Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

Penumbra

K142458

August 29, 2014

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

FDA CDRH DMC
SEP 02 2014
Received

RE: Special 510(k) – Penumbra System ACE

Dear Sir/Madam,

In Compliance with Section 510(k) of the 1976 Medical Device Amendments to the Federal Food, Drug and Cosmetic Act, Penumbra Inc. is notifying the Food and Drug Administration of our intent to add two new Reperfusion Catheters, the ACE 64 and ACE 68 catheters, to the ACE family of Penumbra System® catheters.

Penumbra believes the Reperfusion Catheters ACE 64 and ACE 68 are substantially equivalent to other legally marketed devices included in the Penumbra System®. The Penumbra System® has been cleared under the following 510(k) pre-market notifications:

Predicate Device Listing

510(k) Number / Clearance Date	Name of Predicate Device	Name of Manufacturer
K072718 [28Dec2007]	Penumbra System [026, 032, 041]	Penumbra, Inc.
K090752 [21Sep2009]	Penumbra System [054]	Penumbra, Inc.
K100769 [21May2010]	Penumbra System Separator Flex [026, 032, 041, 054]	Penumbra, Inc.
K113163 [28NOV2011]	Penumbra System® MAX	Penumbra, Inc.
K133317 [13MAY2014]	Penumbra System® and Penumbra System® MAX	Penumbra, Inc.

The subject Reperfusion Catheters ACE 64 and ACE 68 are composed of materials commonly utilized for interventional devices, manufactured using well-characterized and common technologies, and packaged and sterilized using the same materials and methods as the Reperfusion Catheter 5MAX ACE, which was added to the Penumbra System Reperfusion Catheter 054 [K090752] by Letter-To-File in May 2013 as a non-significant

Penumbra, Inc.
1351 Harbor Bay Parkway
Alameda, Ca. 94502
U.S.A.

Regulatory Affairs
F 510.217.6414

www.penumbrainc.com

1-CD

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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change that does not require a new 510(k). Reperfusion Catheter 5MAX ACE data was subsequently reviewed by FDA during the review of K133317 and no issue was identified by FDA for Penumbra's use of the Letter-to-File path for this product.

Penumbra has demonstrated through bench-top testing that the Reperfusion Catheters ACE 64 and ACE 68 are as safe and effective as the aforementioned listed predicate devices.

In this submission, Penumbra Inc. will demonstrate substantial equivalence to the predicate Reperfusion Catheter 5MAX ACE.

Applicant Information

Applicant Name:	Penumbra, Inc.
Applicant Address:	1351 Harbor Bay Parkway Alameda, CA 94502, USA
Phone Number:	510-748-3288
Fax Number:	510-217-6414

Penumbra Inc. requests that the information in this submission be considered confidential, and protected under 21 CFR 807.95, 18 USC 1905, 21 USC 331(j), 5 USC 552, and other applicable laws and provisions. Per the instructions accessed at http://www.fda.gov/cdrh/elecsub.html , an electronic copy is being provided with this submission and it is an exact duplicate of the original paper submission.

If there are any questions regarding this submission, please contact Michaela Mahl, Senior Manager of Regulatory, at 510-748-3288, or via e-mail at michaela.mahl@penumbrainc.com.

Sincerely,

Michaela Mahl

Michaela Mahl, MSBE
Senior Manager, Regulatory Affairs
Phone: (510)748-3288
e-mail: michaela.mahl@penumbrainc.com

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Form Approved: OMB No. 0910-0511 Expiration Date: April 30, 2016. See Instructions for OMB Statement.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE USER FEE COVER SHEET

PAYMENT IDENTIFICATION NUMBER: (b)(4) [redacted]
Write the Payment Identification number on your check.

A completed cover sheet must accompany each original application or supplement subject to fees. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment and mailing instructions can be found at: http://www.fda.gov/oc/mdufma/coversheet.html

1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)

PENUMBRA INC
1351 Harbor Bay Parkway
Alameda
Alameda
CA 94502
US

1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)
*****6819

2. CONTACT NAME
Seth Schulman

2.1 E-MAIL ADDRESS
seth.schulman@penumbrainc.com

2.2 TELEPHONE NUMBER (include Area code)
510-748-3223

2.3 FACSIMILE (FAX) NUMBER (Include Area code)
510-217-6414

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm345263.htm

Select an application type:
[X] Premarket notification(510(k)); except for third party
[ ] 513(g) Request for Information
[ ] Biologics License Application (BLA)
[ ] Premarket Approval Application (PMA)
[ ] Modular PMA
[ ] Product Development Protocol (PDP)
[ ] Premarket Report (PMR)
[ ] 30-Day Notice

3.1 Select a center
[X] CDRH
[ ] CBER

3.2 Select one of the types below
[X] Original Application

Supplement Types:
[ ] Efficacy (BLA)
[ ] Panel Track (PMA, PMR, PDP)
[ ] Real-Time (PMA, PMR, PDP)
[ ] 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)
[ ] YES, I meet the small business criteria and have submitted the required qualifying documents to FDA
[X] NO, I am not a small business

4.1 If Yes, please enter your Small Business Decision Number:

5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA?
[X] YES (All of our establishments have registered and paid the fee, or this is our first device, and we will register and pay the fee within 30 days of FDA's approval/clearance of this device.)
[ ] NO (If "NO," FDA will not accept your submission until you have paid all fees due to FDA. This submission will not be processed; see http://www.fda.gov/cdrh/mdufma for additional information)

6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.
[ ] This application is the first PMA submitted by a qualified small business, including any affiliates
[ ] This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only
[ ] The sole purpose of the application is to support conditions of use for a pediatric population
[ ] The application is submitted by a state or federal government entity for a device that is not to be distributed commercially

7. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA).
[ ] YES [X] NO

PAPERWORK REDUCTION ACT STATEMENT
Public reporting burden for this collection of information is estimated to average 18 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to the address below.

Department of Health and Human Services, Food and Drug Administration, Office of Chief Information Officer, 8455 Colesville Road, COLE-14-14253 Silver Spring, MD 20993-0002
[Please do NOT return this form to the above address, except as it pertains to comments on the burden estimate.]

8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION
(b)(4) [redacted]

13-Jun-2014

Form FDA 3601 (01/2007)

"Close Window" Print Cover sheet

Error - Couldn't merge file with following reason - PdfReader not opened with owner password
0900262181cd5328.pdf
System attempted to attach the file. Please look at attachments to open this file manually.

Records processed under FOIA Request # 2015-4313, Released by CDRH on 10-08-2015

See OMB Statement on Reverse. Form Approved: OMB No. 0910-0625 Expiration Date: 2-28-2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank (42 U.S.C. § 282(j))

(For submission with an application/submission, including amendments, supplements, and resubmissions, under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.)

SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. NAME OF SPONSOR/APPLICANT/SUBMITTER
   Penumbra, Inc.

2. DATE OF THE APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
   29 Aug 2014

3. ADDRESS *(Number, Street, State, and ZIP Code)*
   1351 Harbor Bay Parkway
   Alameda, CA 94502 USA

4. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
   (Tel.) 510-748-3288
   (Fax) 510-217-6414

PRODUCT INFORMATION

5. **FOR DRUGS/BIOLOGICS:** Include Any/All Available Established, Proprietary and/or Chemical/Biochemical/Blood/Cellular/Gene Therapy Product Name(s)
   FOR DEVICES: Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)
   (Attach extra pages as necessary)

   Penumbra System ACE

APPLICATION / SUBMISSION INFORMATION

6. TYPE OF APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES

   ☐ IND ☐ NDA ☐ ANDA ☐ BLA ☐ PMA ☐ HDE ☒ 510(k) ☐ PDP ☐ Other

7. INCLUDE IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/OTHER NUMBER *(If number previously assigned)*
   TBD

8. SERIAL NUMBER ASSIGNED TO APPLICATION/SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES
   TBD

CERTIFICATION STATEMENT / INFORMATION

9. CHECK ONLY ONE OF THE FOLLOWING BOXES *(See instructions for additional information and explanation)*

   ☒ A. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, do not apply because the application/submission which this certification accompanies does not reference any clinical trial.

   ☐ B. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, do not apply to any clinical trial referenced in the application/submission which this certification accompanies.

   ☐ C. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, enacted by 121 Stat. 823, Public Law 110-85, apply to one or more of the clinical trials referenced in the application/submission which this certification accompanies and that those requirements have been met.

10. IF YOU CHECKED BOX C, IN NUMBER 9, PROVIDE THE NATIONAL CLINICAL TRIAL (NCT) NUMBER(S) FOR ANY "APPLICABLE CLINICAL TRIAL(S)," UNDER 42 U.S.C. § 282(j)(1)(A)(i), SECTION 402(j)(1)(A)(i) OF THE PUBLIC HEALTH SERVICE ACT, REFERENCED IN THE APPLICATION/ SUBMISSION WHICH THIS CERTIFICATION ACCOMPANIES *(Attach extra pages as necessary)*

    NCT Number(s):

The undersigned declares, to the best of her/his knowledge, that this is an accurate, true, and complete submission of information. I understand that the failure to submit the certification required by 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the Public Health Service Act, and the knowing submission of a false certification under such section are prohibited acts under 21 U.S.C. § 331, section 301 of the Federal Food, Drug, and Cosmetic Act.
Warning: A willfully and knowingly false statement is a criminal offense, U.S. Code, title 18, section 1001.

11. SIGNATURE OF SPONSOR/APPLICANT/SUBMITTER OR AN AUTHORIZED REPRESENTATIVE (Sign)
    Michaela Mahl

12. NAME AND TITLE OF THE PERSON WHO SIGNED IN NO. 11
    (Name) Michaela Mahl
    (Title) Senior Manager, Regulatory Affairs

13. ADDRESS *(Number, Street, State, and ZIP Code) (of person identified in Nos. 11 and 12)*
    1351 Harbor Bay Parkway
    Alameda, CA 94502 USA

14. TELEPHONE AND FAX NUMBERS *(Include Area Code)*
    (Tel.) 510-748-3288
    (Fax) 510-217-6414

15. DATE OF CERTIFICATION
    29 Aug 2014

PSC Publishing Services (301) 443-6740 EF

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

Form Approved: OMB No. 0910-0120; Expiration Date: 1/31/2017

Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☐ Traditional ☒ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 13485:2012 (ISO 13485:2003) Medical devices- Quality management systems- Requirements for regulatory purposes

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☐	☒
FDA Recognition number [3]	#N/A	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 13485:2012 (ISO 13485:2003) Medical devices - Quality management systems- Requirements for regulatory purposes

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

❖ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 1 hour per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

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Department of Health and Human Services
Food and Drug Administration

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TYPE OF 510(K) SUBMISSION

☐ Traditional ☒ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 14971:20 12 (ISO 14971 :2007/(R)2010) Medical devices-- Application of risk management to medical devices

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#5-70	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: N/A

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 14971:20 12 (ISO 14971 :2007/(R)2010) Medical devices-- Application of risk management to medical devices

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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Food and Drug Administration

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TYPE OF 510(K) SUBMISSION

☐ Traditional ☒ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 10993-1:2009/AC:2010- Biological evaluation of medical devices - Part 1: Eval & Testing within a risk management proce

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#2-179	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☒	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☒	☐
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: FDA Bluebook Memorandum 095-1 "Use of International Standard ISO I 0993"

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 10993-1:2009/AC:2010- Biological evaluation of medical devices - Part 1: Eval & Testing within a risk management proce

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
6.2.2.2	Cytotoxicity	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖
Test selection: MEM Elution

DESCRIPTION
Test lab: Nelson Labs 6280 South Redwood Road, Salt Lake City, UT 84123

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
6.2.2.4	Irritation (including intracutaneous reactivity)	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖
Test selection: Guinea Pig Maximization Sensitization Test, Magnusson-Kligman Method

DESCRIPTION
Test lab: Nelson Labs 6280 South Redwood Road, Salt Lake City, UT 84123

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
6.2.2.9	Haemocompatibility	☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖
Test selection: complement activation- C3a and SCSb-9 through enzyme assay, direct contact and extract method.

DESCRIPTION
Test lab: Nelson Labs 6280 South Redwood Road, Salt Lake City, UT 84123

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

❖ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☐ Traditional ☒ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 11135-1:2007 - Sterilization of health care products — Ethylene oxide — Part 1

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#14-331	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 11135-1:2007 - Sterilization of health care products — Ethylene oxide — Part 1

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
Annex B	Conservative determination of lethal rate of the sterilization process - Overkill	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖
Overkill approach sterilization process selected

DESCRIPTION
Sterilization agent: Sterigenics US, LLC. 5725 W. Harold Gatty Drive, Salt Lake City, UT 84116

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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Department of Health and Human Services
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(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☐ Traditional ☒ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 10993-7:2008/AC:2009- Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#14-335	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: N/A

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 10993-7:2008/AC:2009- Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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Penumbra

August 29, 2014

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Special 510(k) – Penumbra System ACE

Dear Sir/Madam,

In Compliance with Section 510(k) of the 1976 Medical Device Amendments to the Federal Food, Drug and Cosmetic Act, Penumbra Inc. is notifying the Food and Drug Administration of our intent to add two new Reperfusion Catheters, the ACE 64 and ACE 68 catheters, to the ACE family of Penumbra System® catheters.

Penumbra believes the Reperfusion Catheters ACE 64 and ACE 68 are substantially equivalent to other legally marketed devices included in the Penumbra System®. The Penumbra System® has been cleared under the following 510(k) pre-market notifications:

Predicate Device Listing

510(k) Number / Clearance Date	Name of Predicate Device	Name of Manufacturer
K072718 [28Dec2007]	Penumbra System [026, 032, 041]	Penumbra, Inc.
K090752 [21Sep2009]	Penumbra System [054]	Penumbra, Inc.
K100769 [21May2010]	Penumbra System Separator Flex [026, 032, 041, 054]	Penumbra, Inc.
K113163 [28NOV2011]	Penumbra System® MAX	Penumbra, Inc.
K133317 [13MAY2014]	Penumbra System® and Penumbra System® MAX	Penumbra, Inc.

The subject Reperfusion Catheters ACE 64 and ACE 68 are composed of materials commonly utilized for interventional devices, manufactured using well-characterized and common technologies, and packaged and sterilized using the same materials and methods as the Reperfusion Catheter 5MAX ACE, which was added to the Penumbra System Reperfusion Catheter 054 [K090752] by Letter-To-File in May 2013 as a non-significant

Penumbra, Inc.
1351 Harbor Bay Parkway
Alameda, Ca. 94502
U.S.A.

Regulatory Affairs
F 510.217.6414

www.penumbrainc.com

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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change that does not require a new 510(k). Reperfusion Catheter 5MAX ACE data was subsequently reviewed by FDA during the review of K133317 and no issue was identified by FDA for Penumbra's use of the Letter-to-File path for this product.

Penumbra has demonstrated through bench-top testing that the Reperfusion Catheters ACE 64 and ACE 68 are as safe and effective as the aforementioned listed predicate devices.

In this submission, Penumbra Inc. will demonstrate substantial equivalence to the predicate Reperfusion Catheter 5MAX ACE.

Applicant Information

Applicant Name:	Penumbra, Inc.
Applicant Address:	1351 Harbor Bay Parkway Alameda, CA 94502, USA
Phone Number:	510-748-3288
Fax Number:	510-217-6414

Penumbra Inc. requests that the information in this submission be considered confidential, and protected under 21 CFR 807.95, 18 USC 1905, 21 USC 331(j), 5 USC 552, and other applicable laws and provisions. Per the instructions accessed at http://www.fda.gov/cdrh/elecsub.html , an electronic copy is being provided with this submission and it is an exact duplicate of the original paper submission.

If there are any questions regarding this submission, please contact Michaela Mahl, Senior Manager of Regulatory, at 510-748-3288, or via e-mail at michaela.mahl@penumbrainc.com.

Sincerely,

Michaela Mahl

Michaela Mahl, MSBE
Senior Manager, Regulatory Affairs
Phone: (510)748-3288
e-mail: michaela.mahl@penumbrainc.com

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Appendix 3: Representative Labels
Appendix 4: Instructions for Use

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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1 Introduction

In Compliance with Section 510(k) of the 1976 Medical Device Amendments to the Federal Food, Drug and Cosmetic Act, Penumbra Inc. is notifying the Food and Drug Administration of our intent to add two new Reperfusion Catheters, the ACE 64 and ACE 68 catheters, to the ACE family of Penumbra System® catheters.

Penumbra believes the Reperfusion Catheters ACE 64 and ACE 68 are substantially equivalent to other legally marketed devices included in the Penumbra System®. The Penumbra System® has been cleared under the following 510(k) pre-market notifications:

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K100769 [21May2010]	Penumbra System Separator Flex [026, 032, 041, 054]	Penumbra, Inc.
K113163 [28NOV2011]	Penumbra System® MAX	Penumbra, Inc.
K133317 [13MAY2014]	Penumbra System® and Penumbra System® MAX	Penumbra, Inc.

The subject Reperfusion Catheters ACE 64 and ACE 68 are composed of materials commonly utilized for interventional devices, manufactured using well-characterized and common technologies, and packaged and sterilized using the same materials and methods as the Reperfusion Catheter 5MAX ACE, which was added to the Penumbra System Reperfusion Catheter 054 [K090752] by Letter-To-File in May 2013 as a non-significant change that does not require a new 510(k). Reperfusion Catheter 5MAX ACE data was subsequently reviewed by FDA during the review of K133317 and no issue was identified by FDA for Penumbra's use of the Letter-to-File path for this product.

The Reperfusion Catheters ACE 64 and ACE 68 will be individually packaged.

Penumbra has demonstrated through bench-top testing that the Reperfusion Catheters ACE 64 and ACE 68 are as safe and effective as the aforementioned listed predicate devices.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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1.1 Required Information

(under Sections 510(k), 513(f) and 512(i) of the Act, and Subpart E of 21 CFR, Part 807.87)

Device Trade or Proprietary Name:	Penumbra System® ACE
Project Name:	Reperfusion Catheter ACE 64 & ACE 68
Device Common or Usual or Classification Name:	Catheter, Percutaneous (Product Code: NRY)
Device Classification:	Class II
Classification Panel:	Neurology
Regulation Number per 21 CFR:	870.1250 (NRY)
Reason for 510(k):	Adding new Reperfusion Catheters to the Penumbra System
Action taken to comply with Section 514 of the Act for Performance Standards:	No performance standards exist for this device.
Prior submissions for the same device:	There have been no prior submissions for the ACE 64 or ACE 68 Reperfusion Catheters.
Prior approval/clearance for components or accessories:	The Separator 054 and Separator 5MAX, which are compatible with the Reperfusion Catheters ACE 64 and ACE 68, were previously cleared by FDA under K090752, K100769 and K113163.
Proposed labels, Labeling and Advertisements:	See Section 6
For Class III Devices Only, a Class III Summary and Class III Certification:	Not Applicable.
Device Photographs/ Drawings	See Section 3.2
Marketed Device to Which Equivalence is Claimed Including an Identification of Similar Products, Materials, Design Considerations, Energy Expected to Be Used/Delivered, and Operational Principles:	See Section 3.4
Statement of Similarities and/or Differences with the Marketed Devices:	See Sections 3.4 and 7
Data to Show Consequences and Effects of Modifications to a Device:	Not Applicable.
Truthfulness and Accuracy Statement:	See Section 2
510(k) Summary per 21 CFR Part 807.92 or statement per 21 CFR Part 807.93	See Section 8
Financial Certification/Disclosure Statement, per 21 CFR 54:	Not Applicable. The Reperfusion Catheters ACE 64 and ACE 68 were not tested in human subjects.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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1.2 Additional Information

Submitter's Name and Address:	Penumbra, Inc. 1351 Harbor Bay Parkway Alameda, CA 94502 USA Establishment Registration # 3005168196
Primary Contact Person, Title, Telephone and FAX Numbers and Email:	Michaela Mahl Senior Manager, Regulatory Affairs TEL: 510-748-3288 FAX: 510-217-6414 E-MAIL: michaela mahl@penumbrainc.com
Alternate Contact Person, Title, Telephone and FAX Numbers and Email:	Seth A. Schulman Director, Regulatory Affairs TEL: 510-748-3223 FAX: 510-217-6414 E-MAIL: seth.schulman@penumbrainc.com
Table of Contents with Pagination:	See section titled "Table of Contents" of this application.
Manufacturing Facility Name and Address:	Penumbra, Inc. 1351 Harbor Bay Parkway Alameda, CA 94502 USA
Sterilization Site Name and Address:	Sterigenics US, LLC 5725 W. Harold Gatty Drive Salt Lake City, Utah 84116 USA
Product Characterization Data:	See Section 5
Physical/Mechanical Test Reports:	See Section 5.2 [summary only]
Safety/Biocompatibility Test Reports:	See Section 5.1 [summary only]
Effectiveness Test Reports:	See Section 5 [summary only]
Stability Information:	See Section 5.4
Packaging Information:	See Section 5.5
Sterilization Information:	See Section 5.3
Software Information:	Not Applicable – no software is utilized with this device.
Hardware Information:	Not Applicable – no hardware is utilized with this device.
Is the Device Subject to Issues that Have Been Addressed in Specific Guidance Documents?	Guidance on 510(k) - Short-term & long-term intravascular catheters (1995) Guidance - General Considerations for Animal Studies for Cardiovascular Devices (2010)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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2 Truthful and Accuracy Statement

[as required by 21 CFR 807.87(k)]

I certify that, in my capacity as Senior Manager of Regulatory Affairs for Penumbra Inc., I believe to the best of my knowledge that all data and information submitted in this pre-market notification are truthful and accurate and that no material facts have been omitted.

Michaela Mahl

29 Aug 2014

Michaela Mahl
Senior Manager, Regulatory Affairs
Penumbra, Inc.
Phone: (510)748-3288
FAX: (510) 217-6414
Email: michaela.mahl@penumbrainc.com

Date

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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3 Device Description

3.1 Description

The Penumbra System was designed to remove thrombus from large intracranial vessels by aspirating the proximal side of the thrombus using the Penumbra Reperfusion Catheter, Penumbra Separator, and Penumbra Aspiration Tubing. The Penumbra System was cleared under K072718, K090752, K100769, K113163 & K133317. The Reperfusion Catheter 5MAX ACE was added to the Penumbra System Reperfusion Catheter 054 [K090752] by Letter-To-File. The Penumbra Aspiration Tubing is connected to the Penumbra Aspiration Pump and Penumbra Pump/Canister Tubing (K051758 & K122756).

The Penumbra System (Figure 1) is designed to remove thrombus from the vasculature using continuous aspiration. The Reperfusion Catheter targets aspiration from the pump directly to the thrombus. The Separator may be used to clear the lumen of the Reperfusion Catheter should it become blocked with thrombus. The use of the Separator may not be necessary when using a Reperfusion Catheter with an I.D. of 0.054in or larger. The Reperfusion Catheter is introduced through a guide catheter or long femoral sheath and into the intracranial vasculature and guided over a neurovascular guidewire to the site of the primary occlusion. The Penumbra Reperfusion Catheter is used with the Aspiration Pump to aspirate thrombus from an occluded vessel. As needed, a Penumbra Separator may be deployed from the Reperfusion Catheter to assist with thrombus removal. The Penumbra Separator is advanced and retracted through the Penumbra Reperfusion Catheter at the proximal margin of the primary occlusion to facilitate clearing of the thrombus from the Reperfusion Catheter tip. For the aspiration source, the Penumbra Reperfusion Catheter is used in conjunction with the Aspiration Pump, which is connected using the Penumbra Aspiration Tubing and the Penumbra Pump/Canister Tubing. The Penumbra Reperfusion Catheter is provided with a steam shaping mandrel and rotating hemostasis valve, and a peelable sheath. The Penumbra Separator is provided with an introducer and torque device. The devices are visible under fluoroscopy.

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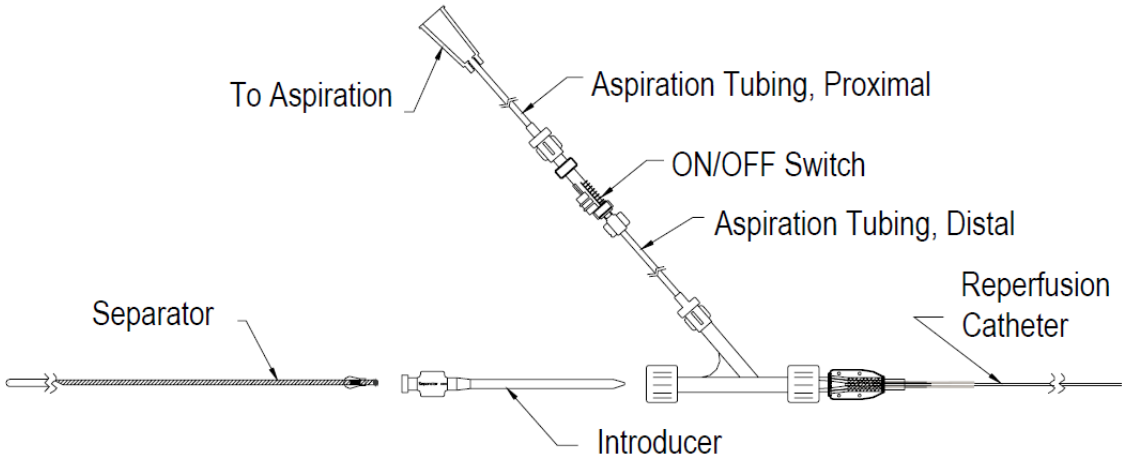
Figure 1: Assembled Penumbra System for Thrombus Debulking



The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.

The ACE 64 and ACE 68 Reperfusion Catheters are additional larger catheters to the currently available Penumbra System Reperfusion Catheters. The subject Reperfusion Catheters ACE 64 and ACE 68 are substantially equivalent to the current available Reperfusion Catheter 5MAX ACE. The subject Reperfusion Catheters ACE 64 and ACE 68 will have a slightly larger I.D.s and will be available in five different length configurations.
The Reperfusion Catheters ACE 64 and ACE 68 are compatible with the currently available Separator 054 and Separator 5MAX.

Both the ACE 64 and ACE 68 Reperfusion Catheters will be separately available in one packing configuration including a packaging hoop, card, rotating hemostasis value (RHV), a 6F peelable sheath, and a 0.038” shaping mandrel.

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3.2 ACE 64 and ACE 68 Reperfusion Catheters

The subject ACE 64 and ACE 68 Reperfusion Catheters are variable stiffness catheters with a proximal shaft that utilize a hybrid coil reinforcement of stainless steel flat wire and round wire (stainless steel round wire on Reperfusion Catheter ACE 64 and (b)(4) [redacted] round wire on Reperfusion Catheter ACE 68) to provide proximal support necessary for improved trackability while maintaining the durability and kink resistance associated with round wire coil reinforcement[1]. The distal shaft of both the ACE 64 and ACE 68 Catheters are coiled with 0.0025" (b)(4) [redacted] wire. No new materials are added and all of the materials in the subject Reperfusion Catheters ACE 64 and ACE 68 are present on the predicate Reperfusion Catheter 5MAX ACE. However, additional blended Pebax extrusions have been added to the Reperfusion Catheters ACE 64 and ACE 68, which provide a smoother material transition from the stiffer proximal materials to the softer distal materials to enable continuous flexibility, trackability and a kink resistant profile.

Both of the Reperfusion Catheters ACE 64 and ACE 68 will be available in the same five different lengths offerings, and their Size Chart can be found in Table 2 and Table 3. The "64" and "68" number convention for both catheters serves to identify their nominal distal inner diameters (ID). These inner diameters have been increased from the distal ID of 0.060 in minimum of the predicate Reperfusion Catheter 5MAX ACE. Both of the Reperfusion Catheters ACE 64 and ACE 68 are only available with a straight tip. Pictures of the Reperfusion Catheters ACE 64 and ACE 68 and their hubs are shown in Figure 2. Both the Reperfusion Catheters ACE 64 and ACE 68 are compatible with the Separator 054 and the Separator 5MAX, should the use of a Separator be needed.

[1] (b)(4) [redacted]

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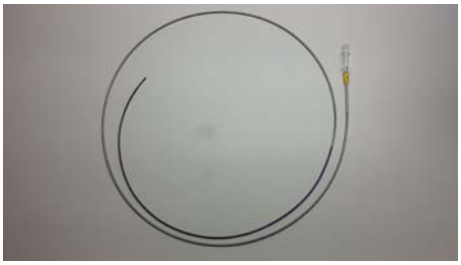
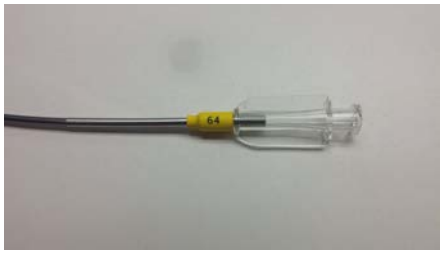
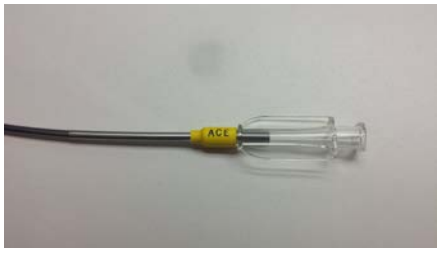
Figure 2: Reperfusion Catheters ACE 64 and ACE 68

	Reperfusion Catheter ACE 64	Reperfusion Catheter ACE 68
Catheter		
Tip		
Hub Side 1		
Hub Side 2		

The engineering drawings [SAs] for the Reperfusion Catheters ACE 64 [SA-7083-XX] and the ACE 68 [SA-7240-XX] can be found in:

Appendix 1: Engineering Drawings – ACE 64 and ACE 68

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Table 2: ACE 64 - Device Size Chart - per Product Specification [Nominal Values]

Catalog No.	Working Length	Coating Length	Distal Flex Length	OD (proximal)	ID (proximal)	OD (distal)	ID (distal)
5MAXACE064	132.0 ± 2.0 cm [132 cm]	30 ± 10 cm [30 cm]	30.0 ± 2.2 cm [30 cm]	0.084" Max [0.080" = 2.03mm]	0.068" Min [0.068" = 1.73mm]	0.080" Max [0.0755" = 1.92mm]	0.064" Min [0.064" = 1.63mm]
5MAXACE064L127	127.0 ± 2.0 cm [127 cm]						
5MAXACE064L125	125.0 ± 2.0 cm [125 cm]						
5MAXACE064L120	120.0 ± 2.0 cm [120 cm]						
5MAXACE064L115	115.0 ± 2.0 cm [115 cm]						

Table 3: ACE 68 - Device Size Chart - per Product Specification [Nominal Values]

Catalog No.	Working Length	Coating Length	Distal Flex Length	OD (proximal)	ID (proximal)	OD (distal)	ID (distal)
5MAXACE068	132.0 ± 2.0 cm [132 cm]	30 ± 10 cm [30 cm]	30.0 ± 2.2 cm [30 cm]	0.084" Max [0.080" = 2.03mm]	0.068" Min [0.068" = 1.73mm]	0.084" Max [0.080" = 2.03mm]	0.068" Min [0.068" = 1.73mm]
5MAXACE068L127	127.0 ± 2.0 cm [127 cm]						
5MAXACE068L125	125.0 ± 2.0 cm [125 cm]						
5MAXACE068L120	120.0 ± 2.0 cm [120 cm]						
5MAXACE068L115	115.0 ± 2.0 cm [115 cm]						

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3.3 Reperfusion Catheter ACE 64 & ACE 68 – Catalog Numbers & Descriptions

Table 4: ACE 64 & ACE 68: Catalog Numbers and Descriptions

Catalog Number	Description
5MAXACE064L115	Reperfusion Catheter ACE 64, 115 cm
5MAXACE064L120	Reperfusion Catheter ACE 64, 120 cm
5MAXACE064L125	Reperfusion Catheter ACE 64, 125 cm
5MAXACE064L127	Reperfusion Catheter ACE 64, 127 cm
5MAXACE064	Reperfusion Catheter ACE 64, 132 cm
5MAXACE068L115	Reperfusion Catheter ACE 68, 115 cm
5MAXACE068L120	Reperfusion Catheter ACE 68, 120 cm
5MAXACE068L125	Reperfusion Catheter ACE 68, 125 cm
5MAXACE068L127	Reperfusion Catheter ACE 68, 127 cm
5MAXACE068	Reperfusion Catheter ACE 68, 132 cm

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3.4 Comparison to Predicate Devices

Table 5: Predicate Device Comparison

System Name	Penumbra System Reperfusion Catheter	Penumbra System ACE Reperfusion Catheter	
Device Name	**5MAX ACE**	**ACE 64**	**ACE 68**
510(k) No.	K090752	To be determined	
Classification	Class II, NRY	SAME	
Indication	The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.	SAME	
Materials			
Proximal hub	Grilamid (TR55-LX)	SAME	
Strain Relief [Hub Sleeve]	Grilamid (TR55)	SAME	
Strain Relief	Stainless Steel, 304	SAME	
ID Band	Polyolefin, PET yellow [black ink]	SAME	
Catheter Shaft			
Distal Extrusions	Tecoflex 80A, Pellethane 80A, Pebas 35D, Pebax 35D/40D Blend, Pebax 40D, Pebax 55D, Pebax 63D	Pellethane 80A, Tecoflex 80A, Tecoflex 80A/Pebax 35D, Pebax 35D, Pebax 35D/40D Blend, Pebax 40D, Pebax 40D/55D Blend, Pebax 55D, Pebax 63D	
Proximal Extrusions	Pebax 55D, Pebax 72D, Vestamid	Pebax 55D, Pebax 72D, Vestamid	Pebax 55D/72D Blend, Pebax 72D, Vestamid
Proximal Coil Reinformcement	SS flat (0.002 in x 0.007 in)	SS flat (0.0015 in x 0.006 in) and SS round (0.0025 in)	SS flat (0.0015 in x 0.006 in) and NiTi round (0.0025 in)
Extrusion Colorants	Clear/ Natural or Purple	SAME	
Tip Shape	Straight	SAME	
Markerband	C-cut Pt/Ir band	SAME	
Coating	SRDX Harmony (proprietary)	SAME	
Dimensions			
Proximal OD	0.083 in Max	0.084 in Max	0.084 in Max
Proximal ID	0.068 in Min	0.068 in Min	0.068 in Min
Distal OD	0.074 in Max	0.080 in Max	0.084 in Max
Distal ID	0.060 in Min	0.064 in Min	0.068 in Min

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System Name	Penumbra System Reperfusion Catheter	Penumbra System ACE Reperfusion Catheter	
Device Name	**5MAX ACE**	**ACE 64**	**ACE 68**
Effective Length	125, 127, 132 cm	115, 120, 125, 127, 132 cm	
Coating Length	30 cm	SAME	
Accessories			
Peelable Sheath	PTFE	SAME	
Rotating Hemostasis Valve	Polycarbonate, silicone o-ring	SAME	
Shaping Mandrel	0.038in OD	SAME	
Packaging Materials			
Pouch	Polyester/Polyethylene/ Tyvek®	SAME	
Packaging Hoop	Polyethylene	SAME	
Packaging Card	Polyethylene	SAME	
Display Carton	SBS Paperboard	SAME	
Packaging Configuration	Individual	SAME	
Sterilization	EtO	SAME	
Shelf-Life	36 Months	SAME	

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4 Design Control Activities

4.1 Summary of Design Control Activities

The subject Penumbra System ACE devices, were developed in accordance with the Penumbra Design Control System. The Design Control system at Penumbra has been implemented in accordance with the US FDA Quality System Regulation, EN ISO 13485[2], and Medical Device Directive.[3] The intent of the Design Control system is to establish and meet the requirements of the Design Control activities relative to product reliability and safety during product design and development, to establish Design Control responsibilities and documentation requirements, and to specify the policies for approval, release, modification, compilation, and retention of Design Control documents. All products designed and developed by Penumbra follow this Design Control system. A (b)(4) [redacted]

(b)(4) [redacted]

[2] EN ISO 13485:2012 Medical Devices - Quality Management Systems - Requirements For Regulatory Purposes
[3] 93/42/EEC Medical Device Directives (as amended, including 2007/47/EC)

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(b)(4)

[redacted]

4.2 Risk Analysis

(b)(4)

[redacted]

[4] EN ISO 14971:2012 Medical devices – Application of risk management to medical devices

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(b)(4) [redacted]

Appendix 2: (b)(4) [redacted] Reperfusion Catheters ACE 64 and ACE 68

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4.3 Declaration of Conformity with Design Controls

Verification Activities: To the best of my knowledge, all verification and validation activities, as required by the risk analysis for the modification, were performed by the designated individual(s) and the results demonstrated that the predetermined acceptance criteria were met.

Michaela Mahl — 29 Aug 2014

Michaela Mahl
Senior Manager of Regulatory Affairs
Penumbra, Inc.

Date

Manufacturing Facility: The Penumbra, Inc. manufacturing facility at 1351 Harbor Bay Parkway, Alameda, CA 94502 USA, is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review.

29 Aug 2014

Ben Tompkins
VP of R&D
Penumbra, Inc.

Date

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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5 Device Performance

As required under Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, a summary of any information regarding safety and effectiveness of the device follows.

Included in this section are descriptions of the testing which substantiates the safe and effective performance of the subject Penumbra System ACE devices (Reperfusion Catheters ACE 64 and ACE 68) as well as their substantial equivalence to the predicate devices:

- Biocompatibility
- Design Verification (Bench-Top Testing)
- Design Validation (GLP Animal Testing)

The subject Penumbra System ACE devices (Reperfusion Catheters ACE 64 and ACE 68) met all established requirements.

5.1 Biocompatibility

Evidence of the biocompatibility of the Reperfusion Catheters ACE 64 and ACE 68 is derived from a series of previously performed studies listed and summarized in Table 6. The studies were selected in accordance with EN ISO 10993-1[5] guidelines. The studies were selected in accordance with EN ISO 10993-1 guidelines (Biological Evaluation of Medical Devices) for a limited exposure (< 24 hours), externally communicating device with circulating blood contact. All studies were conducted pursuant to 21 CFR, Part 58, Good Laboratory Practices (GLP).

Table 6: EN ISO-10993 GLP Testing Summary

Test	Acceptance Criteria	Results	Pass / Fail
In Vitro Cytotoxicity	Sample extracts must yield cell lysis grade 2 or lower	Grade 1: Slight	Pass
Sensitization	Test Group shall yield Grade < 1 score on Magnusson and Kligman scale (provided control Grade < 1)	Grade 0: No visible change	Pass

[5] EN ISO 10993-1: 2009/AC:2010 Biological Evaluation of Medical Devices, Part 1: Evaluation and testing within a risk management process

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Test	Acceptance Criteria	Results	Pass / Fail
Acute Intracutaneous Reactivity (Irritation)	The difference in the mean test article and mean control score must be grade 1.0 or lower	Grade ≤ 1.0 difference between mean test article and mean control score	Pass
Systemic Toxicity			
Acute Systemic Toxicity	Sample extracts must not cause the following: • > 10% weight loss in 3 or more test animals • Mortality of 2 or more test animals • Abnormal behavior in 2 or more test animals	No evidence of systemic toxicity from sample extracts • No weight loss (all gained weight) • No death • All test animals appeared normal	Pass
Rabbit Pyrogen Study	Sample Extracts must not cause a total rise in body temperature of ≥0.5°C	Non-pyrogenic: No evidence of material-mediated pyrogenicity; no single animal had a total body temperature rise of ≥0.5°C	Pass
Hemocompatibility			
In Vitro Hemolysis	Sample extracts must be non-hemolytic (≤ 2% hemolytic index)	Non-hemolytic: Hemolytic Index = 0.70% Corrected Hemolytic index = 0.00%	Pass
Complement Activation	The concentrations of C3a and SC5b-9 in the test samples are statistically similar to the predicate (Exposure Control & Ref Material) control and statistically lower than the positive control for all exposure times	The test sample concentrations of C3a and SC5b-9 were statistically similar or lower than the predicate control sample concentrations, and statistically lower than the positive control sample concentrations at all three exposure times	Pass
Dog Thrombogenicity	The device must be non-thrombogenic after 4 hours *in vivo* when compared to a control device (Boston Scientific Excelsior SL-10 microcatheter)	No significant thrombosis with a Grade of 0 was observed in 2 out 2 test site and 2 out of 2 control sites. Based on the evaluation criteria, the amount of thrombosis was not considered significant	Pass

5.1.1 Summary and Conclusions

As all materials used in Reperfusion Catheters ACE 64 and ACE 68 have previously successfully passed biocompatibility testing no additional biocompatibility testing is necessary. In summary, non-clinical testing found the Reperfusion Catheters ACE 64 and

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ACE 68 to be non-cytotoxic, non-reactive (short and long-term implantation), non-sensitizing, a non-irritant, and non-toxic (acute systemic).

The Reperfusion Catheters ACE 64 and ACE 68 meet the requirements of USP and EN ISO 10993-1, Biological Evaluation of Medical Devices for limited exposure (≤ 24 hours), externally communicating devices with circulating blood contact. With these acceptable results, this data provides supportive evidence that the materials used in the Reperfusion Catheters ACE 64 and ACE 68 are safe for the intended use.

5.2 Design Verification / Validation

5.2.1 Introduction

(b)(4)

[redacted]

5.2.2 Design Verification (Bench-Top Testing)

(b)(4)

[redacted]

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The summary of the testing performed on the subject Reperfusion Catheters ACE 64 and ACE 68 are listed below in Table 7 and Table 8.

Table 7: Design Verification (Bench-Top Testing) Summary – ACE 64

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Dimensional/ Visual Inspection	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Simulated Use [Intracranial Access & Vessel Access Entry Performance]	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Coating Integrity	(b)	Coating has not delaminated, peeled, or flaked after simulated use	100% Must meet Specification (b)(4)	100% Pass
Particulate Testing (Reperfusion Catheter ACE 64 Hydrophilic Coating)	(b)	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification (b)(4)	10µm 100% Pass 25µm 100% Pass
Particulate Testing (Reperfusion Catheter ACE 64/Separator 5MAX (Flex 054))	(b)	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification (b)(4)	10µm 100% Pass 25µm 100% Pass
Coating Integrity	(b)	Coating is not grossly damaged after undergoing particulate testing	100% Must meet Specification (b)(4)	100% Pass
Hub/Catheter Air Aspiration	(b)	When negative pressure is pulled, no air may leak into hub	100% Must meet Specification (b)(4)	100% Pass

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Attribute	Sample Size	Specification	Acceptance Criteria	Results
Pressure Test	(b)	45 psi for 30 sec MIN	100% Must meet Specification (b)(4)	100% Pass
Reperfusion Catheter ACE (b /Sheath or 8F Guide compatibility (Friction Force)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Reperfusion Catheter ACE (l(b) .014" Guidewire compatibility (Friction Force)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Markerband Section Bond Strength	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Bond Strength (b)(4))	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Bond Strength (b)(4)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Bond Strength (b)(4)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
(b)(4) l Joints: (b)(4)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass

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Attribute	Sample Size	Specification	Acceptance Criteria	Results
Hub to Shaft Bond Strength	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Hub to Hypotube Bond Strength	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Elongation to Failure – Reperfusion Catheter	(b)	% Elongation ≥ 5%	100% Must meet Specification (b)(4) (b)(4)	100% Pass
Corrosion	(b)	No visible corrosion on Reperfusion Catheter (b)(4) immediately after Corrosion Testing procedure	100% Must meet Specification (b)(4)	100% Pass

Table 8: Design Verification (Bench-Top Testing) Summary – ACE 68

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Dimensional/ Visual Inspection	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Simulated Use [Intracranial Access & Vessel Access Entry Performance]	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Coating Integrity	(b)	Coating has not delaminated, peeled, or flaked after simulated use	100% Must meet Specification (b)(4)	100% Pass
Particulate Testing (Reperfusion Catheter (b)(4) Hydrophilic Coating)	(b)	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification (b)(4)	10µm 100% Pass 25µm 100% Pass

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Attribute	Sample Size	Specification	Acceptance Criteria	Results
Particulate Testing (Reperfusion Catheter (b)(4) (b)	(b)	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification Statistical Confidence Level: C	10µm 100% Pass 25µm 100% Pass
Coating Integrity	(b)	Coating is not grossly damaged after undergoing particulate testing	100% Must meet Specification (b)(4)	100% Pass
Hub / Catheter Air Aspiration	(b)	When negative pressure is pulled, no air may leak into hub	100% Must meet Specification (b)(4)	100% Pass
Pressure Test	(b)	45 psi for 30 sec MIN	100% Must meet Specification (b)(4) (b	100% Pass
Reperfusion Catheter (b)(4) / Sheath or 8F Guide compatibility (Friction Force)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Reperfusion Catheter (b)(4) / 0.014" Guidewire compatibility (Friction Force)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Markerband Section Bond Strength	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Bond Strength (b)(4)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass
Bond Strength (b)(4)	(b)	(b)(4)	100% Must meet Specification (b)(4)	100% Pass

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Attribute	Sample Size	Specification	Acceptance Criteria	Results
Bond Strength (b)(4) [redacted] (b)	[redacted]	(b)(4) [redacted]	100% Must meet Specification (b)(4) [redacted]	100% Pass
(b)(4) [redacted] Joints: (b)(4) [redacted]	(b) [redacted]	(b)(4) [redacted]	100% Must meet Specification (b)(4) [redacted]	100% Pass
Hub to Shaft Bond Strength	(b) [redacted]	(b)(4) [redacted]	100% Must meet Specification (b)(4) [redacted]	100% Pass
Hub to Hypotube Bond Strength	(b) [redacted]	(b)(4) [redacted]	100% Must meet Specification (b)(4) [redacted] (b) [redacted] (b)(4) [redacted]	100% Pass
Elongation to Failure – Reperfusion Catheter	(b) [redacted]	% Elongation ≥ 5%	100% Must meet Specification (b)(4) [redacted]	100% Pass
Corrosion	(b) [redacted]	No visible corrosion on Reperfusion Catheter ACE 68 immediately after Corrosion Testing procedure	100% Must meet Specification (b)(4) [redacted]	100% Pass

5.2.3 Design Validation (GLP Animal Testing)

The safety and performance of the ACE 64 and ACE 68 Reperfusion Catheters were evaluated in the accepted porcine vascular model in accordance with the "Code of Federal Regulations of the Food and Drug Administration 21 CFR, Part 58 – Good Laboratory Practices for Nonclinical Laboratory Studies." (b)(4) [redacted]
(b)(4) [redacted]

(b)(4) [redacted]

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(b)(4) [redacted]

No gross pathologic abnormalities were noted in any animal. (b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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5.2.4 Summary and Conclusion

The physical and mechanical properties of the ACE 64 and ACE 68 Reperfusion Catheters were assessed using standard test methods and pre-determined acceptance criteria. The data gathered establish that the subject ACE 64 and ACE 68 Reperfusion Catheters meet performance specifications, are safe and effective for their labeled indication, and are substantially equivalent to the predicate device.

5.3 Sterilization

Penumbra has procedures in place to routinely monitor and control the sterilization of manufactured devices in accordance with EN ISO 11135-1[6]. Ethylene oxide (EtO) (b)(4)

(b)(4)

[6] EN ISO 11135-1:2007 Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Table 9: Comparative Resistance - Acceptance Criteria and Results

Test	Acceptance Criteria	Results
(b)(4) [redacted]		

(b)(4) Testing

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Table 10: (b)(4) Testing Testing Results

(b)(4) Testing

[redacted]

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5.4 Expiration Dating (Stability)

Shelf-Life/Packaging validation testing was performed (b)(4) Testing [redacted] (b)(4) Testing [redacted]

Table 11: Shelf-life – Testing Results

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Dimensional/ Visual Inspection	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Simulated Use [Intracranial Access & Vessel Access Entry Performance]	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Particulate Testing (Reperfusion Catheter (b)(4) (b) Hydrophilic Coating)	(b)	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Particulate Testing (Reperfusion Catheter (b)(4) (b)(4) 4 Separator)	(b)	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Hub / Catheter Air Aspiration	(b)	No air may leak into hub	100% Must meet Specification	100% Pass
Pressure Test	(b)	45 psi for 30 sec MIN	100% Must meet Specification	100% Pass
(b)(4) (b)(4) Bond Strength	(b) b	(b)(4) Minimum	100% Must meet Specification	100% Pass
(b) Joint (((b)(4)) Bond Strength	(b)	(b)(4) Minimum	100% Must meet Specification	100% Pass
(b) Joint ((((b)(4) Bond Strength	(b)	(b)(4) Minimum	100% Must meet Specification	100% Pass

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Attribute	Sample Size	Specification	Acceptance Criteria	Results
Mid-Joint: (Pebax 55D – Pebax 72D) Bond Strength	(b) [redacted]	0.75 lb Minimum	100% Must meet Specification	100% Pass
Proximal Joints: (Pebax 72D – Vestamid) Bond Strength	(b) [redacted]	0.75 lb Minimum	100% Must meet Specification	100% Pass
Hub to Shaft Bond Strength	(b) [redacted]	2.0 lb Minimum	100% Must meet Specification	100% Pass
Hub to Hypotube Bond Strength	(b) [redacted]	2.0 lb Minimum	100% Must meet Specification	100% Pass
Elongation to Failure – Reperfusion Catheter	(b) [redacted]	% Elongation ≥ 5%	100% Must meet Specification Statistical Confidence Level: A	100% Pass

Based on these existing shelf-life test results the Reperfusion Catheters ACE 64 and ACE 68 will be labelled with a 36-month shelf-life.

5.5 Packaging

The packaging materials for the subject Reperfusion Catheters ACE 64 and ACE 68 are identical to that of the predicate Reperfusion Catheter 5MAX ACE and are commonly utilized materials.

The Reperfusion Catheters ACE 64 and ACE 68 components are affixed to a packaging card, whereas the catheter itself is inside a protective hoop [see Figure 3], which is then placed in a heat-sealed PET/PE/Tyvek® pouch to maintain sterility post EtO sterilization. The inner pouch is then placed in a display box for further protection. Both the inner pouch and display box receive a product label. An Instruction For Use (IFU) is placed inside the display box of each unit.

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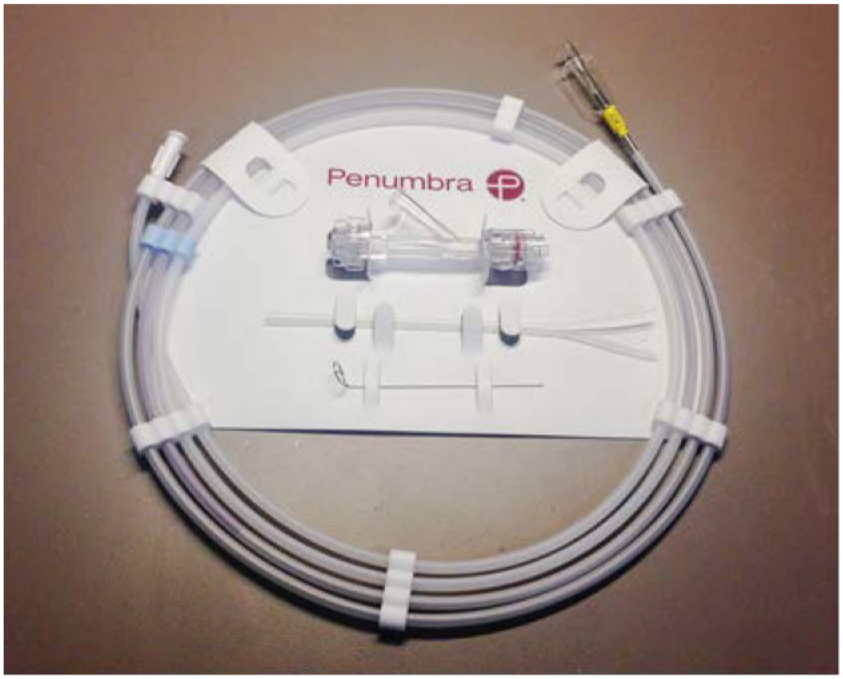
Figure 3: Reperfusion Catheter ACE - Packaged w/ Accessories



The Reperfusion Catheter ACE 64 and ACE 68 will remain sterile unless the pouch is opened, damaged, or the "Use By" date has passed.

Table 12 lists the materials utilized for each packaging component of the Reperfusion Catheters ACE 64 and ACE 68.

Table 12: Penumbra System ACE – Packaging Materials

Packaging Component	Material
Pouch	Polyester/Polyethylene/Tyvek®
Packaging hoop	Polyethylene
Packaging card	Polyethylene
Display box	SBS Paperboard

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6 Labeling

The subject Penumbra System ACE devices (Reperfusion Catheters ACE 64 and ACE 68) utilize the labeling described below for the established packaging configuration.

Each label is used for a distinct purpose with the necessary information to ensure clear identification and traceability of the product. Following is a description of the use of each label.

- Unit/Display Box Label – Placed on the external surface of both the Pouch and Display Box.
- Package Insert [Instructions for Use] – Included in display box.

Final label stock will incorporate a combination of pre-printed content and Lot specific "print on demand" information.

Copies of the proposed representative labels and the Instructions for Use are provided in:

Appendix 3: Representative Labels

Appendix 4: Instructions for Use

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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7 Rationale for Substantial Equivalence

The subject Penumbra System ACE devices (Reperfusion Catheters ACE 64 and ACE 68) are substantially equivalent to the predicate Reperfusion Catheter 5MAX ACE which was added to the Reperfusion Catheter 054 (K090752). The subject devices have the identical intended use and employ the same fundamental technology as the predicate device. The subject devices are substantially equivalent with regard to design, function, packaging, indications, sterilization, and manufacturing specifications, but differ (b)(4) [redacted] (b)(4) [redacted] Please note that these modifications do not alter the subject device's functional or biocompatibility profile. Like the predicate device, the subject device is indicated for use in the same population of patients for the identical treatment modality.

Design:	The subject and predicate devices are substantially equivalent with respect to design characteristic.
Function:	The subject and predicate devices are substantially equivalent with respect to functional characteristics.
Manufacturing:	The subject and predicate devices are manufactured with commonly utilized manufacturing technologies.
Materials:	The subject and predicate devices are all composed of biocompatible materials with the necessary functional characteristics to perform their intended use.
Design Characteristics:	The subject and predicate devices all maintain appropriate design characteristics, which enable the devices to function as needed for their intended use.
Performance Characteristics:	The subject and predicate devices performed in a substantially equivalent manner in *in vivo* studies.
Indications:	The subject and predicate devices maintain identical indications.
Packaging:	The subject and predicate devices utilize identical packaging configurations designed to protect the product through its labeled shelf-life.
Sterilization:	The subject and predicate devices are terminally sterilized and maintain a SAL of 10^{-6}.
Labeling:	The subject and predicate devices have similar labeling.

7.1 Substantial Equivalence Decision Making Process

The "510(k) 'Substantial Equivalence' Decision-Making Process (Detailed)" decision tree (ODE Guidance Memo #K86-3) was utilized to make a determination of substantial equivalence of the Reperfusion Catheters ACE 64 and ACE 68 to other currently marketed products. In accordance with the above-mentioned guidance, the answers to the following questions lead to a determination of substantial equivalence:

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1. **Does the new device have the same indication statements?**
   Yes. The subject Reperfusion Catheters ACE 64 and ACE 68 and the predicate device have the identical indications statement.

2. **Does the new device have the same intended use and may be "Substantially Equivalent"?**
   Yes. The subject and predicate devices have the identical intended use and as evidenced by this 510(k) submission, and may be considered "Substantially Equivalent."

3. **Does the new device have the same technological characteristics, e.g., design, materials, etc.?**
   (b)(4) [redacted].

4. **Could the Characteristics affect safety or effectiveness?**
   Yes. As is true with any device modification that incorporates the use of a different material composition and/or dimensions, the new characteristic has the potential to affect safety or effectiveness.

5. **Do the new characteristics raise new types of safety or effectiveness questions?**
   (b)(4) [redacted]

6. **Do accepted scientific methods exist for assessing the effects of the new characteristics?**
   Yes. Accepted scientific methods exist for the evaluation of all the issues raised in question 5. All of these questions have been assessed for the subject device utilizing similar methods as those, which have been previously reviewed and accepted by the agency for other interventional products.

7. **Are performance data available to assess the effects of the new characteristics?**
   Yes. Included in this submission are the summaries of the biocompatibility, bench-top, GLP animal data and shelf-life data, which assess the effects of the new characteristics.

8. **Performance data demonstrate equivalence?**
   Yes. The data included in this submission establish the substantial equivalence to the predicate device.

"Substantially Equivalent Determination"

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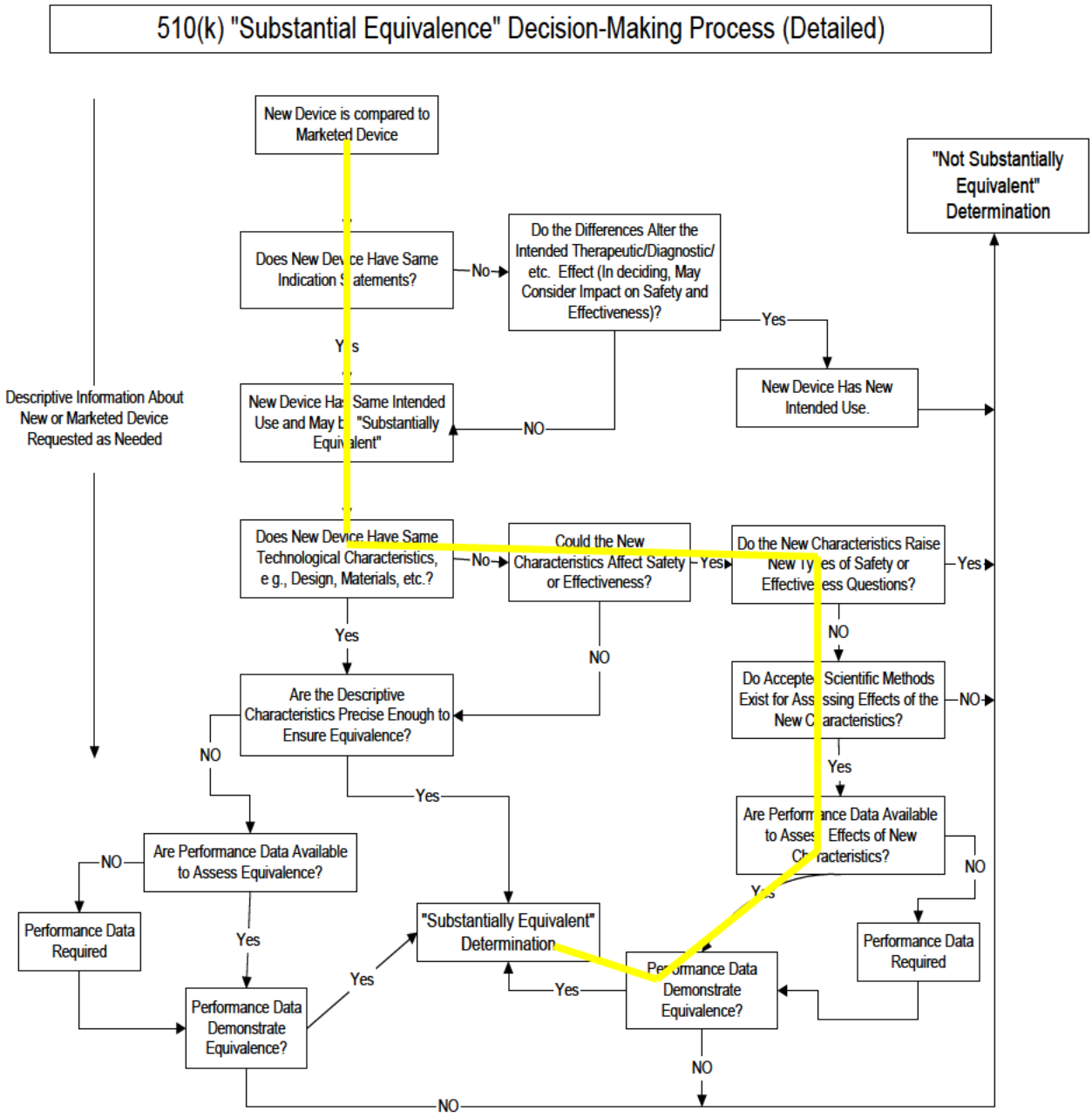
7.2 Substantial Equivalence Flowchart



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8 510(k) Summary of Safety & Effectiveness

(as required by 21 CFR 807.92)

Pursuant to Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, Penumbra Inc. is providing the summary of Substantial Equivalence for the Penumbra System ACE.

8.1 Sponsor/Applicant Name and Address

Penumbra, Inc.
1351 Harbor Bay Parkway
Alameda, CA 94502 USA

8.2 Sponsor Contact Information

Michaela Mahl
Senior Manager, Regulatory Affairs
Phone: (510) 748-3288
FAX: (510) 217-6414
Email: michaela.mahl@penumbrainc.com

8.3 Date of Preparation of 510(k) Summary

August 29, 2014

8.4 Device Trade or Proprietary Name

Penumbra System ACE

8.5 Device Classification

Regulatory Class:	II
Classification Panel:	Neurology
Classification Name:	Catheter, Thrombus Removal
Regulation Number:	21 CFR §870.1250
Product Code:	NRY

8.6 Predicate Devices

510(k) Number / Clearance Date	Name of Predicate Device	Name of Manufacturer
K072718 [28Dec2007], K090752 [21Sep2009], K100769 [21May2010], K113163 [28NOV2011], K133317 [13MAY2014]	Penumbra System / Penumbra System MAX®	Penumbra, Inc. 1351 Harbor Bay Parkway Alameda, CA 94502 USA

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.7 Predicate Comparison

System Name	**Penumbra System/Penumbra System MAX**	**Penumbra System ACE**
Device	**Predicate Device**	**Subject Device**
510(k) No.	K090752	To be determined
Classification	Class II, NRY	SAME
Indication	The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.	SAME
Materials	Medical Grade Plastic, Stainless Steel/Nitinol & Pt/Ir Band	SAME
Coating	Hydrophilic coating	SAME
Dimensions	Appropriately sized for the target vasculature	SAME
Packaging Materials		
Pouch	Polyester/Polyethylene/ Tyvek®	SAME
Hoop	Polyethylene	SAME
Display Carton	SBS Paperboard	SAME
Packaging Configuration	Individual	SAME
Sterilization	EtO	SAME
Shelf-Life	36 Months	SAME

8.8 Device Description

The Penumbra System ACE components are additional components to the currently available Penumbra System / Penumbra System MAX. The Penumbra System ACE components provide a larger lumen to assist in the efficient removal of thrombus from the neurovasculature. The devices are provided sterile, non-pyrogenic, and intended for single use only.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.9 Intended Use

The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.

8.10 Summary of Non-Clinical Data

As required under Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, a summary of any information regarding safety and effectiveness of the device follows.

Included in this section are summary descriptions of the testing, which substantiates the safe and effective performance of the subject Penumbra System ACE as well as its substantial equivalence to the predicate devices:

- Biocompatibility
- Design Verification (Bench-Top Testing)
- Design Validation (GLP Animal Testing)

The subject Penumbra System ACE devices met all established requirements.

8.10.1 Biocompatibility Testing

Biocompatibility tests conducted on the materials of the Penumbra System ACE devices were selected in accordance with EN ISO 10993 -1 guidelines (Biological Evaluation of Medical Devices) for limited duration (<24 hours), external communicating devices, contacting circulating blood. All studies were conducted pursuant to 21 CFR, Part 58, Good Laboratory Practices. In summary, non-clinical testing found the Penumbra System ACE devices to be biocompatible according to the requirements of EN ISO 10993 requirements. The following tests were performed and all tests passed successfully:

Test	Acceptance Criteria	Results	Pass / Fail
In Vitro Cytotoxicity	Sample extracts must yield cell lysis grade 2 or lower	Grade 1: Slight	Pass
Sensitization	Test Group shall yield Grade < 1 score on Magnusson and Kligman scale (provided control Grade < 1)	Grade 0: No visible change	Pass
Acute Intracutaneous Reactivity (Irritation)	The difference in the mean test article and mean control score must be grade 1.0 or lower	Grade ≤ 1.0 difference between mean test article and mean control score	Pass

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Test	Acceptance Criteria	Results	Pass / Fail
Systemic Toxicity			
Acute Systemic Toxicity	Sample extracts must not cause the following: • > 10% weight loss in 3 or more test animals • Mortality of 2 or more test animals • Abnormal behavior in 2 or more test animals	No evidence of systemic toxicity from sample extracts • No weight loss (all gained weight) • No death • All test animals appeared normal	Pass
Rabbit Pyrogen Study	Sample Extracts must not cause a total rise in body temperature of ≥0.5°C	Non-pyrogenic: No evidence of material-mediated pyrogenicity; no single animal had a total body temperature rise of ≥0.5°C	Pass
Hemocompatibility			
In Vitro Hemolysis	Sample extracts must be non-hemolytic (≤ 2% hemolytic index)	Non-hemolytic: Hemolytic Index = 0.70% Corrected Hemolytic index = 0.00%	Pass
Complement Activation	The concentrations of C3a and SC5b-9 in the test samples are statistically similar to the predicate (Exposure Control & Ref Material) control and statistically lower than the positive control for all exposure times	The test sample concentrations of C3a and SC5b-9 were statistically similar or lower than the predicate control sample concentrations, and statistically lower than the positive control sample concentrations at all three exposure times	Pass
Dog Thrombogenicity	The device must be non-thrombogenic after 4 hours *in vivo* when compared to a control device (Boston Scientific Excelsior SL-10 microcatheter)	No significant thrombosis with a Grade of 0 was observed in 2 out 2 test site and 2 out of 2 control sites. Based on the evaluation criteria, the amount of thrombosis was not considered significant	Pass

In summary non-clinical testing substantiates that the Penumbra System ACE devices are non-cytotoxic, non-sensitizing, non-irritating, non-toxic, non-pyrogenic, non-hemolytic, and non-thrombogenic.

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8.10.2 Bench-top Testing

The physical and mechanical properties of the Penumbra System ACE devices were assessed using standard test methods and pre-determined acceptance criteria. The following tests were performed and all tests passed successfully:

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Dimensional/ Visual Inspection	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Simulated Use [Intracranial Access & Vessel Access Entry Performance]	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Coating Integrity	(b) [redacted]	Coating has not delaminated, peeled, or flaked after simulated use	100% Must meet Specification	100% Pass
Particulate Testing (Reperfusion Catheter Hydrophilic Coating)	(b) [redacted]	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Particulate Testing (Reperfusion Catheter /Separator)	(b) [redacted]	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Coating Integrity	(b) [redacted]	Coating is not grossly damaged after undergoing particulate testing	100% Must meet Specification	100% Pass
Hub/Catheter Air Aspiration	(b) [redacted]	When negative pressure is pulled, no air may leak into hub	100% Must meet Specification	100% Pass
Pressure Test	(b) [redacted]	45 psi for 30 sec MIN	100% Must meet Specification	100% Pass
Reperfusion Catheter/Sheath or 8F Guide & 0.014" Guidewire compatibility (Friction Force)	(b) [redacted]	Maximum value per specification	100% Must meet Specification	100% Pass
Markerband Section Bond Strength	(b) [redacted]	Minimum value per specification	100% Must meet Specification	100% Pass
Joint Sections Bond Strength	(b) [redacted]	Minimum value per specification	100% Must meet Specification	100% Pass

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Attribute	Sample Size	Specification	Acceptance Criteria	Results
Hub to Shaft & Hub to Hypotube Bond Strength	(b) [redacted]	Minimum value per specification	100% Must meet Specification	100% Pass
Elongation to Failure – Reperfusion Catheter	(b) [redacted]	% Elongation ≥ 5%	100% Must meet Specification	100% Pass
Corrosion	(b) [redacted]	No visible corrosion on Reperfusion Catheter immediately after Corrosion Testing procedure	100% Must meet Specification	100% Pass

The results of the tests appropriately address the physical and mechanical performance expectations of the device. This is further supported by the surgical handling and performance results reported in the *in vivo* study. Based on these overall results, the physical and mechanical properties of the subject Penumbra System ACE devices are acceptable for the intended use and substantially equivalent to the predicate device.

8.10.3 Animal Study

An animal study was conducted to evaluate the safe use of the Penumbra System ACE devices in a swine model. The study concluded that:

- No vessel injury was noted on the final angiograms following the vessel response procedure.
- No abnormal gross or histology findings were noted in test vessel segments.
- The use of the Penumbra System ACE devices resulted in no significant vascular response in these experimental conditions.

8.10.4 Summary of Substantial Equivalence

The subject Penumbra System ACE devices are substantially equivalent to the predicate device with regard to intended use, operating principle, design concept, materials, shelf-life, packaging and sterilization processes.

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9 Statement of Indication for Use

Indications for Use

510(k) Number (if known): _____

Device Name:___ Penumbra System ACE _____

Indications for Use:

The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.

Prescription Use____X_____ AND/OR Over The Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

(b)(4) Schematic Drawings

(b)(4) Schematic Drawings

[redacted]

(b)(4) Schematic Drawings

(b)(4) Schematic Drawings

[redacted]

(b)(4) Schematic Drawings

(b)(4) Schematic Drawings

(b)(4) Specifications

[redacted]

(b)(4) Specifications

(b)(4) Specifications

(b)(4) Specifications

(b)(4) Specifications

[redacted]

(b)(4) Schematic Drawings

[redacted]

(b)(4) Schematic Drawings

(b)(4) Schematic Drawings

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(b)(4) Schematic Drawings

(b)(4) Schematic Drawings

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(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4)

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(b)(4)

[redacted]

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(b)(4)

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(b)(4)

[redacted]

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(b)(4) [redacted]

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(b)(4)

[redacted]

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(b)(4)

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(b)(4)

[redacted]

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(b)(4)

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(b)(4)

[redacted]

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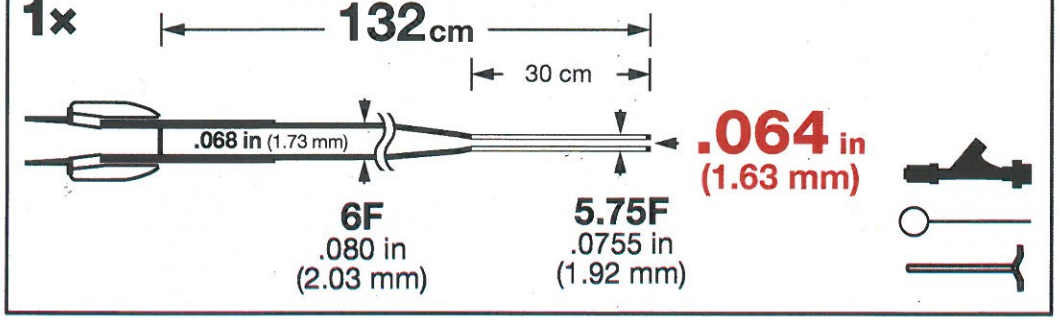
Penumbra

Penumbra System® ACE™

64 Reperfusion Catheter

1×



Rx Only

Use By 使用截止日期 2003-05

REF Catalog Number 型号 5MAXACE064

LOT Lot Number 批号 F12345

STERILE EO Sterile (ethylene oxide) 灭菌（环氧乙烷）

Nonpyrogenic 无热原

Do not resterilize 切勿重新灭菌

Single use only. Do not reuse. 仅供一次性使用。切勿重复使用。

Latex-free 不含胶乳

Attention, see Instructions for Use. 注意，请参阅使用说明。

+M4245MAXACE0640H

+$$80105 03F12345HB

ACE64 Reperfusion Catheter 132 cm
REF 5MAXACE064
LOT F12345

ACE64 Reperfusion Catheter 132 cm
REF 5MAXACE064
LOT F12345

ACE64 Reperfusion Catheter 132 cm
REF 5MAXACE064
LOT F12345

Penumbra System® ACE

制造商

Manufacturer:
Penumbra, Inc.
1351 Harbor Bay Parkway
Alameda, CA 94502, USA
Tel: 1.888.BRAIN06
(1.888.272.4606)
1.510.748.3200
Fax: 1.510.748.3232

EC REP 欧盟授权代表

EU Representative:
MedPass International Ltd.
Windsor House, Bretforton
Evesham, Worcestershire WR11 7JJ, UK

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Suite 3, Level 5, 1 Oxford Street
Darlinghurst NSW 2010, Australia
Tel: 1300 817 025
Fax: 1300 817 026
Email: order.anz@penumbrainc.com

8051.A

ACE64 Reperfusion Catheter REF 5MAXACE064 132 cm Use By 2003-05

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

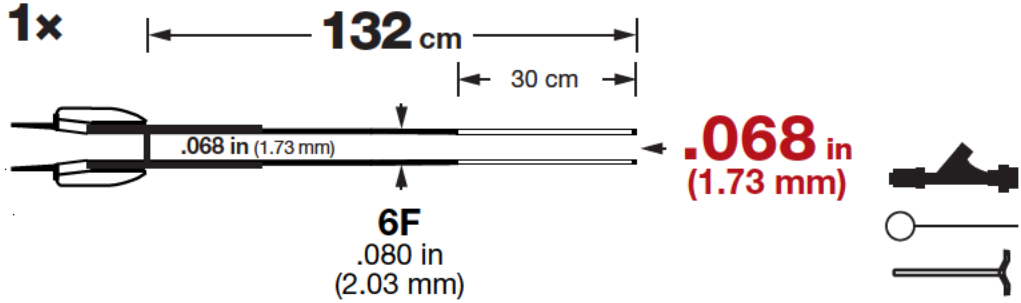
Records processed under FOIA Request # 2015-5433 Released by CDRH on 10-08-2015

Penumbra

Penumbra System® ACE™

68 Reperfusion Catheter

1×



Use By
使用截止日期 2015-01

REF Catalog Number
型号 **5MAXACE068**

LOT Lot Number
批号 F12345

STERILE EO Sterile (ethylene oxide)
灭菌（环氧乙烷）

Nonpyrogenic
无热原

Do not resterilize
切勿重新灭菌

Single use only. Do not reuse.
仅供一次性使用。切勿重复使用。

LATEX Latex-free
不含胶乳

Attention, see Instructions for Use.
注意，请参阅使用说明。

Placeholder 1

Placeholder 2

Rx Only

ACE 68 Reperfusion Catheter 132 cm
REF 5MAXACE068
LOT F12345
Penumbra System® ACE

ACE 68 Reperfusion Catheter 132 cm
REF 5MAXACE068
LOT F12345
Penumbra System® ACE

ACE 68 Reperfusion Catheter 132 cm
REF 5MAXACE068
LOT F12345
Penumbra System® ACE

制造商

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8056.01

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

ACE 68 Reperfusion Catheter REF 5MAXACE068 132 cm Use By 2015-01

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English

Device Description

The Penumbra System® is comprised of several devices:

- Penumbra Reperfusion Catheter
- Penumbra Aspiration Pump
- Penumbra Pump/Canister Tubing
- Penumbra Aspiration Tubing
- Penumbra Separator

The Penumbra System is designed to remove thrombus from the vasculature using continuous aspiration. The Reperfusion Catheter targets aspiration from the pump directly to the thrombus. The Separator may be used to clear the lumen of the Reperfusion Catheter should it become blocked with thrombus. The use of the Separator may not be necessary when using a Reperfusion Catheter with an I.D. of 0.054in or larger. The Reperfusion Catheter is introduced through a guide catheter or long femoral sheath and into the intracranial vasculature and guided over a neurovascular guidewire to the site of the primary occlusion. The Penumbra Reperfusion Catheter is used with the Aspiration Pump to aspirate thrombus from an occluded vessel. As needed, a Penumbra Separator may be deployed from the Reperfusion Catheter to assist with thrombus removal. The Penumbra Separator is advanced and retracted through the Penumbra Reperfusion Catheter at the proximal margin of the primary occlusion to facilitate clearing of the thrombus from the Reperfusion Catheter tip. For the aspiration source, the Penumbra Reperfusion Catheter is used in conjunction with the Aspiration Pump, which is connected using the Penumbra Aspiration Tubing and the Penumbra Pump/Canister Tubing. The Penumbra Reperfusion Catheter is provided with a steam shaping mandrel and rotating hemostasis valve, and a peelable sheath. The Penumbra Separator is provided with an introducer and torque device. The devices are visible under fluoroscopy.

Indication for Use

The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.

Contraindications

There are no known contraindications.

Warnings

- The Penumbra System should only be used by physicians who have received appropriate training in interventional neuro-endovascular techniques and treatment of acute ischemic stroke.
- Do not advance, retract or use any component of the Penumbra System against resistance without careful assessment of the cause using fluoroscopy. If the cause cannot be determined, withdraw the device or system as a unit. Unrestrained torquing or forced insertion of the catheter or separator against resistance may result in damage to the device or vessel.
- Do not use the Penumbra System with a pump other than the Penumbra Aspiration Pump.

Precautions

- The device is intended for single use only. Do not resterilize or reuse. Resterilization and/or Reuse may result in ineffective catheter coating lubrication, which may result in high friction and the inability to access the target neuro vasculature location.
- Do not use kinked or damaged devices. Do not use open or damaged packages. Return all damaged devices and packaging to the manufacturer/ distributor.
- Use prior to the "Use By" date.
- Use the Penumbra System in conjunction with fluoroscopic visualization.
- When performing aspiration, ensure that the Penumbra Aspiration Tubing valve is open for only the minimum time needed to remove thrombus. Excessive aspiration or failure to close the Penumbra Aspiration Tubing valve when aspiration is complete is not recommended.
- The Penumbra Separator is not intended for use as a neurovascular guidewire. If repositioning of the Penumbra Reperfusion Catheter is necessary during the revascularization procedure, such reposition should be performed over an appropriate neurovascular guidewire using standard microcatheter and guidewire techniques.
- Do not use automated high-pressure contrast injection equipment with the Penumbra Reperfusion Catheter because it may damage the device.
- Administration of anticoagulants and antiplatelets should be suspended until 24 hours post-treatment. Medical management and acute post stroke care should follow the ASA guidelines.[1] Any neurological deterioration should be evaluated by urgent CT scan and other evaluations as indicated according to investigator/hospital best practice.
- The total time allowed to achieve patient revascularization is 120 minutes of using the Penumbra System.

Potential Adverse Events

Possible complications include, but are not limited to, the following:

- allergic reaction and anaphylaxis from contrast media
- acute occlusion
- air embolism
- arteriovenous fistula
- death
- device malfunction
- distal embolization
- emboli
- false aneurysm formation
- hematoma or hemorrhage at access site
- inability to completely remove thrombus
- infection
- intracranial hemorrhage
- ischemia
- kidney damage from contrast media
- neurological deficits including stroke
- vessel spasm, thrombosis, dissection, or perforation

Procedure

1. Refer to **Warnings, Precautions**, and **Potential Adverse Events** prior to use.
2. As each device of the Penumbra System is used, remove the device from the packaging, and inspect for damage or for kinks.
3. Prepare Penumbra System devices for use by flushing the packaging hoop and device with heparinized saline (includes Penumbra Reperfusion Catheter and Penumbra Separator only).
4. Prepare a guide catheter or long femoral sheath according to the manufacturer's *Instructions for Use*.
5. Place the guide catheter or long femoral sheath into the appropriate cerebral artery that is proximal to the thrombus occlusion site.

Penumbra Reperfusion Catheter Preparation and Use

1. Confirm vessel diameter, and select an appropriate size Penumbra Reperfusion Catheter (See **Table 1**).
2. The Penumbra Reperfusion Catheter tip may be shaped using the steam shaping mandrel provided.
3. Attach the rotating hemostasis valve provided to the Penumbra Reperfusion Catheter.
4. Attach the Penumbra Aspiration Tubing to the Aspiration Pump and turn on the Aspiration Pump (Refer to the Aspiration Pump *Operation Manual*). Allow the Aspiration Pump to run for at least one minute prior to use, and confirm that the Aspiration gauge reads −20inHg. Ensure the valve on the Penumbra

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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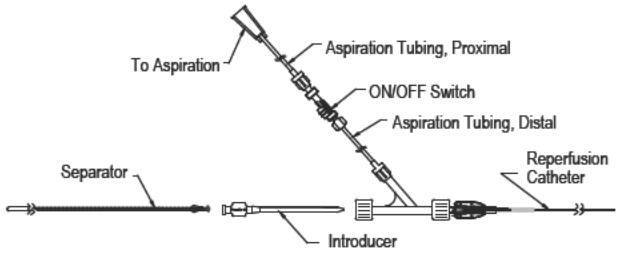
Aspiration Tubing is switched to the OFF position.

5. Connect the Aspiration Tubing to the side port of the rotating hemostasis valve as shown in **Figure 1**.

Figure 1 – Assembled Aspiration System with Penumbra Separator



6. Insert the Penumbra Reperfusion Catheter into a rotating hemostasis valve connected to the proximal hub of a guide catheter. If a guide catheter is not used, insert the Penumbra Reperfusion Catheter through the valve of the long femoral sheath using the peelable sheath. After inserting the Penumbra Reperfusion Catheter, remove the peelable sheath from the vascular sheath, and peel from the Penumbra Reperfusion Catheter shaft.
7. Using conventional catheterization techniques under fluoroscopic guidance, advance the Penumbra Reperfusion Catheter into the target vessel over an appropriate neurovascular guidewire. Position the Penumbra Reperfusion Catheter proximal to the thrombus. Remove the guidewire from the Penumbra Reperfusion Catheter.
8. To begin aspiration, open the valve on the Penumbra Aspiration Tubing to the ON position. To stop aspiration, switch the valve on the Penumbra Aspiration Tubing to the OFF position, and turn off the Aspiration Pump.
9. Using a 5cc or 10cc syringe, aspirate approximately 5cc of blood from the Penumbra Reperfusion Catheter to remove any thrombus that may remain in the catheter.
10. Obtain a post-treatment angiogram by injecting contrast media through the guide catheter.

Penumbra Separator Preparation and Use

1. If needed, select an appropriate size Penumbra Separator corresponding to the Reperfusion Catheter (see **Table 1**).

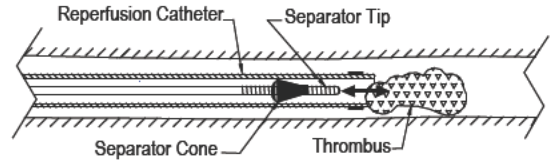
Table 1 – Separator/Reperfusion Catheter Device Size Selection

Vessel Size (mm)	Penumbra Reperfusion Catheter	Penumbra Separator
< 2.0	026	026
2.0 to 3.0	032 / 3MAX	032 / 3MAX
3.0 to 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX / ACE	054 / 5MAX

NOTE: Access to the site of occlusion may be aided by the triaxial use of a compatible inner microcatheter.

2. Using the introducer sheath provided, insert the Penumbra Separator through the rotating hemostasis valve and into the proximal hub of the Penumbra Reperfusion Catheter.
3. To begin aspiration, open the valve on the Penumbra Aspiration Tubing to the ON position, and advance/retract the Penumbra Separator to assist with aspiration and removal of the thrombus from the Reperfusion Catheter as shown in **Figure 2**.

Figure 2 – Thrombus Aspiration Using the Penumbra Separator



4. To stop aspiration, switch the valve on the Penumbra Aspiration Tubing to the OFF position, and turn off the Aspiration Pump.
5. Remove the Penumbra Separator, if used.
6. If necessary, additional Penumbra Separators and Reperfusion Catheters may be used to further remove thrombus at the discretion of the physician.

Clinical Data Summary

The Penumbra Pivotal trial was a prospective, single arm trial to assess the safety and effectiveness of the Penumbra System. A total of 125 patients were enrolled at 24 international centers. Main entry criteria were NIH Stroke Scale (NIHSS) score ≥ 8, presentation within 8 hours of symptom onset, and an occlusion (TIMI 0 or 1) of a treatable intracranial vessel. Patients who presented within 3 hours from symptom onset must have been ineligible for or refractory to rtPA therapy. Primary endpoints were revascularization of the target vessel (TIMI 2 or 3) and incidence of procedural serious adverse events (SAE). All patients were followed and assessed up to 90 days from the procedure.

Statistical Analysis

A sample size of 125 was selected for this study in order to generate at least 115 evaluable patients. A patient was considered evaluable if the patient met eligibility requirements for primary endpoint assessment and was treated with the Penumbra System. Since this was an uncontrolled study, a formal hypothesis test was not planned for the overall response rate for establishing a TIMI grade of 2 or 3. Standard descriptive statistics for categorical endpoints were the number and percent of patients with each level of the endpoint. For numeric endpoints, the standard descriptive statistics included the number of non-missing observations (n), the mean, the median, the standard deviation, the minimum value, and the maximum value.

Study Procedures

Arterial access to the target vessel was achieved using standard percutaneous technique and a four-vessel digital subtraction angiography was performed to define the angio-architecture of the occluded vascular segment. Each patient was required to have their cerebral large vessel occlusion confirmed by angiography and a site of primary occlusion designated a priori by the investigator. If the occlusion is in a treatable vessel, an appropriate guide catheter was positioned and the Penumbra Reperfusion Catheter advanced to the proximal end of the occluded target vessel. A patient was considered enrolled when the Reperfusion Catheter was deployed from the guide catheter.

Key Inclusion Criteria

- Clinical signs consistent with acute ischemic stroke, including:
  - Sudden numbness or weakness of face or extremities
  - Sudden confusion, trouble speaking or understanding speech
  - Sudden trouble walking, dizziness, or loss of balance
- From 18 to 79 years of age
- Neurological deficit resulting in a NIH Stroke Scale (NIHSS) score ≥ 8
- Complete occlusion (TIMI Grade 0) or contrast penetration with minimal perfusion but no distal branch filling (TIMI Grade I) in intracranial vessels accessible to the Penumbra Stroke System
- Signed informed consent
- Present within 8 hours of stroke symptom onset

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- Ineligible or refractory to intravenous rtPA therapy if presenting within 3 hours of symptom onset

Key Exclusion Criteria
- Evidence of rapidly improving neurological signs of stroke at time of enrollment
- NIHSS >30 or coma
- Females who are pregnant
- Vessel tortuosity too difficult to allow endovascular access
- Known hemorrhagic diathesis, coagulation deficiency, or on oral anticoagulant therapy with an INR >3.0
- PTT greater than 2 times the lab normal
- Admission platelets <30,000
- Pre-existing neurological or psychiatric disease that could confound the study results
- Known severe allergy to contrast media
- Uncontrolled hypertension (defined as systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg)
- CT evidence of the following conditions on presentation:
  - Significant mass effect with midline shift
  - Large hypodensity region >1/3 of the middle cerebral artery territory
  - Evidence of intracranial hemorrhage
- Angiographic evidence of an arterial stenosis proximal to the occlusion that could prevent thrombus removal
- Angiographic evidence of preexisting arterial injury
- Life expectancy less than 90 days
- Participation in another clinical investigation that could confound the evaluation of the study device

Summary of reasons for exclusion of enrolled subjects, especially those based on angiographic criteria
No enrolled patient was excluded for angiographic reasons.

Primary Effectiveness Endpoint
The Primary Effectiveness Endpoint was revascularization of the occluded target vessel. Revascularization was defined by a TIMI score of II or III following use of the Penumbra System only and prior to the use of any additional or adjunctive devices or therapies. Angiographic results were adjudicated by an independent Core Laboratory.

Effectiveness	% (n/N) [95% CI]†
Primary Effectiveness Endpoint (TIMI score of II or III) *TIMI scores before adjunctive therapies are used*	81.6% (102/125) [73.7%, 88.0%]
Post-Device Revascularization Success (TIMI ≥ 2) *Any Adjunctive Therapy Use Considered Treatment Failure*	81.6% (102/125) [73.7%, 88.0%]
Post-Device Revascularization Success (TIMI ≥ 2) *Any IA Lytic Use Considered Treatment Failure*	81.6% (102/125) [73.7%, 88.0%]

†Exact Clopper-Pearson confidence intervals

Primary Safety Endpoint
The Primary Safety Endpoint was incidence of device and/or procedure-related serious adverse events that occurred during the procedure as reported by the investigator. There were 18 procedural events reported in 16 patients (12.8%). Among these, 4 events in 3 patients were rated as serious by the CEC (2.4%).

Composite Adverse Events during the procedure	% (n/N) [95% CI]†
Composite SAE during the procedure	2.4% (3/125)
Primary Safety Endpoint: Composite Procedure/Device related SAE during the procedure	2.4% (3/125)

†Exact Clopper-Pearson confidence intervals

Each specific SAE through 90 days occurring in more than 2% of patients

SAE	% (n/N)
Composite SAEs	52.0% (65/125)
Cerebral Edema	11.2% (14/125)
ICH	8.0% (10/125)
Respiratory Dysfunction/Failure	8.0% (10/125)
Worsening Symptoms of Qualifying Stroke	7.2% (9/125)
Infection	5.6% (7/125)
Other Pulmonary Complications	5.6% (7/125)
Pneumonia	4.0% (5/125)
Cardiac Arrhythmia	3.2% (4/125)
Access Site Complication	2.4% (3/125)
Myocardial Infarction	2.4% (3/125)
Peripheral Vascular Complication	2.4% (3/125)
Renal Dysfunction/Failure	2.4% (3/125)
Stroke in New Territory	2.4% (3/125)

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Categorization of AEs through 90 days Under Anatomical System

Anatomical System	% (n/N)
Nervous System Disorders	62.4% (78/125)
Infections and Infestations	44.0% (55/125)
Cardiac Disorders	28.8% (36/125)
Metabolism and Nutrition Disorders	25.6% (32/125)
General Disorders and Administration Site Conditions	24.8% (31/125)
Respiratory, Thoracic and Mediastinal Disorders	24.8% (31/125)
Injury, Poisoning and Procedural Complications	18.4% (23/125)
Gastrointestinal Disorders	16.0% (20/125)
Blood and Lymphatic System Disorders	14.4% (18/125)
Vascular Disorder	11.2% (14/125)
Psychiatric Disorders	10.4% (13/125)
Renal and Urinary Disorders	8.0% (10/125)
Hepatobiliary Disorders	4.0% (5/125)
Investigations	3.2% (4/125)
Skin and Subcutaneous Tissue Disorders	3.2% (4/125)
Neoplasms Benign, Malignant and Unspecified (Incl Cysts And Polyps)	2.4% (3/125)
Musculoskeletal and Connective Tissue Disorders	0.8% (1/125)

SYMBOLS GLOSSARY

		Attention, see instructions for use	
Rx Only		Prescription only – US Federal Law restricts this device to use by or on the order of a physician	
		Nonpyrogenic	
STERILE EO		Sterilized using ethylene oxide	
	Manufacturer	EC REP	EU Representative
LOT	Lot number		Do not reuse
	Use by	REF	Catalogue number
STERILIZE	Do not resterilize	LATEX	Latex free

WARRANTY

Penumbra, Inc. (Penumbra) warrants that reasonable care has been used in the design and manufacture of this device. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warran ies of merchantability or fitness for a par icular use. Handling, storage, cleaning, and sterilization of this device as well as other factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond Penumbra's control directly affect the device and the results obtained from its use. Penumbra's obligation under this warranty is limited to the repair or replacement of this device and Penumbra shall not be liable for any incidental or consequential loss, damage, or expense directly or indirectly arising from he use of this device. Penumbra neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with his device. Penumbra assumes no liability with respect to devices reused, reprocessed, or resterilized and makes no warranties, expressed or implied, including but not limited to merchantability or fitness for intended use, with respect to such device.

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Deutsch

Produktbeschreibung

Das Penumbra System® besteht aus mehreren Produkten:

- Penumbra Reperfusionskatheter
- Penumbra Aspirationspumpe
- Penumbra Pumpen-/Behälterschlauch
- Penumbra Aspirationsschlauch
- Penumbra Separator

Das Penumbra System ist für die Entfernung von Thromben aus dem Gefäßsystem mittels kontinuierlicher Aspiration vorgesehen. Der Reperfusionskatheter leitet die Aspiration von der Pumpe direkt zum Thrombus. Der Separator kann verwendet werden, um im Falle einer Blockade Thrombusmaterial aus dem Lumen des Reperfusionskatheters zu beseitigen. Wenn ein Reperfusionskatheter mit einem Innendurchmesser ab 1,37 mm (0,054 Zoll) verwendet wird, ist der Einsatz des Separators eventuell nicht erforderlich. Der Reperfusionskatheter wird über einen Führungskatheter oder eine lange femorale Schleuse in die intrakranielle Vaskulatur eingeführt und mithilfe eines neurovaskulären Führungsdrahtes zur primären Okklusionsstelle geführt. Der Penumbra Reperfusionskatheter wird zusammen mit der Aspirationspumpe eingesetzt, um den Thrombus aus einem verschlossenen Gefäß abzusaugen. Bei Bedarf wird der Penumbra Separator vom Reperfusionskatheter freigesetzt, um die Thrombusentfernung zu erleichtern. Der Penumbra Separator wird am proximalen Rand der primären Okklusion durch den Penumbra Reperfusionskatheter vorgeschoben und zurückgezogen, um die Beseitigung des Thrombus aus der Spitze des Reperfusionskatheters zu erleichtern. Die Aspirationsquelle besteht aus dem Penumbra Reperfusionskatheter und der Aspirationspumpe, die über den Penumbra Aspirationsschlauch und den Penumbra Pumpen-/Behälterschlauch angeschlossen ist. Der Lieferumfang des Penumbra Reperfusionskatheters umfasst einen Dampfformmandrin und ein rotierendes Hämostaseventil sowie eine abziehbare Schleuse. Der Penumbra Separator wird zusammen mit einer Einführschleuse und einer Drehvorrichtung geliefert. Die Produkte sind unter Röntgendurchleuchtung sichtbar.

Indikationen

Das Penumbra System ist zur Revaskularisierung von Patienten mit einem akuten ischämischen Schlaganfall als Folge von Verschlusskrankheiten in den großen intrakraniellen Blutgefäßen (innerhalb der A. carotis interna, der A. cerebri media – Segmente M1 und M2, der A. basilaris und der A. vertebralis) vorgesehen. Der Eingriff muss innerhalb von 8 Stunden nach Einsetzen der Symptome durchgeführt werden.

Kontraindikationen

Es liegen keine bekannten Kontraindikationen vor.

Warnhinweise

- Das Penumbra System darf nur von Ärzten mit einer adäquaten Ausbildung in interventionellen neuro-endovaskulären Techniken und Behandlung eines akuten ischämischen Schlaganfalls eingesetzt werden.
- Keine Komponente des Penumbra Systems darf gegen einen Widerstand vorgeschoben, zurückgezogen oder benutzt werden, ohne zuvor die Ursache des Widerstands unter Durchleuchtung sorgfältig zu beurteilen. Falls keine Ursache bestimmt werden kann, muss das Produkt bzw. System als Ganzes zurückgezogen werden. Eine ungehinderte Drehung oder erzwungene Einführung des Katheters bzw. Separators gegen einen Widerstand kann zu Schäden am Produkt oder zu Gefäßverletzungen führen.
- Das Penumbra System darf nur mit der Penumbra Aspirationspumpe verwendet werden.

Vorsichtsmassnahmen

- Das Produkt ist nur zum einmaligen Gebrauch bestimmt. Nicht resterilisieren oder wiederverwenden. Eine Resterilisation und/oder Wiederverwendung kann dazu führen, dass die Gleiteigenschaften der Katheterbeschichtung unwirksam werden, wodurch es zu einer hohen Reibung und der Unfähigkeit zum Zutritt in das neurovaskuläre Zielgefäß kommen kann.
- Produkte mit Knickstellen oder Schäden dürfen nicht verwendet werden. Inhalt bei offener oder beschädigter Verpackung nicht verwenden. Beschädigte Produkte und Verpackungen an den Hersteller/Vertriebspartner zurücksenden.
- Vor Ablauf des angegebenen Verwendbarkeitsdatums verwenden.
- Das Penumbra System ist unter Durchleuchtung zu verwenden.
- Bei der Aspiration sicherstellen, dass das Ventil des Penumbra Aspirationsschlauchs nur für den zur Thrombusentfernung erforderlichen Mindestzeitraum geöffnet ist. Eine übermäßige Aspiration bzw. das Versäumnis, das Ventil des Penumbra Aspirationsschlauchs nach Abschluss der Aspiration zu schließen, werden nicht empfohlen.
- Der Penumbra Separator ist nicht für die Verwendung als neurovaskulärer Führungsdraht vorgesehen. Sollte der Penumbra Reperfusionskatheter während des Revaskularisierungseingriffs neu positioniert werden müssen, muss diese Umpositionierung mithilfe eines geeigneten neurovaskulären Führungsdrahtes und unter Anwendung von Standard-Techniken für Mikrokatheter und Führungsdrähte vorgenommen werden.
- Keinen automatisierten Hochdruckinjektor für Kontrastmittel mit dem Penumbra Reperfusionskatheter verwenden, da dies zu Schäden am Produkt führen könnte.
- Thrombozytenaggregationshemmer und Antikoagulanzien sollten bis 24 Stunden nach dem Eingriff ausgesetzt werden. Das medikamentöse Management und die akute Schlaganfallnachsorge sollten gemäß den ASA (American Stroke Association)-Richtlinien durchgeführt werden.[1] Jegliche neurologische Verschlechterung sollte umgehend mit einem CT-Scan oder einem anderen gemäß der empfohlenen Praxis des Prüfarztes/Krankenhauses angezeigten Verfahren untersucht werden.
- Bei der Verwendung des Penumbra Systems beträgt die max. Zeitdauer bis zum Erreichen der Patienten-Revaskularisierung 120 Minuten.

Potenzielle unerwünschte Ereignisse

Zu den möglichen Komplikationen gehören u.a. die folgenden:

- akute Okklusion
- arteriovenöse Fistel
- Bildung eines falschen Aneurysmas
- distale embolische Verschleppung
- durch Kontrastmittel ausgelöste allergische Reaktion und Anaphylaxe
- Emboli
- Gefäßspasmus, -thrombose, -dissektion oder -perforation
- Hämatome oder Blutungen an der Zugangsstelle
- Infektion
- intrakranielle Blutung
- Ischämie
- Luftembolie
- neurologische Ausfälle einschließlich Schlaganfall
- Nicht mögliche vollständige Entfernung des Thrombus
- Nierenschäden durch Kontrastmittel
- Produktfehlfunktion
- Tod

Eingriff

1. Vor der Verwendung die Abschnitte **Warnhinweise, Vorsichtsmaßnahmen** und **Potenzielle unerwünschte Ereignisse** durchlesen.
2. Jedes Produkt des Penumbra Systems vor Gebrauch aus der Verpackung nehmen und auf Schäden oder Knicke untersuchen.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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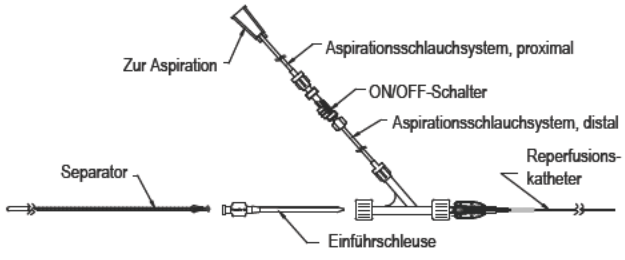
3. Die Produkte des Penumbra Systems zur Verwendung vorbereiten, indem die Schutzspirale und das Produkt mit heparinisierter Kochsalzlösung gespült werden (nur für Penumbra Reperfusionskatheter und Penumbra Separator).
4. Einen Führungskatheter bzw. eine lange femorale Schleuse entsprechend der *Gebrauchsanweisung* des Herstellers vorbereiten.
5. Den Führungskatheter bzw. die lange femorale Schleuse proximal zur Thrombusverschlussstelle in der entsprechenden Gehirnarterie positionieren.

Penumbra Reperfusionskatheter – Vorbereitung und Verwendung

1. Den Gefäßdurchmesser bestimmen und den Penumbra Reperfusionskatheter (siehe **Tabelle 1**) der geeigneten Größe auswählen.
2. Die Spitze des Penumbra Reperfusionskatheters kann mit dem im Lieferumfang enthaltenen Dampfformmandrin geformt werden.
3. Das im Lieferumfang enthaltene rotierende Hämostaseventil an den Penumbra Reperfusionskatheter anschließen.
4. Den Penumbra Aspirationsschlauch an die Aspirationspumpe anschließen und diese einschalten (siehe das *Betriebshandbuch* der Aspirationspumpe). Die Aspirationspumpe mindestens eine Minute vor Gebrauch laufen lassen und überprüfen, ob das Aspirationsmanometer −508 mmHg (−20 inHg) anzeigt. Sicherstellen, dass das Ventil am Penumbra Aspirationsschlauch in der Position OFF (AUS) steht.
5. Den Aspirationsschlauch wie in **Abbildung 1** gezeigt am Seitenanschluss des rotierenden Hämostaseventils anschließen.

Abbildung 1 – Montiertes Aspirationssystem mit Penumbra Separator



6. Den Penumbra Reperfusionskatheter in ein rotierendes Hämostaseventil einführen, das am proximalen Ansatz eines Führungskatheters angebracht ist. Wenn kein Führungskatheter verwendet wird, den Penumbra Reperfusionskatheter mithilfe der abziehbaren Schleuse durch das Ventil der langen femoralen Schleuse einführen. Nach der Einführung des Penumbra Reperfusionskatheters die abziehbare Schleuse aus der Gefäßschleuse entfernen und vom Schaft des Penumbra Reperfusionskatheters abziehen.
7. Unter Röntgendurchleuchtung und gemäß den herkömmlichen Katheterisierungsmethoden den Penumbra Reperfusionskatheter über einen geeigneten neurovaskulären Führungsdraht in das Zielgefäß vorschieben. Den Penumbra Reperfusionskatheter proximal zum Thrombus platzieren. Den Führungsdraht aus dem Penumbra Reperfusionskatheter entfernen.
8. Um mit der Aspiration zu beginnen, das Ventil am Penumbra Aspirationsschlauch in die Position ON (EIN) stellen. Das Ventil am Penumbra Aspirationsschlauch zum Beenden der Aspiration in die Position OFF (AUS) drehen und die Aspirationspumpe ausschalten.
9. Mit einer 5-ml- oder 10-ml-Spritze ca. 5 ml Blut aus dem Penumbra Reperfusionskatheter aspirieren, um einen eventuell im Katheter verbliebenen Thrombus zu entfernen.
10. Ein postinterventionelles Angiogramm erstellen, indem Kontrastmittel durch den Führungskatheter injiziert wird.

Penumbra Separator – Vorbereitung und Verwendung

1. Sofern erforderlich, einen Penumbra Separator der geeigneten Größe entsprechend dem Reperfusionskatheter auswählen (siehe **Tabelle 1**).

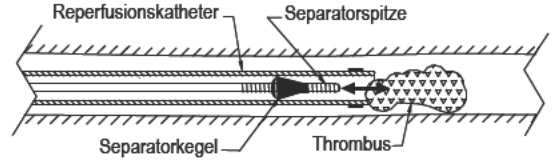
Tabelle 1 – Größenauswahl für Separator und Reperfusionskatheter

Gefäßgröße (mm)	Penumbra Reperfusionskatheter	Penumbra Separator
< 2,0	026	026
2,0 bis 3,0	032 / 3MAX	032 / 3MAX
3,0 bis 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

HINWEIS: Der Zugang zur Okklusionsstelle kann durch die triaxiale Verwendung eines kompatiblen inneren Mikrokatheters erleichtert werden.

2. Den Penumbra Separator mithilfe der mitgelieferten Einführschleuse in das rotierende Hämostaseventil und den proximalen Ansatz des Penumbra Reperfusionskatheters einführen.
3. Um mit der Aspiration zu beginnen, das Ventil am Penumbra Aspirationsschlauch in die Position ON (EIN) stellen und den Penumbra Separator zurückziehen/vorschieben, um die Aspiration und die Entfernung des Thrombus (wie in **Abbildung 2** dargestellt) aus dem Reperfusionskatheter zu erleichtern.

Abbildung 2 – Thrombus-Aspiration mithilfe des Penumbra Separators



4. Zum Beenden der Aspiration das Ventil am Penumbra Aspirationsschlauch in die Position OFF (AUS) drehen und die Aspirationspumpe ausschalten.
5. Den Penumbra Separator (sofern verwendet) entfernen.
6. Es können ggf. weitere Exemplare des Penumbra Separators und Reperfusionskatheters zur Entfernung des Thrombus eingesetzt werden, wenn dies vom Arzt als erforderlich erachtet wird.

Zusammenfassung der klinischen Daten

Bei der Penumbra Pivotalstudie handelte es sich um eine prospektive, einarmige Studie zur Beurteilung von Sicherheit und Wirksamkeit des Penumbra Systems. Insgesamt wurden 125 Patienten an 24 Zentren in mehreren Ländern in die Studie aufgenommen. Die wichtigsten Aufnahmekriterien waren ein Score auf der NIH-Schlaganfall-Skala (NIHSS) von ≥ 8, Vorstellung innerhalb von 8 Stunden nach Einsetzen der Symptome sowie eine Okklusion (TIMI 0 oder 1) eines für die Behandlung zugänglichen Gefäßes. Bei Vorstellung des Patienten innerhalb von 3 Stunden nach Einsetzen der Symptome waren Untauglichkeit für die rt-PA-Therapie bzw. deren Unwirksamkeit vorgeschrieben. Die primären Endpunkte waren die Revaskularisierung des Zielgefäßes (TIMI 2 oder 3) und die Inzidenz von schwerwiegenden unerwünschten Ereignissen (SUE) während des Eingriffs. Alle Patienten wurden nach dem Eingriff bis zu 90 Tage lang betreut und beurteilt.

Statistische Analyse

Für diese Studie wurde eine Stichprobengröße von 125 festgelegt, um mindestens 115 beurteilungsfähige Patienten zu erhalten. Dabei galt ein Patient als beurteilungsfähig, wenn er die Eignungsvoraussetzungen für die Beurteilung

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der primären Endpunkte erfüllte und mit dem Penumbra System behandelt wurde. Da es sich hier um eine nicht kontrollierte Studie handelte, war keine formelle Prüfung der Hypothese zur Gesamt-Ansprechensrate beim Erreichen des TIMI-Grades 2 oder 3 vorgesehen. Die üblichen deskriptiven Statistiken für die Kategorie-Endpunkte waren Anzahl und Prozentsatz der Patienten auf jeder Stufe des Endpunktes. Bei numerischen Endpunkten waren die üblichen deskriptiven Statistiken die Anzahl der nicht fehlenden Beobachtungen (n), der Mittelwert, der Medianwert, die Standardabweichung, das Minimum und das Maximum.

Studieneingriffe
Der arterielle Zugang zum Zielgefäß erfolgte mittels herkömmlicher perkutaner Techniken; die Angio-Architektur des okkludierten Gefäßsegments wurde dabei mittels digitaler Subtraktionsangiographie an vier Gefäßen definiert. Für jeden Patienten war der angiographische Nachweis der Okklusion eines großen Hirngefäßes und die A-priori-Festlegung einer primären Okklusionsstelle durch den Prüfarzt vorgeschrieben. Bei Okklusion in einem für die Behandlung zugänglichen Gefäß wurde ein geeigneter Führungskatheter platziert und der Penumbra Reperfusionskatheter an das proximale Ende des okkludierten Zielgefäßes vorgeschoben. Patienten galten als in die Studie aufgenommen, sobald der Reperfusionskatheter aus dem Führungskatheter vorgeschoben wurde.

Wichtigste Einschlusskriterien
- Mit einem akuten ischämischen Schlaganfall vereinbare klinische Zeichen, darunter:
  - Plötzliches Auftreten von Taubheit oder Schwächegefühl im Gesicht oder in den Extremitäten
  - Plötzliches Auftreten von Verwirrung, Sprachstörung oder Störung des Sprachverständnisses
  - Plötzliches Auftreten von Gehstörung, Schwindel oder Gleichgewichtsstörung
- Alter zwischen 18 und 79 Jahren
- Neurologische Störung mit einem Score auf der NIH-Schlaganfall-Skala (NIHSS) von ≥ 8
- Vollständiger Verschluss (TIMI-Grad 0) oder Kontrastmittelpenetration mit minimaler Perfusion, jedoch ohne Füllung der distalen Äste (TIMI-Grad 1) in den intrakraniellen Gefäßen, die dem Penumbra Stroke System zugänglich sind
- Unterschriebene Einwilligungserklärung nach Aufklärung
- Vorstellung innerhalb von 8 Stunden nach Einsetzen der Schlaganfallsymptome
- Untauglichkeit für die intravenöse rt-PA-Therapie bzw. deren Unwirksamkeit bei Vorstellung innerhalb von 3 Stunden nach Einsetzen der Symptome

Wichtigste Ausschlusskriterien
- Nachweis über sich rasch bessernde neurologische Schlaganfallzeichen zum Zeitpunkt der Aufnahme in die Studie
- NIHSS > 30 oder Koma
- Schwangerschaft
- Für den endovaskulären Zugang zu stark verschlungene Gefäße
- Bekannte hämorrhagische Diathese oder Blutungsneigung oder orale Antikoagulanzientherapie bei einem INR > 3,0
- PTT mehr als doppelt so hoch wie der normale Laborwert
- Thrombozyten bei Aufnahme < 30.000
- Vorbestehende neurologische oder psychiatrische Erkrankung, die die Studienergebnisse verfälschen könnte
- Bekannte schwere Allergie auf Kontrastmittel
- Schlecht eingestellte Hypertonie (definiert als systolischer Blutdruck > 185 mmHg bzw. diastolischer Blutdruck > 110 mmHg)
- CT-Nachweis folgender Erkrankungen bei Vorstellung:
  - Signifikanter Masseneffekt mit Mittellinienverschiebung
  - Große hypodense Region mit einer Ausdehnung von > 1/3 des ACM-Stromgebiets
  - Nachweis einer intrakraniellen Hämorrhagie
- Angiografischer Nachweis einer Arterienstenose proximal des Verschlusses, die eine Thrombusentfernung verhindern könnte
- Angiografischer Nachweis einer vorbestehenden Arterienverletzung
- Lebenserwartung unter 90 Tagen
- Teilnahme an einer anderen klinischen Untersuchung, die die Auswertung der Studie verfälschen könnte

Zusammenfassung der Gründe für einen Ausschluss bereits aufgenommener Patienten, insbesondere aufgrund angiographischer Kriterien
Es wurden keine bereits aufgenommenen Patienten aufgrund angiographischer Befunde ausgeschlossen.

Primärer Wirksamkeitsendpunkt
Der primäre Wirksamkeitsendpunkt war die Revaskularisierung des verschlossenen Zielgefäßes. Revaskularisierung war definiert als TIMI-Score II oder III im Anschluss an den Einsatz ausschließlich des Penumbra Systems, vor dem Einsatz etwaiger weiterer bzw. unterstützender Produkte oder Therapien. Die angiographischen Ergebnisse wurden von einem unabhängigen Zentrallabor beurteilt.

Wirksamkeit	% (n/N) [95%-KI]†
Primärer Wirksamkeitsendpunkt (TIMI-Score II oder III) *TIMI-Scores vor dem Einsatz unterstützender Therapien*	81,6 % (102/125) [73,7 %, 88,0 %]
Revaskularisierungserfolg nach dem Produkteinsatz (TIMI ≥ 2) *Jeglicher Einsatz unterstützender Therapien galt als Fehlschlag der Behandlung*	81,6 % (102/125) [73,7 %, 88,0 %]
Revaskularisierungserfolg nach dem Produkteinsatz (TIMI ≥ 2) *Jeglicher Einsatz von i.a. Lytika galt als Fehlschlag der Behandlung*	81,6 % (102/125) [73,7 %, 88,0 %]

†Exakte Konfidenzintervalle nach Clopper-Pearson

Primärer Sicherheitsendpunkt
Der primäre Sicherheitsendpunkt war die Inzidenz von produkt- und/oder eingriffsbedingten schwerwiegenden unerwünschten Ereignissen, die nach Angaben des Prüfarztes während des Eingriffs auftraten. Den Prüfärzten zufolge kam es zu 18 Ereignissen während des Eingriffs bei 16 Patienten (12,8 %). Von diesen wurden 4 Ereignisse bei 3 Patienten (2,4 %) von der CEC als schwerwiegend eingestuft.

Zusammengesetzte unerwünschte Ereignisse während des Eingriffs	% (n/N) [95%-KI]†
Zusammengesetzte SUE während des Eingriffs	2,4 % (3/125)
Primärer Sicherheitsendpunkt: Zusammengesetzte eingriffs-/produktbedingte SUE während des Eingriffs	2,4 % (3/125)

†Exakte Konfidenzintervalle nach Clopper-Pearson

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Alle einzelnen SUE bis einschließlich 90 Tage, die bei mehr als 2 % der Patienten auftraten

SUE	% (n/N)
Zusammengesetzte SUE	52,0 % (65/125)
Hirnödem	11,2 % (14/125)
ICB	8,0 % (10/125)
Atemdysfunktion/-insuffizienz	8,0 % (10/125)
Sich verschlechternde Symptome des zur Aufnahme führenden Schlaganfalls	7,2 % (9/125)
Infektion	5,6 % (7/125)
Sonstige Lungenkompl kationen	5,6 % (7/125)
Pneumonie	4,0 % (5/125)
Herzrhythmusstörungen	3,2 % (4/125)
Komplikationen an der Zugangsstelle	2,4 % (3/125)
Myokardinfarkt	2,4 % (3/125)
Periphere Gefäßkomplikation	2,4 % (3/125)
Nierendysfunktion/-insuffizienz	2,4 % (3/125)
Schlaganfall in einem neuen Bereich	2,4 % (3/125)

Einstufung der UE bis einschließlich 90 Tage nach anatomischen Systemen

Anatomisches System	% (n/N)
Störungen des Nervensystems	62,4 % (78/125)
Infektionen und Besiedlungen	44,0 % (55/125)
Herzstörungen	28,8 % (36/125)
Störungen von Stoffwechsel und Nahrungsaufnahme	25,6 % (32/125)
Allgemeine Störungen und Beschwerden an der Verabreichungsstelle	24,8 % (31/125)
Atem-, Brust- und Mediastinumstörungen	24,8 % (31/125)
Verletzungen, Vergiftungen und Komplikationen während des Eingriffs	18,4 % (23/125)
Magen-Darm-Störungen	16,0 % (20/125)
Störungen des Blut- und Lymphsystems	14,4 % (18/125)
Gefäßstörungen	11,2 % (14/125)
Psychiatrische Störungen	10,4 % (13/125)
Störungen des Nieren- und Harnsystems	8,0 % (10/125)
Leber-Gallen-Störungen	4,0 % (5/125)
Explorationen	3,2 % (4/125)
Störungen von Haut und Subkutangewebe	3,2 % (4/125)
Neoplasien (benigne, maligne und nicht abgeklärte, inkl. Zysten und Polypen)	2,4 % (3/125)
Störungen von Muskel-Skelett-Apparat und Bindegewebe	0,8 % (1/125)

Erläuterung der Symbole

	Achtung! Siehe Gebrauchsanweisung		
Rx Only	Verschre bungspflichtig – Laut Bundesgesetz der USA darf dieses Produkt ausschließlich von einem Arzt oder auf Anordnung eines Arztes verwendet werden		
	Nicht pyrogen		
STERILE EO	Steril (Ethylenoxid)		
	Hersteller	EC REP	Bevollmächtigter in der EU
LOT	Chargennummer		Nicht wiederverwenden
	Zu verwenden bis	REF	Katalognummer
STERILIZE	Nicht resterilisieren	LATEX	Latexfrei

Gewährleistung

Penumbra, Inc. (Penumbra) sichert zu, dass bei der Konstruktion und Herstellung dieses Produkts angemessene Sorgfalt angewendet wurde. Diese Gewährleistung gilt anstelle jeglicher hier nicht ausdrücklich erwähnter Garantien und ersetzt diese, seien sie ausdrücklicher oder stillschweigender Art, durch Anwendung von Gesetzen oder anderweitig begründet, darunter insbesondere jegliche stillschweigende Garan ie der Handelstauglichkeit oder Eignung für einen bestimmten Zweck. Der Umgang mit diesem Produkt und seine Aufbewahrung, Reinigung, Sterilisation sowie andere Faktoren in Zusammenhang mit dem Patienten, der Diagnose, der Behandlung, den chirurgischen Eingriffen und anderen Umständen außerhalb der Kontrolle von Penumbra haben einen direkten Einfluss auf das Produkt und die bei seiner Anwendung erzielten Ergebnisse. Die Haftung von Penumbra im Rahmen dieser Gewährleistung beschränkt sich auf die Reparatur oder den Ersatz dieses Produkts. Penumbra ist nicht haftbar für Begleit- oder Folgeschäden, Verluste oder Kosten, die sich unmittelbar oder mittelbar aus der Anwendung dieses Produkts ergeben. Penumbra übernimmt keinerlei weitere oder zusätzliche Haftung oder Verantwortung in Zusammenhang mit diesem Produkt und erteilt auch keinen anderen Personen die Befugnis zu einer derartigen Übernahme. Penumbra übernimmt keinerlei Haftung für wiederverwendete, wiederaufbereitete oder resterilisierte Produkte und gibt keine Garantie ausdrücklicher oder stillschweigender Art, insbesondere zur Handelstauglichkeit oder Eignung für einen bestimmten Zweck, für derartige Produkte.

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Italiano

Descrizione del dispositivo

Il sistema Penumbra System® comprende diversi componenti:

- Catetere di riperfusione Penumbra
- Pompa di aspirazione Penumbra
- Tubo contenitore/pompa Penumbra
- Tubo di aspirazione Penumbra
- Separatore Penumbra

Il sistema Penumbra System è previsto per la rimozione di trombi dal sistema vascolare tramite aspirazione continua. Il catetere di riperfusione dirige direttamente verso il trombo la forza di aspirazione proveniente dalla pompa. Il separatore può essere usato per liberare il lume del catetere di riperfusione, qualora quest'ultimo fosse ostruito dal trombo. Quando si utilizza un catetere di riperfusione con diametro interno pari o superiore a 1,37 mm (0,054 pollici), è possibile che il separatore non sia necessario. Il catetere di riperfusione viene introdotto in un catetere guida o una guaina femorale lunga e all'interno dei vasi intracranici e, tramite una guida neurovascolare, viene condotto fino al sito dell'occlusione primaria. Il catetere di riperfusione Penumbra viene utilizzato assieme alla pompa di aspirazione per aspirare trombi da un vaso occluso. Se necessario, per favorire la rimozione del trombo è possibile fare avanzare un separatore Penumbra dal catetere di riperfusione. Il separatore Penumbra viene fatto avanzare e retratto attraverso il catetere di riperfusione Penumbra, in corrispondenza del margine prossimale dell'occlusione primaria, allo scopo di agevolare il distacco del trombo dalla punta del catetere di riperfusione. Per quanto riguarda la fonte di aspirazione, il catetere di riperfusione Penumbra viene usato insieme alla pompa di aspirazione, la quale è collegata tramite il tubo di aspirazione Penumbra e il tubo contenitore/pompa Penumbra. Il catetere di riperfusione Penumbra è dotato di un mandrino di sagomatura a vapore, una valvola emostatica rotante e una guaina distaccabile. Il separatore Penumbra è dotato di un introduttore e di un dispositivo di torsione. I dispositivi sono visibili in fluoroscopia.

Indicazioni per l'uso

Il sistema Penumbra System è indicato per la rivascolarizzazione di pazienti affetti da ictus ischemico acuto, secondario a malattia occlusiva dei grandi vasi intracranici (arterie carotide interna, cerebrale media – segmenti M1 e M2, basilare e vertebrale), entro 8 ore dall'insorgenza dei sintomi.

Controindicazioni

Non esiste alcuna controindicazione nota.

Avvertenze

- Il sistema Penumbra System deve essere utilizzato esclusivamente da medici specializzati in tecniche interventistiche neuro-endovascolari e nel trattamento dell'ictus ischemico acuto.
- Qualora si riscontri resistenza, non fare avanzare, retrarre o usare alcun componente del sistema Penumbra System senza aver prima determinato la causa di tale resistenza tramite fluoroscopia. Se non è possibile determinare la causa, rimuovere il dispositivo o il sistema come unità. Una torsione eccessiva o l'introduzione forzata del catetere o del separatore contro una resistenza possono danneggiare il dispositivo o il vaso.
- Usare il sistema Penumbra System esclusivamente con la pompa di aspirazione Penumbra.

Precauzioni

- Il dispositivo è esclusivamente monouso. Non risterilizzare né riutilizzare. La risterilizzazione e/o il riutilizzo possono rendere inefficace la lubrificazione del rivestimento del catetere, con conseguente aumento dell'attrito e impossibilità di raggiungere la posizione desiderata nel sistema neurovascolare.
- Non utilizzare dispositivi deformati o danneggiati. Non usare confezioni aperte o danneggiate. Restituire al fabbricante/distributore tutti i dispositivi danneggiati e le relative confezioni.
- Usare prima della data di scadenza ("Usare entro").
- Il sistema Penumbra System va usato sotto visualizzazione fluoroscopica.
- Durante l'aspirazione, controllare che la valvola del tubo di aspirazione Penumbra rimanga aperta solo per il tempo minimo necessario per la rimozione del trombo. L'aspirazione eccessiva o la mancata chiusura della valvola del tubo di aspirazione Penumbra al termine dell'aspirazione sono condizioni non raccomandabili.
- Il separatore Penumbra è controindicato per l'uso come guida neurovascolare. Se durante la procedura di rivascolarizzazione fosse necessario riposizionare il catetere di riperfusione Penumbra, eseguire il riposizionamento usando una guida neurovascolare adeguata, con tecniche standard che prevedano l'uso di una guida e di un microcatetere.
- Con il catetere di riperfusione Penumbra, non usare attrezzature automatiche per l'iniezione di mezzo di contrasto ad alta pressione, in quanto potrebbero danneggiare il dispositivo.
- La somministrazione di anticoagulanti e antipiastrinici deve essere sospesa fino a 24 ore dopo l'intervento. La gestione medica e la cura successive all'ictus acuto devono essere conformi alle linee guida dell'ASA.[1] Qualsiasi deterioramento neurologico deve essere valutato tramite una TAC d'urgenza e altre metodiche, in accordo con le migliori pratiche del ricercatore/ospedaliere.
- Il tempo totale concesso per ottenere la rivascolarizzazione del paziente è di 120 minuti con il sistema Penumbra System.

Possibili eventi avversi

Tra le possibili complicanze vi sono:

- danni renali causati dal mezzo di contrasto
- decesso
- deficit neurologici, incluso ictus
- ematoma o emorragia presso il sito di accesso
- emboli
- embolia gassosa
- embolizzazione distale
- emorragia intracranica
- fistola artero-venosa
- formazione di pseudoaneurismi
- impossibilità di rimozione completa del trombo
- infezione
- ischemia
- malfunzionamento del dispositivo
- occlusione acuta
- reazione allergica e anafilassi causate dal mezzo di contrasto
- vasopasmo, trombosi, dissezione o perforazione del vaso

Procedura

1. Prima dell'uso, fare riferimento alle sezioni **Avvertenze, Precauzioni** e **Possibili eventi avversi**.
2. Prima dell'uso di ciascun dispositivo del sistema Penumbra System, estrarli dalla confezione e controllare che non presentino danni o deformazioni.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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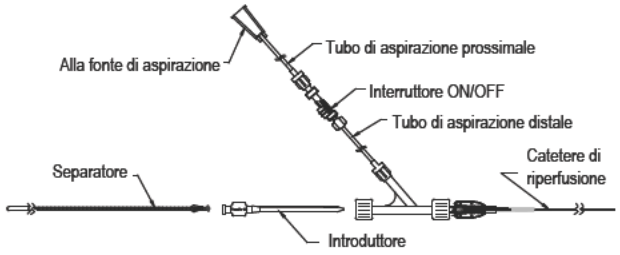
3. Preparare per l'uso i dispositivi del sistema Penumbra System, irrigando con soluzione fisiologica eparinizzata la spirale di confezionamento e il dispositivo (inclusi solo il catetere di riperfusione Penumbra e il separatore Penumbra).
4. Preparare un catetere guida o una guaina femorale lunga in base alle *Istruzioni per l'uso* del produttore.
5. Introdurre il catetere guida o la guaina femorale lunga nell'arteria cerebrale appropriata, prossimale al sito dell'occlusione trombotica.

Preparazione e uso del catetere di riperfusione Penumbra

1. Confermare il diametro del vaso e selezionare un catetere di riperfusione Penumbra di dimensioni adeguate (**Tabella 1**).
2. La punta del catetere di riperfusione Penumbra può essere modellata usando il mandrino di sagomatura a vapore fornito in dotazione.
3. Collegare la valvola emostatica rotante in dotazione al catetere di riperfusione Penumbra.
4. Collegare il tubo di aspirazione Penumbra alla pompa di aspirazione e accendere la pompa (fare riferimento al *Manuale d'uso* della pompa di aspirazione). Lasciare funzionare la pompa per almeno un minuto prima dell'uso, quindi controllare che la lettura dell'indicatore di aspirazione corrisponda a −508 mmHg (−20 pollHg). Controllare che la valvola sul tubo di aspirazione Penumbra si trovi nella posizione OFF (spento).
5. Collegare il tubo di aspirazione all'attacco laterale della valvola emostatica rotante, come illustrato nella **Figura 1**.

Figura 1 – Sistema di aspirazione montato con il separatore Penumbra



6. Introdurre il catetere di riperfusione Penumbra nella valvola emostatica rotante collegata al raccordo prossimale di un catetere guida. Qualora non si utilizzi un catetere guida, inserire il catetere di riperfusione Penumbra attraverso la valvola della guaina femorale lunga, utilizzando la guaina distaccabile. Dopo aver inserito il catetere di riperfusione Penumbra, rimuovere la guaina distaccabile dalla guaina vascolare e distaccarla dallo stelo del catetere di riperfusione Penumbra.
7. Facendo uso delle tecniche convenzionali di cateterismo in fluoroscopia, fare avanzare il catetere di riperfusione Penumbra nel vaso target lungo una guida neurovascolare adeguata. Posizionare il catetere di riperfusione Penumbra in posizione prossimale rispetto al trombo. Rimuovere la guida dal catetere di riperfusione Penumbra.
8. Per avviare l'aspirazione, aprire la valvola sul tubo di aspirazione Penumbra collocandola nella posizione ON (acceso). Per interrompere l'aspirazione, portare la valvola sul tubo di aspirazione Penumbra sulla posizione OFF (spento) e spegnere la pompa di aspirazione.
9. Con una siringa da 5 ml o da 10 ml, aspirare circa 5 ml di sangue dal catetere di riperfusione Penumbra in modo da eliminare eventuali residui trombotici dal catetere.
10. Ottenere un angiogramma post-trattamento iniettando mezzo di contrasto attraverso il catetere guida.

Preparazione e uso del separatore Penumbra

1. Se necessario, scegliere un separatore Penumbra di dimensioni adeguate corrispondente al catetere di riperfusione (**Tabella 1**).

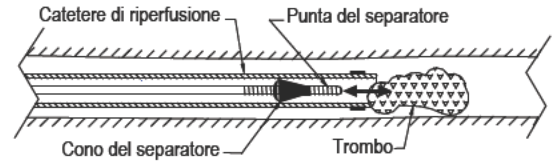
Tabella 1 – Scelta delle dimensioni del catetere di riperfusione/separatore

Dimensioni vaso (mm)	Catetere di riperfusione Penumbra	Separatore Penumbra
< 2,0	026	026
da 2,0 a 3,0	032 / 3MAX	032 / 3MAX
da 3,0 a 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

NOTA: per agevolare l'accesso al sito dell'occlusione è possibile servirsi di un microcatetere interno compatibile con sistema triassiale.

2. Usando la guaina di introduzione fornita in dotazione, inserire il separatore Penumbra nella valvola emostatica rotante e nel raccordo prossimale del catetere di riperfusione Penumbra.
3. Per avviare l'aspirazione, aprire la valvola sul tubo di aspirazione Penumbra sulla posizione ON (acceso), e fare avanzare/retrarre il separatore Penumbra per favorire l'aspirazione e la rimozione del trombo dal catetere di riperfusione, come illustrato nella **Figura 2**.

Figura 2 – Aspirazione del trombo tramite il separatore Penumbra



4. Per interrompere l'aspirazione, portare la valvola sul tubo di aspirazione Penumbra sulla posizione OFF (spento) e spegnere la pompa di aspirazione.
5. Rimuovere il separatore Penumbra, se utilizzato.
6. Se necessario, a discrezione del medico è possibile usare separatori e cateteri di riperfusione Penumbra aggiuntivi per l'ulteriore rimozione di materiale trombotico.

Riepilogo dei dati clinici

Lo studio clinico registrativo Penumbra è uno studio prospettico a braccio singolo, che è stato eseguito per determinare la sicurezza e l'efficacia del sistema Penumbra System. Sono stati arruolati 125 pazienti presso 24 centri internazionali. I principali criteri di arruolamento erano un punteggio sulla scala dell'ictus del National Institutes of Health (NIHSS) ≥ 8, la presentazione del paziente entro 8 ore dall'insorgenza dei sintomi e un'occlusione (TIMI 0 o 1) di un vaso intracranico trattabile. I pazienti che si presentavano entro 3 ore dall'insorgenza dei sintomi dovevano essere non idonei o refrattari alla terapia con rt-PA. Gli endpoint primari erano la rivascolarizzazione del vaso target (TIMI 2 e 3) e l'incidenza di eventi avversi gravi (SAE) di natura procedurale. Tutti i pazienti sono stati seguiti e valutati fino a 90 giorni dopo la procedura.

Analisi statistica

Per questo studio è stata selezionata una dimensione del campione di 125 soggetti, allo scopo di generare almeno 115 pazienti valutabili. Un paziente veniva considerato valutabile qualora soddisfacesse i requisiti di ammissibilità per la valutazione dell'endpoint primario e fosse stato trattato con il sistema

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Penumbra System. Poiché si trattava di uno studio non controllato, non era previsto un test di ipotesi formale per l'indice di risposta globale per la determinazione di un grado TIMI 2 o 3. Le statistiche descrittive standard per gli endpoint categorici erano il numero e la percentuale di pazienti con ciascun livello dell'endpoint. Per quanto riguarda gli endpoint numerici, le statistiche descrittive standard includevano il numero di osservazioni esistenti (n), la media, la mediana, la deviazione standard, il valore minimo e il valore massimo.

Procedure dello studio
L'accesso arterioso al vaso target è stato ottenuto utilizzando la tecnica percutanea standard ed è stata eseguita un'angiografia digitale sottrattiva a quattro vasi per definire l'angio-architettura del segmento vascolare occluso. Ciascun paziente doveva avere un'occlusione di un vaso cerebrale maggiore, confermata da angiografia, e un sito di occlusione primaria designato a priori dal ricercatore. Se l'occlusione si trovava in un vaso trattabile, veniva posizionato un catetere guida adeguato e il catetere di riperfusione Penumbra veniva fatto avanzare fino all'estremità prossimale del vaso target occluso. Un paziente veniva considerato arruolato al momento del posizionamento del catetere di riperfusione dal catetere guida.

Criteri chiave di inclusione nello studio
- Segni clinici compatibili con l'ictus ischemico acuto, compresi i seguenti:
  - improvviso intorpidimento o debolezza del viso o delle estremità
  - improvvisa confusione, difficoltà di parola o di comprensione del parlato
  - improvvisi problemi di deambulazione, vertigini o perdita dell'equilibrio
- età compresa tra i 18 e i 79 anni
- deficit neurologico con conseguente punteggio sulla scala dell'ictus del National Institutes of Health (NIHSS) ≥ 8
- occlusione completa (grado TIMI 0) o penetrazione del mezzo di contrasto con perfusione minima ma senza riempimento del ramo distale (grado TIMI 1) in vasi intracranici accessibili con il sistema Penumbra System per ictus
- firma del modulo di consenso informato
- presentazione entro 8 ore dall'insorgenza dei sintomi di ictus
- non idoneità o refrattarietà alla terapia endovenosa con rt-PA, in caso di presentazione entro 3 ore dall'insorgenza dei sintomi

Criteri chiave di esclusione dallo studio
- evidenza di segni neurologici di ictus in rapido miglioramento al momento dell'arruolamento
- NIHSS > 30 o coma
- donne in gravidanza
- tortuosità vascolare troppo accentuata per permettere l'accesso endovascolare
- diatesi emorragica nota, deficit della coagulazione o terapia anticoagulante orale con INR > 3,0
- tempo di tromboplastina parziale superiore al doppio del valore normale di laboratorio
- piastrine al ricovero < 30.000
- patologie neurologiche o psichiatriche preesistenti capaci di confondere i risultati dello studio
- nota allergia grave al mezzo di contrasto
- ipertensione non controllata (definita come pressione sistolica > 185 mmHg o pressione diastolica > 110 mmHg)
- evidenza suffragata da TAC delle seguenti condizioni al momento della presentazione:
  - vistoso effetto massa con spostamento della linea mediana
  - ampia area di ipodensità > 1/3 della regione dell'arteria cerebrale media
  - evidenza di emorragia intracranica
- evidenza angiografica di stenosi arteriosa prossimale all'occlusione, capace di impedire la rimozione del trombo
- evidenza angiografica di una lesione arteriosa preesistente
- speranza di vita inferiore a 90 giorni
- partecipazione ad altre indagini cliniche capaci di confondere la valutazione del dispositivo oggetto di studio

Riepilogo delle cause di esclusione di soggetti arruolati, in particolare di quelle basate su criteri angiografici
Nessuno dei pazienti arruolati è stato escluso per cause angiografiche.

Endpoint primario di efficacia
L'endpoint primario di efficacia era la rivascolarizzazione del vaso target occluso. La rivascolarizzazione veniva definita da un punteggio TIMI 2 o 3 in seguito all'uso del solo sistema Penumbra System e prima dell'uso di qualsiasi altro dispositivo o terapia. I risultati angiografici sono stati sottoposti al giudizio di un laboratorio centrale indipendente.

Efficacia	% (n/N) [IC 95%]†
Endpoint primario di efficacia (punteggio TIMI 2 o 3) *Punteggi TIMI prima dell'uso di terapie aggiuntive*	81,6% (102/125) [73,7%, 88,0%]
Successo della rivascolarizzazione post-dispositivo (TIMI ≥ 2) *Impiego di qualsiasi terapia aggiuntiva considerato come fallimento del trattamento*	81,6% (102/125) [73,7%, 88,0%]
Successo della rivascolarizzazione post-dispositivo (TIMI ≥ 2) *Impiego di qualsiasi lisi IA considerato come fallimento del trattamento*	81,6% (102/125) [73,7%, 88,0%]

†Intervalli di confidenza esat i di Clopper-Pearson

Endpoint primario di sicurezza
L'endpoint primario di sicurezza era l'incidenza di eventi avversi gravi associati al dispositivo e/o alla procedura, verificatisi durante la procedura come segnalato dal ricercatore. Sono stati segnalati 18 eventi procedurali in 16 pazienti (12,8%). Di questi, 4 eventi in 3 pazienti sono stati definiti gravi dal CEC (2,4%).

Eventi avversi compositi durante la procedura	% (n/N) [IC 95%]†
SAE compositi durante la procedura	2,4% (3/125)
Endpoint primario di sicurezza: SAE composito associato alla procedura/al dispositivo durante la procedura	2,4% (3/125)

†Intervalli di confidenza esat i di Clopper-Pearson

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Singoli SAE specifici nel corso di 90 giorni verificatisi in più del 2% dei pazienti

SAE	% (n/N)
SAE compositi	52,0% (65/125)
Edema cerebrale	11,2% (14/125)
Emorragia intracerebrale	8,0% (10/125)
Disfunzione/insufficienza respiratoria	8,0% (10/125)
Peggioramento dei sintomi di ictus come evento qualificante	7,2% (9/125)
Infezione	5,6% (7/125)
Altre complicanze polmonari	5,6% (7/125)
Polmonite	4,0% (5/125)
Aritmia cardiaca	3,2% (4/125)
Complicanza nel sito di accesso	2,4% (3/125)
Infarto miocardico	2,4% (3/125)
Complicanza vascolare periferica	2,4% (3/125)
Disfunzione/insufficienza renale	2,4% (3/125)
Ictus in un'altra regione	2,4% (3/125)

Categorizzazione degli AE nei 90 giorni suddivisi per sistema anatomico

Sistema anatomico	% (n/N)
Disturbi del sistema nervoso	62,4% (78/125)
Infezioni e infestazioni	44,0% (55/125)
Disturbi cardiaci	28,8% (36/125)
Disturbi metabolici e alimentari	25,6% (32/125)
Disturbi generici e condizioni nel sito di somministrazione	24,8% (31/125)
Disturbi respiratori, toracici e mediastinici	24,8% (31/125)
Infortuni, avvelenamento e complicanze procedurali	18,4% (23/125)
Disturbi gastrointestinali	16,0% (20/125)
Disturbi del sistema circolatorio e linfatico	14,4% (18/125)
Disturbi vascolari	11,2% (14/125)
Disturbi psichiatrici	10,4% (13/125)
Disturbi renali e urinari	8,0% (10/125)
Disturbi epatobiliari	4,0% (5/125)
Indagini	3,2% (4/125)
Disturbi cutanei e dei tessuti sottocutanei	3,2% (4/125)
Neoplasie benigne, maligne e aspecifiche (comprese cisti e polipi)	2,4% (3/125)
Disturbi muscoloscheletrici e del tessuto connettivo	0,8% (1/125)

LEGENDA DEI SIMBOLI

	Attenzione, vedere le istruzioni per l'uso		
Rx Only	Solo su prescrizione – La legge federale degli Stati Uniti autorizza l'uso di questo prodotto esclusivamente su prescrizione medica		
	Apirogeno		
STERILE EO	Sterilizzato con ossido di etilene		
	Fabbricante	EC REP	Rappresentante nell'UE
LOT	Numero di lotto		Non riutilizzare
	Usare entro	REF	Numero di catalogo
STERILIZE	Non risterilizzare	LATEX	Non contiene lattice

GARANZIA

Penumbra, Inc. (Penumbra) garantisce che il presente dispositivo è stato progettato e fabbricato con cura ragionevole. Questa garanzia sostituisce ed esclude tutte le altre garanzie non espressamente citate in questa sede, sia esplicite che tacite in forza di legge o altro, incluse – senza limitazione – tutte le garanzie implicite di commerciabilità e idoneità a un uso particolare. La manipolazione, conservazione, pulizia e sterilizzazione di questo dispositivo, nonché altri fattori correlati al paziente, alla diagnosi, al trattamento, alle procedure chirurgiche e ad altri fattori che esulano dal controllo di Penumbra, influiscono direttamente sul dispositivo e sui risultati ottenuti dal suo uso. L'obbligo di Penumbra ai sensi della presente garanzia è limitato alla riparazione o sostituzione di questo dispositivo; Penumbra non potrà essere ritenuta responsabile di perdite, danni o costi incidentali o conseguenti, derivati direttamente o indirettamente dall'uso di questo dispositivo. Penumbra non si assume, né autorizza terzi ad assumersi per suo conto, alcuna ulteriore responsabilità connessa all'uso di questo dispositivo. Penumbra non si assume alcuna responsabilità in caso di riutilizzo, riprocessamento o risterilizzazione dei dispositivi e per tali dispositivi non concede alcuna garanzia, né esplicita né tacita, incluse – senza limitazione – le garanzie di commerciabilità e idoneità per l'uso previsto.

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Descripción del dispositivo

Penumbra System® está formado por varios dispositivos:

- Catéter de reperfusión de Penumbra
- Bomba de aspiración de Penumbra
- Tubo de contenedor/bomba de Penumbra
- Tubo de aspiración de Penumbra
- Separador de Penumbra

Penumbra System está diseñado para eliminar trombos de la vasculatura mediante una aspiración continua. El catéter de reperfusión dirige la aspiración desde la bomba directamente al trombo. El separador puede utilizarse para limpiar la luz del catéter de reperfusión en caso de que se bloquee con el trombo. Es posible que el uso del separador no sea necesario si se utiliza un catéter de reperfusión con un DI de 1,37 mm (0,054 in) o más. El catéter de reperfusión se introduce mediante un catéter guía o una vaina femoral larga dentro de la vasculatura intracraneal y se conduce a través de una guía neurovascular hasta el lugar de la oclusión primaria. El catéter de reperfusión de Penumbra se utiliza con la bomba de aspiración para aspirar trombos de un vaso obstruido. Según sea necesario, podrá desplegar un separador de Penumbra desde un catéter de reperfusión para ayudar con la eliminación de trombos. El separador de Penumbra se avanza y retrae a través del catéter de reperfusión de Penumbra en el margen proximal de la oclusión primaria para facilitar el despeje del trombo de la punta del catéter de Penumbra. En lo que se refiere a la fuente de aspiración, el catéter de perfusión de Penumbra se utiliza junto con la bomba de aspiración, que se conecta mediante el tubo de aspiración de Penumbra y el tubo de contenedor/bomba de Penumbra. El catéter de reperfusión de Penumbra se ofrece con un mandril de modelado al vapor y una válvula hemostática giratoria y una vaina extraíble. El separador de Penumbra se ofrece con un introductor y un dispositivo de torsión. Los dispositivos son visibles mediante radioscopia.

Indicaciones de uso

Penumbra System está diseñado para la revascularización de pacientes con un accidente cerebrovascular isquémico agudo secundario a una enfermedad oclusiva de los vasos grandes intracraneales (dentro de la carótida interna, los segmentos medios cerebrales, M1 y M2, y las arterias vertebrales y la basilar) en las 8 horas siguientes al inicio de los síntomas.

Contraindicaciones

No hay contraindicaciones conocidas.

Advertencias

- Penumbra System únicamente deberían utilizarlo médicos con formación adecuada en las técnicas de intervención neurovasculares y el tratamiento de accidentes cerebrovasculares isquémicos agudos.
- Si nota resistencia al hacer avanzar o retroceder, o utilizar cualquier componente de Penumbra System, no continúe sin antes evaluar detenidamente la causa mediante radioscopia. Si no puede determinar la causa, retire el dispositivo o el sistema como una unidad. Un giro sin restricción o una inserción forzada del catéter o del separador en contra de la resistencia podrían provocar daños en el dispositivo o en el vaso.
- No utilice Penumbra System con una bomba que no sea la bomba de aspiración Penumbra.

Precauciones

- El dispositivo está indicado para un solo uso. No lo reesterilice ni lo reutilice. La reesterilización y/o reutilización puede provocar una lubricación del recubrimiento del catéter ineficaz, lo que podría producir alta fricción y la incapacidad para acceder a la ubicación neurovascular objetivo.
- No utilice dispositivos acodados o dañados. No utilice paquetes abiertos o dañados. Devuelva todos los dispositivos y los paquetes dañados al fabricante o al distribuidor.
- Utilice el producto antes de la fecha de caducidad.
- Utilice Penumbra System junto con visualización radioscópica.
- Cuando realice la aspiración, asegúrese de que la válvula del tubo de aspiración de Penumbra esté abierto solo para el tiempo mínimo necesario para eliminar el trombo. No se recomienda una aspiración excesiva ni no cerrar la válvula del tubo de aspiración de Penumbra cuando la aspiración no haya concluido.
- El separador de Penumbra no está diseñado para usarse como una guía neurovascular. Si necesita recolocar el catéter de reperfusión de Penumbra durante el procedimiento de revascularización, dicha recolocación deberá realizarse sobre una guía neurovascular adecuada con un microcatéter y técnicas de guía estándar.
- No utilice un equipo automatizado de inyección de contraste a alta presión con el catéter de reperfusión de Penumbra, ya que esto podría dañar el dispositivo.
- La administración de anticoagulantes y antiagregantes plaquetarios deberá suspenderse hasta 24 después del tratamiento. El tratamiento médico y los cuidados intensivos posteriores al accidente cerebrovascular deberán seguir las directrices de la ASA.[1] Cualquier deterioro neurológico deberá evaluarse mediante una exploración de TC urgente y otras evaluaciones, según lo indicado por el investigador/prácticas recomendadas del hospital.
- El tiempo total permitido para conseguir la revascularización del paciente es de 120 minutos de uso de Penumbra System.

Posibles episodios adversos

Entre las posibles complicaciones se incluyen, entre otras, las siguientes:

- daños renales por el medio de contraste
- déficits neurológicos, incluido el accidente cerebrovascular
- embolia gaseosa
- embolización distal
- émbolos
- espasmo, trombosis, disección o perforación vasculares
- fístula arteriovenosa
- formación de aneurismas falsos
- funcionamiento incorrecto del dispositivo
- hematoma o hemorragia en el sitio de acceso
- hemorragia intracraneal
- incapacidad de eliminar completamente el trombo
- infección
- isquemia
- muerte
- oclusión aguda
- reacción alérgica y anafilaxis producidas por los medios de contraste

Procedimiento

1. Consulte las **advertencias, precauciones** y **posibles episodios adversos** antes de usar el producto.
2. A medida que utilice cada dispositivo de Penumbra System, extráigalo del paquete e inspecciónelo en busca de daños o acodamientos.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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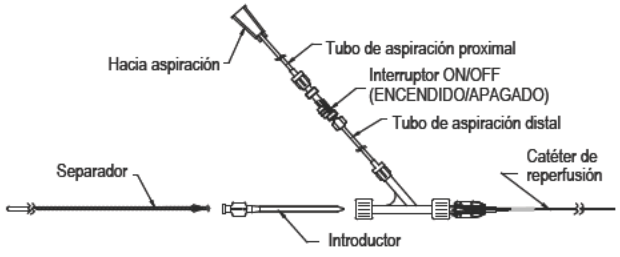
3. Prepare los dispositivos Penumbra System para su uso lavando el aro de embalaje y el dispositivo con solución salina heparinizada (solo incluye el catéter de reperfusión de Penumbra y el separador de Penumbra).
4. Prepare un catéter guía o una vaina femoral larga de acuerdo con las *instrucciones de uso* del fabricante.
5. Coloque el catéter guía o la vaina femoral larga en la arteria cerebral adecuada proximal al sitio de oclusión del trombo.

Preparación y uso del catéter de reperfusión de Penumbra

1. Confirme el diámetro del vaso y seleccione un catéter de reperfusión de Penumbra del tamaño adecuado (consulte la **tabla 1**).
2. Se puede dar forma a la punta del catéter de reperfusión de Penumbra con el mandril de modelado al vapor suministrado.
3. Acople la válvula hemostática giratoria proporcionada al catéter de reperfusión de Penumbra.
4. Conecte el tubo de aspiración de Penumbra a la bomba de aspiración y actívela (consulte el *Manual de funcionamiento* de la bomba de aspiración). Haga funcionar la bomba de aspiración durante al menos un minuto antes de utilizarla y confirme que el indicador de aspiración se encuentre en −508 mm Hg (−20 in Hg). Asegúrese de que la válvula del tubo de aspiración de Penumbra esté en la posición OFF (APAGADO).
5. Conecte el tubo de aspiración al orificio lateral de la válvula hemostática giratoria, como se muestra en la **figura 1**.

Figura 1. Sistema de aspiración ensamblado con separador de Penumbra



6. Inserte el catéter de reperfusión de Penumbra en una válvula hemostática giratoria conectada al conector proximal de un catéter guía. Si no se utiliza un catéter guía, inserte el catéter de reperfusión de Penumbra a través de la válvula de la vaina femoral larga con una vaina extraíble. Después de insertar el catéter de reperfusión de Penumbra, saque la vaina extraíble de la vaina vascular y retírela del eje del catéter de reperfusión de Penumbra.
7. Con las técnicas de cateterización convencionales mediante orientación radioscópica, avance el catéter de reperfusión de Penumbra hacia el interior del vaso objetivo sobre una guía neurovascular adecuada. Coloque el catéter de reperfusión de Penumbra proximal con respecto al trombo. Retire la guía del catéter de reperfusión de Penumbra.
8. Para iniciar la aspiración, abra la válvula del tubo de aspiración de Penumbra en la posición ON (ENCENDIDO). Para detener la aspiración, lleve la válvula del tubo de aspiración de Penumbra a la posición OFF (APAGADO) y, a continuación, apague la bomba de aspiración.
9. Con ayuda de una jeringa de 5 o 10 ml, aspire aproximadamente 5 ml de sangre del catéter de reperfusión de Penumbra para extraer cualquier trombo que pudiera quedar en el catéter.
10. Obtenga un angiograma posterior al tratamiento inyectando medio de contraste a través del catéter guía.

Preparación y uso del separador de Penumbra

1. En caso necesario, seleccione un separador de Penumbra del tamaño adecuado correspondiente al catéter de reperfusión (consulte la **tabla 1**).

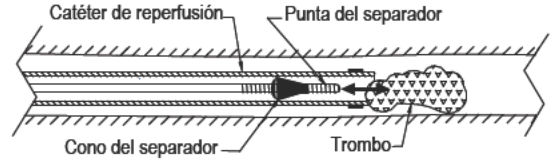
Tabla 1. Selección del tamaño del dispositivo separador/catéter de reperfusión

Tamaño del vaso (mm)	Catéter de reperfusión de Penumbra	Separador de Penumbra
< 2,0	026	026
2,0-3,0	032 / 3MAX	032 / 3MAX
3,0-4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

NOTA: Es posible facilitar el acceso al sitio de la oclusión mediante el uso triaxial de un microcatéter interno compatible.

2. Mediante la vaina introductora proporcionada, inserte el separador de Penumbra a través de la válvula hemostática giratoria y hacia el interior del conector proximal del catéter de reperfusión de Penumbra.
3. Para comenzar la aspiración, lleve la válvula del tubo de aspiración de Penumbra a la posición ON (ENCENDIDO) y avance/retraiga el separador de Penumbra para facilitar la aspiración y la extracción del trombo del catéter de reperfusión, como se muestra en la **figura 2**.

Figura 2. Aspiración del trombo mediante el separador de Penumbra



4. Para detener la aspiración, lleve la válvula del tubo de aspiración de Penumbra a la posición OFF (APAGADO) y, a continuación, apague la bomba de aspiración.
5. Extraiga el separador de Penumbra, si se usa.
6. Si resulta necesario, y a criterio del médico, es posible usar separadores y catéteres de reperfusión de Penumbra adicionales para seguir extrayendo trombos.

Resumen de datos clínicos

El ensayo esencial de Penumbra fue un estudio prospectivo, de un solo grupo para evaluar la seguridad y la eficacia de Penumbra System. Se inscribieron un total de 125 pacientes en 24 centros internacionales. Los principales criterios de entrada fueron una puntuación en la escala de accidentes cerebrovasculares del instituto estadounidense de salud (NIHSS) ≥ 8, la presentación en las 8 horas posteriores al inicio de los síntomas y una oclusión (TIMI 0 o 1) de un vaso intracraneal tratable. Los pacientes que se presentaron en las 3 horas posteriores al inicio de los síntomas deberán haber resultado no aptos o refractarios para el tratamiento con rtPA. Los criterios principales de valoración fueron la revascularización del vaso objetivo (TIMI 2 o 3) y la incidencia de episodios adversos graves (EAG) procedimentales. Se realizó un seguimiento de todos los pacientes y se les evaluó hasta 90 días después del procedimiento.

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Análisis estadístico
Se seleccionó un tamaño de muestra de 125 para este estudio con el fin de generar un mínimo de 115 pacientes evaluables. Se consideró que un paciente era evaluable si este cumplía los requisitos de elegibilidad para el criterio principal de valoración y se le había tratado con Penumbra System. Este fue un estudio sin control, de modo que no se planificó una prueba de hipótesis normal para la tasa de respuesta general con el fin de establecer una categoría de TIMI de 2 o 3. Las estadísticas descriptivas estándar para los criterios categóricos de valoración fueron el número y el porcentaje de pacientes con cada nivel del criterio de valoración. En el caso de los criterios numéricos de valoración, las estadísticas descriptivas estándar incluyeron el número de observaciones no ausentes (n), la media, la mediana, la desviación estándar, el valor mínimo y el valor máximo.

Procedimientos del estudio
El acceso arterial al vaso objetivo se logró con una técnica percutánea estándar y se realizó una angiografía de sustracción digital de cuatro vasos para definir una angioarquitectura del segmento vascular ocluido. Todos los pacientes debían sufrir una oclusión de un vaso cerebral grande confirmada mediante angiografía y presentar un sitio de oclusión principal designado «a priori» por el investigador. Si la oclusión era en un vaso tratable, se colocó un catéter guía adecuado y el catéter de reperfusión de Penumbra se avanzó hasta el extremo proximal del vaso objetivo ocluido. Los pacientes se consideraron inscritos una vez desplegado el catéter de reperfusión desde el catéter guía.

Criterios clave de inclusión
- Signos clínicos coherentes con un accidente cerebrovascular isquémico agudo, incluidos:
  - Insensibilidad o debilidad repentina en la cara o las extremidades
  - Confusión repentina, problemas para hablar o para comprender el habla
  - Problemas repentinos para caminar, mareos o pérdida del equilibrio
- De 18 a 79 años
- Déficit neurológico con una puntuación en la escala NIHSS ≥ 8
- Oclusión completa (categoría de TIMI 0) o penetración del contraste con una perfusión mínima pero sin relleno de la rama distal (categoría de TIMI I) en los vasos intracraneales accesibles al dispositivo Penumbra System para accidentes cerebrovasculares
- Consentimiento informado firmado
- Presente en las 8 horas posteriores al inicio de los síntomas del accidente cerebrovascular
- No apto o refractario al tratamiento con rtPA intravenoso si se presenta en las 3 horas posteriores al inicio de los síntomas

Criterios clave de exclusión
- Pruebas de señales neurológicas de accidente cerebrovascular que mejoran rápidamente en el momento de la inscripción
- NIHSS > 30 o coma
- Mujeres embarazadas
- Tortuosidad de los vasos demasiado complicada como para permitir el acceso endovascular
- Diátesis hemorrágica conocida, deficiencia en la coagulación o tratamiento oral con anticoagulantes con una RNI > 3,0
- TTP mayor que el doble del valor normal en laboratorio
- Plaquetas en el momento del ingreso < 30 000
- Enfermedad neurológica o psiquiátrica preexistente que podría confundir los resultados del estudio
- Alergia grave conocida al medio de contraste
- Hipertensión no controlada (definida como una presión sanguínea sistólica > 185 mm Hg o presión sanguínea diastólica > 110 mm Hg)
- Pruebas de TC de las afecciones siguientes en el momento de la presentación:
  - Efecto de masa significativo con desviación de la línea media
  - Región con hipodensidad grande > 1/3 del territorio arterial medio del cerebro
  - Pruebas de hemorragia intracraneal
- Pruebas angiográficas de estenosis arterial proximal a la oclusión que podría impedir la extracción del trombo
- Pruebas angiográficas de lesiones arteriales preexistentes
- Esperanza de vida de menos de 90 días
- Participación en otra investigación clínica que podría confundir la evaluación del dispositivo del estudio

Resumen de motivos de exclusión de sujetos inscritos, especialmente de aquellos basados en criterios angiográficos
No se excluyó a ningún paciente inscrito por motivos angiográficos.

Criterio principal de valoración de eficacia
El criterio principal de valoración de eficacia fue la revascularización del vaso objetivo ocluido. La revascularización se definió con una puntuación de TIMI de II o III tras el uso de solo Penumbra System y antes del uso de cualquier otro dispositivo o tratamiento adicional o complementario. Los resultados angiográficos los adjudicó un laboratorio principal independiente.

Eficacia	% (n/N) [IC 95 %]†
Criterio principal de valoración de eficacia (puntuación de TIMI de II o III) *Puntuaciones de TIMI antes de utilizar los tratamientos complementarios*	81,6 % (102/125) [73,7 %, 88,0 %]
Éxito de revascularización después del dispositivo (TIMI ≥ 2) *Cualquier uso de tratamiento complementario considerado error de tratamiento*	81,6 % (102/125) [73,7 %, 88,0 %]
Éxito de revascularización después del dispositivo (TIMI ≥ 2) *Cualquier uso lítico IA considerado error de tratamiento*	81,6 % (102/125) [73,7 %, 88,0 %]

†Intervalos de confianza de Clopper-Pearson exactos

Criterio principal de valoración de seguridad
El criterio principal de valoración de seguridad fue la incidencia de episodios adversos graves del dispositivo y/o relacionados con el procedimiento ocurridos durante el procedimiento según lo comunicado por el investigador. Se produjeron 18 episodios adversos procedimentales comunicados en 16 pacientes (12,8 %). Entre estos, CEC clasificó como graves 4 episodios adversos en 3 pacientes (2,4 %).

Episodios adversos compuestos durante el procedimiento	% (n/N) [IC 95 %]†
EAG compuestos durante el procedimiento	2,4 % (3/125)
Criterio principal de valoración de seguridad: EAG compuestos relacionados con el dispositivo/procedimiento durante el procedimiento	2,4 % (3/125)

†Intervalos de confianza de Clopper-Pearson exactos

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Todos los EAG específicos a lo largo de 90 días que se hayan producido en más del 2 % de los pacientes

EAG	% (n/N)
EAG compuestos	52,0 % (65/125)
Edema cerebral	11,2 % (14/125)
HIC	8,0 % (10/125)
Disfunción/fallo respiratorio	8,0 % (10/125)
Síntomas de empeoramiento del accidente cerebrovascular que cumple los criterios	7,2 % (9/125)
Infección	5,6 % (7/125)
Otras complicaciones pulmonares	5,6 % (7/125)
Neumonía	4,0 % (5/125)
Arritmia cardiaca	3,2 % (4/125)
Complicación en el sitio de acceso	2,4 % (3/125)
Infarto de miocardio	2,4 % (3/125)
Complicación vascular periférica	2,4 % (3/125)
Disfunción/fallo renal	2,4 % (3/125)
Accidente cerebrovascular en una nueva zona	2,4 % (3/125)

Categorización de los EA a lo largo de 90 días con un sistema anatómico

Sistema anatómico	% (n/N)
Alteraciones del sistema nervioso	62,4 % (78/125)
Infecciones e infestaciones	44,0 % (55/125)
Trastornos cardiacos	28,8 % (36/125)
Trastornos del metabolismo y la nutrición	25,6 % (32/125)
Trastornos generales y condiciones del sitio de administración	24,8 % (31/125)
Trastornos respiratorios, torácicos y mediastínicos	24,8 % (31/125)
Lesiones, envenenamiento y complicaciones procedimentales	18,4 % (23/125)
Trastornos gastrointestinales	16,0 % (20/125)
Trastornos sanguíneos y del sistema linfático	14,4 % (18/125)
Trastorno vascular	11,2 % (14/125)
Trastornos psiquiátricos	10,4 % (13/125)
Trastornos renales y urinarios	8,0 % (10/125)
Trastornos hepatobiliares	4,0 % (5/125)
Investigaciones	3,2 % (4/125)
Trastornos cutáneos y subcutáneos	3,2 % (4/125)
Neoplasmas benignos, malignos y no especificados (incluidos quistes y pólipos)	2,4 % (3/125)
Trastornos musculoesqueléticos y del tejido conectivo	0,8 % (1/125)

Glosario de símbolos

		Atención, consultar las instrucciones de uso	
Rx Only		Solamente con receta: Las leyes federales estadounidenses restringen el uso de este dispositivo a médicos o por prescripción facultativa	
		Apirógeno	
STER LE EO		Esterilizado con óxido de etileno	
	Fabricante	EC REP	Representante en la UE
LOT	Número de lote		No reutilizar
	Fecha de caducidad	REF	Número de catálogo
STERILIZE	No reesterilizar	LATEX	Sin látex

Garantía

Penumbra, Inc. (Penumbra) garantiza que se ha tenido una precaución razonable en el diseño y la fabricación de este dispositivo. Esta garantía sustituye y excluye a todas las demás garantías no expresamente establecidas en este documento, ya sean expresas o implícitas, por proceso jurídico o de otro modo, incluida, entre otras, cualquier garantía implícita de comerciabilidad o idoneidad para un uso particular. La manipulación, el almacenamiento, la limpieza y la esterilización de este dispositivo, así como otros factores relacionados con el paciente, el diagnóstico, el tratamiento, los procedimientos quirúrgicos y otros asuntos ajenos al control de Penumbra, afectan directamente al dispositivo y a los resultados obtenidos al usarlo. La obligación de Penumbra en virtud de esta garantía se limita a la reparación o sustitución de este dispositivo, y Penumbra no será responsable de ningún daño, pérdida o gasto incidental o emergente que surja directa o indirectamente del uso de este dispositivo. Penumbra no asume ni autoriza a ninguna otra persona que las asuma por ella ninguna otra obligación u obligaciones adicionales, ni ninguna responsabilidad con respecto a este dispositivo. Penumbra no asume ninguna responsabilidad con respecto a dispositivos reutilizados, reprocesados o reesterilizados y no ofrece garantía alguna, expresa o implícita, incluidas a modo de ejemplo, las de comerciabilidad o idoneidad para el uso indicado, con respecto a dichos dispositivos.

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Magyar

Az eszköz leírása

A Penumbra System® rendszer több eszközből áll:

- Penumbra reperfúziós katéter
- Penumbra szívópumpa
- Penumbra pumpa/tartály csatlakozócsöve
- Penumbra szívócső
- Penumbra szeparátor

A Penumbra System rendszer az érrendszerben található thrombusok folyamatos leszívás révén történő eltávolítására szolgál. A reperfúziós katéter a pumpa szívóhatását közvetlenül a thrombusra irányítja. A reperfúziós katéter lumene a szeparátorral tisztítható ki, ha thrombus zárja el. Legalább 1,37 mm (0,054 hüvelyk) belső átmérőjű reperfúziós katéter használata esetén a szeparátor használata felesleges lehet. A reperfúziós katétert egy vezetőkatéteren vagy hosszú femoralis hüvelyen keresztül kell felvezetni a koponyán belüli érrendszerbe, és neurovaszkuláris vezetődrót mentén kell a primer elzáródás helyére irányítani. A Penumbra reperfúziós katéter a szívópumpával együtt az elzáródott érben található thrombus leszívására szolgál. Ha szükséges, a reperfúziós katéterből kitolható egy Penumbra szeparátor a thrombus eltávolításának elősegítésére. A Penumbra szeparátor a Penumbra reperfúziós katéteren keresztül előretolható és visszahúzható a primer elzáródás proximális szélénél, ezzel elősegítve a thrombus eltávolítását a reperfúziós katéter csúcsáról. A szívóforrásnál a Penumbra reperfúziós katéter a szívópumpával együtt használatos; utóbbi csatlakoztatása a Penumbra szívócsővel és a Penumbra pumpa/tartály csatlakozócsövével történik. A Penumbra reperfúziós katéterhez gőzformázó szár, forgó vérzéscsillapító szelep és lehúzható hüvely van mellékelve. A Penumbra szeparátorhoz bevezetőeszköz és forgatóeszköz van mellékelve. Az eszközök fluoroszkópos ellenőrzés mellett láthatóak.

Használati javallatok

A Penumbra System rendszer a tünetek jelentkezésétől számított 8 órán belüli revascularisatióhoz szolgál olyan betegekben, akiket akut ischaemiás stroke ért a koponyán belüli nagyméretű ér (az arteria carotis interna, az arteria cerebri media – M1 és M2 szegmens, az arteria basilaris és az arteria vertebralis) elzáródásos betegsége következtében.

Ellenjavallatok

Nincsenek ismert ellenjavallatok.

„Vigyázat” szintű figyelmeztetések

- A Penumbra System rendszert csak olyan orvos használhatja, aki az intervenciós neuroendovascularis technikákra és az akut ischaemiás stroke kezelésére vonatkozóan megfelelő képzésben részesült.
- Ha ellenállást tapasztal, akkor mindaddig ne tolja előre és ne húzza vissza a Penumbra System rendszer egyetlen komponensét sem, amíg fluoroszkópia segítségével gondosan meg nem állapította az ellenállás okát. Amennyiben az ok nem állapítható meg, egy egységként húzza vissza az eszközt vagy a rendszert. A katéter vagy a szeparátor szabad elforgatása vagy erőltetett behelyezése az eszköz vagy az ér károsodását eredményezheti.
- A Penumbra szívópumpán kívül semmilyen más pumpával ne használja a Penumbra System rendszert.

Óvintézkedések

- Az eszköz kizárólag egyszeri használatra szolgál. Tilos újrasterilizálni vagy ismételten felhasználni! Az újrasterilizálás és/vagy ismételt használat nyomán a katéter bevonatának síkosítása hatástalannak bizonyulhat, ami erős súrlódást eredményezhet, és meghiúsíthatja a neurovasculatura célhelyéhez való hozzáférést.
- Tilos használni az eszközt, ha meghurkolódott vagy megsérült! A nyitott vagy sérült csomagokat tilos használni! Juttassa vissza az összes sérült eszközt a csomagolással együtt a gyártóhoz/forgalmazóhoz.
- A „Felhasználható a következő időpontig” jelzésű időpont előtt felhasználandó.
- A Penumbra System rendszert fluoroszkópiás megjelenítéssel együtt használja.
- Amikor leszívást hajt végre, ügyeljen arra, hogy a Penumbra szívócső szelepe csak a thrombus eltávolításához szükséges legrövidebb ideig legyen nyitva. Nem ajánlott túlzott szívást alkalmazni, illetve elmulasztani a Penumbra szívócső szelepének elzárását a szívás befejezésekor.
- A Penumbra szeparátor nem használható neurovascularis vezetődrótként. Ha a revascularisatiós eljárás során szükségessé válik a Penumbra reperfúziós katéter áthelyezése, akkor az áthelyezést megfelelő neurovascularis vezetődrót mentén kell végrehajtani standard mikrokatéteres és vezetődrótos technikák alkalmazásával.
- Ne használjon nagynyomású kontrasztanyag-befecskendező automatát a Penumbra reperfúziós katéterhez, mert azzal kárt tehet az eszközben.
- Az alvadásgátlók és thrombocytagátlók adagolását a kezelés utáni 24 órára fel kell függeszteni. Az orvosi ellátás és az akut stroke utáni ápolás az ASA irányelveinek megfelelően kell, hogy történjen.[1] A neurológiai állapot bármilyen romlását sürgős CT-vizsgálattal és a vizsgáló szakember/a kórház legjobb módszerei által kijelölt egyéb értékelőeljárásokkal kell értékelni.
- A beteg revascularisatiójának végrehajtására engedélyezett teljes idő: a Penumbra System rendszer 120 percnyi használata.

Lehetséges nemkívánatos események

A lehetséges szövődmények közé tartoznak egyebek mellett a következők:

- a thrombus teljes eltávolításának meghiúsulása
- akut elzáródás
- álaneurysma kialakulása
- arteriovenosus fistula
- az eszköz működési hibája
- disztális embolizáció
- embolus
- érgörcs, trombózis, dissectio vagy perforáció
- fertőzés
- haematoma vagy vérzés a hozzáférés helyén
- halál
- ischaemia
- kontrasztanyag által kiváltott allergiás reakció és anafilaxis
- kontrasztanyag miatti vesekárosodás
- koponyán belüli vérzés
- légembólia
- neurológiai deficitek, beleértve a stroke-ot is

Eljárás

1. Használat előtt tekintse át a **„Vigyázat” szintű figyelmeztetések, Óvintézkedések** és **Lehetséges nemkívánatos események** c. részeket.
2. Amikor a Penumbra System rendszer egyes eszközeinek felhasználására kerül a sor, távolítsa el az adott eszközt a csomagolásából, majd vizsgálja meg, hogy nem sérült-e, és nincs-e meghurkolódva.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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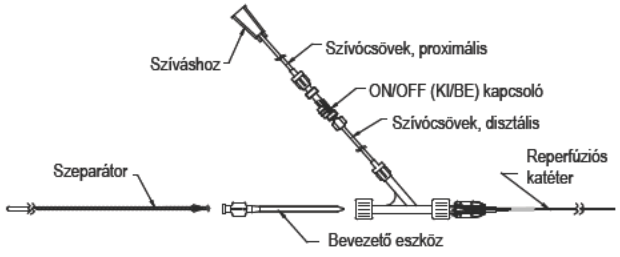
3. Készítse elő a Penumbra System rendszer eszközeit a használatra; ehhez heparinos fiziológiás sóoldattal öblítse át a védőtekercset és az eszközt (csak a Penumbra reperfúziós katétert és a Penumbra szeparátort).
4. Készítsen elő egy vezetőkatétert vagy egy hosszú femoralis hüvelyt a gyártó *használati utasításának* megfelelően.
5. Helyezze a vezetőkatétert vagy hosszú femoralis hüvelyt a thrombus által elzárt helyhez képest proximális helyzetű megfelelő arteria cerebralisba.

A Penumbra reperfúziós katéter előkészítése és használata

1. Ellenőrizze az ér átmérőjét, és válassza ki a megfelelő méretű Penumbra reperfúziós katétert (lásd **1. táblázat**).
2. A Penumbra reperfúziós katéter csúcsa a mellékelt gőzformázó szárral formázható.
3. Csatlakoztassa a mellékelt forgó vérzéscsillapító szelepet a Penumbra reperfúziós katéterhez.
4. Csatlakoztassa Penumbra szívócsövet a szívópumpához, és kapcsolja be a szívópumpát (lásd a *Felhasználói kézikönyv* Szívópumpa c. részét). Használat előtt legalább egy percig járassa a szívópumpát, és győződjön meg róla, hogy a szívásmérő –508 mmHg (–20 inHg) értéket mutat. Győződjön meg róla, hogy a Penumbra szívócsövön lévő szelep „OFF” (ki) állásban van.
5. Csatlakoztassa a szívócsövet a forgó vérzéscsillapító szelep oldalnyílásához az **1. ábrán** látható módon.

1. ábra – Összeszerelt szívórendszer Penumbra szeparátorral



6. Vezesse a Penumbra reperfúziós katétert a vezetőkatéter proximális kónuszához csatlakoztatott forgó vérzéscsillapító szelepbe. Ha nem használ vezetőkatétert, akkor a lehúzható hüvely segítségével vezesse át a Penumbra reperfúziós katétert a hosszú femoralis hüvely szelepén. A Penumbra reperfúziós katéter bevezetése után távolítsa el a lehúzható hüvelyt a vaszkuláris hüvelyről, és húzza le a Penumbra reperfúziós katéter száráról.
7. Hagyományos katéterezési technikákat használva, fluoroszkópos ellenőrzés mellett tolja előre a Penumbra reperfúziós katétert a célérbe egy megfelelő neurovascularis vezetődrót mentén. Pozicionálja a Penumbra reperfúziós katétert a thrombushoz képest proximális helyzetbe. Távolítsa el a vezetődrótot a Penumbra reperfúziós katéterből.
8. A leszívás megkezdéséhez az „ON” (be) állásba fordítva nyissa ki a Penumbra szívócsövön lévő szelepet. A leszívás leállításához fordítsa „OFF” (ki) állásba a Penumbra szívócsövön lévő szelepet, és kapcsolja ki a szívópumpát.
9. 5 ml-es vagy 10 ml-es fecskendővel szívjon fel kb. 5 ml vért a Penumbra reperfúziós katéterből az esetlegesen a katéterben maradt thrombusok eltávolításához.
10. Készítsen kezelés utáni angiogramot; ehhez fecskendezzen be kontrasztanyagot a vezetőkatéteren keresztül.

A Penumbra szeparátor előkészítése és használata

1. Szükség esetén válasszon a reperfúziós katéternek megfelelő méretű Penumbra szeparátort (lásd **1. táblázat**).

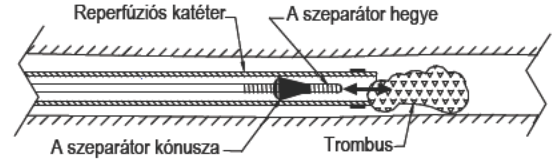
1. táblázat – Szeparátor/reperfúziós katéter méretének kiválasztása

Ér mérete (mm)	Penumbra reperfúziós katéter	Penumbra szeparátor
< 2,0	026	026
2,0–3,0	032 / 3MAX	032 / 3MAX
3,0–4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

MEGJEGYZÉS: Az elzáródás helyéhez való hozzáférés megkönnyíthető kompatibilis belső mikrokatéter triaxiális alkalmazásával.

2. A mellékelt bevezetőhüvely segítségével vezesse a Penumbra szeparátort a forgó vérzéscsillapító szelepen át a Penumbra reperfúziós katéter proximális kónuszába.
3. A leszívás megkezdéséhez az „ON” (be) állásba fordítva nyissa ki a Penumbra szívócsövön lévő szelepet, majd a szívásnak és a thrombus reperfúziós katéterből történő eltávolításának az elősegítése érdekében tolja előre/húzza vissza a Penumbra szeparátort a **2. ábrán** látható módon.

2. ábra – Thrombus leszívása a Penumbra szeparátorral



4. A leszívás leállításához fordítsa „OFF” (ki) állásba a Penumbra szívócsövön lévő szelepet, és kapcsolja ki a szívópumpát.
5. Ha használ Penumbra szeparátort, távolítsa el.
6. Amennyiben szükséges, az orvos belátása szerint további Penumbra szeparátorok és reperfúziós katéterek használhatók a thrombus további eltávolításához.

Klinikai adatok összefoglalása

A Penumbra pivotális vizsgálat a Penumbra System rendszer biztonságosságának és hatásosságának felmérésére szolgáló prospektív, egycsoportos vizsgálat volt. Összesen 125 beteg vett benne részt 24 nemzetközi vizsgálati központban. A fő beválasztási kritériumok a következők voltak: a NIH Stroke skálán (NIHSS) legalább 8-as érték, kivizsgálásra jelentkezés a tünetek jelentkezésétől számított 8 órán belül, valamint egy kezelhető koponyán belüli ér elzáródása (TIMI = 0 vagy 1). A tünetek jelentkezésétől számított 3 órán belül kivizsgálásra jelentkező betegeknek vagy alkalmatlanoknak kellett lenniük az rtPA-terápiára, vagy állapotuknak az rtPA-terápiával nem befolyásolhatónak kellett lennie. Az elsődleges végpontok a következők voltak: a célér revascularisatiója (TIMI = 2 vagy 3), illetve az eljárással kapcsolatos súlyos nemkívánatos események jelentkezése. Az összes beteg állapotát az eljárástól számított legfeljebb 90 napon át követték és értékelték.

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Statisztikai elemzés
A vizsgálathoz 125 fős mintát választottak, hogy legalább 115 értékelhető beteg legyen. Egy beteg akkor minősült értékelhetőnek, ha megfelelt az elsődleges végpont értékeléséhez kapcsolódó beválasztási követelményeknek, és a Penumbra System rendszerrel lett kezelve. Mivel kontrollcsoport nélküli vizsgálat volt, nem terveztek formális hipotézistesztet az összesített kimeneteli arányokra a 2 vagy 3 TIMI-érték megállapítására. A kategóriák végpontjaihoz használt standard leíró statisztikai mutatók a végpontok egyes szintjeihez tartozó betegszámok és betegszázalékok voltak. A számértékszerű végpontok esetében a standard leíró statisztikai mutatók között szerepelt a nem hiányzó megfigyelések száma (n), a középérték, a medián, a szórás, a minimumérték és a maximumérték.

A tanulmányban alkalmazott eljárások
A célérhez való artériás hozzáférés standard perkután technikával lett biztosítva, és négyeres digitális kivonási algoritmusú angiográfiát végeztek az elzáródott érszegmens angiográfiai szerkezetének meghatározására. Mindegyik beteg esetében előírás volt, hogy a nagyméretű agyi ér elzáródását angiográfiával megerősítsék, és hogy a vizsgáló szakember előzetesen kijelölje az elsődleges elzáródás helyét. Ha az elzáródás kezelhető érben volt, megfelelő vezetőkatétert helyeztek be, és a Penumbra reperfúziós katétert az elzáródott célér proximális végéhez tolták előre. Egy beteg akkor minősült a vizsgálatban résztvevőnek, amikor a reperfúziós katétert a vezetőkatéterből kitolták.

Fő beválasztási kritériumok
- Az akut ischaemiás stroke-kal konzisztens klinikai jelek, egyebek között:
  - Arc vagy végtagok hirtelen zsibbadása vagy gyengesége
  - Hirtelen zavartság, beszédprobléma vagy beszédértési probléma
  - Hirtelen járási probléma, szédülés vagy egyensúlyvesztés
- 18–79 éves életkor
- A NIH Stroke skálán (NIHSS) legalább 8 értéket eredményező neurológiai deficit
- Teljes elzáródás (TIMI-érték: 0) vagy kontrasztanyag behatolása minimális perfúzióval, de a disztális ág kitöltése nélkül (TIMI-érték: I) a stroke-okhoz használt Penumbra System rendszer számára hozzáférhető, koponyán belüli erekbe
- Aláírt tájékozott beleegyező nyilatkozat
- Kivizsgálásra jelentkezés a stroke tüneteinek jelentkezésétől számított 8 órán belül
- A tünetek jelentkezésétől számított 3 órán belül kivizsgálásra jelentkező betegek esetében: intravénás rtPA-terápiára való alkalmatlanság vagy az intravénás rtPA-terápiával nem befolyásolható állapot

Fő kizárási kritériumok
- A stroke neurológiai jeleinek gyors javulására utaló bizonyítékok a beválasztás időpontjában
- 30 fölötti NIHSS-érték vagy kóma
- Terhesség
- Az erek olyan fokú kanyargóssága, amely nehezen teszi lehetővé az endovaszkuláris hozzáférést
- Ismert vérzéses diathesis, véralvadási elégtelenség, vagy orális alvadásgátló terápia INR > 3,0 értékkel
- A laboratóriumi normális érték kétszeresét meghaladó PTT
- Felvételkor mért thrombocytaszám < 30 000
- Előzetesen meglévő neurológiai vagy pszichiátriai betegség, mely összezavarhatja a vizsgálat eredményeit
- Ismert súlyos allergia a kontrasztanyaggal szemben
- Kontrollálatlan magas vérnyomás (definíció szerint 185 mmHg-t meghaladó szisztolés nyomás vagy 110 mmHg-t meghaladó diasztolés nyomás)
- CT által szolgáltatott bizonyítékok az alábbi állapotokról a kivizsgálásra jelentkezéskor:
  - Jelentős tömeghatás középvonal-eltolódással
  - Nagyméretű – a középső arteria cerebralis területének 1/3-ánál nagyobb kiterjedésű – alacsony sűrűségű terület
  - Koponyán belüli vérzés bizonyítéka
- Bizonyíték az elzáródáshoz képest proximális helyzetű artériaszűkületre, mely megakadályozhatja a thrombus eltávolítását
- Előzetesen meglévő artériasérülés angiográfiás bizonyítéka
- 90 napnál rövidebb várható élettartam
- Részvétel másik klinikai vizsgálatban, amely összezavarhatja a vizsgált eszköz értékelését

A beválasztott alanyok kizárási okainak összefoglalása, különös tekintettel az angiográfiai kritériumon alapulókra
Egyetlen beválasztott beteg sem lett kizárva angiográfiai okokból.

Elsődleges hatásossági végpont
Az elsődleges hatásossági végpont az elzáródott célér revascularisatiója volt. A revascularisatio definíció szerint II-es vagy III-as TIMI-értéknek felel meg kizárólag a Penumbra System rendszer használata nyomán, minden további vagy kiegészítő eszköz vagy terápia alkalmazása előtt. Az angiográfiás eredményeket egy független törzslaboratórium állapította meg.

Hatásosság	% (n/N) [95% CI]†
Elsődleges hatásossági végpont (TIMI-érték: II vagy III) *Kiegészítő terápia alkalmazása előtti TIMI-értékek*	81,6% (102/125) [73,7%, 88,0%]
Sikeres revascularisatio az eszköz használatát követően (TIMI ≥ 2) *Bármilyen kiegészítő terápia alkalmazása esetén a kezelés sikertelennek minősül*	81,6% (102/125) [73,7%, 88,0%]
Sikeres revascularisatio az eszköz használatát követően (TIMI ≥ 2) *Bármilyen artérián belüli lyticus terápia alkalmazása esetén a kezelés sikertelennek minősül*	81,6% (102/125) [73,7%, 88,0%]

†Pontos Clopper–Pearson-konfidenciaintervallumok

Elsődleges biztonságossági végpont
Az elsődleges biztonságossági végpont a vizsgáló szakember jelentése szerint az eljárás során bekövetkezett és az eszközzel, illetve az eljárással kapcsolatos súlyos nemkívánatos események előfordulása volt. 18 eljárással kapcsolatos eseményről számoltak be 16 betegben (12,8%). Ezek közül 3 betegen bekövetkezett 4 eseményt minősített súlyosnak a Klinikai események bizottsága (CEC) (2,4%).

Az eljárás során bekövetkezett nemkívánatos események összesítése	% (n/N) [95% CI]†
Az eljárás során bekövetkezett súlyos nemkívánatos események összesítése	2,4% (3/125)
Elsődleges biztonságossági végpont: Az eljárás során bekövetkezett és eljárással/eszközzel kapcsolatos súlyos nemkívánatos események összesítése	2,4% (3/125)

†Pontos Clopper–Pearson-konfidenciaintervallumok

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A betegek több mint 2%-ában 90 napon belül bekövetkezett specifikus súlyos nemkívánatos események

Súlyos nemkívánatos esemény	% (n/N)
Súlyos nemkívánatos események összesítése	52,0% (65/125)
Agyödéma	11,2% (14/125)
Koponyán belüli vérzés	8,0% (10/125)
Légzési rendellenesség/elégtelenség	8,0% (10/125)
A kritériumoknak megfelelő stroke súlyosbodó tünetei	7,2% (9/125)
Fertőzés	5,6% (7/125)
Egyéb tüdővel kapcsolatos szövődmények	5,6% (7/125)
Tüdőgyulladás	4,0% (5/125)
Szívritmuszavar	3,2% (4/125)
Hozzáférési hellyel kapcsolatos szövődmények	2,4% (3/125)
Szívizominfarktus	2,4% (3/125)
Perifériás erekkel kapcsolatos szövődmények	2,4% (3/125)
Veseműködés rendellenessége/veseelégtelenség	2,4% (3/125)
Stroke új területen	2,4% (3/125)

90 napon belül bekövetkezett súlyos nemkívánatos események osztályozása az anatómiai rendszer szerint

Anatómiai rendszer	% (n/N)
Idegrendszeri rendellenességek	62,4% (78/125)
Fertőzések és parazitafertőzések	44,0% (55/125)
Szívvel kapcsolatos rendellenességek	28,8% (36/125)
Metabolizmussal és táplálkozással kapcsolatos rendellenességek	25,6% (32/125)
Általános rendellenességek és beadási hellyel kapcsolatos problémák	24,8% (31/125)
Légzési, mellkasi és mediastinalis rendellenességek	24,8% (31/125)
Sérülés, mérgezés és eljárással kapcsolatos szövődmények	18,4% (23/125)
Gastrointestinalis rendellenességek	16,0% (20/125)
Vér- és nyirokrendszeri rendellenességek	14,4% (18/125)
Vaszkuláris rendellenességek	11,2% (14/125)
Pszichiátriai rendellenességek	10,4% (13/125)
Vesével és vizeléssel kapcsolatos rendellenességek	8,0% (10/125)
Hepatobiliaris rendellenességek	4,0% (5/125)
Kivizsgálások	3,2% (4/125)
Bőrrel és bőr alatti szövettel kapcsolatos rendellenességek	3,2% (4/125)
Jóindulatú, rosszindulatú és meghatározatlan neoplazmák (egyebek között ciszták és polipok)	2,4% (3/125)
Musculoskeletalis és kötőszöveti rendellenességek	0,8% (1/125)

SZIMBÓLUMOK MAGYARÁZATA

		Figyelem, lásd a használati utasítást	
Rx Only		Vényköteles – az Egyesült Államok szövetségi törvényei értelmében ez az eszköz csak orvos által vagy orvosi rendelvényre használható	
		Nem pirogén	
STERILE EO		Etilén-oxiddal sterilizálva	
	Gyártó	EC REP	Képviselő az EU-ban
LOT	Tételszám		Tilos ismételten felhasználni
	Felhasználható a következő időpontig	REF	Katalógusszám
STERILIZE	Tilos újrasterilizálni	LATEX	Latexmentes

SZAVATOSSÁG

A Penumbra, Inc. (Penumbra) szavatolja, hogy ezen eszköz tervezése és gyártása során megfelelő mértékű gondossággal jártak el. Ez a szavatosság minden egyéb szavatosságot helyettesít, és kizár minden egyéb, itt nem részletezett kifejezett szavatosságot, illetve törvény alapján vagy egyéb módon meghatározott kellékszavatosságot, ideértve egyebek között az értékesíthetőségre vagy adott célra való megfelelésre vonatkozó kellékszavatosságot is. Az eszköz kezelése, tárolása, isztítása és sterilizálása, csakúgy, mint a beteggel, a diagnózissal, a kezeléssel, a műtéti eljárásokkal kapcsolatos tényezők és a Penumbra ellenőrzésén kívül eső egyéb tényezők közvetlen hatással vannak az eszközre és a használata révén kapott eredményekre. A jelen szavatosság keretében a Penumbra kötelezettsége az eszköz javítására vagy cseréjére korlátozódik, és a Penumbra nem felel az eszköz használatából közvetlenül vagy közvetetten adódó bármiféle járulékos vagy következményes veszteségért, kárért, illetve költségért. Az eszközzel kapcsolatban a Penumbra semmilyen egyéb vagy további felelősséget vagy kötelezettséget nem vállal, és nem hatalmaz fel senkit, hogy vállaljon. A Penumbra nem vállal semmilyen felelősséget az újrafelhasznált, újrafeldolgozott vagy újrasterilizált eszközökkel kapcsolatban, és ilyen eszközökkel kapcsolatban semmilyen kifejezett szavatosságot vagy kellékszavatosságot nem vállal, ideértve egyebek között az értékesíthetőségre vagy egy adott célra való megfelelésre vonatkozó kellékszavatosságot is.

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Français

Description du dispositif

Le Penumbra System® est composé de plusieurs dispositifs :

- Cathéter de reperfusion Penumbra
- Pompe d'aspiration Penumbra
- Tubulure pompe/réservoir Penumbra
- Tubulure d'aspiration Penumbra
- Séparateur Penumbra

Le Penumbra System est conçu pour l'extraction de thrombus du système vasculaire par aspiration continue. Le cathéter de reperfusion permet de cibler l'aspiration de la pompe sur le thrombus. Le séparateur peut être utilisé pour évacuer la lumière du cathéter de reperfusion si elle est obstruée par le thrombus. L'utilisation du séparateur n'est pas nécessaire lorsqu'un cathéter de reperfusion avec un Ø int. de 1,37 mm (0,054 po) ou plus est utilisé. Le cathéter de reperfusion est introduit par un cathéter guide ou une gaine fémorale longue dans le réseau vasculaire intracrânien et guidé sur un guide neuro-vasculaire vers le site de l'occlusion principale. Le cathéter de reperfusion Penumbra est utilisé en conjonction avec la pompe d'aspiration Penumbra pour aspirer le thrombus et l'extraire du vaisseau occlus. Le séparateur Penumbra peut être déployé à partir du cathéter de reperfusion pour faciliter l'extraction du thrombus. Le séparateur Penumbra est avancé et rétracté par le cathéter de reperfusion Penumbra, au niveau du bord proximal de l'occlusion principale, pour faciliter l'extraction du thrombus de l'extrémité du cathéter de reperfusion. Pour la source d'aspiration, le cathéter de reperfusion Penumbra est utilisé en conjonction avec la pompe d'aspiration, qui est raccordée par la tubulure d'aspiration Penumbra et la tubulure pompe/réservoir Penumbra. Le cathéter de reperfusion Penumbra est fourni avec un mandrin de modelage à la vapeur, une valve hémostatique rotative et une gaine pelable. Le séparateur Penumbra est fourni avec un introducteur et un dispositif de contrôle du couple. Les dispositifs sont visibles sous radioscopie.

Indications

L'utilisation du Penumbra System est indiquée dans la revascularisation de patients souffrant d'un accident vasculaire cérébral ischémique consécutif à une atteinte occlusive d'un gros vaisseau intracrânien (dans l'artère carotide interne, les segments M1 et M2 de l'artère cérébrale moyenne, les artères basilaire et vertébrale) dans les 8 heures suivant l'apparition des symptômes.

Contre-indications

Il n'existe aucune contre-indication connue.

Avertissements

- Le système Penumbra System doit uniquement être utilisé par des médecins ayant reçu la formation adéquate aux techniques interventionnelles neuro-endovasculaires et au traitement d'un accident vasculaire cérébral ischémique aigu.
- Ne pas avancer, rétracter ni utiliser un composant du Penumbra System en cas de résistance sans en évaluer soigneusement la cause sous radioscopie. Si la cause ne peut pas être déterminée, retirer le dispositif ou le système d'un seul tenant. Une torsion libre ou une introduction forcée du cathéter ou du séparateur contre résistance risque d'endommager le dispositif ou le vaisseau.
- Ne pas utiliser le Penumbra System avec une pompe autre que la pompe d'aspiration Penumbra.

Mises en garde

- Ce dispositif est exclusivement à usage unique. Ne pas restériliser ni réutiliser. Toute restérilisation et/ou réutilisation risque d'entraver la lubrification du revêtement du cathéter, ce qui est susceptible de causer une friction élevée et d'empêcher l'accès à l'emplacement ciblé dans le système neurovasculaire.
- Ne pas utiliser des dispositifs entortillés ou endommagés. Ne pas utiliser des emballages ouverts ou endommagés. Retourner les dispositifs et emballages endommagés au fabricant/distributeur.
- Utiliser avant la date de péremption.
- Utiliser le Penumbra System sous contrôle radioscopique.
- Lors de l'aspiration, s'assurer que la valve de la tubulure d'aspiration Penumbra n'est ouverte que pendant la durée minimale nécessaire à l'élimination du thrombus. Il est déconseillé d'effectuer une aspiration excessive ou de ne pas fermer la valve de la tubulure d'aspiration Penumbra quand l'aspiration est terminée.
- Le séparateur Penumbra n'est pas destiné à servir de guide neurovasculaire. En cas de repositionnement nécessaire du cathéter de reperfusion Penumbra lors de la procédure de revascularisation, procéder sur un guide neurovasculaire adapté en appliquant des techniques standard par microcathéter et guide.
- Ne pas utiliser d'équipement automatisé d'injection à haute pression de produit de contraste avec le cathéter de reperfusion Penumbra au risque d'endommager ce dernier.
- L'administration d'anticoagulants et d'antiplaquettaires doit être suspendue pendant les 24 heures suivant le traitement. La prise en charge médicale et les soins post-accident vasculaire cérébral aigu doivent se conformer aux directives de l'ASA.[1] Toute dégradation neurologique doit être évaluée au moyen d'un tomodensitogramme d'urgence et d'autres moyens d'évaluation tels qu'indiqués par les pratiques exemplaires définies par l'investigateur ou l'hôpital.
- La durée totale allouée pour parvenir à la revascularisation d'un patient en utilisant le Penumbra System est de 120 minutes.

Événements indésirables potentiels

Les complications possibles incluent notamment :

- décès
- déficits neurologiques, y compris AVC
- dysfonctionnement du dispositif
- embolie
- embolie gazeuse
- embolisation distale
- fistule artérioveineuse
- formation de faux anévrisme
- hématome ou hémorragie au niveau du site d'accès
- hémorragie intracrânienne
- incapacité d'extraire complètement le thrombus
- infection
- ischémie
- lésion rénale causée par le produit de contraste
- occlusion aiguë
- réaction allergique et anaphylaxie dues au produit de contraste
- spasme, thrombose, dissection ou perforation du vaisseau

Procédure

1. Avant utilisation, consulter les **avertissements,** les **mises en garde** et les **événements indésirables potentiels**.
2. Au moment de l'utilisation de chaque dispositif du Penumbra System, retirer ledit dispositif du conditionnement et vérifier qu'il n'est pas endommagé ou entortillé.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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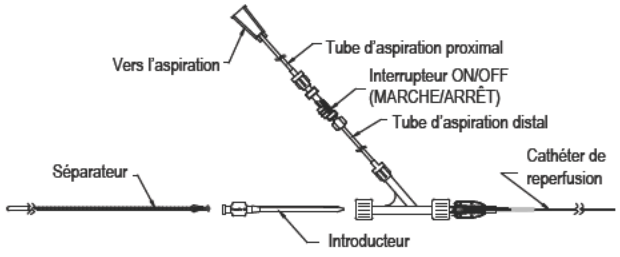
3. Préparer les dispositifs du Penumbra System en rinçant l'arceau d'emballage et le dispositif avec du sérum physiologique hépariné (cette instruction ne concerne que le cathéter de reperfusion Penumbra et le séparateur Penumbra).
4. Préparer un cathéter guide ou une gaine fémorale longue conformément au *Mode d'emploi* du fabricant.
5. Placer le cathéter guide ou la gaine fémorale longue dans l'artère cérébrale correcte, proximale au site d'occlusion du thrombus.

Préparation et utilisation du cathéter de reperfusion Penumbra

1. Confirmer le diamètre du vaisseau et sélectionner un cathéter de reperfusion Penumbra de taille correcte (voir le **Tableau 1**).
2. L'extrémité du cathéter de reperfusion Penumbra peut être modelée à l'aide du mandrin de modelage à la vapeur fourni.
3. Fixer la valve hémostatique rotative fournie au cathéter de reperfusion Penumbra.
4. Fixer la tubulure d'aspiration Penumbra à la pompe d'aspiration et allumer cette dernière (consulter le *Manuel d'utilisation* de la pompe d'aspiration). Permettre à la pompe d'aspiration de fonctionner pendant au moins une minute avant l'utilisation, et confirmer que la jauge d'aspiration indique −508 mmHg (−20 inHg). S'assurer que la valve de la tubulure d'aspiration Penumbra est en position OFF (fermée).
5. Raccorder la tubulure d'aspiration à l'orifice latéral de la valve hémostatique rotative, comme illustré à la **Figure 1**.

Figure 1 – Système d'aspiration assemblé avec le séparateur Penumbra



6. Insérer le cathéter de reperfusion Penumbra dans une valve hémostatique rotative fixée sur l'embase proximale d'un cathéter guide. Si un cathéter guide n'est pas utilisé, insérer le cathéter de reperfusion Penumbra par la valve de la gaine fémorale longue en utilisant la gaine pelable. Après avoir inséré le cathéter de reperfusion Penumbra, retirer la gaine pelable de la gaine vasculaire et la peler pour l'ôter du corps du cathéter de reperfusion Penumbra.
7. En utilisant des techniques conventionnelles de cathétérisme sous guidage radioscopique, avancer le cathéter de reperfusion Penumbra dans le vaisseau cible sur un guide neurovasculaire approprié. Positionner le cathéter de reperfusion Penumbra en amont du thrombus. Retirer le guide du cathéter de reperfusion Penumbra.
8. Pour commencer l'aspiration, mettre la valve de la tubulure d'aspiration Penumbra en position ON (ouverte). Pour arrêter l'aspiration, mettre la valve de la tubulure d'aspiration Penumbra en position OFF (fermée) et éteindre la pompe d'aspiration.
9. À l'aide d'une seringue de 5 ou 10 ml, aspirer environ 5 ml de sang du cathéter de reperfusion Penumbra pour éliminer tout thrombus susceptible de rester dans le cathéter.
10. Réaliser une angiographie post-traitement en injectant un produit de contraste par le cathéter guide.

Préparation et utilisation du séparateur Penumbra

1. Selon les besoins, sélectionner un séparateur Penumbra de la taille appropriée qui correspond au cathéter de reperfusion (voir le **Tableau 1**).

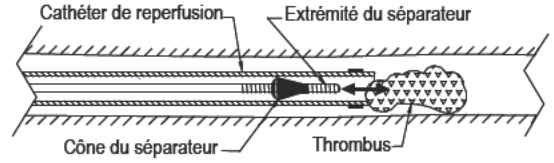
Tableau 1 – Sélection de taille du séparateur/ cathéter de reperfusion

Taille du vaisseau (mm)	Cathéter de reperfusion Penumbra	Séparateur Penumbra
< 2,0	026	026
2,0 à 3,0	032 / 3MAX	032 / 3MAX
3,0 à 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

REMARQUE : L'accès au site d'occlusion peut être facilité par l'utilisation triaxiale d'un microcathéter interne compatible.

2. À l'aide de la gaine d'introduction fournie, insérer le séparateur Penumbra par la valve hémostatique rotative et dans l'embase proximale du cathéter de reperfusion Penumbra.
3. Pour commencer l'aspiration, mettre la valve de la tubulure d'aspiration Penumbra en position ON (ouverte), et avancer/rétracter le séparateur Penumbra pour faciliter l'aspiration et l'extraction du thrombus du cathéter de reperfusion, comme illustré à la **Figure 2**.

Figure 2 – Aspiration d'un thrombus à l'aide du séparateur Penumbra



4. Pour arrêter l'aspiration, mettre la valve de la tubulure d'aspiration Penumbra en position OFF (fermée) et éteindre la pompe d'aspiration.
5. Retirer le séparateur Penumbra, s'il a été utilisé.
6. Selon les besoins, des séparateurs Penumbra et des cathéters de reperfusion Penumbra supplémentaires peuvent être utilisés pour une extraction de thrombus plus poussée, à la discrétion du médecin.

Résumé des données cliniques

L'essai pivot Penumbra était un essai prospectif à bras unique visant à évaluer la sécurité et l'efficacité du Penumbra System. Au total, 125 patients étaient inscrits dans 24 centres internationaux. Les principaux critères d'inclusion étaient un score > 8 sur l'échelle NIHSS (National Institutes of Health Stroke Score), la présentation du patient dans les 8 heures suivant l'apparition des symptômes, et une occlusion (score de recanalisation TIMI 0 ou 1) d'un vaisseau intracrânien traitable. Les patients s'étant présentés dans les 3 heures suivant l'apparition des symptômes devaient avoir été inéligibles pour le traitement par activateur du plasminogène tissulaire recombinant (rt-PA) ou réfractaires à ce traitement. Les critères primaires étaient la revascularisation du vaisseau cible (TIMI 2 ou 3) et l'incidence des effets indésirables graves liés à la procédure (EIG). Tous les patients ont été suivis et évalués jusqu'à 90 jours à partir de la date de la procédure.

Analyse statistique

Une taille d'échantillon de 125 a été choisie pour cette étude afin d'avoir au moins 115 patients évaluables. Un patient était considéré évaluable s'il répondait aux exigences d'éligibilité pour l'évaluation du critère primaire et s'il avait été traité avec le Penumbra System. Puisqu'il s'agissait d'une étude

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non contrôlée, un test d'hypothèse formel n'a pas été prévu pour le taux de réponse global pour l'établissement d'une score TIMI 2 ou 3. Les statistiques descriptives standard pour les critères catégoriques étaient le nombre et le pourcentage des patients avec chaque niveau du critère. Pour les critères numériques, les statistiques descriptives standard comprenaient le nombre d'observations non manquantes (n), la moyenne, la médiane, l'écart-type, la valeur minimale et la valeur maximale.

Procédures de l'étude
L'accès artériel au vaisseau cible a été obtenu selon une technique percutanée standard et une angiographie par soustraction numérique de quatre vaisseaux a été réalisée pour définir l'angioarchitecture du segment vasculaire occlus. L'occlusion d'un gros vaisseau cérébral devait être confirmée par angiographie pour chaque patient, et un site d'occlusion primaire était désigné a priori par l'investigateur. Si l'occlusion se situait dans un vaisseau traitable, un cathéter guide était mis en place et le cathéter de reperfusion Penumbra était avancé jusqu'à l'extrémité proximale du vaisseau cible occlus. Un patient était considéré comme inscrit quand le cathéter de reperfusion était déployé du cathéter guide.

Critères d'inclusion clés
- Les signes cliniques évoquant un AVC ischémique aigu, notamment :
  - Engourdissement ou faiblesse soudains du visage ou des extrémités
  - Confusion soudaine, difficulté à parler ou à comprendre
  - Difficulté soudaine à marcher, étourdissements ou perte d'équilibre
- Âge compris entre 18 et 79 ans
- Déficit neurologique entraînant un score NIHSS ≥ 8
- Occlusion complète (TIMI 0) ou pénétration du produit de contraste avec perfusion minime, mais sans remplissage de branche distale (TIMI I), dans des vaisseaux intracrâniens accessibles au Penumbra System pour AVC
- Consentement éclairé signé
- Présentation du patient dans les 8 heures suivant l'apparition des symptômes
- Patient inéligible au traitement par rt-PA intraveineux ou réfractaire à ce traitement, s'il s'est présenté dans les 3 heures suivant l'apparition des symptômes

Critères d'exclusion clé
- Preuve de l'amélioration rapide des signes neurologiques de l'AVC au moment de l'inscription
- Score NIHSS > 30 ou coma
- Femmes enceintes
- Tortuosité trop prononcée pour permettre l'accès endovasculaire
- Diathèse hémorragique documentée, trouble de la coagulation ou traitement anticoagulant oral avec un INR > 3,0
- PTT supérieur à 2 fois la normale de laboratoire
- Numération plaquettaire à l'admission < 30 000
- Maladie neurologique ou psychiatrique préexistante susceptible de confondre les résultats de l'étude
- Allergie sévère documentée aux produits de contraste
- Hypertension non contrôlée (définie comme une tension artérielle systolique > 185 mmHg ou une tension artérielle diastolique > 110 mmHg)
- Présence, constatée par tomodensitogramme, des conditions suivantes sur présentation du patient :
  - Important effet de masse significatif avec déviation de la ligne médiane
  - Grande région d'hypodensité > 1/3 du territoire de l'artère cérébrale moyenne
  - Constatation d'hémorragie intracrânienne
- Preuve angiographique d'une sténose artérielle en amont de l'occlusion qui pourrait empêcher l'extraction du thrombus
- Preuve angiographique de lésion artérielle préexistante
- Espérance de vie inférieure à 90 jours
- Participation à une autre étude clinique qui pourrait confondre l'évaluation du dispositif d'étude

Résumé des raisons justifiant l'exclusion de sujets inscrits, en particulier celles basées sur des critères angiographiques
Aucun patient inscrit n'a été exclu pour des raisons angiographiques.

Critère d'efficacité primaire
Le critère d'efficacité primaire était la revascularisation du vaisseau cible occlus. La revascularisation était définie par un score TIMI de II ou III après l'utilisation du Penumbra System seulement et avant l'utilisation de dispositifs ou thérapies complémentaires ou d'appoint. Les résultats angiographiques ont été analysés par un laboratoire central indépendant.

Efficacité	% (n/N) [IC à 95 %]†
Critère d'efficacité primaire (score TIMI de II ou III) *Scores TIMI avant les traitements adjuvants*	81,6 % (102/125) [73,7 %, 88,0 %]
Succès de la revascularisation après mise en place du dispositif (TIMI ≥ 2) *Toute utilisation de traitement adjuvant considérée comme un échec thérapeutique*	81,6 % (102/125) [73,7 %, 88,0 %]
Succès de la revascularisation après mise en place du dispositif (TIMI ≥ 2) *Toute utilisation d'agent lytique IA considérée comme un échec thérapeutique*	81,6 % (102/125) [73,7 %, 88,0 %]

†Intervalles de confiance exacts de Clopper-Pearson

Critère de sécurité primaire
Le critère de sécurité primaire était l'incidence d'événements indésirables graves liés au dispositif et/ou à la procédure s'étant produits au cours de la procédure, tel que rapportée par l'investigateur. 18 événements de procédure ont été rapportés chez 16 patients (12,8 %). Parmi ceux-ci, 4 événements chez 3 patients ont été classés graves par le CEC (2,4 %).

Effets indésirables composites au cours de la procédure	% (n/N) [IC à 95 %]†
EIG composite au cours de la procédure	2,4 % (3/125)
Critère de sécurité primaire : EIG composite lié à la procédure/au dispositif au cours de la procédure	2,4 % (3/125)

†Intervalles de confiance exacts de Clopper-Pearson

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Chaque EIG spécifique, sur une période de 90 jours, se produisant chez plus de 2 % des patients

EIG	% (n/N)
EIG composites	52,0 % (65/125)
Œdème cérébral	11,2 % (14/125)
HIC	8,0 % (10/125)
Insuffisance/défaillance respiratoire	8,0 % (10/125)
Aggravation des symptômes de l'AVC élig ble	7,2 % (9/125)
Infection	5,6 % (7/125)
Autres complications pulmonaires	5,6 % (7/125)
Pneumonie	4,0 % (5/125)
Arythmie cardiaque	3,2 % (4/125)
Complication au site d'accès	2,4 % (3/125)
Infarctus du myocarde	2,4 % (3/125)
Complication vasculaire périphérique	2,4 % (3/125)
Insuffisance/défaillance rénale	2,4 % (3/125)
AVC autrement situé	2,4 % (3/125)

Catégorisation des EI sur 90 jours selon la localisation anatomique

Localisation anatomique	% (n/N)
Troubles du système nerveux	62,4 % (78/125)
Infections et infestations	44,0 % (55/125)
Affections cardiaques	28,8 % (36/125)
Troubles métaboliques et nutritionnels	25,6 % (32/125)
Troubles généraux et états au site d'administration	24,8 % (31/125)
Troubles respiratoires, thoraciques et médiastinaux	24,8 % (31/125)
Lésions, intoxications et complications procédurales	18,4 % (23/125)
Affections gastro-intestinales	16,0 % (20/125)
Affections hématologiques et du système lymphatique	14,4 % (18/125)
Trouble vasculaire	11,2 % (14/125)
Troubles psychiatriques	10,4 % (13/125)
Affections des reins et des voies urinaires	8,0 % (10/125)
Affections hépatobiliaires	4,0 % (5/125)
Investigations	3,2 % (4/125)
Affections cutanées et des tissus sous-cutanés	3,2 % (4/125)
Tumeurs bénignes, malignes et non précisées (incl kystes et polypes)	2,4 % (3/125)
Affections musculo-squelettiques et des tissus conjonctifs	0,8 % (1/125)

GLOSSAIRE DES SYMBOLES

		Attention, consulter le mode d'emploi	
Rx Only		Sur ordonnance uniquement – Conformément à la législation fédérale des États-Unis, ce dispositif ne peut être utilisé que par un médecin ou sur ordonnance médicale	
		Non pyrogène	
STER LE EO		Stérilisé à l'oxyde d'éthylène	
	Fabricant	EC REP	Mandataire pour l'UE
LOT	Numéro du lot		Ne pas réutiliser
	Date de péremption	REF	N° de référence
STERILIZE	Ne pas restériliser	LATEX	Sans latex

GARANTIE

Penumbra, Inc. (Penumbra) garantit avoir pris des précautions raisonnables lors de la conception et la fabrication de ce dispositif. Cette garantie remplace et exclut toutes les autres garanties non expressément citées aux présentes, expresses ou implicites, par effet de la loi ou autre, notamment mais sans s'y limiter toutes les garanties implicites de qualité marchande ou d'aptitude à un usage particulier. La manipulation, la conservation, le nettoyage et la stérilisation de ce dispositif ainsi que d'autres facteurs relatifs au patient, au diagnostic, au traitement, aux interventions chirurgicales et à d'autres paramètres échappant au contrôle de Penumbra peuvent directement affecter le dispositif et les résultats obtenus par son utilisation. La responsabilité de Penumbra au titre de cette garantie se limite à la réparation ou au remplacement de ce dispositif, et Penumbra ne pourra pas être tenue pour responsable en cas de pertes, dommages ou frais indirects ou consécutifs découlant directement ou indirectement de l'utilisation de ce disposi if. Penumbra n'assume pas, et n'autorise aucune personne à assumer en son nom, d'autres responsabilités en rapport avec ce dispositif. Penumbra n'assume aucune responsabilité en ce qui concerne les dispositifs réutilisés, retraités ou restérilisés et ne fait aucune garan ie, expresse ou implicite, notamment mais sans s'y limiter toute garantie de qualité marchande ou d'aptitude à l'usage prévu, relativement à ces disposi ifs.

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Περιγραφη της συσκευης

Το Penumbra System® αποτελείται από αρκετές συσκευές:

- Καθετήρα επαναιμάτωσης Penumbra
- Αντλία αναρρόφησης Penumbra
- Σωλήνα αντλίας/δοχείου Penumbra
- Σωλήνα αναρρόφησης Penumbra
- Διαχωριστή Penumbra

Το Penumbra System έχει σχεδιαστεί για αφαίρεση θρόμβου από το αγγειακό σύστημα χρησιμοποιώντας συνεχή αναρρόφηση. Ο καθετήρας επαναιμάτωσης κατευθύνει την αναρρόφηση από την αντλία απευθείας στο θρόμβο. Ο διαχωριστής μπορεί να χρησιμοποιηθεί για τη διάνοιξη του αυλού του καθετήρα επαναιμάτωσης σε περίπτωση που αποφραχθεί με θρόμβο. Η χρήση του διαχωριστή ενδέχεται να μην είναι απαραίτητη όταν χρησιμοποιείται καθετήρας επαναιμάτωσης με εσωτερική διάμετρο 1,37 mm (0,054 ίντσες) ή μεγαλύτερη. Ο καθετήρας επαναιμάτωσης εισάγεται μέσω οδηγού καθετήρα ή μηριαίου θηκαριού μεγάλου μήκους στο ενδοκρανιακό αγγειακό σύστημα και κατευθύνεται πάνω από ένα νευροαγγειακό οδηγό σύρμα προς τη θέση της πρωτογενούς απόφραξης.
Ο καθετήρας επαναιμάτωσης Penumbra χρησιμοποιείται σε συνδυασμό με την αντλία αναρρόφησης για την αναρρόφηση θρόμβου από αποφραγμένο αγγείο. Όποτε είναι απαραίτητο, ένας διαχωριστής Penumbra μπορεί να εκπτυχθεί από τον καθετήρα επαναιμάτωσης για να βοηθήσει στην αφαίρεση του θρόμβου.
Ο διαχωριστής Penumbra προωθείται και αποσύρεται μέσω του καθετήρα επαναιμάτωσης Penumbra στο εγγύς όριο της πρωτογενούς απόφραξης για να διευκολύνει την εξάλειψη του θρόμβου από το άκρο του καθετήρα επαναιμάτωσης.
Όσον αφορά την πηγή αναρρόφησης, ο καθετήρας επαναιμάτωσης Penumbra χρησιμοποιείται σε συνδυασμό με την αντλία αναρρόφησης, η οποία συνδέεται χρησιμοποιώντας το σωλήνα αναρρόφησης Penumbra και το σωλήνα αντλίας/δοχείου Penumbra. Ο καθετήρας επαναιμάτωσης Penumbra παρέχεται με αξονίσκο διαμόρφωσης με ατμό, περιστροφική αιμοστατική βαλβίδα και αποκολλούμενο θηκάρι. Ο διαχωριστής Penumbra παρέχεται με εισαγωγέα και συσκευή στρέψης. Οι συσκευές είναι ορατές υπό ακτινοσκόπηση.

Ενδειξεις χρησης

Το Penumbra System προορίζεται για χρήση στην επαναγγείωση ασθενών με οξύ ισχαιμικό εγκεφαλικό επεισόδιο μετά από ενδοκρανιακή αποφρακτική νόσο μεγάλου αγγείου (εντός της εσωτερικής καρωτιδικής, έσω εγκεφαλικής – τμήματα M1 και M2, βασικής και σπονδυλικής αρτηρίας) εντός 8 ωρών από την έναρξη των συμπτωμάτων.

Αντενδειξεις

Δεν υπάρχουν γνωστές αντενδείξεις.

Προειδοποιησεις

- Το Penumbra System θα πρέπει να χρησιμοποιείται αποκλειστικά από ιατρούς που έχουν εκπαιδευτεί κατάλληλα σε επεμβατικές νευρο-ενδοαγγειακές τεχνικές και στη θεραπεία οξέος ισχαιμικού εγκεφαλικού επεισοδίου.
- Μην προωθείτε, μην αποσύρετε και μην χρησιμοποιείτε οποιοδήποτε εξάρτημα του Penumbra System εάν συναντήσετε αντίσταση, πρ ν αξιολογήσετε προσεκτικά την αιτία μέσω ακτινοσκόπησης. Εάν η αιτία δεν μπορεί να προσδιοριστεί, αποσύρετε τη συσκευή ή το σύστημα ως ενιαία μονάδα. Η ανεξέλεγκτη συστροφή ή βίαιη εισαγωγή του καθετήρα ή του διαχωριστή υπό αντίσταση ενδέχεται να προκαλέσει βλάβη στη συσκευή ή το αγγείο.
- Μην χρησιμοποιείτε το Penumbra System με αντλία διαφορετική από την αντλία αναρρόφησης Penumbra.

Προφυλαξεις

- Η συσκευή προορίζεται για μία μόνο χρήση. Μην την αποστειρώνετε και μην τη χρησιμοποιείτε ξανά. Η επαναποστείρωση ή/και η επαναχρησιμοποίηση ενδέχεται να έχουν ως αποτέλεσμα ανεπαρκή λίπανση της επικάλυψης του καθετήρα, με πιθανό επακόλουθο υψηλή τριβή και αδυναμία προσπέλασης της επιθυμητής νευροαγγειακής θέσης.
- Μην χρησιμοποιείτε συσκευές που έχουν υποστεί στρεβλώσεις ή ζημιά. Μην χρησιμοποιείτε συσκευασίες που έχουν ανοιχθεί ή υποστεί ζημιά. Επιστρέψτε όλες τις συσκευές και συσκευασίες που έχουν υποστεί ζημιά στον κατασκευαστή/διανομέα.
- Να χρησιμοποιείται πριν από την ημερομηνία λήξης.
- Χρησιμοποιείτε το Penumbra System σε συνδυασμό με ακτ νοσκοπική απεικόνιση.
- Κατά τη διενέργεια αναρρόφησης, βεβαιωθείτε ότι η βαλβίδα του σωλήνα αναρρόφησης Penumbra είναι ανοικτή μόνο για τον ελάχιστο χρόνο που απαιτείται για την αφαίρεση του θρόμβου. Υπερβολική αναρρόφηση ή μη κλείσιμο της βαλβίδας του σωλήνα αναρρόφησης Penumbra όταν η αναρρόφηση έχει ολοκληρωθεί δεν συνιστάται.
- Ο διαχωριστής Penumbra δεν προορίζεται για χρήση ως νευροαγγειακό οδηγό σύρμα. Εάν απαιτείται επανατοποθέτηση του καθετήρα επαναιμάτωσης Penumbra κατά τη διάρκεια της διαδικασίας επαναγγείωσης, η επανατοποθέτηση αυτή θα πρέπει να διενεργηθεί περνώντας τον καθετήρα πάνω από κατάλληλο νευροαγγειακό οδηγό σύρμα, χρησιμοποιώντας τυπικές τεχνικές μικροκαθετήρων και οδηγών συρμάτων.
- Μην χρησιμοποιείτε αυτοματοποιημένο εξοπλισμό έγχυσης σκιαγραφικής ουσίας υπό υψηλή πίεση σε συνδυασμό με τον καθετήρα επαναιμάτωσης Penumbra διότι υπάρχει πιθανότητα να προκληθεί ζημιά στη συσκευή.
- Η χορήγηση αντιπηκτικής και αντιαιμοπεταλιακής αγωγής πρέπει να αναστέλλεται μέχρι 24 ώρες μετά τη θεραπεία. Κατά την ιατρική αντιμετώπιση και τη φροντίδα μετά από οξύ εγκεφαλικό επεισόδιο πρέπει να τηρούνται οι κατευθυντήριες οδηγίες του ASA.[1] Τυχόν νευρολογική επιδείνωση πρέπει να αξιολογείται με επείγουσα αξονική τομογραφία και άλλες αξιολογήσεις όπως ενδείκνυται σύμφωνα με τη βέλτιστη πρακτική του ερευνητή/νοσοκομείου.
- Ο συνολικός χρόνος που επιτρέπεται για την επίτευξη της επαναγγείωσης του ασθενούς είναι 120 λεπτά χρήσης του Penumbra System.

Πιθανες ανεπιθυμητες ενεργειες

Οι πιθανές επιπλοκές περιλαμβάνουν μεταξύ άλλων και τις εξής:

- αγγειόσπασμος, θρόμβωση, διαχωρισμός ή διάτρηση αγγείου
- αδυναμία πλήρους αφαίρεσης του θρόμβου
- αιμάτωμα ή αιμορραγία στη θέση πρόσβασης
- αλλεργική αντίδραση και αναφυλαξία από σκιαγραφική ουσία
- αρτηριοφλεβώδες συρίγγιο
- δυσλειτουργία της συσκευής
- έμβολα
- εμβολή αέρα
- ενδοκρανιακή αιμορραγία
- θάνατος
- ισχαιμία
- λοίμωξη
- νευρολογικά ελλείμματα, συμπεριλαμβανομένου του εγκεφαλικού επεισοδίου
- νεφρική βλάβη από τη σκιαγραφική ουσία
- οξεία απόφραξη
- περιφερική εμβολή
- σχηματισμός ψευδοανευρύσματος

Διαδικασια

1. Ανατρέξτε στις ενότητες **Προειδοποιήσεις**, **Προφυλάξεις** και **Πιθανές ανεπιθύμητες ενέργειες** πριν από τη χρήση.
2. Καθώς χρησιμοποιούνται όλες οι συσκευές του Penumbra System, αφαιρέστε κάθε συσκευή από τη συσκευασία και επιθεωρήστε την για ζημιά ή στρεβλώσεις.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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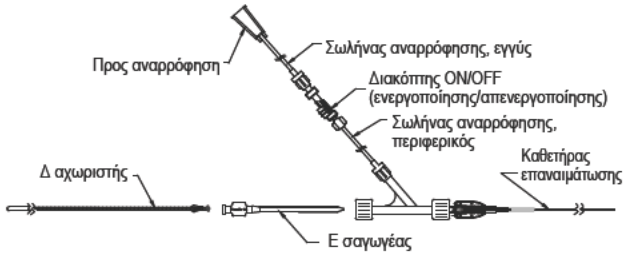
3. Προετοιμάστε τις συσκευές του Penumbra System για χρήση, εκπλένοντας τη στεφάνη συσκευασίας και τη συσκευή με ηπαρινισμένο αλατούχο διάλυμα (περιλαμβάνει τον καθετήρα επαναιμάτωσης Penumbra και το διαχωριστή Penumbra μόνο).
4. Προετοιμάστε έναν οδηγό καθετήρα ή μηριαίο θηκάρι μεγάλου μήκους σύμφωνα με τις *Οδηγίες Χρήσης* του κατασκευαστή.
5. Τοποθετήστε τον οδηγό καθετήρα ή το μηριαίο θηκάρι μεγάλου μήκους στην κατάλληλη εγκεφαλική αρτηρία που βρίσκεται εγγύς της θέσης απόφραξης από το θρόμβο.

Προετοιμασια και χρηση του καθετηρα επαναιματωσης Penumbra

1. Επιβεβαιώστε τη διάμετρο του αγγείου και επιλέξτε έναν καθετήρα επαναιμάτωσης Penumbra κατάλληλου μεγέθους (Βλ. **πίνακα 1**).
2. Το άκρο του καθετήρα επαναιμάτωσης Penumbra μπορεί να διαμορφωθεί χρησιμοποιώντας τον άξονα διαμόρφωσης με ατμό που παρέχεται.
3. Συνδέστε την παρεχόμενη περιστροφική αιμοστατική βαλβίδα στον καθετήρα επαναιμάτωσης Penumbra.
4. Συνδέστε το σωλήνα αναρρόφησης Penumbra στην αντλία αναρρόφησης και ενεργοποιήστε την αντλία αναρρόφησης (Ανατρέξτε στο *Εγχειρίδιο λειτουργίας* της αντλίας αναρρόφησης). Αφήστε την αντλία αναρρόφησης να λειτουργήσει για τουλάχιστον ένα λεπτό πριν από τη χρήση και επιβεβαιώστε ότι το μανόμετρο της αντλίας αναρρόφησης αναγράφει −508 mmHg (−20 inHg). Βεβαιωθείτε ότι η βαλβίδα στο σωλήνα αναρρόφησης Penumbra είναι γυρισμένη στη θέση OFF (απενεργοποίηση).
5. Συνδέστε το σωλήνα αναρρόφησης με την πλευρική θύρα της περιστροφικής αιμοστατικής βαλβίδας, όπως φαίνεται στο **Σχήμα 1**.

Σχήμα 1 – Συναρμολογημένο σύστημα αναρρόφησης με διαχωριστή Penumbra



6. Εισαγάγετε τον καθετήρα επαναιμάτωσης Penumbra σε μια περιστροφική αιμοστατική βαλβίδα συνδεδεμένη στον εγγύς ομφαλό του οδηγού καθετήρα. Αν δεν χρησιμοποιηθεί οδηγός καθετήρας, εισαγάγετε τον καθετήρα επαναιμάτωσης Penumbra μέσω της βαλβίδας του μηριαίου θηκαριού μεγάλου μήκους χρησιμοποιώντας το αποκολλούμενο θηκάρι. Αφού εισάγετε τον καθετήρα επαναιμάτωσης Penumbra, αφαιρέστε το αποκολλούμενο θηκάρι από το αγγειακό θηκάρι και αποκολλήστε το από το στέλεχος του καθετήρα επαναιμάτωσης Penumbra.
7. Με τη χρήση συμβατικών τεχνικών καθετηριασμού υπό ακτινοσκοπική καθοδήγηση, προωθήστε τον καθετήρα επαναιμάτωσης Penumbra πάνω από κατάλληλο νευροαγγειακό οδηγό σύρμα και εισαγάγετέ τον στο αγγείο-στόχο. Τοποθετήστε τον καθετήρα επαναιμάτωσης Penumbra εγγύς του θρόμβου. Αφαιρέστε το οδηγό σύρμα από τον καθετήρα επαναιμάτωσης Penumbra.
8. Για να ξεκινήσετε την αναρρόφηση, ανοίξτε τη βαλβίδα του σωλήνα αναρρόφησης Penumbra στη θέση ON (ενεργοποίηση). Για να σταματήσει η αναρρόφηση, τοποθετήστε τη βαλβίδα του σωλήνα αναρρόφησης Penumbra στη θέση OFF (απενεργοποίηση) και απενεργοποιήστε την αντλία αναρρόφησης.
9. Με τη χρήση σύριγγας των 5 ml ή 10 ml, αναρροφήστε περίπου 5 ml αίματος από τον καθετήρα επαναιμάτωσης Penumbra, ώστε να αφαιρεθεί τυχόν θρόμβος που ενδέχεται να παραμένει εντός του καθετήρα.
10. Διενεργήστε αγγειογραφία μετά τη θεραπεία με έγχυση σκιαγραφικής ουσίας διαμέσου του οδηγού καθετήρα.

Προετοιμασια και χρηση του διαχωριστη Penumbra

1. Εάν χρειάζεται, επιλέξτε έναν διαχωριστή Penumbra κατάλληλου μεγέθους, ο οποίος να ταιριάζει με τον καθετήρα επαναιμάτωσης (βλ. **Πίνακα 1**).

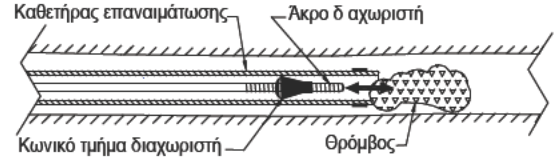
Πίνακας 1 – Επιλογή μεγέθους διαχωριστή/καθετήρα επαναιμάτωσης

Μέγεθος αγγείου (mm)	Καθετήρας επαναιμάτωσης Penumbra	Διαχωριστής Penumbra
< 2,0	026	026
2,0 έως 3,0	032 / 3MAX	032 / 3MAX
3,0 έως 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

ΣΗΜΕΙΩΣΗ: Η προσπέλαση της θέσης της απόφραξης μπορεί να διευκολυνθεί μέσω της τριαξονικής χρήσης ενός συμβατού εσωτερικού μικροκαθετήρα.

2. Με το παρεχόμενο θηκάρι εισαγωγής, εισαγάγετε το διαχωριστή Penumbra διαμέσου της περιστροφικής αιμοστατικής βαλβίδας και προωθήστε τον στον εγγύς ομφαλό του καθετήρα επαναιμάτωσης Penumbra.
3. Για να αρχίσει η αναρρόφηση, ανοίξτε τη βαλβίδα του σωλήνα αναρρόφησης Penumbra στη θέση ON (ενεργοποίηση) και προωθήστε/αποσύρετε το διαχωριστή Penumbra, ώστε να διευκολύνετε την αναρρόφηση και αφαίρεση του θρόμβου από τον καθετήρα επαναιμάτωσης, όπως φαίνεται στο **Σχήμα 2**.

Σχήμα 2 – Αναρρόφηση θρόμβου με τη χρήση του διαχωριστή Penumbra



4. Για να σταματήσει η αναρρόφηση, τοποθετήστε τη βαλβίδα του σωλήνα αναρρόφησης Penumbra στη θέση OFF (απενεργοποίηση) και απενεργοποιήστε την αντλία αναρρόφησης.
5. Αφαιρέστε το διαχωριστή Penumbra, εάν χρησιμοποιείται.
6. Εάν χρειαστεί, είναι δυνατό να χρησιμοποιηθούν πρόσθετοι διαχωριστές και καθετήρες επαναιμάτωσης Penumbra, ώστε να γίνει περαιτέρω αφαίρεση του θρόμβου κατά την κρίση του ιατρού.

Συνοπτικη παρουσιαση κλινικων δεδομενων

Η κύρια μελέτη Penumbra ήταν μια προοπτική μελέτη μονού σκέλους για την αξιολόγηση της ασφάλειας και της αποτελεσματικότητας του Penumbra System. Στη μελέτη εντάχθηκαν 125 ασθενείς σε 24 διεθνή κέντρα. Κύρια κριτήρια εισαγωγής ήταν η βαθμολογία NIH Stroke Scale (NIHSS) ≥ 8, εμφάνιση εντός 8 ωρών από την έναρξη των συμπτωμάτων και απόφραξη (TIMI 0 ή 1) ενός θεραπεύσιμου ενδοκρανιακού αγγείου. Ασθενείς που εμφανίστηκαν εντός 3 ωρών από την έναρξη των συμπτωμάτων περιελήφθησαν εφόσον ήταν μη επιλέξιμοι ή ανθεκτικοί στη θεραπεία με rtPA. Πρωτεύοντα καταληκτικά σημεία ήταν η επαναγγείωση του αγγείου στόχου (TIMI 2 ή 3) και η επίπτωση των σχετικών με τη διαδικασία σοβαρών ανεπιθύμητων ενεργειών (ΣΑΕ). Όλοι οι ασθενείς παρακολουθήθηκαν και αξιολογήθηκαν έως και 90 ημέρες μετά τη διαδικασία.

Στατιστική ανάλυση

Για την παρούσα μελέτη επιλέχθηκε μέγεθος δείγματος 125 ασθενών προκειμένου να προκύψουν τουλάχιστον 115 αξιολογήσιμοι ασθενείς. Ένας ασθενής θεωρήθηκε αξιολογήσιμος εάν πληρούσε τις απαιτήσεις ένταξης στη μελέτη για την αξιολόγηση του πρωτεύοντος καταληκτικού σημείου και εάν υποβλήθηκε σε θεραπεία με το Penumbra System. Επειδή επρόκειτο για μελέτη χωρίς ομάδα ελέγχου, δεν σχεδιάστηκε μια κανονική δοκιμασία ελέγχου υπόθεσης

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για το συνολικό ποσοστό ανταπόκρισης για επίτευξη βαθμού TIMI 2 ή 3. Τα τυπικά περιγραφικά στατιστικά δεδομένα για τα κατηγορικά καταληκτικά σημεία περιελάμβαναν τον αριθμό και το ποσοστό των ασθενών με κάθε επίπεδο του καταληκτικού σημείου. Για τα αριθμητικά καταληκτικά σημεία, τα τυπικά περιγραφικά στατιστικά δεδομένα περιελάμβαναν τον αριθμό των διαθέσιμων παρατηρήσεων (n), τη μέση τιμή, τη διάμεση τιμή, την τυπική απόκλιση, την ελάχιστη τιμή και τη μέγιστη τιμή.

Διαδικασίες μελέτης
Αρτηριακή πρόσβαση στο αγγείο-στόχο επιτεύχθηκε χρησιμοποιώντας τυπική διαδερμική τεχνική και πραγματοποιήθηκε ψηφιακή αφαιρετική αγγειογραφία τεσσάρων αγγείων για να καθοριστεί η αρχιτεκτονική του αποφραγμένου αγγειακού τμήματος. Κάθε ασθενής έπρεπε να έχει την απόφραξη μεγάλου εγκεφαλικού αγγείου του επιβεβαιωμένη με αγγειογραφία και περιοχή πρωτογενούς απόφραξης προσδιορισμένη εκ των προτέρων από τον ερευνητή. Εάν η απόφραξη αφορούσε θεραπεύσιμο αγγείο, τοποθετούνταν κατάλληλος οδηγός καθετήρας και ο καθετήρας επαναιμάτωσης Penumbra προωθούνταν στο εγγύς άκρο του αποφραγμένου αγγείου-στόχο. Ο ασθενής θεωρούνταν ενταγμένος στη μελέτη εφόσον ο καθετήρας επαναιμάτωσης Penumbra απελευθερωνόταν από τον οδηγό καθετήρα.

Βασικά κριτήρια ένταξης
- Κλινικά σημεία συμβατά με οξύ ισχαιμικό εγκεφαλικό επεισόδιο, όπως:
  - Αιφνίδιο μούδιασμα ή αδυναμία του προσώπου ή των άκρων
  - Αιφνίδια σύγχυση, δυσκολία στην ομιλία ή την κατανόηση του προφορικού λόγου
  - Αιφνίδια δυσκολία στη βάδιση, ζάλη ή απώλεια της ισορροπίας
- Από 18 έως 79 ετών
- Νευρολογικό έλλειμμα που οδηγεί σε βαθμολογία NIH Stroke Scale (NIHSS) ≥ 8
- Πλήρης απόφραξη (βαθμός TIMI 0) ή είσοδος σκιαγραφικής ουσίας με ελάχιστη αιμάτωση αλλά έλλειψη πλήρωσης του άπω τμήματος του κλάδου (βαθμός TIMI I) ενδοκρανιακών αγγείων προσβάσιμων στο Penumbra System για εγκεφαλικά επεισόδια
- Υπογεγραμμένη συγκατάθεση κατόπ ν συνεννόησης
- Εμφάνιση του ασθενούς εντός 8 ωρών από την εμφάνιση συμπτωμάτων του εγκεφαλικού επεισοδίου
- Ασθενείς που εμφανίστηκαν εντός 3 ωρών από την έναρξη των συμπτωμάτων περιελήφθησαν εφόσον ήταν μη επιλέξιμοι ή ανθεκτικοί στη θεραπεία με rtPA

Βασικά κριτήρια αποκλεισμού
- Ενδείξεις ταχείας βελτίωσης των νευρολογικών σημείων του εγκεφαλικού επεισοδίου κατά τη χρονική στιγμή της ένταξης στη μελέτη
- NIHSS > 30 ή κώμα
- Έγκυες γυναίκες
- Ελίκωση αγγείου τέτοια που δεν επιτρέπει την ενδοαγγειακή προσπέλαση
- Γνωστή αιμορραγική διάθεση, διαταραχές πηκτικότητας ή από του στόματος θεραπεία με αντιπηκτικά με INR > 3,0
- PTT με τιμή μεγαλύτερη από 2 φορές τη φυσιολογική τιμή του εργαστηρίου
- Αριθμός αιμοπεταλίων κατά την εισαγωγή < 30.000
- Προϋπάρχουσα νευρολογική ή ψυχιατρική νόσος που θα μπορούσε να προκαλέσει σύγχυση στα αποτελέσματα της μελέτης
- Γνωστή σοβαρή αλλεργία σε σκιαγραφική ουσία
- Μη ελεγχόμενη υπέρταση (που ορίζεται ως συστολική αρτηριακή πίεση > 185 mmHg ή διαστολική αρτηριακή πίεση > 110 mmHg)
- Ένδειξη των ακολούθων καταστάσεων στην αξονική τομογραφία κατά την εμφάνιση του ασθενούς:
  - Σημαντική χωρακατακτητική δράση (mass effect) με παρεκτόπιση της μέσης γραμμής
  - Μεγάλη υπόπυκνη περιοχή > 1/3 της περιοχής αιμάτωσης της μέσης εγκεφαλικής αρτηρίας
  - Ένδειξη ενδοκρανιακής αιμορραγίας
- Αγγειογραφική ένδειξη αρτηριακής στένωσης εγγύς της απόφραξης που θα μπορούσε να παρεμποδίσει την αφαίρεση του θρόμβου
- Αγγειογραφική ένδειξη προϋπάρχουσας αρτηριακής βλάβης
- Προσδόκιμο ζωής μικρότερο από 90 ημέρες
- Συμμετοχή σε άλλη κλινική έρευνα που θα μπορούσε να προκαλέσει σύγχυση κατά την αξιολόγηση της υπό μελέτη συσκευής

Συνοπτική παρουσίαση των λόγων αποκλεισμού επιλεγμένων ασθενών, ιδιαίτερα αυτών που βασίζονται σε αγγειογραφικά κριτήρια
Κανένας επιλεγμένος ασθενής δεν αποκλείστηκε για αγγειογραφικούς λόγους.

Πρωτεύον καταληκτικό σημείο αποτελεσματικότητας
Το πρωτεύον καταληκτικό σημείο αποτελεσματικότητας ήταν η επαναγγείωση του αποφραγμένου αγγείου-στόχου. Η επαναγγείωση ορίστηκε από μια βαθμολογία TIMI II ή III μετά από τη χρήση του Penumbra System και μόνον και πριν από τη χρήση οποιασδήποτε συμπληρωματικής ή πρόσθετης συσκευής ή θεραπείας. Τα αγγειογραφικά αποτελέσματα αξιολογήθηκαν από ανεξάρτητο κεντρικό εργαστήριο.

Αποτελεσματικότητα	% (n/N) [95% ΔΕ]†
Πρωτεύον καταληκτικό σημείο αποτελεσματικότητας (βαθμολογία TIMI II ή III) *Βαθμολογίες TIMI πριν από τη χρήση συμπληρωματικών θεραπειών*	81,6% (102/125) [73,7%, 88,0%]
Επιτυχία επαναγγείωσης μετά τη χρήση της συσκευής (TIMI ≥ 2) *Η χρήση οποιασδήποτε συμπληρωματικής θεραπείας θεωρήθηκε αποτυχία*	81,6% (102/125) [73,7%, 88,0%]
Επιτυχία επαναγγείωσης μετά τη χρήση της συσκευής (TIMI ≥ 2) *Η χρήση οποιασδήποτε ενδοαρτηριακής θρομβολυτικής θεραπείας θεωρήθηκε αποτυχία*	81,6% (102/125) [73,7%, 88,0%]

†Διαστήματα εμπιστοσύνης Clopper-Pearson (Exact)

Πρωτεύον καταληκτικό σημείο ασφάλειας
Το πρωτεύον καταληκτικό σημείο ασφάλειας ήταν η επίπτωση σοβαρών ανεπιθύμητων ενεργειών που σχετίζονται με τη συσκευή και/ή τη διαδικασία τα οποία συνέβησαν κατά τη διάρκεια της διαδικασίας όπως αναφέρθηκαν από τον ερευνητή. Αναφέρθηκαν 18 σχετικές με τη διαδικασία ενέργειες σε 16 ασθενείς (12,8%). Μεταξύ αυτών, 4 ενέργειες σε 3 ασθενείς αξιολογήθηκαν από την Επιτροπή Κλινικών Συμβάντων (CEC) ως σοβαρές (2,4%).

Σύνθετες ανεπιθύμητες ενέργειες κατά τη διάρκεια της διαδικασίας	% (n/N) [95% ΔΕ]†
Σύνθετες σοβαρές ανεπιθύμητες ενέργειες κατά τη διάρκεια της διαδικασίας	2,4% (3/125)
Πρωτεύον καταληκτικό σημείο ασφάλειας: Σύνθετες σχετικές με τη διαδικασία/συσκευή ανεπιθύμητες ενέργειες κατά τη διάρκεια της διαδικασίας	2,4% (3/125)

†Διαστήματα εμπιστοσύνης Clopper-Pearson (Exact)

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Κάθε ΣΑΕ σε διάρκεια 90 ημερών που συνέβη σε ποσοστό ασθενών μεγαλύτερο από 2%

ΣΑΕ	% (n/N)
Σύνθετα ΣΑΕ	52,0% (65/125)
Εγκεφαλικό οίδημα	11,2% (14/125)
Ενδοεγκεφαλική αιμορραγία	8,0% (10/125)
Αναπνευστική δυσλειτουργία/ανεπάρκεια	8,0% (10/125)
Επιδείνωση συμπτωμάτων διαγνωσμένου εγκεφαλικού επεισοδίου	7,2% (9/125)
Λοίμωξη	5,6% (7/125)
Άλλες πνευμονικές επιπλοκές	5,6% (7/125)
Πνευμονία	4,0% (5/125)
Καρδιακή αρρυθμία	3,2% (4/125)
Επιπλοκή στο σημείο προσπέλασης	2,4% (3/125)
Έμφραγμα του μυοκαρδίου	2,4% (3/125)
Επιπλοκή περιφερικού αγγειακού συστήματος	2,4% (3/125)
Νεφρική δυσλειτουργία/ανεπάρκεια	2,4% (3/125)
Εγκεφαλικό επεισόδιο σε νέα περιοχή	2,4% (3/125)

Κατηγοριοποίηση ΑΕ σε διάστημα 90 ημερών ανά ανατομικό σύστημα

Ανατομικό σύστημα	% (n/N)
Διαταραχές του νευρικού συστήματος	62,4% (78/125)
Λοιμώξεις και μολύνσεις	44,0% (55/125)
Καρδιακές διαταραχές	28,8% (36/125)
Μεταβολικές και διατροφικές διαταραχές	25,6% (32/125)
Γενικές διαταραχές και καταστάσεις που αφορούν το σημείο χορήγησης	24,8% (31/125)
Αναπνευστικές, θωρακικές και μεσοθωρακικές διαταραχές	24,8% (31/125)
Τραυματισμός, δηλητηρίαση και επιπλοκές που σχετίζονται με τη διαδικασία	18,4% (23/125)
Γαστρεντερικές διαταραχές	16,0% (20/125)
Διαταραχές του αγγειακού και του λεμφικού συστήματος	14,4% (18/125)
Αγγειακή διαταραχή	11,2% (14/125)
Ψυχιατρικές διαταραχές	10,4% (13/125)
Νεφρικές και ουρολογικές διαταραχές	8,0% (10/125)
Διαταραχές ηπατοχοληφόρου συστήματος	4,0% (5/125)
Υπό έρευνα	3,2% (4/125)
Δερματικές και υποδόριες διαταραχές	3,2% (4/125)
Καλοήθη, κακοήθη και μη καθορισμένα νεοπλάσματα (συμπ/μένων κύστεων και πολύποδων)	2,4% (3/125)
Μυοσκελετικές διαταραχές και διαταραχές του συνδετικού ιστού	0,8% (1/125)

Γλωσσαρι συμβολων

	Προσοχή, βλ. οδηγίες χρήσης		
Rx Only	Χορηγείται μόνο με ιατρική συνταγή - Η ομοσπονδιακή νομοθεσία των Η.Π.Α. επιτρέπει τη χρήση της συσκευής αυτής μόνο από ιατρό ή κατόπιν εντολής ιατρού		
	Μη πυρετογόνο		
STERILE EO	Αποστειρωμένο με χρήση οξειδίου του αιθυλενίου		
	Κατασκευαστής	EC REP	Αντιπρόσωπος στην Ε.Ε.
LOT	Κωδικός παρτίδας		Μην επαναχρησιμοποιείτε
	Ημερομηνία λήξης	REF	Αριθμός καταλόγου
STERILIZE	Μην επαναποστειρώνετε	LATEX	Χωρίς λάτεξ

Εγγυηση

Η Penumbra, Inc. (Penumbra) εγγυάται ότι έχει δοθεί η δέουσα προσοχή κατά το σχεδιασμό και την κατασκευή της παρούσας συσκευής. Η παρούσα εγγύηση αντικαθιστά και ακυρώνει όλες τις άλλες εγγυήσεις που δεν ορίζονται ρητά στο παρόν, ρητές ή συναγόμενες δια νόμου ή άλλως, συμπεριλαμβανομένων, μεταξύ άλλων, συναγόμενων εγγυήσεων εμπορευσιμότητας ή καταλληλότητας για συγκεκριμένο σκοπό. Ο χειρισμός, η φύλαξη, ο καθαρισμός και η αποστείρωση της παρούσας συσκευής, καθώς και άλλοι παράγοντες που σχετίζονται με τον ασθενή, τη διάγνωση, τη θεραπεία, τις χειρουργικές επεμβάσεις και άλλα ζητήματα πέραν του ελέγχου της Penumbra επηρεάζουν άμεσα τη συσκευή και τα αποτελέσματα που επιτυγχάνονται με τη χρήση της. Η υποχρέωση της Penumbra σύμφωνα με την παρούσα εγγύηση περιορίζεται στην επισκευή ή αντικατάσταση αυτής της συσκευής και η Penumbra δε θα είναι υπεύθυνη για τυχόν θετική ή αποθετική απώλεια, ζημία ή δαπάνη που προκύπτει άμεσα ή έμμεσα από τη χρήση της παρούσας συσκευής. Η Penumbra ούτε αναλαμβάνει ούτε εξουσιοδοτεί οποιοδήποτε άλλο πρόσωπο να αναλάβει αντ' αυτής οποιαδήποτε άλλη ή πρόσθετη υποχρέωση ή ευθύνη σε σχέση με την παρούσα συσκευή. Η Penumbra δεν αναλαμβάνει καμία ευθύνη σε σχέση με συσκευές που έχουν επαναχρησιμοποιηθεί, υποστεί επανεπεξεργασία ή επαναποστειρωθεί και δεν παρέχει καμία εγγύηση, ρητή ή συναγόμενη, συμπεριλαμβανομένων, μεταξύ άλλων, συναγόμενων εγγυήσεων εμπορευσιμότητας ή καταλληλότητας για συγκεκριμένο σκοπό, σχετικά με τέτοιες συσκευές.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Popis prostředku

Systém Penumbra System® sestává z několika zařízení:

- reperfuzní katetr Penumbra
- odsávací čerpadlo Penumbra
- hadička čerpadla/kanystru Penumbra
- odsávací hadička Penumbra
- separátor Penumbra

Systém Penumbra System je určen k odstranění trombu z vaskulatury pomocí průběžného odsávání. Reperfuzní katetr zaměřuje odsávání z čerpadla přímo k trombu. Separátor se může použít k vyčištění lumenu reperfuzního katetru, pokud dojde k jeho ucpání trombem. Použití separátoru nemusí být nutné, pokud se používá reperfuzní katetr s vnitřním průměrem 1,37 mm (0,054 palce) nebo větší. Reperfuzní katetr se zavádí skrz vodicí katetr nebo pomocí dlouhého femorálního sheathu do intrakraniálních cév a je naváděn přes neurovaskulární vodicí drát do místa primární okluze. Reperfuzní katetr Penumbra se používá spolu s odsávacím čerpadlem k odsátí trombu z okludované cévy. Podle potřeby se může separátor Penumbra rozvinout z reperfuzního katetru na pomoc při odstraňování trombu. Separátor Penumbra se posunuje vpřed a vytahuje zpět skrz reperfuzní katetr Penumbra na proximálním okraji místa primární okluze. To usnadňuje odstranění trombu z hrotu reperfuzního katetru. Co se týče zdroje odsávání, reperfuzní katetr Penumbra se používá ve spojení s odsávacím čerpadlem, které je připojeno pomocí odsávací hadičky Penumbra a hadičky čerpadla/kanystru Penumbra. Reperfuzní katetr Penumbra se dodává s mandrénem tvarovaným parou, rotačním hemostatickým ventilem a odlupovacím sheathem. Separátor Penumbra se dodává se zavaděčem a otáčecím zařízením. Zařízení jsou viditelná skiaskopicky.

Indikace pro použití

Systém Penumbra System je určen k použití při revaskularizaci u pacientů s akutní ischemickou mozkovou příhodou následkem okluzního onemocnění velkých intrakraniálních cév (v řečišti a. carotis interna, a. cerebri media – segmenty M1 a M2, a. basillaris a aa. vertebrales) v průběhu 8 hodin od nástupu symptomů.

Kontraindikace

Žádné kontraindikace nejsou známy.

Varování

- Systém Penumbra System mohou používat pouze lékaři, kteří byli náležitě proškoleni v intervenčních neuro-endovaskulárních technikách a léčbě akutní ischemické mozkové příhody.
- Žádnou součást systému Penumbra System neposunujte vpřed, nevyjímejte ani nepoužívejte proti odporu bez předchozího pečlivého skiaskopického vyhodnocení příčiny odporu. Pokud příčinu nelze stanovit, prostředek nebo systém vyjměte jako jednu jednotku. Neřízené kroucení nebo násilné zavedení katetru nebo separátoru proti odporu může způsobit poškození prostředku nebo cévy.
- Systém Penumbra System používejte pouze s odsávacím čerpadlem Penumbra.

Upozornění

- Tento prostředek je určen pouze k jednorázovému použití. Neresterilizujte ani nepoužívejte opakovaně. Resterilizace a/nebo opakované použití mohou vést k neúčinné lubrikaci povlaku katetru, což může způsobit vysoké tření a nemožnost zpřístupnit cílové neurovaskulární místo.
- Zasmyčkované nebo poškozené prostředky nepoužívejte. Nepoužívejte, je-li obal otevřen nebo poškozen. Všechny poškozené prostředky a obaly vraťte výrobci/distributorovi.
- Nepoužívejte po datu použitelnosti.
- Systém Penumbra System používejte ve spojení se skiaskopickou vizualizací.
- Při odsávání se ujistěte, že ventil odsávací hadičky Penumbra je otevřený pouze po minimální dobu nutnou k odstranění trombu. Nedoporučuje se nadměrné odsávání nebo neuzavření ventilu odsávací hadičky Penumbra po dokončení odsávání.
- Separátor Penumbra není určen k použití jako neurovaskulární vodicí drát. V případě nutnosti úpravy polohy reperfuzního katetru Penumbra v průběhu revaskularizačního zákroku je nutné tuto úpravu provést po vhodném neurovaskulárním vodicím drátu pomocí standardních technik využívajících mikrokatetr a vodicí drát.
- S reperfuzním katetrem Penumbra nepoužívejte automatické vysokotlaké injektory kontrastní látky, neboť by mohlo dojít k poškození prostředku.
- Podávání antikoagulačních a protidestičkových látek je třeba pozastavit na 24 hodin po zákroku. Lékařská péče a akutní péče po mozkové příhodě se musí řídit pokyny ASA.[1] Jakékoli neurologické poruchy je nutné vyhodnotit pomocí urgentního skenu CT a dalšími metodami, jak je indikováno dle nejlepší praxe zkoušejícího/nemocnice.
- Celkový čas povolený k dosažení revaskularizace u pacienta s použitím systému Penumbra System je 120 minut.

Potenciální nežádoucí příhody

K možným komplikacím patří mimo jiné:

- alergická reakce a anafylaxe z kontrastní látky;
- akutní uzávěr;
- arteriovenózní píštěl;
- distální embolizace;
- embolie;
- hematom nebo krvácení v místě přístupu;
- chybná funkce přístroje;
- infekce;
- ischémie;
- nemožnost úplného odstranění trombu;
- nitrolebeční krvácení;
- neurologické deficity včetně mozkové příhody;
- poškození ledvin kontrastní látkou;
- spasmus, trombóza, disekce nebo perforace cévy;
- úmrtí;
- vytvoření nepravého aneuryzmatu;
- vzduchová embolie.

Postup

1. Před použitím si přečtěte části **Varování, Upozornění** a **Potenciální nežádoucí příhody**.
2. Při použití jakéhokoli zařízení systému Penumbra System vyjměte zařízení z obalu a zkontrolujte, zda není poškozené nebo zauzlené.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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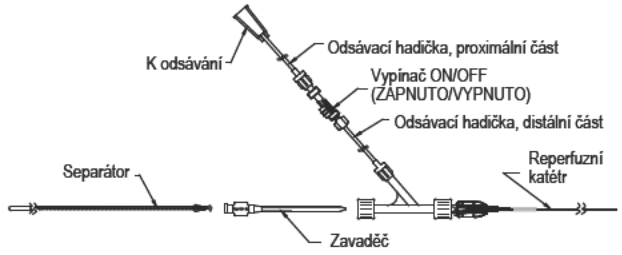
3. Zařízení systému Penumbra System připravte k použití propláchnutím ochranného obalu a zařízení heparinyzovaným fyziologickým roztokem (týká se pouze reperfuzního katetru Penumbra a separátoru Penumbra).
4. Připravte si vodicí katetr nebo dlouhý femorální sheath dle *Návodu k použití* výrobce.
5. Zaveďte vodicí katetr nebo dlouhý femorální sheath do příslušné mozkové artérie, která leží proximálně od místa okluze trombem.

Příprava a použití reperfuzního katetru Penumbra

1. Potvrďte průměr cévy a vyberte vhodnou velikost reperfuzního katetru Penumbra (viz **tabulka 1**).
2. Hrot repefuzního katetru Penumbra se může tvarovat pomocí dodaného mandrénu tvarovaného parou.
3. K reperfuznímu katetru Penumbra připojte dodaný rotační hemostatický ventil.
4. Odsávací hadičku Penumbra připojte k odsávacímu čerpadlu a čerpadlo zapněte (viz *Provozní příručka* odsávacího čerpadla). Před použitím nechte odsávací čerpadlo alespoň jednu minutu běžet a zkontrolujte, zda ukazatel odsávání ukazuje −508 mm Hg (−20 palců Hg). Zkontrolujte, zda je ventil na odsávací hadičce Penumbra přepnutý do polohy OFF (vypnuto).
5. Připojte odsávací hadičku k bočnímu portu rotačního hemostatického ventilu, jak je zobrazeno na **obrázku 1**.

Obrázek 1 – Sestavený odsávací systém se separátorem Penumbra



6. Vložte reperfuzní katetr Penumbra do rotačního hemostatického ventilu, který je připojen k proximálnímu ústí vodicího katetru. Pokud se vodicí katetr nepoužije, zasuňte reperfuzní katetr Penumbra skrz ventil dlouhého femorálního sheathu pomocí slupovacího sheathu. Po zasunutí reperfuzního katetru Penumbra vyjměte slupovací sheat z vaskulárního sheathu a sloupněte jej z tubusu reperfuzního katetru Penumbra.
7. Konvenčními katetrizačními technikami pod skiaskopickým naváděním zasunujte reperfuzní katetr Penumbra do cílové cévy po vhodném neurovaskulárním vodicím drátu. Reperfuzní katetr Penumbra umístěte proximálně od trombu. Vyjměte vodicí drát z reperfuzního katetru Penumbra.
8. Pro zahájení odsávání otevřete ventil na odsávací hadičce Penumbra do polohy ON (zapnuto). Odsávání zastavíte přepnutím ventilu na odsávací hadičce Penumbra do polohy OFF (vypnuto) a vypnutím odsávacího čerpadla.
9. Pomocí 5ml nebo 10ml stříkačky odsajte přibližně 5 ml krve z reperfuzního katetru Penumbra pro odstranění trombu, který mohl zůstat v katetru.
10. Po zákroku zhotovte angiogram vstříknutím kontrastní látky skrz vodicí katetr.

Příprava a použití separátoru Penumbra

1. V případě potřeby vyberte vhodnou velikost separátoru Penumbra, která odpovídá reperfuznímu katetru (viz **tabulka 1**).

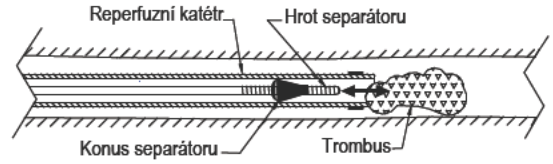
Tabulka 1 – Volba velikosti separátoru/reperfuzního katetru

Velikost cévy (mm)	Reperfuzní katetr Penumbra	Separátor Penumbra
< 2,0	026	026
2,0 až 3,0	032 / 3MAX	032 / 3MAX
3,0 až 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

POZNÁMKA: Přístup k místu okluze je možné usnadnit triaxiálním použitím kompatibilního vnitřního mikrokatetru.

2. Pomocí dodaného zaváděcího sheathu zaveďte separátor Penumbra přes rotační hemostatický ventil do proximálního ústí reperfuzního katetru Penumbra.
3. Odsávání zahájíte tak, že otevřete ventil na odsávací hadičce Penumbra do polohy ON (zapnuto) a separátor Penumbra vysunete a zasunete zpět na pomoc při odsávání a odstranění trombu z reperfuzního katetru, viz **obrázek 2**.

Obrázek 2 – Odsátí trombu pomocí separátoru Penumbra



4. Odsávání zastavíte přepnutím ventilu na odsávací hadičce Penumbra do polohy OFF (vypnuto) a vypnutím odsávacího čerpadla.
5. Vyjměte separátor Penumbra, pokud ho používáte.
6. Je-li to nutné, je možné na základě rozhodnutí lékaře použít další separátory Penumbra a reperfuzní katetry Penumbra k dalšímu odstranění trombu.

Přehled klinických dat

Pivotní studie Penumbra byla prospektivní studie prováděná v jedné větvi k vyhodnocení bezpečnosti a účinnosti systému Penumbra System. Ve 24 mezinárodních centrech do ní bylo zařazeno celkem 125 pacientů. Hlavní vstupní kritéria zahrnovala skóre NIHSS ≥ 8, dostavení se do 8 hodin po nástupu příznaků a okluze (TIMI 0 nebo 1) léčitelné intrakraniální cévy. Pacienti, kteří se dostavili do 3 hodin po nástupu příznaků, se nesměli kvalifikovat pro léčbu rtPA, nebo na ni nereagovali. Primární cílové parametry zahrnovaly revaskularizaci cílové cévy (TIMI 2 nebo 3) a výskyt závažných nežádoucích příhod při zákroku. Všichni pacienti byli sledováni a vyhodnocováni po období až 90 dnů po zákroku.

Statistická analýza

Pro tuto studii byl vybrán vzorek 125 pacientů, aby bylo zajištěno alespoň 115 vyhodnotitelných pacientů. Pacient byl považován za vyhodnotitelného, pokud splňoval kritéria vhodnosti pro vyhodnocení primárního cílového parametru a byl ošetřen systémem Penumbra System. Protože se jednalo o nekontrolovanou studii, nebyl plánován oficiální test hypotézy pro celkový poměr léčebné odpovědi při dosažení stupně TIMI 2 nebo 3. Standardní deskriptivní statistické údaje pro kategorie cílových parametrů zahrnovaly počet a procento pacientů s každou úrovní cílového parametru. U numerických

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cílových parametrů zahrnovaly standardní deskriptivní statistické údaje počet nechybějících pozorování (n), průměr, medián, směrodatnou odchylku, minimální hodnotu a maximální hodnotu.

Postupy studie
Arteriální přístup k cílové cévě byl dosažen pomocí standardní perkutánní techniky. Byla provedena čtyřcévová digitální subtrakční angiografie za účelem definování angio-architektury okludovaného cévního segmentu. U každého pacienta musela být angiograficky potvrzená okluze velké cerebrální cévy a zkoušející musel předem určit místo primární okluze. Pokud okluze byla v léčitelné cévě, byl zaveden vhodný vodicí katetr a reperfuzní katetr Penumbra byl zasunut na proximální konec okludované cílové cévy. Pacient byl považován za zařazeného okamžikem vysunutí reperfuzního katetru z vodicího katetru.

Hlavní kritéria pro zařazení
- Klinické známky konzistentní s akutní ischemickou mozkovou příhodou zahrnující:
  - Náhlé znecitlivění nebo slabost obličeje nebo končetin
  - Náhlou zmatenost, problémy s mluvením a porozuměním
  - Náhlý problém s chůzí, točení hlavy nebo ztrátu rovnováhy
- Pacient ve věku od 18 do 79 let
- Neurologický deficit vedoucí ke skóre NIHSS ≥ 8
- Úplná okluze (TIMI stupeň 0) nebo průnik kontrastní látky s minimální perfuzí, ale bez naplnění distálních větví (TIMI stupeň I) v intrakraniálních cévách přístupných pro systém pro léčbu mozkových příhod Penumbra System
- Podepsaný informovaný souhlas
- Pacient se dostavil do 8 hodin po nástupů příznaků mozkové mrtvice
- Pokud se pacient dostavil do 3 hodin po nástupu příznaků, nekvalifikoval se pro rtPA terapii nebo na ni nereagoval

Hlavní kritéria pro vyřazení
- Důkazy rychle se zlepšujících neurologických známek mozkové příhody v době zařazení
- NIHSS > 30 nebo kóma
- Těhotné ženy
- Vinutost cév příliš obtížná pro endovaskulární přístup
- Známá hemoragická diatéza, nedostatečná koagulace nebo pacient na perorální antikoagulační terapii s INR > 3,0
- PTT vyšší než dvojnásobek normální laboratorní hodnoty
- Krevní destičky při příjmu < 30 000
- Existující neurologické nebo psychiatrické onemocnění, které by mohlo zmást výsledky studie
- Známá závažná alergie na kontrastní látku
- Nekontrolovaná hypertenze (definovaná jako systolický krevní tlak > 185 mm Hg nebo diastolický krevní tlak > 110 mm Hg)
- CT důkazy níže uvedených stavů při příjmu:
  - Významný masivní efekt s posunem středové čáry
  - Velká oblast hypodenzity > 1/3 území střední mozkové artérie
  - Důkazy nitrolebečního krvácení
- Angiografické důkazy arteriální stenózy proximálně k okluzi, která by mohla zabránit odstranění trombu
- Angiografické důkazy existujícího poranění artérie
- Očekávaná doba života kratší než 90 dnů
- Účast v jiném klinickém hodnocení, která by mohla zmást vyhodnocení hodnoceného prostředku

Souhrn důvodů pro vyloučení zařazených pacientů, obzvláště těch, které jsou založeny na angiografických kritériích
Žádný zařazený pacient nebyl vyloučen z angiografických důvodů.

Primární cílový parametr účinnosti
Primárním cílovým parametrem účinnosti byla revaskularizace okludované cílové cévy. Revaskularizace byla definována jako TIMI skóre II nebo III po použití pouze systému Penumbra System a před použitím dalších nebo podpůrných zařízení nebo terapií. Angiografické výsledky hodnotila nezávislá centrální laboratoř.

Účinnost	% (n/N) [95 % interval spolehlivosti]†
Primární cílový parametr účinnosti (TIMI skóre II nebo III) *Jsou použita TIMI skóre před použitím podpůrné léčby*	81,6 % (102/125) [73,7 %, 88,0 %]
Úspěch po revaskularizaci pomocí prostředku (TIMI ≥ 2) *Každé použití podpůrné léčby se považuje za selhání léčby*	81,6 % (102/125) [73,7 %, 88,0 %]
Úspěch po revaskularizaci pomocí prostředku (TIMI ≥ 2) *Každé použití intraarteriální lytické terapie se považuje za selhání léčby*	81,6 % (102/125) [73,7 %, 88,0 %]

†Přesné intervaly spolehlivos i podle Clopper-Pearsona

Primární cílový parametr bezpečnosti
Primárním cílovým parametrem bezpečnosti byl výskyt závažné nežádoucí příhody související s prostředkem nebo zákrokem, ke kterému došlo při zákroku podle hlášení zkoušejícího. U 16 pacientů bylo hlášeno 18 příhod při zákroku (12,8 %). Z nich 4 příhody u 3 pacientů byly výborem pro klinické příhody vyhodnoceny jako závažné (2,4 %).

Kompozitní nežádoucí příhody při zákroku	% (n/N) [95 % interval spolehlivosti]†
Kompozitní závažné nežádoucí příhody při zákroku	2,4 % (3/125)
Primární cílový parametr bezpečnosti: Kompozitní závažné nežádoucí příhody při zákroku související se zákrokem/zařízením	2,4 % (3/125)

†Přesné intervaly spolehlivos i podle Clopper-Pearsona

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Každá specifická závažná nežádoucí příhoda, která nastala v období do 90 dnů u více než 2 % pacientů

Závažná nežádoucí příhoda	% (n/N)
Kompozitní závažné nežádoucí příhody	52,0 % (65/125)
Mozkový edém	11,2 % (14/125)
Nitrolebeční krvácení	8,0 % (10/125)
Respirační dysfunkce/selhání	8,0 % (10/125)
Zhoršující se příznaky kvalifikující se mozkové příhody	7,2 % (9/125)
Infekce	5,6% (7/125)
Jiné plicní komplikace	5,6% (7/125)
Zápal plic	4,0 % (5/125)
Srdeční arytmie	3,2 % (4/125)
Komplikace v místě vstupu	2,4 % (3/125)
Infarkt myokardu	2,4 % (3/125)
Periferní vaskulární komplikace	2,4 % (3/125)
Renální dysfunkce/selhání	2,4 % (3/125)
Mozková příhoda v novém území	2,4 % (3/125)

Kategorizace nežádoucích příhod po období 90 dnů podle anatomických systémů

Anatomický systém	% (n/N)
Poruchy nervového systému	62,4 % (78/125)
Infekce a infestace	44,0 % (55/125)
Srdeční poruchy	28,8 % (36/125)
Poruchy metabolismu a výživy	25,6 % (32/125)
Celkové poruchy a reakce v místě apl kace	24,8 % (31/125)
Respirační, hrudní a mediastinální poruchy	24,8 % (31/125)
Poranění, otravy a procedurální komplikace	18,4 % (23/125)
Gastrointestinální poruchy	16,0 % (20/125)
Poruchy krve a lymfatického systému	14,4 % (18/125)
Cévní porucha	11,2 % (14/125)
Psychiatrické poruchy	10,4% (13/125)
Poruchy ledvin a močových cest	8,0 % (10/125)
Poruchy jater a žlučových cest	4,0 % (5/125)
Vyšetření	3,2 % (4/125)
Poruchy kůže a podkožní tkáně	3,2 % (4/125)
Novotvary benigní, maligní a blíže neurčené (zahrnující cysty a polypy)	2,4 % (3/125)
Poruchy svalové a kosterní soustavy a pojivové tkáně	0,8 % (1/125)

VYSVĚTLENÍ SYMBOLŮ

		Pozor, prostudujte návod k použití	
Rx Only		Pouze na lékařský předpis – federální zákony USA omezují použití tohoto prostředku jen na lékaře nebo na lékařský předpis	
		Nepyrogenní	
STER LE EO		Sterilizováno ethylenoxidem	
	Výrobce	EC REP	Pověřený zástupce pro EU
LOT	Číslo šarže		Nepoužívejte opakovaně
	Použitelné do	REF	Katalogové číslo
	Neprovádějte resterilizaci	LATEX	Neobsahuje latex

ZÁRUKA

Společnost Penumbra, Inc., (Penumbra) zaručuje, že konstrukci a výrobě tohoto prostředku byla věnována přiměřená péče. Tato záruka je jediným vyjádřením záručních podmínek a vylučuje jakékoli jiné záruky, které zde nejsou výslovně uvedeny, ať se jedná o záruky vyjádřené, či mlčky předpokládané na základě právních předpisů či na jiném základě, mimo jiné také včetně všech předpokládaných záruk prodejnos i či připravenosti k určitému účelu. Manipulace, uskladnění, čištění a sterilizace tohoto prostředku, stejně jako další faktory vztahující se k pacientovi, diagnóze, léčbě, chirurgickým postupům a další problematice, která je mimo kontrolu společnosti Penumbra, mají přímý vliv na prostředek a na výsledky jeho použití. Závazky společnosti Penumbra, vyplývající z této záruky, jsou omezeny na opravu nebo výměnu tohoto prostředku a společnost Penumbra není zodpovědná za žádné náhodné nebo následné ztráty, škody ani výdaje přímo nebo nepřímo vyplývající z použití tohoto prostředku. Společnost Penumbra nepřebírá žádnou jinou nebo další odpovědnost v souvislos i s tímto prostředkem, ani v tomto smyslu neopravňuje žádnou osobu. Společnost Penumbra nepřebírá žádnou odpovědnost za prostředky, které byly opakovaně používány, oše řeny nebo sterilizovány, a k takovým prostředkům neposkytuje žádné záruky, ať vyjádřené, nebo mlčky předpokládané, mimo jiné ani záruku jejich prodejnosti nebo připravenosti k určitému účelu.

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Dansk

Produktbeskrivelse

Penumbra System® består af flere forskellige dele:

- Penumbra-reperfusionskateter
- Penumbra-aspirationspumpe
- Penumbra-pumpe/cylinderrør
- Penumbra-aspirationsslange
- Penumbra-separator

Penumbra System er beregnet til at fjerne tromber i vaskulaturen ved brug af kontinuerlig aspiration. Reperfusionskatetret er beregnet til at aspirere fra pumpen direkte til tromben. Separatoren kan bruges til at rydde lumen i reperfusionskateteret, hvis det bliver blokeret pga. tromben. Det er muligvis ikke nødvendigt at benytte separatoren, hvis et reperfusionskateter anvendes, som har en indv. diam. på 1,37 mm (0,054 tommer) eller større. Reperfusionskatetret indføres gennem et ledekateter eller et langt femoralt hylster og ind i den intrakraniale vaskulatur og føres over en neurovaskulær guidewire til det sted, hvor den primære okklusion er. Penumbra-reperfusionskatetret bruges sammen med aspirationspumpen til aspiration af tromben fra det okkluderede kar. Penumbra-separatoren kan efter behov anlægges fra reperfusionskatetret som en hjælp til fjernelse af tromben. Penumbra-separatoren føres fremad og trækkes tilbage igennem Penumbra-reperfusionskatetret ved den proksimale kant af den primære okklusion, hvor den letter fjernelsen af tromben fra reperfusionskatetrets spids. Som aspirationskilde anvendes Penumbra-reperfusionskatetret sammen med aspirationspumpen, som tilkobles vha. Penumbra-aspirationslangen og Penumbra-pumpen/-cylinderrøret. Penumbra-reperfusionskatetret leveres med en dorn til dampformning og en roterende hæmostaseventil samt et aftageligt hylster. Penumbra-separatoren leveres desuden med en indførings- og vridningsanordning. Disse anordninger kan ses under fluoroskopi.

Tilsigtet anvendelse

Penumbra System er beregnet til brug ved revaskularisering af patienter med akut iskæmisk apopleksi sekundært til intrakranial okklusionssygdom af store kar (a. carotis interna, a. cerebri media – M1- og M2-segmenter, a. basilaris og a. vertebralis) inden for 8 timer efter start af symptomer.

Kontraindikationer

Der er ingen kendte kontraindikationer.

Advarsler

- Penumbra System bør kun anvendes af læger, der har modtaget den relevante uddannelse i neurovaskulære interventionsteknikker og behandling af akut iskæmisk apopleksi.
- Hverken instrumentet eller nogen del af Penumbra System må fremføres, trækkes tilbage eller anvendes, hvis der mærkes modstand, uden nøje vurdering af årsagen ved brug af fluoroskopi. Hvis årsagen ikke kan påvises, skal instrumentet eller systemet trækkes tilbage som en enhed. Ubehersket vridning eller tvungen indsætning af katetret eller separatoren under modstand kan resultere i beskadigelse af instrumentet eller karret.
- Penumbra System må ikke anvendes med andre pumper end Penumbra-aspirationspumpen.

Forholdsregler

- Instrumentet er kun beregnet til engangsbrug. Må ikke resteriliseres eller genanvendes. Resterilisering og/eller genanvendelse kan resultere i virkningsløs smøring af katetrets belægning, hvilket kan resultere i høj modstand og manglende evne til at opnå adgang til det ønskede sted i den neurologiske vaskulatur.
- Instrumentet må ikke anvendes, hvis det er knækket eller beskadiget. Pakker må ikke anvendes, hvis de er åbnede eller beskadigede. Returner alle beskadigede instrumenter med emballage til producenten/forhandleren.
- Anvendes før udløbsdatoen.
- Anvend Penumbra System med gennemlysning.
- Under aspirationen skal det sikres, at Penumbra-aspirationsslangens ventil kun er åben, så længe det varer at fjerne tromben. For kraftig aspiration eller undladelse af at lukke Penumbra-aspirationsslangens ventil efter udførelsen af aspirationen anbefales ikke.
- Penumbra-separatoren er ikke beregnet til brug som en neurovaskulær guidewire. Hvis det er nødvendigt at omplacere Penumbra-reperfusionskatetret i løbet af revaskulariseringsproceduren, skal dette gøres over den korrekte type neurovaskulær guidewire ved brug af standard mikrokateter- og guidewireteknikker.
- Brug ikke trykinjektionsudstyr til kontraststoffet sammen med Penumbra-reperfusionskatetret, da dette udstyr kan beskadige instrumentet.
- Administration af antikoagulantika og trombocythæmmende midler må først finde sted 24 timer efter behandlingen. Den medicinske behandling og akutte pleje efter apopleksien skal følge ASA-retningslinjerne.[1] Enhver form for neurologisk svækkelse skal straks evalueres med CT-scanning og andre evalueringer som indiceret, i overenstemmelse med investigatorens/hospitalets praksis.
- Den samlede tid, der er tilladt til at opnå revaskularisering af patienten, er 120 minutters brug af Penumbra System.

Mulige uønskede hændelser

Mulige komplikationer inkluderer, men er ikke begrænset til, følgende:

- akut okklusion
- allergisk reaktion og anafylaksi pga. kontraststof
- arteriovenøs fistel
- dannelse af falsk aneurisme
- distal embolisering
- død
- emboli
- hæmatom eller blødning på adgangsstedet
- infektion
- instrumentfejl
- intrakranial hæmoragi
- iskæmi
- karspasme, trombose, dissektion eller perforering
- luftemboli
- manglende evne til at fjerne tromben helt
- neurologisk deficit, inklusive apopleksi
- nyreskader forårsaget af kontraststoffer

Procedure

1. Der henvises til **Advarsler, Forholdsregler** og **Mulige uønskede hændelser** inden brug.
2. Når hvert instrument i Penumbra System bruges, skal det tages ud af emballagen og inspiceres for tegn på skader eller knæk.
3. Klargør Penumbra System instrumenterne ved at skylle emballageringen og instrumentet med hepariniseret saltvand (kun Penumbra-reperfusionskatetret og Penumbra-separatoren).

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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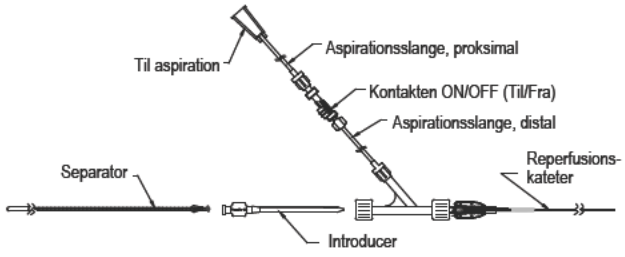
4. Klargør et ledekateter eller et langt femoralt hylster i hht. producentens *brugsanvisning*.
5. Placer ledekatetret eller det lange femorale hylster i den hjernearterie, der ligger proksimalt for okklusionsstedet med tromben.

Klargøring og brug af Penumbra-reperfusionskatetret

1. Bekræft karrets diameter, og vælg et Penumbra-reperfusionskateter i rette størrelse (se **Tabel 1**).
2. Spidsen på Penumbra-reperfusionskatetret kan formes ved hjælp af den vedlagte dorn til dampformning.
3. Fastgør den vedlagte roterende hæmostaseventil til Penumbra-reperfusionskatetret.
4. Fastgør Penumbra-aspirationsslangen til aspirationspumpen, og tænd for aspirationspumpen (der henvises til aspirationspumpens *brugervejledning*). Lad aspirationspumpen køre i mindst et minut før brug og bekræft, at aspirationsmåleren står på -508 mmHg (-20 inHg). Sørg for, at ventilen på Penumbra-aspirationsslangen står på OFF (Fra).
5. Slut aspirationsslangen til sideporten på den roterende hæmostaseventil som vist på **Figur 1**.

Figur 1 – Samlet aspirationssystem med Penumbra-separator



6. Sæt Penumbra-reperfusionskatetret ind i en roterende hæmostaseventil, der er koblet til den proksimale muffe på et ledekateter. Hvis et ledekateter ikke anvendes, føres Penumbra-reperfusionskatetret igennem ventilen på det lange femorale hylster vha. det aftagelige hylster. Efter indføring af Penumbra-reperfusionskatetret fjernes det aftagelige hylster fra den vaskulære sheath og fra Penumbra-reperfusionskatetrets skaft.
7. Brug konventionelle kateterisationsteknikker under gennemlysning, og før Penumbra-reperfusionskatetret fremad ind i målkarret hen over den korrekte type neurovaskulær guidewire. Anlæg Penumbra-reperfusionskatetret proksimalt for tromben. Fjern guidewiren fra Penumbra-reperfusionskatetret.
8. Indled aspirationen ved at åbne ventilen på Penumbra-aspirationsslangen til positionen ON (Til). Sæt ventilen på Penumbra-aspirationsslangen på OFF (Fra) for at standse aspiration, og sluk for aspirationspumpen.
9. Aspirer ca. 5 ml blod fra Penumbra-reperfusionskatetret med en 5 eller 10 ml sprøjte for at fjerne en eventuel trombe, der stadig er i katetret.
10. Tag et angiogram efter indgrebet ved at injicere kontraststof gennem ledekatetret.

Klargøring og brug af Penumbra-separatoren

1. Hvis det er nødvendigt vælges en Penumbra-separator i rette størrelse, svarende til reperfusionskatetret (se **Tabel 1**).

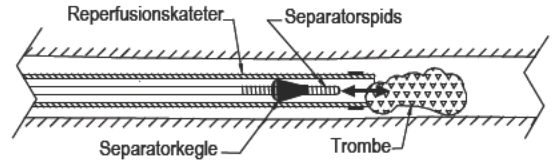
Tabel 1 – Valg af størrelser på separator/reperfusionskateter

Karstørrelse (mm)	Penumbra-reperfusionskateter	Penumbra-separator
< 2,0	026	026
2,0 til 3,0	032 / 3MAX	032 / 3MAX
3,0 til 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

BEMÆRK: Adgang til okklusionsstedet kan lettes ved triaksial brug af et kompatibelt indvendigt mikrokateter.

2. Anvend den vedlagte indføringssheath til at indsætte Penumbra-separatoren gennem den roterende hæmostaseventil og ind i den proksimale muffe på Penumbra-reperfusionskatetret.
3. Åbn ventilen på Penumbra-aspirationsslangen, så den står på ON (Til) for at påbegynde aspiration, og fremfør/tilbagetræk derefter Penumbra-separatoren som en hjælp til aspiration og fjernelse af tromben fra reperfusionskatetret som vist i **Figur 2**.

Figur 2 – Trombeaspiration med Penumbra-separatoren



4. Sæt ventilen på Penumbra-aspirationsslangen på OFF (Fra) for at standse aspiration, og sluk for aspirationspumpen.
5. Fjern Penumbra-separatoren, hvis den blev anvendt.
6. Hvis det er nødvendigt, kan der efter lægens skøn bruges yderligere Penumbra-separatorer og Penumbra-reperfusionskatetre til yderligere at fjerne tromber.

Oversigt over kliniske data

Det pivotale Penumbra-forsøg var et prospektivt enkelt-arms forsøg, der vurderede sikkerheden og effektiviteten af Penumbra System. I alt 125 patienter blev tilmeldt på 24 internationale centre. Primære kriterier for deltagelse var en NIHSS score på ≥ 8, udvisning af tegn inden for 8 timer fra start af symptomer, og en okklusion (TIMI 0 eller 1) i et intrakranialt kar, som kunne behandles. Patienter, som udviste tegn inden for 3 timer fra start af symptomerne, har ikke opfyldt kravene for behandling med rtPA eller har været terapiresistente. Primære endepunkter var revaskularisering af målkarret (TIMI 2 eller 3) og forekomst af procedurerelaterede alvorlige uønskede hændelser (SAE). Alle patienter blev fulgt op og evalueret op til 90 dage efter proceduren.

Statistisk analyse

En prøvestørrelse på 125 blev valgt til dette forsøg for at finde mindst 115 evaluerbare patienter. En patient blev anset for evaluerbar, hvis patienten opfyldte deltagelseskravene for evalueringen af primære endepunkter og blev behandlet med Penumbra System. Da dette var et ikke-kontrolleret forsøg, var der ikke planlagt en test af en formel hypotese for den samlede responsrate til etablering af en TIMI-grad på 2 eller 3. Den beskrivende standardstatistik for kategoriske endepunkter var antallet og procentdelen af patienter med hvert

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endepunktsniveau. For numeriske endepunkter inkluderede den beskrivende standardstatistik antallet af ikke-manglende observationer (n), middelværdi, median, standardafvigelse, minimumsværdi og maksimumsværdi.

Forsøgsprocedurer
Adgang til målkarret blev opnået ved brug af standard perkutan teknik og digital subtraktionsangiografi for fire kar for at definere den angiografiske arkitektur af det okkluderede karsegment. Det var et krav, at hver patient fik den cerebrale karokklusion bekræftet med angiografi og at et sted for den primære okklusion blev udpeget på forhånd af investigatoren. Hvis okklusionen forekom i et kar, der kunne behandles, blev et ledekateter i rette størrelse anlagt, og Penumbra-reperfusionskatetret blev ført fremad til den proksimale ende af det okkluderede målkar. En patient blev anset for at deltage, når reperfusionskatetret blev anlagt fra ledekatetret.

Vigtigste inklusionskriterier
- Kliniske tegn, som stemte overens med akut iskæmisk apopleksi, herunder:
  - pludselig følelsesløshed eller svaghed i ansigt eller ekstremiteter
  - pludselig forvirring, talebesvær eller vanskeligt at forstå tale
  - pludselige problemer med at gå, svimmelhed eller tab af balance
- Mellem 18 og 79 år
- Neurologisk deficit resulterende i en NIHSS-score på ≥ 8
- Komplet okklusion (TIMI-grad 0) eller kontraststofpenetration med minimal perfusion men uden fyldning af distale kargrene (TIMI-grad I) i intrakraniale kar, til hvilke Penumbra System til apopleksi havde adgang
- Underskrevet samtykkeerklæring
- Til stede inden for 8 timer fra start af symptomer
- Opfyldte ikke krav eller var terapiresistent over for intravenøs rtPA, hvis udviste tegn inden for 3 timer fra start af symptomer

Vigtigste eksklusionskriterier
- Tegn på hurtig forbedring af neurologiske tegn på apopleksi på indrulleringsstidspunktet
- NIHSS > 30 eller coma
- Kvinder, der er gravide
- Slyngede kar, der gjorde endovaskulær adgang for vanskelig
- Kendt blødningsdiatese, koagulationsdefekt eller fik oral antikoagulationsbehandling med INR på > 3,0
- PTT mere end 2 gange laboratoriets normalværdi
- Trombocyttal ved indlæggelse på < 30.000
- Neurologisk eller psykisk lidelse i anamnesen, der kunne påvirke forsøgsresultaterne
- Kendt alvorlig allergisk reaktion over for kontraststof
- Ukontrolleret hypertension (defineret som systolisk blodtryk på > 185 mmHg eller diastolisk blodtryk på > 110 mmHg)
- CT-baserede tegn på følgende tilstande ved præsentation:
  - Betydelig masseeffekt med midlinjeskift
  - Stort hypodensitetsområde på > 1/3 af midterste del af arteria cerebri-område
  - Bevis på intrakranial hæmoragi
- Angiografiske tegn på arteriel stenose proksimalt for okklusionen, der kunne forhindre fjernelse af trombe
- Angiografiske tegn på præeksisterende arteriel skade
- Forventet levetid på under 90 dage
- Deltagelse i anden klinisk forskning, der kunne påvirke evalueringen af dette system

Oversigt over årsager til eksklusion af indrullerede forsøgspersoner, især årsager baseret på angiografiske kriterier
Ingen indrulleret patient blev ekskluderet af angiografiske årsager.

Primært endepunkt for effektivitet
Det primære endepunkt for effektivitet var revaskularisering af det okkluderede målkar. Revaskularisering blev defineret vha. en TIMI-score på II eller III efter brug udelukkende af Penumbra System og før brug af yderligere eller andre alternative systemer eller behandlinger. Angiografiske resultater blev bedømt af et selvstændigt centrallaboratorium.

Effektivitet	% (n/N) [95 % CI]†
Primært endepunkt for effektivitet (TIMI-score på II eller III) *TIMI-scorer før anvendelse af andre behandlinger*	81,6 % (102/125) [73,7 %, 88,0 %]
Effektivitet af revaskularisering efter brug af system (TIMI ≥ 2) *Brug af andre behandlinger anset for mislykket behandling*	81,6 % (102/125) [73,7 %, 88,0 %]
Effektivitet af revaskularisering efter brug af system (TIMI ≥ 2) *Brug af intra-arteriel lytisk behandling anset for mislykket behandling*	81,6 % (102/125) [73,7 %, 88,0 %]

†Clopper-Pearson (exact-metode) konfidensintervaller

Primært endepunkt for sikkerhed
Det primære endepunkt for sikkerhed var incidensen af system- og/eller procedurerelaterede alvorlige uønskede hændelser, der opstod i løbet af proceduren som rapporteret af investigatoren. Der blev rapporteret 18 procedurerelaterede hændelser hos 16 patienter (12,8 %). Blandt disse blev 4 hændelser hos 3 patienter kategoriseret som alvorlige af CEC (Clinical Events Committee) (2,4 %).

Sammenlagte uønskede hændelser i løbet af proceduren	% (n/N) [95 % CI]†
Sammenlagte SAE'er i løbet af proceduren	2,4 % (3/125)
Primært endepunkt for sikkerhed: Sammenlagte procedure-/systemrelaterede SAE'er under proceduren	2,4 % (3/125)

†Clopper-Pearson (exact-metode) konfidensintervaller

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Hver specifik SAE i løbet af 90 dage, som opstod hos mere end 2 % af patienter

Alvorlige uønskede hændelser (SAE)	% (n/N)
Sammenlagte SAE'er	52,0 % (65/125)
Hjerneødem	11,2 % (14/125)
Hjerneblødning	8,0 % (10/125)
Åndedrætsbesvær/-svigt	8,0 % (10/125)
Forværring af symptomer på kvalificerende apopleksi	7,2 % (9/125)
Infektion	5,6 % (7/125)
Andre lungekomplikationer	5,6 % (7/125)
Lungebetændelse	4,0 % (5/125)
Hjertearytmier	3,2 % (4/125)
Komplikationer på adgangssted	2,4 % (3/125)
Myokardieinfarkt	2,4 % (3/125)
Perifer vaskulær komplikation	2,4 % (3/125)
Nedsat nyrefunktion/nyresvigt	2,4 % (3/125)
Apopleksi i nyt område	2,4 % (3/125)

Kategorisering af uønskede hændelser i løbet af 90 dage under anatomisk system

Anatomisk system	% (n/N)
Lidelser i nervesystem	62,4 % (78/125)
Infektioner og infestationer	44,0 % (55/125)
Hjertesygdomme	28,8 % (36/125)
Stofskifte- og ernæringssygdomme	25,6 % (32/125)
Generelle lidelser og forhold på administrationssted	24,8 % (31/125)
Respiratoriske, torakale og mediastinale lidelser	24,8 % (31/125)
Tilskadekomst, forgiftning og procedurerelaterede kompl kationer	18,4 % (23/125)
Mave-tarm-lidelser	16,0 % (20/125)
Lidelser i blod og lymfesystem	14,4 % (18/125)
Karsygdomme	11,2 % (14/125)
Sindslidelser	10,4 % (13/125)
Nyre- og urinvejslidelser	8,0 % (10/125)
Lever-/galdesygdomme	4,0 % (5/125)
Undersøgelser	3,2 % (4/125)
Sygdomme i hud og subkutant væv	3,2 % (4/125)
Neoplasmer - benigne, maligne og uspecificerede (inkl. cyster og polypper)	2,4 % (3/125)
Muskuloskeletale og bindevævslidelser	0,8 % (1/125)

SYMBOLFORKLARING

		Bemærk: Se brugsanvisning	
Rx Only		Receptpligtig – Ifølge amerikansk lovgivning må anordningen kun bruges af en læge eller på dennes anvisning	
		Ikke-pyrogen	
STER LE EO		Steril (ethylenoxid)	
	Producent	EC REP	Forhandler i EU
LOT	Lotnr.		Kun til engangsbrug
	Anvendes inden	REF	Katalognummer
STERILIZE	Må kke resteriliseres	LATEX	Latexfri

GARANTI

Penumbra, Inc. (Penumbra) garanterer, at al rimelig omhu er anvendt ved instrumentets udformning og fremstilling. Denne garanti træder i stedet for og udelukker alle andre garantier, der ikke udtrykkeligt nævnes heri, hvad enten garantierne er udtrykkelige eller underforståede ifølge loven eller på anden måde, inklusive, men ikke begrænset til, underforståede garantier om salgbarhed eller egnethed til bestemt anvendelse. Håndtering, opbevaring, rengøring og sterilisering af dette instrument samt andre faktorer, der vedrører patienten, diagnosen, behandlingen, kirurgiske procedurer og andre forhold, der er uden for Penumbras kontrol, påvirker direkte produktet og resultaterne opnået ved dets anvendelse. Penumbras forpligtelser i henhold til denne garanti begrænses til reparation eller udskiftning af dette instrument, og Penumbra hæfter ikke for nogen som helst følgeskade eller driftstab, beskadigelse eller udgift opstået direkte eller indirekte som følge af produktets anvendelse. Penumbra hverken påtager sig eller autoriserer andre personer til på sine vegne at påtage sig yderligere ansvar i forbindelse med dette instrument. Penumbra påtager sig intet ansvar med hensyn til genbrugte, omarbejdede eller resteriliserede instrumenter og giver ingen garanti, udtrykt eller underforstået, inklusive, men ikke begrænset til, salgbarhed eller egnethed til bestemt anvendelse af et sådant instrument.

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Svenska

Produktbeskrivning

Penumbra System® består av flera anordningar:

- Penumbra reperfusionskateter
- Penumbra aspirationspump
- Penumbra pump-/behållarslang
- Penumbra aspirationsslang
- Penumbra avskiljare

Penumbra System är avsett för att avlägsna tromber från kärlsystemet genom kontinuerlig aspiration. Reperfusionskatetern riktar aspirationen från pumpen direkt mot tromben. Avskiljaren kan användas för att rensa reperfusionskateterns lumen om det skulle blockeras av en tromb. Det är eventuellt inte nödvändigt att använda avskiljaren vid användning av en reperfusionskateter med en ID på 1,37 mm (0,054 tum) eller större. Reperfusionskatetern förs genom en styrkateter eller en lång femoralishylsa in i den intrakraniella vaskulaturen och över en neurovaskulär ledare till det primära ocklusionsstället. Penumbra reperfusionskateter används tillsammans med aspirationspumpen för att aspirera en tromb från ett ockluderat kärl. Vid behov kan en Penumbra avskiljare utplaceras från reperfusionskatetern för att underlätta avlägsnandet av tromben. Penumbra avskiljare förs fram och dras tillbaka genom Penumbra reperfusionskateter i den primära ocklusionens proximala kant för att underlätta avlägsnande av tromben från reperfusionskateterns spets. Aspirationskällan består av Penumbra reperfusionskateter i kombination med aspirationspumpen, som är ansluten med hjälp av Penumbra aspirationsslang och Penumbra pump-/behållarslang. Penumbra reperfusionskateter levereras med en ångformningsmandrin och en roterande hemostasventil samt en avskalbar hylsa. Penumbra avskiljare levereras med en introducer och en åtdragningsanordning. Anordningarna är synliga under fluoroskopi.

Indikationer för användning

Penumbra System är avsett att användas för revaskularisering hos patienter som drabbats av akut ischemisk stroke sekundärt till en ocklusiv sjukdom i ett stort intrakraniellt kärl (i inre halsartären, mellersta hjärnartären – segment M1 och M2, basilarartären och kotartärerna) inom 8 timmar efter de första symptomen.

Kontraindikationer

Det finns inga kända kontraindikationer.

Varningar

- Penumbra System får användas endast av läkare som har genomgått lämplig utbildning inom interventionella neuroendovaskulära tekniker och behandling av akut ischemisk stroke.
- Om motstånd påträffas får ingen komponent i Penumbra System föras fram, dras tillbaka eller användas utan en föregående noggrann bedömning av orsaken med hjälp av fluoroskopi. Om orsaken inte kan fastställas ska anordningen eller systemet dras ut som en enda enhet. Okontrollerad vridning eller forcerad införing av katetern eller avskiljaren mot motstånd kan orsaka skada på anordningen eller kärlet.
- Använd inte Penumbra System tillsammans med någon annan pump än Penumbra aspirationspump.

Försiktighetsåtgärder

- Anordningen är avsedd endast för engångsbruk. Får inte omsteriliseras eller återanvändas. Omsterilisering och/eller återanvändning kan leda till ineffektiv smörjning av kateterbeläggningen, vilket kan orsaka hög friktion och oförmåga att skapa åtkomst till det neurovaskulära målstället.
- Använd inte knickade eller skadade anordningar. Använd inte öppna eller skadade förpackningar. Returnera alla skadade anordningar och förpackningar till tillverkaren/återförsäljaren.
- Används före ”Använd före”-datumet.
- Använd Penumbra System tillsammans med fluoroskopisk avbildning.
- Vid aspiration ska det säkerställas att ventilen på Penumbra aspirationsslang är öppen endast under den minimala tid som krävs för att avlägsna tromben. Alltför omfattande aspiration eller underlåtelse att stänga ventilen på Penumbra aspirationsslang när aspirationen har slutförts rekommenderas inte.
- Penumbra avskiljare är inte avsedd att användas som en neurovaskulär ledare. Om det blir nödvändigt att flytta Penumbra reperfusionskateter under revaskulariseringsingreppet ska en sådan förflyttning utföras över lämplig neurovaskulär ledare med standardtekniker med mikrokateter och ledare.
- Använd inte utrustning för automatisk högtrycksinjektion av kontrastmedel tillsammans med Penumbra reperfusionskateter eftersom detta kan skada anordningen.
- Administration av koagulationshämmande och blodplättshämmande medel bör inte ske förrän 24 timmar efter behandlingen. Sjukvårdshanteringen och akutvården efter stroke ska följa riktlinjerna från ASA.[1] En eventuell neurologisk försämring ska bedömas genom en akut DT-undersökning och andra bedömningar som är indicerade enligt sjukhusets bästa praxis.
- Den sammanlagda tid som är tillåten för att uppnå revaskularisering av patienten är 120 minuters användning av Penumbra System.

Möjliga biverkningar

Möjliga komplikationer inkluderar, men begränsas inte till, följande:

- akut ocklusion,
- allergisk reaktion mot och anafylaxis orsakad av kontrastmedlet,
- arteriovenös fistel,
- bildning av falskt aneurysm,
- distal embolisering,
- dödsfall,
- emboli,
- funktionsfel hos anordningen,
- hematom eller hemorragi vid åtkomststället,
- infektion,
- intrakraniell blödning,
- ischemi,
- kärlspasm, -trombos, -dissektion eller -perforation,
- luftemboli,
- neurologiska skador, inklusive stroke,
- njurskada orsakad av kontrastmedlet,
- oförmåga att avlägsna tromben fullständigt.

Ingrepp

1. Läs **Varningar, Försiktighetsåtgärder** och **Möjliga biverkningar** före användning.
2. Allteftersom du använder var och en av anordningarna i Penumbra System ska du ta ut anordningen från förpackningen och inspektera den avseende skada och avseende knickar.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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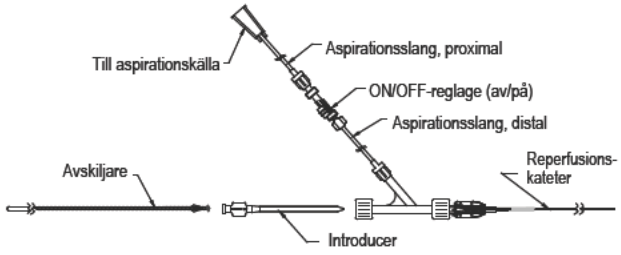
3. Förbered anordningarna i Penumbra System för användning genom att spola förpackningsringen och anordningen med hepariniserad koksaltlösning (omfattar endast Penumbra reperfusionskateter och Penumbra avskiljare).
4. Förbered en styrkateter eller en lång femoralishylsa enligt tillverkarens *bruksanvisning*.
5. Placera styrkatetern eller den långa femoralishylsan i lämplig hjärnartär som ligger proximalt om platsen med trombocklusion.

Förberedelse och användning av Penumbra reperfusionskateter

1. Bekräfta kärldiametern och välj en Penumbra reperfusionskateter i lämplig storlek (se **tabell 1**).
2. Spetsen på Penumbra reperfusionskateter kan formas med hjälp av den medföljande ångformningsmandrinen.
3. Fäst den medföljande roterande hemostasventilen vid Penumbra reperfusionskateter.
4. Anslut Penumbra aspirationsslang till aspirationspumpen och starta aspirationspumpen (se *användarhandboken* för aspirationspumpen). Låt aspirationspumpen gå i minst en minut innan den används. Kontrollera att det står -508 mmHg (-20 tumHg) på aspirationsmätaren. Kontrollera att ventilen på Penumbra aspirationsslang står i läget OFF (av).
5. Anslut aspirationsslangen till sidoporten på den roterande hemostasventilen, enligt **figur 1**.

Figur 1 – Monterat aspirationssystem med Penumbra avskiljare



6. För in Penumbra reperfusionskateter i en roterande hemostasventil ansluten till en styrkateters proximala fattning. Om ingen styrkateter används ska du föra in Penumbra reperfusionskateter genom ventilen på den långa femoralishylsan med hjälp av den avskalbara hylsan. Efter införingen av Penumbra reperfusionskateter avlägsnar du den avskalbara hylsan från den vaskulära hylsan och skalar av den från Penumbra reperfusionskateters skaft.
7. Använd konventionell katetriseringsteknik under fluoroskopisk vägledning för att föra fram Penumbra reperfusionskateter in i målkärlet över en lämplig neurovaskulär ledare. Placera Penumbra reperfusionskateter proximalt om tromben. Avlägsna ledaren från Penumbra reperfusionskateter.
8. Påbörja aspirationen genom att öppna ventilen på Penumbra aspirationsslang till läget ON (på). Stäng av aspirationen genom att ställa om ventilen på Penumbra aspirationsslang till läget OFF (av) och stäng av aspirationspumpen.
9. Använd en 5 ml- eller 10 ml-spruta och sug upp ca 5 ml blod från Penumbra reperfusionskateter för att avlägsna eventuella trombrester i katetern.
10. Ta ett angiogram efter behandlingen genom att injicera kontrastmedel genom styrkatetern.

Förberedelse och användning av Penumbra avskiljare

1. Välj en Penumbra avskiljare i lämplig storlek, motsvarande reperfusionskatetern (se **tabell 1**), vid behov.

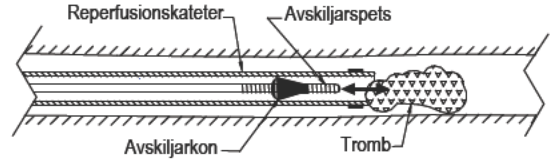
Tabell 1 – Val av anordningsstorlek för avskiljare/reperfusionskateter

Kärlstorlek (mm)	Penumbra reperfusionskateter	Penumbra avskiljare
< 2,0	026	026
2,0 till 3,0	032 / 3MAX	032 / 3MAX
3,0 till 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

ANMÄRKNING: Åtkomsten till ocklusionsstället kan underlättas genom treaxlig användning av en kompatibel inre mikrokateter.

2. Använd den medföljande introducerhylsan för att föra Penumbra avskiljare genom den roterande hemostasventilen och in i Penumbra reperfusionskateters proximala fattning.
3. Påbörja aspirationen genom att öppna ventilen på Penumbra aspirationsslang till läget ON (på) och för fram/dra tillbaka Penumbra avskiljare för att underlätta aspirationen och avlägsnandet av tromben från reperfusionskatetern, enligt **figur 2**.

Figur 2 – Trombaspiration med hjälp av Penumbra avskiljare



4. Stäng av aspirationen genom att ställa om ventilen på Penumbra aspirationsslang till läget OFF (av) och stäng av aspirationspumpen.
5. Avlägsna Penumbra avskiljare, om den har använts.
6. Vid behov kan fler Penumbra avskiljare och Penumbra reperfusionskatetrar användas, efter läkarens gottfinnande, i syfte att ytterligare reducera tromben.

Sammanfattning av kliniska data

Penumbra piråprövning var en prospektiv, enarmad prövning avsedd att bedöma säkerheten och effektiviteten hos Penumbra System. Sammanlagt 125 patienter enrollerades vid 24 internationella centra. De huvudsakliga ingångskriterierna var en poäng på NIH-strokeskalan (NIHSS) ≥ 8, att patienten infunnit sig inom 8 timmar efter de första symptomen och en ocklusion (TIMI 0 eller 1) i ett behandlingsbart intrakraniellt kärl. Patienter som infann sig inom 3 timmar efter de första symptomen fick inte vara tänkbara kandidater för eller måste ha visat sig behandlingsresistenta mot rtPA-behandling. De primära ändpunkterna var revaskularisering av målkärlet (TIMI 2 eller 3) och incidensen av ingreppsrelaterade allvarliga biverkningar. Alla patienter följdes upp och bedömdes under upp till 90 dagar efter ingreppet.

Statistisk analys

En provurvalsstorlek på 125 valdes för den här studien för att generera minst 115 utvärderingsbara patienter. En patient betraktades som utvärderingsbar om patienten uppfyllde kriterierna för bedömningen av den primära ändpunkten och behandlades med Penumbra System. Eftersom det här var en okontrollerad studie planerades inget formellt hypotestest för den

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övergripande svarsfrekvensen för att etablera en TIMI-poäng på 2 eller 3. Den beskrivande standardstatistiken för kategoriska ändpunkter bestod av antalet och procentandelen patienter med varje nivå av ändpunkten. Som numeriska ändpunkter omfattade den beskrivande standardstatistiken antalet icke-saknade observationer (n), medelvärdet, medianvärdet, standardavvikelsen, det lägsta värdet och det högsta värdet.

Studieingrepp
Arteriell åtkomst till målkärlet skapades med perkutan standardteknik och en digital subtraktionsangiografi av fyra kärl genomfördes för att fastställa det ockluderade kärlsegmentets angioarkitektur. Alla patienter måste få sin ocklusion i ett stort hjärnkärl bekräftad genom angiografi och ett primärt ocklusionsställe bestämt på förhand av prövaren. Om ocklusionen fanns i ett behandlingsbart kärl placerades en lämplig styrkateter och Penumbra reperfusionskateter fördes fram till det ockluderade målkärlets proximala ände. En patient ansågs ha enrollerats när reperfusionskatetern utplacerades från styrkatetern.

Huvudsakliga inklusionskriterier
- Kliniska tecken som tyder på akut ischemisk stroke, däribland följande:
  - Plötslig domning eller svaghet i ansikte eller extremiteter.
  - Plötslig förvirring, plötsligt uppkomna svårigheter att tala eller förstå tal.
  - Plötslig yrsel eller förlust av balansen eller plötsligt uppkomna gångsvårigheter.
- I åldrarna 18 till 79 år.
- Neurologiskt bortfall som leder till en poäng på NIH-strokeskalan (NIHSS) ≥ 8.
- Fullständig ocklusion (TIMI-poäng 0) eller kontrastmedelspenetrering med minimal perfusion men ingen fyllning av distala förgreningar (TIMI-poäng I) i intrakraniella kärl som är åtkomliga för Penumbra System för stroke.
- Undertecknat informerat samtycke.
- Infinner sig inom 8 timmar från de första strokesymptomen.
- Behandlingsresistent mot eller inte en tänkbar kandidat för intravenös rtPA-behandling om patienten infinner sig inom 3 timmar från de första symptomen.

Huvudsakliga exklusionskriterier
- Belägg för neurologiska tecken på stroke, som snabbt förbättras, vid tidpunkten för enrollering.
- NIHSS > 30 eller koma.
- Kvinnor som är gravida.
- Slingriga kärl som gör det för svårt att skapa endovaskulär åtkomst.
- Känd hemorragisk diates, koagulationsrubbning eller pågående behandling med koagulationshämmande läkemedel med ett INR-värde > 3,0.
- PTT över 2 gånger det normala laboratorieresultatet.
- Blodplättar vid inskrivning < 30 000.
- Sedan tidigare befintlig neurologisk eller psykiatrisk sjukdom som skulle kunna göra studieresultaten svåra att tolka.
- Känd allvarlig allergi mot kontrastmedel.
- Okontrollerad hypertoni (definieras som ett systoliskt blodtryck > 185 mmHg eller ett diastoliskt blodtryck > 110 mmHg).
- DT-belägg för följande tillstånd vid den tidpunkt då patienten infinner sig:
  - Signifikant masseffekt med förflyttning av mittlinjen.
  - Stort område med hypodensitet > 1/3 av mellersta hjärnartärens område.
  - Belägg för intrakraniell blödning.
- Angiografiska belägg för en arteriell stenos proximalt om ocklusionen som skulle kunna hindra avlägsnandet av tromben.
- Angiografiska belägg för sedan tidigare befintlig artärskada.
- Förväntad livslängd som är kortare än 90 dagar.
- Deltagande i en annan klinisk undersökning, som skulle kunna störa bedömningen av studieanordningen.

Sammanfattning av orsakerna till exklusion av enrollerade patienter, i synnerhet orsaker baserade på angiografiska kriterier
Inga enrollerade patienter exkluderades av angiografiska skäl.

Primär ändpunkt för effektivitet
Den primära ändpunkten för effektivitet var revaskularisering av det ockluderade målkärlet. Revaskularisering definierades som en TIMI-poäng på II eller III efter användning av endast Penumbra System och före användning av några som helst ytterligare eller kompletterande anordningar eller behandlingar. De angiografiska resultaten bedömdes av ett oberoende huvudlaboratorium.

Effektivitet	% (n/N) [95 % KI]†
Primär ändpunkt för effektivitet (TIMI-poäng på II eller III) *TIMI-poäng före användning av kompletterande behandlingar*	81,6 % (102/125) [73,7 %, 88,0 %]
Framgångsrik revaskularisering efter användning av anordningen (TIMI ≥ 2) *All eventuell användning av kompletterande behandling betraktas som ett misslyckande för behandlingen*	81,6 % (102/125) [73,7 %, 88,0 %]
Framgångsrik revaskularisering efter användning av anordningen (TIMI ≥ 2) *All eventuell användning av intraarteriell lytisk behandling betraktas som ett misslyckande för behandlingen*	81,6 % (102/125) [73,7 %, 88,0 %]

†Exakta Clopper-Pearson-konfidensintervall

Primär ändpunkt för säkerhet
Den primära ändpunkten för säkerhet var incidensen av anordnings- och/eller ingreppsrelaterade allvarliga biverkningar som uppstod under ingreppet, enligt vad som rapporterades av prövaren. 18 ingreppsrelaterade biverkningar rapporterades hos 16 patienter (12,8 %). Av dessa klassificerades 4 biverkningar hos 3 patienter som allvarliga av kommittén för kliniska händelser (CEC) (2,4 %).

Sammansatta biverkningar under ingreppet	% (n/N) [95 % KI]†
Sammansatta allvarliga biverkningar under ingreppet	2,4 % (3/125)
Primär ändpunkt för säkerhet: Sammansatta ingrepps-/anordningsrelaterade allvarliga biverkningar under ingreppet	2,4 % (3/125)

†Exakta Clopper-Pearson-konfidensintervall

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Varje specifik allvarlig biverkning under en 90 dagarsperiod som uppträdde hos över 2 % av patienterna

Allvarliga biverkningar	% (n/N)
Sammansatta allvarliga biverkningar	52,0 % (65/125)
Hjärnödem	11,2 % (14/125)
ICH	8,0 % (10/125)
Andningsinsufficiens eller andningssvikt	8,0 % (10/125)
Förvärrande av symptomen på kvalificerande stroke	7,2 % (9/125)
Infektion	5,6 % (7/125)
Övriga lungkomplikationer	5,6 % (7/125)
Pneumoni	4,0 % (5/125)
Hjärtarrytmi	3,2 % (4/125)
Komplikation på åtkomststället	2,4 % (3/125)
Hjärtinfarkt	2,4 % (3/125)
Perifer vaskulär komplikation	2,4 % (3/125)
Njurinsufficiens eller njursvikt	2,4 % (3/125)
Stroke i ett nytt område	2,4 % (3/125)

Kategorisering av biverkningar under en 90 dagarsperiod efter anatomiskt system

Anatomiskt system	% (n/N)
Centrala och perifera nervsystemet	62,4 % (78/125)
Infektioner och infestationer	44,0 % (55/125)
Hjärtat	28,8 % (36/125)
Metabolism och nutrition	25,6 % (32/125)
Allmänna symtom och/eller symtom vid administreringsstället	24,8 % (31/125)
Andningsvägar, bröstkorg och mediastinum	24,8 % (31/125)
Skador och förgiftningar och behandlingskomplikationer	18,4 % (23/125)
Magtarmkanalen	16,0 % (20/125)
Blodet och lymfsystemet	14,4 % (18/125)
Blodkärl	11,2 % (14/125)
Psykiska störningar	10,4 % (13/125)
Njurar och urinvägar	8,0 % (10/125)
Lever och gallvägar	4,0 % (5/125)
Undersökningar	3,2 % (4/125)
Hud och subkutan vävnad	3,2 % (4/125)
Neoplasier; benigna, maligna och ospecificerade (samt cystor och polyper)	2,4 % (3/125)
Muskuloskeletala systemet och bindväv	0,8 % (1/125)

SYMBOLFÖRKLARING

		Obs! Läs bruksanvisningen	
Rx Only		Receptbelagd – enligt USA:s federala lagstiftning får denna produkt endast användas av läkare eller på läkarordination	
		Icke-pyrogen	
STER LE EO		Steriliserad med etylenoxid	
	Tillverkare	EC REP	EU-representant
LOT	Partinummer		Får ej återanvändas
	Använd före	REF	Katalognummer
STERILIZE	Får ej omsteriliseras	LATEX	Latexfri

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Neder-lands

Beschrijving van het hulpmiddel

Het Penumbra System® bestaat uit verschillende hulpmiddelen:

- Penumbra-reperfusiekatheter
- Penumbra-aspiratiepomp
- Penumbra-pomp/container-slang
- Penumbra-aspiratieslang
- Penumbra-separator

Het Penumbra System dient voor de verwijdering van een trombus uit de vasculatuur met behulp van continue aspiratie. Via de reperfusiekatheter wordt de zuiging van de pomp rechtstreeks op de trombus gericht. Met de separator kan het lumen van de reperfusiekatheter worden vrijgemaakt indien dit geblokkeerd raakt met trombusmateriaal. Gebruik van de separator is mogelijk niet nodig wanneer een reperfusiekatheter met een binnendiameter van 1,37 mm (0,054 inch) of groter wordt gebruikt. De reperfusiekatheter wordt via een geleidekatheter of lange femorale schacht ingebracht in de intracraniale vasculatuur en over een neurovasculaire voerdraad opgevoerd naar de plaats van de primaire occlusie. De Penumbra-reperfusiekatheter wordt in combinatie met de aspiratiepomp gebruikt om een trombus weg te zuigen uit een geoccludeerd bloedvat. Zo nodig kan vanuit de reperfusiekatheter een Penumbra-separator worden uitgevouwen om de trombusverwijdering te ondersteunen. De Penumbra-separator wordt opgevoerd en teruggetrokken door de Penumbra-reperfusiekatheter aan de proximale rand van de primaire occlusie om verwijdering van de trombus vanaf de tip van de reperfusiekatheter te vergemakkelijken. Voor wat betreft de aspiratiebron wordt de Penumbra-reperfusiekatheter gebruikt in combinatie met de aspiratiepomp, die wordt aangesloten met behulp van de Penumbra-aspiratieslang en de Penumbra-pomp/container-slang. De Penumbra-reperfusiekatheter wordt geleverd met een stoomvormmandrijn en een draaiende hemostaseklep alsmede een pelbare schacht. De Penumbra-separator wordt geleverd met een introducer en een torsie-instrument. De hulpmiddelen zijn zichtbaar onder fluoroscopie.

Indicatie voor gebruik

Het Penumbra System is bedoeld voor gebruik bij de revascularisatie van patiënten met acute ischemische beroerte secundair aan een occlusie van de grote intracraniale vaten (in de a. carotis interna, a. cerebri media – segmenten M1 en M2, a. basilaris en a. vertebralis) binnen 8 uur na het optreden van de eerste symptomen.

Contra-indicaties

Er zijn geen contra-indicaties bekend.

Waarschuwingen

- Het Penumbra System mag alleen worden gebruikt door artsen met een passende opleiding in interventionele neuro-endovasculaire technieken en de behandeling van acute ischemische beroerte.
- Geen enkele component van het Penumbra System mag tegen weerstand in worden opgevoerd, teruggetrokken of gebruikt zonder eerst de oorzaak van de weerstand zorgvuldig fluoroscopisch te onderzoeken. Als de oorzaak niet kan worden vastgesteld, trek het hulpmiddel of systeem dan als één geheel terug. Ongeremde verdraaiing of geforceerde inbrenging van de katheter of separator tegen weerstand in kan tot beschadiging van het hulpmiddel of bloedvat leiden.
- Gebruik het Penumbra System niet met een andere pomp dan de Penumbra-aspiratiepomp.

Voorzorgsmaatregelen

- Het hulpmiddel is uitsluitend bestemd voor eenmalig gebruik. Niet opnieuw steriliseren of hergebruiken. Opnieuw steriliseren en/of hergebruik kan leiden tot ineffectieve smering van de kathetercoating, waardoor een hoge wrijving kan ontstaan en de doellocatie in de neurovasculatuur mogelijk niet kan worden bereikt.
- Gebruik geen geknikte of beschadigde hulpmiddelen. Gebruik geen open of beschadigde verpakkingen. Retourneer alle beschadigde hulpmiddelen en verpakkingen aan de fabrikant/distributeur.
- Gebruiken vóór de uiterste gebruiksdatum.
- Gebruik het Penumbra System in combinatie met fluoroscopische visualisatie.
- Zorg er bij het aspireren voor dat de klep van de Penumbra-aspiratieslang niet langer wordt opengehouden dan nodig is om de trombus te verwijderen. Overmatige aspiratie of het openhouden van de klep van de Penumbra-aspiratieslang wanneer de aspiratie is voltooid, wordt afgeraden.
- De Penumbra-separator is niet bedoeld voor gebruik als neurovasculaire voerdraad. Als het tijdens de revascularisatieprocedure nodig is de Penumbra-reperfusiekatheter te herpositioneren, dan moet dit over een geschikte neurovasculaire voerdraad worden gedaan met behulp van standaardtechnieken voor microkatheters en voerdraden.
- Er mag geen geautomatiseerde apparatuur voor hogedrukinjectie van contrastmiddel worden gebruikt, aangezien het hulpmiddel hierdoor kan beschadigen.
- Met de toediening van anticoagulantia en trombocytenaggregatieremmers moet worden gewacht tot 24 uur na de behandeling. Medische behandeling en acute zorg na een beroerte moeten voldoen aan de richtlijnen van de ASA.[1] Elke neurologische verslechtering moet met spoed worden onderzocht door middel van een CT-scan en andere onderzoeken op indicatie van de onderzoeker of volgens beste praktijken van het ziekenhuis.
- Bij gebruik van het Penumbra System bedraagt de totale tijd die is toegestaan om revascularisatie bij de patiënt bewerkstelligen 120 minuten.

Mogelijke ongewenste voorvallen

Mogelijke complicaties zijn onder meer, maar niet uitsluitend:

- acute occlusie
- allergische reactie en anafylaxie door contrastmiddel
- arterioveneuze fistel
- distale embolisatie
- embolie
- hematoom of bloeding op de toegangsplaats
- het niet volledig kunnen verwijderen van de trombus
- hulpmiddeldefect
- infectie
- intracraniale bloeding
- ischemie
- luchtembolie
- neurologische uitvalsverschijnselen waaronder beroerte
- nierschade door contrastmiddel
- overlijden
- vaatspasme, trombose, dissectie of perforatie
- vorming van een vals aneurysma

Procedure

1. Lees vóór gebruik de hoofdstukken **Waarschuwingen, Voorzorgsmaatregelen** en **Mogelijke ongewenste voorvallen**.
2. Verwijder elk hulpmiddel van het Penumbra System vóór gebruik uit de verpakking en inspecteer het op schade en knikken.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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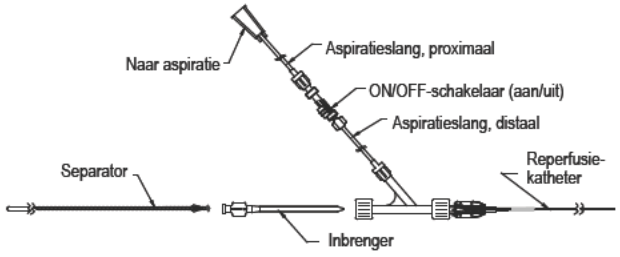
3. Maak hulpmiddelen van het Penumbra System klaar voor gebruik door de verpakkingsring en het hulpmiddel met gehepariniseerde zoutoplossing te spoelen (alleen voor de Penumbra-reperfusiekatheter en Penumbra-separator).
4. Maak een geleidekatheter of lange femorale schacht klaar voor gebruik volgens de *gebruiksaanwijzing* van de fabrikant.
5. Plaats de geleidekatheter of lange femorale schacht in de juiste cerebrale arterie, proximaal van de occlusieplaats met de trombus.

Voorbereiding en gebruik van de Penumbra-reperfusiekatheter

1. Controleer de vaatdiameter en kies een geschikte maat Penumbra-reperfusiekatheter (zie **tabel 1**).
2. De tip van de Penumbra-reperfusiekatheter kan gevormd worden met behulp van de meegeleverde stoomvormmandrijn.
3. Bevestig de meegeleverde draaiende hemostaseklep aan de Penumbra-reperfusiekatheter.
4. Sluit de Penumbra-aspiratieslang aan op de aspiratiepomp en zet de aspiratiepomp aan (zie de *gebruikshandleiding* van de aspiratiepomp). Laat de aspiratiepomp vóór gebruik ten minste één minuut draaien en controleer of de aspiratiemeter -508 mmHg (-20 inHg) aangeeft. Zorg dat de klep op de Penumbra-aspiratieslang in de OFF-stand (uit) staat.
5. Sluit de aspiratieslang aan op de zijpoort van de draaiende hemostaseklep; zie **afbeelding 1**.

Afbeelding 1 – Opgebouwd aspiratiesysteem met Penumbra-separator



6. Steek de Penumbra-reperfusiekatheter in een draaiende hemostaseklep die is aangesloten op het proximale aanzetstuk van de geleidekatheter. Als er geen geleidekatheter wordt gebruikt, steek de Penumbra-reperfusiekatheter dan met behulp van de pelbare schacht door de klep van de lange femorale schacht. Nadat u de Penumbra-perfusiekatheter hebt ingebracht, verwijdert u de pelbare schacht uit de vasculaire schacht en pelt u hem los van de schacht van de Penumbra-perfusiekatheter.
7. Met behulp van conventionele katheterisatietechnieken en onder fluoroscopische geleiding voert u de Penumbra-reperfusiekatheter over een geschikte neurovasculaire voerdraad op in het doelvat. Positioneer de Penumbra-reperfusiekatheter proximaal van de trombus. Verwijder de voerdraad uit de Penumbra-reperfusiekatheter.
8. Om de aspiratie te beginnen, opent u de klep op de Penumbra-aspiratieslang door hem in de ON-stand (aan) te zetten. Om de aspiratie te stoppen, zet u de klep op de Penumbra-aspiratieslang in de OFF-stand (uit) en schakelt u de aspiratiepomp uit.
9. Aspireer met een spuit van 5 ml of 10 ml ongeveer 5 ml bloed uit de Penumbra-reperfusiekatheter om eventueel in de katheter achtergebleven trombusmateriaal te verwijderen.
10. Maak na de behandeling een angiogram door contrastmiddel te injecteren door de geleidekatheter.

Voorbereiding en gebruik van de Penumbra-separator

1. Als een Penumbra-separator nodig is, kiest u een geschikte maat die overeenkomt met die van de reperfusiekatheter (zie **tabel 1**).

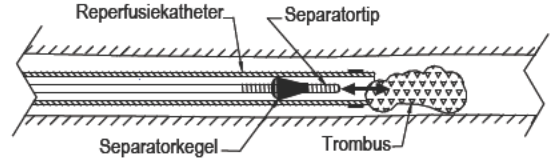
Tabel 1 – Keuze van de maat separator/reperfusiekatheter

Diameter bloedvat (mm)	Penumbra-reperfusiekatheter	Penumbra-separator
< 2,0	026	026
2,0 tot 3,0	032 / 3MAX	032 / 3MAX
3,0 tot 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

OPMERKING: De toegang tot de occlusieplaats kan worden vergemakkelijkt door triaxiaal gebruik van een compatibele inwendige microkatheter.

2. Steek met behulp van de bijgeleverde introducer-huls de Penumbra-separator door de draaiende hemostaseklep in het proximale aanzetstuk van de Penumbra-reperfusiekatheter.
3. Om de aspiratie te beginnen opent u de klep op de Penumbra-aspiratieslang door hem in de ON-stand (aan) te zetten, waarna u de Penumbra-separator opvoert/terugtrekt om de aspiratie en verwijdering van de trombus uit de reperfusiekatheter te ondersteunen; zie **afbeelding 2**.

Afbeelding 2 – Trombusaspiratie met de Penumbra-separator



4. Om de aspiratie te stoppen, zet u de klep op de Penumbra-aspiratieslang in de OFF-stand (uit) en schakelt u de aspiratiepomp uit.
5. Verwijder de Penumbra-separator, indien gebruikt.
6. Indien nodig kunnen extra Penumbra-separators en reperfusiekatheters worden gebruikt om de trombus verder te verwijderen. Dit is ter beoordeling van de arts.

Samenvatting van klinische gegevens

Het Penumbra hoofdonderzoek was een prospectief eenarmig onderzoek ter beoordeling van de veiligheid en effectiviteit van het Penumbra System. Er werden in totaal 125 patiënten in het onderzoek opgenomen, in 24 internationale centra. De voornaamste inclusiecriteria waren een score op de NIH Stroke Scale (NIHSS) ≥ 8, presentatie binnen 8 uur na het optreden van de eerste symptomen en een occlusie (TIMI 0 of 1) van een behandelbaar intracraniaal bloedvat. Voor patiënten die zich binnen 3 uur na de eerste symptomen presenteerden gold bovendien dat ze niet in aanmerking mochten komen voor of refractair moesten zijn tegen behandeling met rtPA ('recombinant tissue plasminogen activator'). Primaire eindpunten waren revascularisatie van het doelvat (TIMI 2 of 3) en de incidentie van procedure-gerelateerde ernstige ongewenste voorvallen ('serious adverse events', SAE's). Alle patiënten werden na de ingreep tot 90 dagen opgevolgd en onder controle gehouden.

Statistische analyse

Voor dit onderzoek werd een steekproefomvang van 125 gekozen om ten minste 115 evalueerbare patiënten te hebben. Een patiënt werd als evalueerbaar beschouwd als hij/zij voldeed aan de geschiktheidsvereisten voor beoordeling van de primaire eindpunten en was behandeld met het Penumbra System.

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Aangezien dit een niet-gecontroleerd onderzoek was, werd geen formele hypothesetest opgezet voor het totale responspercentage voor het bere ken van TIMI-graad 2 of 3. Standaard beschrijvende statistische maten voor categorische eindpunten waren het aantal en percentage patiënten met elk niveau van het eindpunt. De standaard beschrijvende statistische maten voor numerieke eindpunten omvatten het aantal niet-ontbrekende waarnemingen (n), het gemiddelde, de mediaan, de standaarddeviatie, de minimale waarde en de maximale waarde.

Onderzoeksprocedures
Met standaard percutane technieken werd arteriële toegang tot het doelvat verkregen, en er werd vier-vaten digitale subtractieangiografie uitgevoerd om de angioarchitectuur van het geoccludeerde vaatsegment te bepalen. Een vereiste was dat bij elke patiënt occlusie van een groot cerebraal vat angiografisch werd bevestigd en dat er van tevoren door de onderzoeker een plaats van primaire occlusie werd aangegeven. Als de occlusie zich in een behandelbaar bloedvat bevond, werd een geschikte geleidekatheter geplaatst en werd de Penumbra-reperfusiekatheter opgevoerd naar het proximale einde van het geoccludeerde doelvat. Een patiënt werd beschouwd als opgenomen in het onderzoek wanneer de reperfusiekatheter werd uitgevouwen vanuit de geleidekatheter.

Belangrijkste inclusiecriteria
- Klinische verschijnselen die kunnen wijzen op acute ischemische beroerte, waaronder:
  - plotselinge gevoelloosheid of zwakte in het gezicht of de ledematen
  - plotselinge verwardheid, moeite met spreken of met het begrijpen van wat anderen zeggen
  - plotselinge moeite met lopen, duizeligheid of verlies van het evenwichtsgevoel
- Leeftijd tussen 18 en 79 jaar
- Neurologische uitval resulterend in een score op de NIH Stroke Scale (NIHSS) ≥ 8
- Volledige occlusie (TIMI-graad 0) of penetratie van contrastmiddel met minimale perfusie maar zonder vulling van de distale tak (TIMI-graad 1) in intracraniale vaten die toegankelijk zijn voor het Penumbra System voor beroertes
- Ondertekende toestemmingsverklaring
- Presentatie binnen 8 uur na de eerste symptomen van beroerte
- Bij presentatie binnen 3 uur na de eerste symptomen: niet in aanmerking komend voor of refractair tegen intraveneuze rtPA-therapie

Belangrijkste exclusiecriteria
- Aanwijzingen voor snelle verbetering van neurologische verschijnselen van beroerte op het moment van opname in het onderzoek
- NIHSS > 30 of coma
- Zwangerschap
- Zodanig sterk gekronkelde vaten dat endovasculaire toegang te moeilijk is
- Bekende hemorragische diathese, stollingsfactordeficiëntie, of huidige orale antistollingstherapie met een INR-streefwaarde > 3,0
- PTT van meer dan 2 maal de normale laboratoriumwaarde
- Aantal bloedplaatjes bij opname < 30.000
- Reeds bestaande neurologische of psychische aandoening die de onderzoeksresultaten zou kunnen vertroebelen
- Bekende ernstige allergie voor contrastmiddel
- Hypertensie (gedefinieerd als een systolische bloeddruk > 185 mmHg of een diastolische bloeddruk > 110 mmHg) die niet onder controle is
- Bij presentatie CT-bewijs van de volgende condities:
  - aanzienlijk massa-effect met 'midline shift'
  - groot hypodens gebied, > 1/3 van het stroomgebied van de a. cerebri media
  - intracraniale bloeding
- Angiografisch bewijs van een arteriële stenose proximaal van de occlusie die verwijdering van de trombus zou kunnen verhinderen
- Angiografisch bewijs van reeds bestaand arterieel letsel
- Een levensverwachting van minder dan 90 dagen
- Deelname aan een ander klinisch onderzoek waardoor de evaluatie van het onderzoekshulpmiddel zou kunnen worden vertroebeld

Overzicht van redenen voor de exclusie van opgenomen patiënten, in het bijzonder redenen gebaseerd op angiografische criteria
Geen van de opgenomen patiënten werd om angiografische redenen geëxcludeerd.

Primaire effectiviteitseindpunt
Het primaire effectiviteitseindpunt was revascularisatie van het geoccludeerde doelvat. Revascularisatie werd gedefinieerd als een TIMI-score van 2 of 3 na gebruik van alleen het Penumbra System en vóór het gebruik van eventuele bijkomende of aanvullende hulpmiddelen of therapieën. De angiografische resultaten werden beoordeeld door een onafhankelijk kernlaboratorium.

Effectiviteit	% (n/N) [95% BI]†
Primaire effectiviteitseindpunt (TIMI-score van 2 of 3) *TIMI-scores voordat aanvullende therapieën worden gebruikt*	81,6% (102/125) [73,7%, 88,0%]
Succesvolle revascularisatie na gebruik van het hulpmiddel (TIMI ≥ 2) *Gebruik van elke aanvullende therapie wordt opgevat als behandelingsfalen*	81,6% (102/125) [73,7%, 88,0%]
Succesvolle revascularisatie na gebruik van het hulpmiddel (TIMI ≥ 2) *Gebruik van elke intra-arteriële trombolytische therapie wordt opgevat als behandelingsfalen*	81,6% (102/125) [73,7%, 88,0%]

†Betrouwbaarheidsintervallen volgens de 'exacte' methode van Clopper-Pearson

Primaire veiligheidseindpunt
Het primaire veiligheidseindpunt was de incidentie van hulpmiddel- en/of procedure-gerelateerde ernstige ongewenste voorvallen die zich voordeden tijdens de procedure, die door de onderzoeker werden gerapporteerd. Er werden 18 procedure-gerelateerde voorvallen bij 16 patiënten gerapporteerd (12,8%). Hiervan werden 4 voorvallen bij 3 patiënten als ernstig beoordeeld door de CEC ('Clinical Events Committee') (2,4%).

Samengenomen ongewenste voorvallen tijdens de procedure	% (n/N) [95% BI]†
Samengenomen SAE's tijdens de procedure	2,4% (3/125)
Primaire veiligheidseindpunt: Samengenomen procedure-/hulpmiddelgerelateerde SAE's t jdens de procedure	2,4% (3/125)

†Betrouwbaarheidsintervallen volgens de 'exacte' methode van Clopper-Pearson

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Specifieke SAE's die zich in de periode van 90 dagen voordeden bij meer dan 2% van de patiënten

SAE	% (n/N)
Samengenomen SAE's	52,0% (65/125)
Hersenoedeem	11,2% (14/125)
Intracraniale bloeding	8,0% (10/125)
Ademhalingsdisfunctie/-insufficiëntie	8,0% (10/125)
Verergerende symptomen van de kwalificerende beroerte	7,2% (9/125)
Infectie	5,6% (7/125)
Andere pulmonale complicaties	5,6% (7/125)
Pneumonie	4,0% (5/125)
Hartritmestoornissen	3,2% (4/125)
Complicaties op de toegangsplaats	2,4% (3/125)
Myocardinfarct	2,4% (3/125)
Perifere vasculaire complicatie	2,4% (3/125)
Nierdisfunctie/-insufficiëntie	2,4% (3/125)
Beroerte in een nieuw stroomgebied	2,4% (3/125)

AE's in de periode van 90 dagen ingedeeld naar anatomisch systeem

Anatomisch systeem	% (n/N)
Zenuwstelselaandoeningen	62,4% (78/125)
Infecties en parasitaire aandoeningen	44,0% (55/125)
Hartaandoeningen	28,8% (36/125)
Voedings- en stofwisselingsstoornissen	25,6% (32/125)
Algemene aandoeningen en aandoeningen op de toegangsplaats	24,8% (31/125)
Respiratoire, thoracale en mediastinale aandoeningen	24,8% (31/125)
Letsels, intoxicaties en verrichtingscomplicaties	18,4% (23/125)
Gastro-intestinale aandoeningen	16,0% (20/125)
Bloed- en lymfestelselaandoeningen	14,4% (18/125)
Vasculaire aandoeningen	11,2% (14/125)
Psychische stoornissen	10,4% (13/125)
Nier- en urinewegaandoeningen	8,0% (10/125)
Lever- en galwegaandoeningen	4,0% (5/125)
Onderzoeken	3,2% (4/125)
Huid- en onderhuidaandoeningen	3,2% (4/125)
Benigne, maligne en niet-gespecificeerde neoplasmata (incl. cysten en poliepen)	2,4% (3/125)
Skelet-, spierstelsel- en bindweefselaandoeningen	0,8% (1/125)

Verklaring van de symbolen

	Opgelet, zie gebruiksaanwijzing		
Rx Only	Uitsluitend op voorschrift – In de Verenigde Staten mag dit product uitsluitend worden gebruikt door of in opdracht van een arts		
	Niet-pyrogeen		
STER LE EO	Gesteriliseerd met ethyleenoxide		
	Fabr kant	EC REP	Vertegenwoordiger voor de EU
LOT	Partijnummer		Niet opnieuw gebru ken
	Te gebruiken vóór	REF	Catalogusnummer
STERILIZE	Niet opnieuw steriliseren	LATEX	Latexvrij

Garantie

Penumbra, Inc. (Penumbra) garandeert dat aan het ontwerp en de fabricage van dit hulpmiddel alle redelijke zorg is besteed. Deze garantie komt in de plaats van en sluit alle andere garanties uit die hier niet uitdrukkelijk vermeld staan, zij het expliciet of impliciet door de werking van de wet of anderszins, inclusief maar niet beperkt tot, alle impliciete garanties van verkoopbaarheid of geschiktheid voor een bepaald doel. Hantering, opslag, reiniging en sterilisatie van dit hulpmiddel evenals andere factoren met betrekking tot de patiënt, de diagnose, de behandeling, de chirurgische procedures en andere zaken waar Penumbra geen controle over heeft, hebben directe consequenties voor het hulpmiddel en de resultaten die met het gebruik ervan behaald worden. Penumbra's verplichting onder deze garantie is beperkt tot de reparatie of vervanging van dit hulpmiddel en Penumbra zal op geen enkele wijze aansprakelijk zijn voor enige incidentele of gevolgschade, schade of kosten direct of indirect verband houdend met het gebruik van dit hulpmiddel. Penumbra aanvaardt geen enkele andere of aanvullende aansprakelijkheid of verantwoordelijkheid met betrekking tot dit hulpmiddel, noch machtigt zij enige andere persoon om voor haar een dergelijke aansprakelijkheid of verantwoordelijkheid te aanvaarden. Penumbra aanvaardt geen aansprakelijkheid met betrekking tot hergebruikte, opnieuw verwerkte of opnieuw gesteriliseerde hulpmiddelen en geeft geen enkele expliciete of impliciete garantie aangaande dergelijke hulpmiddelen, waaronder, maar niet beperkt tot, verkoopbaarheid of geschiktheid voor het beoogde gebruik.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Opis wyrobu medycznego

W skład Penumbra System® wchodzi kilka urządzeń:

- cewnik reperfuzyjny Penumbra,
- pompa aspiracyjna Penumbra,
- rurki do pompy/pojemnika Penumbra,
- rurki do aspiracji Penumbra,
- separator Penumbra.

Penumbra System jest przeznaczony do usuwania zakrzepów z naczyń krwionośnych za pomocą ciągłej aspiracji. Cewnik reperfuzyjny kieruje aspirację bezpośrednio od pompy do zakrzepu. Separator można stosować do oczyszczania kanału cewnika reperfuzyjnego w razie zablokowania zakrzepem. Przy stosowaniu cewnika reperfuzyjnego o średnicy wewnętrznej wynoszącej co najmniej 1,37 mm (0,054 cala) używanie separatora może nie być konieczne. Cewnik reperfuzyjny jest wprowadzany przez cewnik prowadzący lub długą koszulkę udową do wewnątrzczaszkowego układu naczyniowego i kierowany wzdłuż prowadnika nerwowo-naczyniowego do miejsca pierwotnie niedrożnego. Cewnik reperfuzyjny Penumbra stosuje się wraz z pompą aspiracyjną w celu aspirowania zakrzepu z zatkanego naczynia. W razie konieczności separator Penumbra można rozprężyć z cewnika reperfuzyjnego, co pomaga w usuwaniu zakrzepu. Separator Penumbra jest wysuwany i chowany przez cewnik reperfuzyjny Penumbra na proksymalnym obrzeżu miejsca pierwotnej niedrożności, co ułatwia usuwanie zakrzepu z końcówki cewnika reperfuzyjnego. Gdy chodzi o źródło aspiracji, cewnik reperfuzyjny Penumbra jest stosowany w połączeniu z pompą aspiracyjną, która jest podłączana za pomocą rurek do aspiracji Penumbra i rurki do pompy/pojemnika Penumbra. Cewnik reperfuzyjny Penumbra jest dostarczany z mandrynem kształtowanym nad parą oraz obrotową zastawką hemostatyczną i zdejmowaną koszulką. Separator Penumbra jest dostarczany z introduktorem i urządzeniem skręcającym. Urządzenia te są widoczne w obrazie fluoroskopowym.

Wskazania

Penumbra System jest przeznaczony do stosowania w celu rewaskularyzacji u pacjentów z ostrym udarem niedokrwiennym mózgu spowodowanym chorobą zatorową dużych naczyń wewnątrzczaszkowych (wewnątrz tętnic szyjnych wewnętrznych, środkowych mózgu – segmentów M1 i M2, podstawnych i kręgowych) w ciągu 8 godzin od wystąpienia objawów.

Przeciwwskazania

Brak znanych przeciwwskazań.

Ostrzeżenia

- Penumbra System powinni stosować wyłącznie lekarze, którzy otrzymali odpowiednie przeszkolenie w technikach interwencyjnych nerwowo-naczyniowych, a także w leczeniu ostrego udaru niedokrwiennego mózgu.
- Nie wolno przesuwać do przodu, wycofywać ani stosować żadnego elementu Penumbra System w przypadku wystąpienia oporu bez starannej oceny jego przyczyny za pomocą fluoroskopii. Jeśli ustalenie przyczyny jest niemożliwe, należy wycofać urządzenie lub system w całości. Niekontrolowane przesuwanie lub obracanie urządzenia pomimo oporu może spowodować uszkodzenie naczynia lub urządzenia.
- Nie należy stosować Penumbra System wraz z inną pompą niż pompa aspiracyjna Penumbra.

Środki ostrożności

- Urządzenie jest przeznaczone wyłącznie do jednorazowego użytku. Nie wolno resterylizować ani ponownie używać. Resterylizacja i/lub ponowne użycie mogą zakłócić skuteczność powłoki poślizgowej cewnika, co może spowodować wysoki stopień tarcia i niemożność uzyskania dostępu do docelowej lokalizacji w naczyniach.
- Nie wolno używać urządzeń zapętlonych lub uszkodzonych. Nie wolno używać jeśli opakowanie jest otwarte lub uszkodzone. Zwrócić wszystkie uszkodzone urządzenia i opakowania do producenta lub dystrybutora.
- Zużyć przed upływem terminu ważności.
- Penumbra System należy stosować w połączeniu z wizualizacją fluoroskopową.
- Podczas aspiracji zastawkę rurek do aspiracji Penumbra należy otwierać na możliwie najkrótszy czas, potrzebny do usunięcia zakrzepu. Nie zaleca się nadmiernej aspiracji, podobnie jak nie zaleca się niezamykania zastawki rurek do aspiracji Penumbra po zakończeniu aspiracji.
- Separator Penumbra nie jest przeznaczony do stosowania w charakterze prowadnika w naczyniach układu nerwowego. Jeżeli w trakcie zabiegu rewaskularyzacji konieczna jest zmiana położenia cewnika reperfuzyjnego Penumbra, należy ją wykonać po odpowiednim prowadniku do stosowania w naczyniach układu nerwowego za pomocą standardowych technik z wykorzystaniem mikrocewnika i prowadnika.
- Wraz z cewnikiem reperfuzyjnym Penumbra nie należy używać automatycznych urządzeń do wysokociśnieniowych iniekcji środków kontrastowych, ponieważ może to spowodować uszkodzenie urządzenia.
- Na okres 24 godzin po zabiegu należy zawiesić podawanie środków przeciwkrzepliwych oraz przeciwpłytkowych. Leczenie i opieka w fazie ostrej po wystąpieniu ostrego udaru mózgu powinna być zgodna z wytycznymi Amerykańskiego Stowarzyszenia Udaru Mózgu (ASA).[1] Jakiekolwiek pogorszenie się stanu neurologicznego pacjenta należy ocenić za pomocą badania TK przeprowadzonego w trybie pilnym oraz innych badań zgodnych ze standardami postępowania danego badacza lub szpitala.
- Całkowity dopuszczalny czas do uzyskania rewaskularyzacji pacjenta za pomocą Penumbra System wynosi 120 min.

Potencjalne zdarzenia niepożądane

Możliwe powikłania obejmują m.in.:

- brak możliwości całkowitego usunięcia zakrzepu,
- krwiak lub krwotok w miejscu wprowadzenia urządzenia,
- krwotok wewnątrzczaszkowy,
- niedokrwienie,
- ostre zamknięcie naczynia,
- powstanie tętniaka rzekomego,
- przetokę tętniczo-żylną,
- reakcję alergiczną i anafilaktyczną na środek kontrastowy,
- skurcz, zakrzepica, rozwarstwienie lub perforacja naczynia,
- ubytki neurologiczne, w tym udar,
- uszkodzenie nerek środkami kontrastowymi,
- wadliwe funkcjonowanie urządzenia,
- zakażenie,
- zator powietrzny,
- zatorowość dystalną,
- zatory,
- zgon.

Procedura

1. Przed użyciem należy zapoznać się z **Ostrzeżeniami, Środkami ostrożności** i **Potencjalnymi zdarzeniami niepożądanymi**.
2. Przed użyciem każdego urządzenia wchodzącego w skład Penumbra System należy je wyjąć z opakowania i obejrzeć pod kątem uszkodzeń lub zapętleń.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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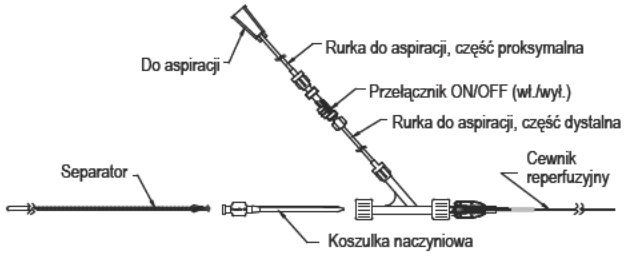
3. Przygotować urządzenia wchodzące w skład Penumbra System do użytku, przepłukując obręcz opakowania i urządzenie heparynizowanym roztworem soli fizjologicznej (dotyczy wyłącznie cewnika reperfuzyjnego Penumbra i separatora Penumbra).
4. Przygotować cewnik prowadzący lub długą koszulkę udową zgodnie z *Instrukcją użycia* producenta.
5. Umieścić cewnik prowadzący lub długą koszulkę udową w odpowiedniej tętnicy mózgowej, proksymalnej względem miejsca zatkania zakrzepem.

Przygotowanie oraz korzystanie z cewnika reperfuzyjnego Penumbra

1. Potwierdzić średnicę naczynia i wybrać odpowiedni rozmiar cewnika reperfuzyjnego Penumbra (patrz **Tabela 1**).
2. Końcówkę cewnika reperfuzyjnego Penumbra można ukształtować za pomocą dostarczonego mandrynu kształtowanego nad parą.
3. Przymocować dostarczony obrotowy zawór hemostatyczny do cewnika reperfuzyjnego Penumbra.
4. Przymocować rurki do aspiracji Penumbra do pompy aspiracyjnej, a następnie włączyć pompę aspiracyjną (patrz *Podręcznik użytkownika* pompy aspiracyjnej). Przed użyciem pompy aspiracyjnej odczekać co najmniej minutę przy włączonej pompie, a następnie sprawdzić, czy wskaźnik aspiracji pokazuje -508 mmHg (-20 inHg). Upewnić się, że zastawka na rurkach do aspiracji Penumbra jest przełączona w pozycję OFF (wył.).
5. Przymocować rurki aspiracyjne do portu bocznego obrotowego zaworu hemostatycznego, jak pokazano na **Rysunku 1**.

Rysunek 1 - Złożony system aspiracji wraz z separatorem Penumbra



6. Wprowadzić cewnik reperfuzyjny Penumbra do obrotowego zaworu hemostatycznego połączonego z proksymalną złączką cewnika prowadzącego. Jeśli cewnik prowadzący nie jest używany, wprowadzić cewnik reperfuzyjny Penumbra przez zawór długiej koszulki udowej, używając zdejmowanej koszulki. Po wprowadzeniu cewnika reperfuzyjnego Penumbra zdjąć zdejmowaną koszulkę z koszulki naczyniowej i z trzonu cewnika reperfuzyjnego Penumbra.
7. Stosując standardowe techniki cewnikowania wspomaganego obrazem fluoroskopowym, wprowadzić cewnik reperfuzyjny Penumbra do naczynia docelowego po odpowiednim prowadniku do stosowania w naczyniach układu nerwowego. Umieścić cewnik perfuzyjny Penumbra proksymalnie do zakrzepu. Wyjąć prowadnik z cewnika reperfuzyjnego Penumbra.
8. Aby rozpocząć aspirację, otworzyć zawór na rurkach do aspiracji Penumbra, ustawiając go w pozycji ON (włączony). Aby przerwać aspirację, przełączyć zastawkę na rurkach do aspiracji Penumbra w pozycję OFF (wyłączony), a następnie wyłączyć pompę aspiracyjną.
9. Korzystając ze strzykawki 5 ml lub 10 ml, pobrać około 5 ml krwi z cewnika reperfuzyjnego Penumbra w celu usunięcia resztek zakrzepu, które mogą znajdować się w cewniku.
10. Wstrzyknąć środki kontrastowe przez cewnik prowadzący i uzyskać angiogram pozabiegowy.

Przygotowanie i użycie separatora Penumbra

1. W razie konieczności wybrać odpowiedni rozmiar separatora Penumbra, odpowiadający cewnikowi reperfuzyjnemu (patrz **Tabela 1**).

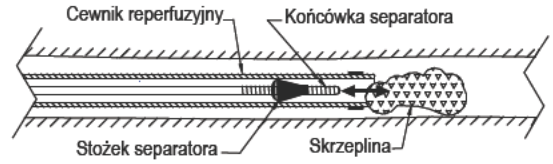
Tabela 1 – Wybór rozmiaru separatora/cewnika reperfuzyjnego

Rozmiar naczynia (mm)	Cewnik reperfuzyjny Penumbra	Separator Penumbra
< 2,0	026	026
2,0 do 3,0	032 / 3MAX	032 / 3MAX
3,0 do 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

UWAGA: Można ułatwić dostęp do miejsca niedrożności poprzez trójosiowe użycie kompatybilnego mikrocewnika wewnętrznego.

2. Korzystając z dostarczonej koszulki wprowadzającej, przeprowadzić separator Penumbra przez obrotowy zawór hemostatyczny i wprowadzić do proksymalnej złączki cewnika reperfuzyjnego Penumbra.
3. Aby rozpocząć aspirację, otworzyć zawór na rurkach do aspiracji Penumbra, przekręcając go w pozycję ON (włączony), po czym wysunąć/wsunąć separator Penumbra, aby wspomóc aspirację i usunięcie zakrzepu z cewnika reperfuzyjnego, jak pokazano na **Rysunku 2**.

Rysunek 2 – Aspiracja zakrzepu za pomocą separatora Penumbra



4. Aby przerwać aspirację, przełączyć zawór na rurkach do aspiracji Penumbra w pozycję OFF (wyłączony), a następnie wyłączyć pompę aspiracyjną.
5. Usunąć separator Penumbra, jeżeli był stosowany.
6. Jeżeli zachodzi taka konieczność, można skorzystać z dodatkowych separatorów Penumbra i cewników reperfuzyjnych Penumbra w celu dalszego usunięcia zakrzepu w zależności od decyzji lekarza.

Podsumowanie danych klinicznych

Główne badanie oceniające system Penumbra stanowiło prospektywne, jednoramienne badanie przeprowadzone w celu oceny bezpieczeństwa i skuteczności stosowania Penumbra System. Do badania włączono ogółem 125 pacjentów w 24 ośrodkach zlokalizowanych w różnych krajach. Głównym kryterium włączenia pacjenta do badania była punktacja ≥ 8 punktów w skali oceny udaru NIH (NIH Stroke Scale, NIHSS), zgłoszenie się w ciągu 8 godzin od wystąpienia objawów oraz zamknięcie (ocena w skali TIMI 0 lub 1) nadającego się do leczenia wewnątrzczaszkowego naczynia krwionośnego. Pacjenci, którzy zgłosili się w ciągu 3 godzin od wystąpienia objawów, musieli nie kwalifikować się do terapii rtPA lub musieli być na nią oporni. Pierwszorzędowe punkty końcowe stanowiła rewaskularyzacja naczynia docelowego (2 lub 3 w skali TIMI) oraz częstość występowania poważnych zdarzeń niepożądanych (SAE) związanych z zabiegiem. Wszystkich pacjentów poddawano badaniom kontrolnym i ocenom przez maksymalnie 90 dni po zabiegu.

Analiza statystyczna

Aby uzyskać co najmniej 115 pacjentów nadających się do oceny, do niniejszego badania wybrano wielkość próby wynoszącą 125 pacjentów. Pacjenta uznawano na nadającego się do oceny, jeżeli spełniał kryteria

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kwalifikacji do oceny pierwszorzędowego punku końcowego i był leczony za pomocą Penumbra System. Ze względu na niewystępowanie w tym badaniu grupy kontrolnej, nie planowano formalnego testu hipotezy dla całkowitego wskaźnika odpowiedzi w odniesieniu do uzyskania wyniku 2 lub 3 w skali TIMI. Standardowe statystyki opisowe dotyczące jakościowych punktów końcowych stanowiły liczba i odsetek pacjentów, u których uzyskano każdy poziom punktu końcowego. W przypadku liczbowych punktów końcowych standardowe statystyki opisowe obejmowały liczbę niepominiętych obserwacji (n), średnią, medianę, odchylenie standardowe, wartość minimalną i maksymalną.

Procedury badania
Dostęp tętniczy do naczynia docelowego uzyskiwano przy użyciu standardowej techniki przezskórnej. Przeprowadzano cyfrową angiografię subtrakcyjną czterech naczyń w celu określenia struktury naczyniowej zamkniętego fragmentu naczynia. Konieczne było potwierdzenie zamknięcia dużego naczynia mózgowego u każdego pacjenta w angiografii i wyznaczenie a priori miejsca pierwotnego zamknięcia naczynia przez badacza. Jeżeli zamknięcie dotyczyło naczynia nadającego się do leczenia, umieszczano odpowiedni cewnik prowadzący i wprowadzano cewnik reperfuzyjny Penumbra do proksymalnego końca zamkniętego naczynia docelowego. Pacjenta uznawano za włączonego do badania w momencie rozprężenia cewnika reperfuzyjnego z cewnika prowadzącego.

Kluczowe kryteria włączenia
- Kliniczne objawy przedmiotowe odpowiadające ostremu udarowi niedokrwiennemu, w tym:
  - nagłe zdrętwienie lub osłabienie twarzy lub kończyn,
  - nagła dezorientacja, zaburzenia mówienia lub rozumienia mowy,
  - nagłe zaburzenia chodzenia, zawroty głowy lub utrata równowagi.
- Wiek 18–79 lat
- Deficyt neurologiczny oceniany w skali oceny udaru (NIHSS) na ≥8
- Całkowite zamknięcie (0 w skali TIMI) lub przechodzenie środka kontrastowego z minimalną perfuzją, ale bez wypełniania gałęzi dystalnych (I w skali TIMI) w naczyniach wewnątrzczaszkowych, do których można uzyskać dostęp za pomocą Penumbra System do leczenia udarów
- Podpisany formularz zgody
- Zgłoszenie się w ciągu 8 godzin od wystąpienia objawów udaru
- W przypadku pacjentów zgłaszających się w ciągu 3 godzin od wystąpienia objawów – pacjent nie kwalifikuje się do terapii dożylnej rtPA lub jest na nią oporny

Kluczowe kryteria wykluczenia
- Potwierdzone dane świadczące o gwałtownej poprawie objawów neurologicznych udaru w czasie kwalifikacji
- Punktacja w skali NIHSS >30 lub śpiączka
- Kobiety w okresie ciąży
- Kręty przebieg naczynia uniemożliwiający uzyskanie dostępu do naczynia
- Rozpoznana skaza krwotoczna, zaburzenia krzepnięcia lub przyjmowanie doustnych leków przeciwzakrzepowych z INR >3,0
- PTT przekraczających ponad dwukrotnie normę laboratoryjną
- Liczba płytek krwi przy przyjęciu <30 000
- Występująca u pacjenta wcześniej choroba neurologiczna lub psychiczna, która może wpłynąć na wyniki badania
- Rozpoznana ciężka alergia na środki kontrastowe
- Niekontrolowane nadciśnienie tętnicze (definiowane jako ciśnienie skurczowe > 185 mmHg lub ciśnienie rozkurczowe >110 mmHg)
- Wynik badania TK przy przyjęciu wskazujący na następujące stany:
  - znaczący efekt masy z przemieszczeniem linii środkowej,
  - duży obszar hipodensyjny, stanowiący >1/3 obszaru ukrwienia przez tętnicę środkową mózgu
  - potwierdzone dane świadczące o krwotoku wewnątrzczaszkowym
- Dane z badania angiograficznego wskazujące na zwężenie tętnicy proksymalnie od miejsca jej zamknięcia, które może uniemożliwić usunięcie zakrzepu
- Dane z badania angiograficznego wskazujące na istniejące wcześniej uszkodzenie tętnicy
- Spodziewana długość życia poniżej 90 dni
- Udział w innym badaniu klinicznym, który może zakłócić ocenę badanego urządzenia

Podsumowanie przyczyn wykluczenia uczestników zakwalifikowanych do udziału w badaniu, szczególnie przyczyn związanych z kryteriami angiograficznymi
Żaden pacjent zakwalifikowany do badania nie został wykluczony z niego z powodu dotyczącego kryteriów angiograficznych.

Pierwszorzędowy punkt końcowy skuteczności
Pierwszorzędowy punkt końcowy skuteczności stanowiła rewaskularyzacja zamkniętego naczynia docelowego. Rewaskularyzację definiowano jako II lub III w skali TIMI po zastosowaniu wyłącznie Penumbra System i przed zastosowaniem jakichkolwiek dodatkowych lub uzupełniających urządzeń lub terapii. Wyniki badań angiograficznych były oceniane przez niezależne centralne laboratorium.

Skuteczność	% (n/N) [95% CI]†
Pierwszorzędowy punkt końcowy skuteczności (II lub III w skali TIMI) *Punktacja w skali TIMI przed zastosowaniem terapii uzupełniających*	81,6% (102/125) [73,7%, 88,0%]
Powodzenie rewaskularyzacji po zastosowaniu urządzenia (TIMI ≥ 2) *Wszelka terapia uzupełniająca po stwierdzeniu niepowodzenia leczenia*	81,6% (102/125) [73,7%, 88,0%]
Powodzenie rewaskularyzacji po zastosowaniu urządzenia (TIMI ≥ 2) *Wszelkie zastosowanie dotętniczych środków fibrynolitycznych po stwierdzeniu niepowodzenia leczenia*	81,6% (102/125) [73,7%, 88,0%]

†Dokładne przedziały ufności Cloppera-Pearsona

Pierwszorzędowy punkt końcowy bezpieczeństwa
Pierwszorzędowy punkt końcowy bezpieczeństwa stanowiła częstość występowania poważnych zdarzeń niepożądanych związanych z urządzeniem i (lub) zabiegiem, które wystąpiły podczas zabiegu – na podstawie zgłoszenia przez badacza. Zgłoszono 18 zdarzeń związanych z zabiegiem, które wystąpiły u 16 pacjentów (12,8%). Spośród nich 4 zdarzenia u 3 pacjentów Komisja ds. Zdarzeń Klinicznych (CEC) oceniła jako poważne (2,4%).

Złożone zdarzenia niepożądane podczas zabiegu	% (n/N) [95% CI]†
Złożone poważne zdarzenia niepożądane podczas zabiegu	2,4% (3/125)
Pierwszorzędowy punkt końcowy bezpieczeństwa: Złożone poważne zdarzenia niepożądane związane z zabiegiem i (lub) urządzeniem podczas zabiegu	2,4% (3/125)

†Dokładne przedziały ufności Cloppera-Pearsona

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Wszystkie określone poważne zdarzenia niepożądane, które wystąpiły w ciągu 90 dni u ponad 2% pacjentów

Poważne zdarzenia niepożądane	% (n/N)
Złożone poważne zdarzenia niepożądane	52,0% (65/125)
obrzęk mózgu	11,2% (14/125)
krwotok śródczaszkowy	8,0% (10/125)
zaburzenia lub niewydolność oddychania	8,0% (10/125)
nasilenie objawów udaru stanowiącego podstawę włączania pacjenta do badania	7,2% (9/125)
zakażenie	5,6% (7/125)
inne powikłania płucne	5,6% (7/125)
zapalenie płuc	4,0% (5/125)
zaburzenia rytmu serca	3,2% (4/125)
powikłania dostępu do miejsca zamknięcia naczynia	2,4% (3/125)
zawał mięśnia sercowego	2,4% (3/125)
powikłania dotyczące naczyń obwodowych	2,4% (3/125)
zaburzenia czynności lub niewydolność nerek	2,4% (3/125)
udar w nowym obszarze	2,4% (3/125)

Przyporządkowanie zdarzeń niepożądanych, które wystąpiły w ciągu 90 dni, do układu anatomicznego

Układ anatomiczny	% (n/N)
zaburzenia układu nerwowego	62,4% (78/125)
zakażenia i zarażenia pasożytnicze	44,0% (55/125)
zaburzenia serca	28,8% (36/125)
zaburzenia metabolizmu i odżywiania	25,6% (32/125)
zaburzenia ogólne i stany w miejscu podania	24,8% (31/125)
zaburzenia układu oddechowego, klatki piersiowej i śródpiersia	24,8% (31/125)
urazy, zatrucia i pow kłania po zabiegach	18,4% (23/125)
zaburzenia żołądka i jelit	16,0% (20/125)
zaburzenia krwi i układu chłonnego	14,4% (18/125)
zaburzenia naczyniowe	11,2% (14/125)
zaburzenia psychiczne	10,4% (13/125)
zaburzenia nerek i dróg moczowych	8,0% (10/125)
zaburzenia wątroby i dróg żółciowych	4,0% (5/125)
badania diagnostyczne	3,2% (4/125)
zaburzenia skóry i tkanki podskórnej	3,2% (4/125)
nowotwory łagodne, złośliwe i nieokreślone (w tym torbiele i polipy)	2,4% (3/125)
zaburzenia mięśniowo-szkieletowe i tkanki łącznej	0,8% (1/125)

Słownik symboli

		Uwaga, sprawdzić w instrukcji użycia	
Rx Only		Tylko na receptę – prawo federalne USA zezwala na sprzedaż tego urządzenia wyłącznie przez lekarza lub na jego zlecenie	
		Produkt niepirogenny	
STER LE EO		Sterylizowano tlenkiem etylenu	
	Producent	EC REP	Przedstawiciel w UE
LOT	Numer partii		Nie używać ponownie
	Termin ważności	REF	Numer katalogowy
	Nie sterylizować ponownie	LATEX	Nie zawiera lateksu

Gwarancja

Firma Penumbra, Inc. (Penumbra) gwarantuje, że przy projektowaniu i produkcji tego urządzenia przestrzegano normalnych zasad staranności. Niniejsza gwarancja zastępuje i wyklucza wszystkie inne gwarancje, z wyjątkiem wyraźnie tu sformułowanych, zarówno wyrażone jak i dorozumiane na podstawie przepisów prawa lub inaczej, w tym m.in. wszelkie dorozumiane gwarancje przydatności handlowej lub zdatności do określonego celu. Na niniejsze urządzenie i wyniki uzyskane z jego użyciem wpływają bezpośrednio: obchodzenie się z produktem, jego przechowywanie, czyszczenie i sterylizacja oraz inne czynniki dotyczące pacjenta, diagnozy, leczenia, procedur chirurgicznych i innych kwestii, na które firma Penumbra nie ma wpływu. Zobowiązanie firmy Penumbra na podstawie tej gwarancji ogranicza się do naprawy lub wymiany tego urządzenia, przy czym Penumbra nie ponosi odpowiedzialności za żadne straty przypadkowe lub wynikowe, uszkodzenia ani koszty wynikające bezpośrednio lub pośrednio z użycia tego urządzenia. Penumbra nie przyjmuje ani nie upoważnia nikogo innego do przyjmowania żadnej innej ani dodatkowej odpowiedzialności w związku z tym urządzeniem. Penumbra nie ponosi żadnej odpowiedzialności w związku z urządzeniami poddanymi ponownemu użyciu, ponownym procesom lub ponownej sterylizacji i nie udziela żadnych gwarancji, wyrażonych ani dorozumianych, w tym m in. dotyczących przydatności handlowej lub zdatności do określonego celu, dotyczących tego rodzaju urządzenia.

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Descrição do dispositivo

O Penumbra System® é constituído por vários componentes:

- Cateter de reperfusão Penumbra
- Bomba de aspiração Penumbra
- Bomba/tubulação do recipiente Penumbra
- Tubos de aspiração Penumbra
- Separador Penumbra

O Penumbra System foi desenvolvido para remover trombos vasculares por meio de aspiração contínua. O cateter de reperfusão orienta a aspiração da bomba diretamente para o trombo. O separador pode ser utilizado para desobstruir o lúmen do cateter de reperfusão caso seja obstruído pelo trombo. A utilização do separador pode não ser necessária quando se utiliza cateter de reperfusão com DI de 1,37 mm (0,054 polegadas) ou mais. O cateter de reperfusão é introduzido no interior da vasculatura intracraniana através de um cateter guia ou de uma bainha femoral comprida, e é orientado, ao longo de um fio-guia neurovascular, até o local da oclusão primária. O cateter de reperfusão Penumbra é utilizado com a bomba de aspiração para aspirar trombos dos vasos ocluídos. Conforme necessário, pode-se liberar o separador Penumbra a partir do cateter de reperfusão para auxiliar a remoção do trombo. O separador Penumbra é avançado e retraído através do cateter de reperfusão Penumbra na margem proximal da oclusão primária para facilitar a remoção do trombo da ponta do cateter de reperfusão. A fonte de aspiração consiste na utilização do cateter de reperfusão Penumbra em conjunto com a bomba de aspiração, que é conectada aos tubos de aspiração Penumbra e à bomba/tubulação do recipiente Penumbra. O cateter de reperfusão Penumbra é fornecido com um mandril para moldagem a vapor e uma válvula hemostática rotativa, e uma bainha removível. O separador Penumbra é fornecido com um introdutor e um dispositivo de torque. Os dispositivos são visíveis sob fluoroscopia.

Indicações de uso

O Penumbra System é indicado para utilização na revascularização de pacientes com AVC isquêmico agudo decorrente de doença oclusiva de grandes vasos intracranianos (artéria carótida interna, artéria cerebral média – segmentos M1 [esfenoidal] e M2 [insular], artéria basilar e artéria vertebral) no prazo de 8 horas desde o início dos sintomas.

Contraindicações

Não existem contraindicações conhecidas.

Advertências

- O Penumbra System só deve ser utilizado por médicos com treinamento adequado em técnicas de intervenção neuro-endovascular e de tratamento de AVC isquêmico agudo.
- Não avance, não retraia nem utilize qualquer componente do Penumbra System se detectar resistência, antes de avaliar com cuidado a causa, com a ajuda de fluoroscopia. Se não for possível determinar a causa, retire o dispositivo ou o sistema como uma unidade. O torque não controlado ou a inserção forçada do cateter ou do separador contra resistência pode resultar em dano do dispositivo ou em lesão no vaso.
- Não utilize o Penumbra System com outra bomba que não seja a bomba de aspiração Penumbra.

Precauções

- O dispositivo destina-se a uma única utilização. Não reesterilize nem reutilize. A reesterilização e/ou reutilização pode resultar em lubrificação ineficaz do revestimento do cateter, o que pode resultar em atrito elevado e na incapacidade para de atingir a localização neurovascular visada.
- Não utilize dispositivos com dobras ou danificados. Não utilize embalagens abertas ou danificadas. Devolva todos os dispositivos danificados e a respectiva embalagem ao fabricante/distribuidor.
- Use antes do término do "Prazo de validade".
- Utilize o Penumbra System em conjunto com a visualização fluoroscópica.
- Ao realizar aspiração, certifique-se de que a válvula da tubulação de aspiração Penumbra esteja aberta apenas durante o tempo mínimo necessário para remover o trombo. Não se recomenda aspirar em excesso nem manter a válvula da tubulação de aspiração Penumbra aberta quando a aspiração estiver concluída.
- O separador Penumbra não se destina a ser utilizado como fio-guia neurovascular. Se for necessário reposicionar o cateter de reperfusão Penumbra durante o procedimento de revascularização, esse reposicionamento deve ser realizado ao longo de um fio-guia neurovascular adequado utilizando-se um microcateter e técnicas padrão de fio-guia.
- Não utilize equipamento automático de alta pressão para a injeção de contraste de alta pressão com o cateter de reperfusão Penumbra, porque pode danificar o dispositivo.
- A administração de agentes anticoagulantes e antiplaquetários deve ser interrompida até 24 horas após o tratamento. A conduta clínica e o tratamento intensivo após AVC devem seguir as diretrizes da ASA.[1] Qualquer deterioração neurológica deve ser avaliada por tomografia computadorizada urgente e por outras avaliações, conforme indicado pelas melhores práticas clínicas e hospitalares.
- O tempo total permitido para atingir a revascularização do paciente é 120 minutos após a utilização do Penumbra System.

Possíveis eventos adversos

As complicações possíveis incluem, mas não se limitam ao seguinte:

- déficits neurológicos, incluindo AVC
- embolia
- embolia gasosa
- embolização distal
- falsa formação de aneurisma
- fístula arteriovenosa
- hematoma ou hemorragia no local de acesso
- hemorragia intracraniana
- incapacidade de remover completamente o trombo
- infecção
- isquemia
- lesão renal devido ao meio de contraste
- mau funcionamento do dispositivo
- morte
- oclusão aguda
- reação alérgica e anafilaxia ao meio de contraste
- vasoespasmo, trombose, dissecação ou perfuração

Procedimento

1. Antes de usar, consulte **Advertências, Precauções** e **Possíveis efeitos indesejáveis**.
2. À medida que for utilizando cada dispositivo do Penumbra System, remova o dispositivo da embalagem e inspecione-o para identificar danos ou dobras.
3. Prepare os dispositivos do Penumbra System para utilização irrigando o aro de proteção e o dispositivo com solução salina heparinizada (inclui apenas o cateter de reperfusão Penumbra e o separador Penumbra).
4. Prepare um cateter guia ou uma bainha femoral comprida de acordo com as *Instruções de uso* do fabricante.
5. Coloque o cateter guia ou a bainha femoral comprida na artéria adequada do cérebro, que se situe proximalmente ao local da oclusão do trombo.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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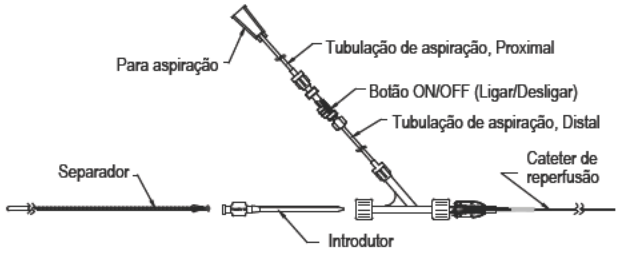
Preparação e utilização do cateter de reperfusão Penumbra

1. Confirme o diâmetro do vaso e escolha um cateter de reperfusão Penumbra de tamanho adequado (Ver **Tabela 1**).
2. O formato da ponta do cateter de reperfusão Penumbra pode ser criado utilizando-se o mandril para moldagem a vapor fornecido.
3. Conecte a válvula hemostática rotativa fornecida ao cateter de reperfusão Penumbra.
4. Conecte a tubulação de aspiração Penumbra à bomba de aspiração e ligue a bomba (consulte o *Manual de utilização* da bomba de aspiração). Deixe a bomba de aspiração funcionar por pelo menos um minuto antes do uso e certifique-se de que o calibrador de aspiração indique −508 mmHg (−20 inHg). Certifique-se de que a válvula na tubulação de aspiração Penumbra esteja na posição OFF (Desligada).
5. Conecte a tubulação de aspiração ao port lateral da válvula hemostática rotativa, conforme ilustrado na **Figura 1**.

Figura 1 – Sistema de aspiração montado com o separador Penumbra



6. Insira o cateter de reperfusão Penumbra numa válvula hemostática rotativa ligada ao conector proximal de um cateter guia. Se o cateter guia não estiver sendo utilizado, insira o cateter de reperfusão Penumbra através da válvula da bainha femoral comprida, usando a bainha removível. Depois de inserir o cateter de reperfusão Penumbra, retire a bainha removível da bainha vascular e solte-a da haste do cateter de reperfusão Penumbra.
7. Utilizando técnicas de cateterização convencionais sob orientação fluoroscópica, avance o cateter de reperfusão Penumbra para o vaso alvo ao longo do fio-guia neurovascular apropriado. Posicione o cateter de reperfusão Penumbra proximalmente ao trombo. Remova o fio-guia do cateter de reperfusão Penumbra.
8. Para iniciar a aspiração, abra a válvula da tubulação de aspiração Penumbra, colocando-a na posição ON (Ligada). Para interromper a aspiração, feche a válvula da tubulação de aspiração Penumbra (posição OFF [Desligada]) e desligue a bomba de aspiração.
9. Utilizando uma seringa de 5 ml ou de 10 ml, aspire cerca de 5 ml de sangue do cateter de reperfusão Penumbra para retirar qualquer trombo que ainda possa estar dentro do cateter.
10. Realize um angiograma pós-tratamento injetando meio de contraste através do cateter guia.

Preparação e uso do separador Penumbra

1. Se necessário, escolha um separador Penumbra de tamanho adequado, correspondente ao cateter de reperfusão (Ver **Tabela 1**).

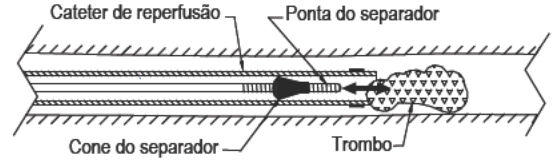
Tabela 1 – Escolha do tamanho do dispositivo do separador/ cateter de reperfusão

Tamanho do vaso (mm)	Cateter de reperfusão Penumbra	Separador Penumbra
< 2,0	026	026
2,0 a 3,0	032 / 3MAX	032 / 3MAX
3,0 a 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

NOTA: O acesso ao local da oclusão pode ser facilitado pela utilização triaxial de um microcateter interno compatível.

2. Utilizando a bainha introdutora fornecida, insira o separador Penumbra através da válvula hemostática rotativa e na parte proximal do canhão do cateter de reperfusão Penumbra.
3. Para iniciar a aspiração, abra a válvula na tubulação de aspiração Penumbra (posição ON [Ligada]) e avance/retraia o separador Penumbra para auxiliar a aspiração e remoção do trombo do cateter de reperfusão, conforme ilustrado na **Figura 2**.

Figura 2 – Aspiração do trombo utilizando o separador Penumbra



4. Para interromper a aspiração, coloque a válvula da tubulação de aspiração Penumbra na posição OFF (Desligada) e desligue a bomba de aspiração.
5. Remova o separador Penumbra, se estiver sendo usado.
6. Se necessário, podem ser utilizados separadores e cateteres de reperfusão Penumbra adicionais para retirar mais trombos, a critério do médico.

Resumo dos dados clínicos

O estudo central Penumbra foi prospectivo e de um só grupo para avaliar a segurança e a eficácia do Penumbra System. Um total de 125 pacientes foram inscritos em 24 centros internacionais. Os principais critérios de inclusão foram escore ≥ 8 na Escala de AVC dos NIH (NIHSS), apresentação no prazo de 8 horas após o início dos sintomas e oclusão (TIMI 0 ou 1) de vaso intracraniano passível de tratamento. Os pacientes que se apresentaram no prazo de 3 horas após o início dos sintomas provavelmente não eram elegíveis ou eram refratários ao tratamento com o fator ativador de plasminogênio tecidual recombinante (rtPA). Os endpoints primários foram a revascularização do vaso alvo (TIMI 2 ou 3) e incidência de eventos adversos graves (EAG) durante o procedimento. Todos os pacientes foram acompanhados e avaliados até 90 dias após o procedimento.

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Análise estatística
Foi selecionada uma amostra de 125 indivíduos para este estudo, visando obter pelo menos 115 pacientes passíveis de avaliação. O paciente foi considerado passível de avaliação se satisfizesse os requisitos de elegibilidade para avaliação do endpoint primário e se tivesse sido tratado com o Penumbra System. Como se trata de um estudo não controlado, não se planejou um teste de hipótese formal para a taxa de resposta global para determinar a classificação TIMI 2 ou 3. A estatística descritiva padrão para os endpoints categóricos foram o número e a porcentagem de pacientes com cada nível do endpoint. Para endpoints numéricos, a estatística descritiva padrão incluiu o número de observações não faltantes (n), a média, a mediana e o desvio padrão, o valor mínimo e o valor máximo.

Procedimentos do estudo
O acesso arterial ao vaso alvo foi obtido utilizando-se técnica percutânea padrão e realizou-se angiografia por subtração digital de quatro vasos para definir a angioarquitetura do segmento vascular ocluído. Foi necessário confirmar a oclusão de grandes vasos cerebrais em cada paciente, por meio de angiografia, além do local de oclusão primária designado a priori pelo investigador. Se a oclusão estivesse em vaso passível de tratamento, posicionava-se um cateter guia apropriado e o cateter de reperfusão Penumbra era avançado para a extremidade proximal do vaso alvo ocluído. Os pacientes foram considerados inscritos no estudo quando o cateter de reperfusão era liberado a partir do cateter guia.

Principais critérios de inclusão
- Sinais clínicos compatíveis com AVC isquêmico agudo, incluindo:
  - Perda de sensibilidade ou fraqueza súbita na face ou nos membros
  - Confusão súbita, dificuldade de articular e expressar a linguagem ou de compreendê-la.
  - Dificuldade súbita para caminhar, tonturas ou desequilíbrio
- Idade entre 18 e 79 anos
- Déficit neurológico que resultou em escore ≥ 8
- Oclusão completa (TIMI Grau 0) ou penetração de contraste com perfusão mínima, mas sem enchimento de ramo distal (TIMI Grau I) nos vasos intracranianos acessíveis ao Penumbra System para AVC
- Termo de consentimento livre e esclarecido assinado
- Apresentar-se no prazo de 8 horas após início dos sintomas de AVC
- Não ser elegível ou ser refratário ao tratamento com o fator rtPA intravenoso em apresentação no prazo de 3 horas desde o início dos sintomas

Principais critérios de exclusão
- Evidência de restabelecimento rápido dos sinais neurológicos do AVC no momento da inscrição
- NIHSS > 30 ou coma
- Mulheres grávidas
- Extrema tortuosidade do vaso, não permitindo o acesso endovascular
- Diátese hemorrágica conhecida, deficiência de coagulação ou tratamento com anticoagulante oral e índice internacional normalizado (INR) > 3,0
- Tempo parcial de tromboplastina (TPT) 2 vezes maior que o valor de referência do laboratório
- Contagem de plaquetas < 30.000
- Doença neurológica ou psiquiátrica preexistente que pudesse confundir os resultados do estudo
- Alergia grave conhecida ao meio de contraste
- Hipertensão não controlada (definida como pressão sistólica > 185 mmHg ou pressão diastólica > 110 mmHg)
- Evidências tomográficas das seguintes condições no momento da apresentação:
  - Efeito de massa significante e desvio da linha média
  - Grande área de hipodensidade > 1/3 da região da artéria cerebral média
  - Evidência de hemorragia intracraniana
- Evidência angiográfica de estenose arterial proximal à oclusão que pudesse impedir a remoção do trombo
- Evidência angiográfica de lesão arterial preexistente
- Expectativa de vida inferior a 90 dias
- Participação em outra pesquisa clínica que pudesse confundir a avaliação do dispositivo do presente estudo

Resumo dos motivos para exclusão dos indivíduos inscritos, principalmente com base em critérios angiográficos
Nenhum paciente inscrito foi excluído por motivos angiográficos.

Endpoint primário de eficácia
O endpoint primário de eficácia foi a revascularização do vaso alvo ocluído. Revascularização foi definida apenas pelo escore TIMI II ou III após a utilização do Penumbra System e antes do uso de qualquer outro dispositivo ou tratamento complementar. Os resultados angiográficos foram determinados por um laboratório central independente.

Eficácia	% (n/N) [IC 95%]†
Endpoint primário de eficácia (escore TIMI II ou III) *Uso dos escores TIMI antes de tratamentos complementares*	81,6% (102/125) [73,7%, 88,0%]
Sucesso da revascularização após uso do dispositivo (TIMI ≥ 2) *Qualquer terapia complementar foi considerada falha do tratamento*	81,6% (102/125) [73,7%, 88,0%]
Sucesso da revascularização após utilização do dispositivo (TIMI ≥ 2) *A utilização de qualquer terapia trombolítica intra-arterial foi considerada falha do tratamento*	81,6% (102/125) [73,7%, 88,0%]

†Intervalos de confiança exatos de Clopper-Pearson

Endpoint primário de segurança
O endpoint primário de segurança foi a incidência de eventos adversos graves relacionados com o dispositivo e/ou com o procedimento, ocorridos durante a intervenção, de acordo com o relato do investigador. Foram relatados 18 eventos relacionados com o procedimento em 16 pacientes (12,8%). Entre eles, 4 eventos em 3 pacientes foram classificados como graves por um comitê de avaliação de eventos clínicos (2,4%).

Eventos adversos combinados durante o procedimento	% (n/N) [IC 95%]†
EAG combinados durante o procedimento	2,4% (3/125)
Endpoint primário de segurança: EAG combinados relacionados com o procedimento/dispositivo durante o procedimento	2,4% (3/125)

†Intervalos de confiança exatos de Clopper-Pearson

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Todos os EAG específicos durante 90 dias, constatados em mais de 2% dos pacientes

EAG	% (n/N)
EAG combinados	52,0% (65/125)
Edema cerebral	11,2% (14/125)
Hemorragia intracerebral	8,0% (10/125)
Disfunção/insuficiência respiratória	8,0% (10/125)
Sintomas de agravamento de AVC qualificado	7,2% (9/125)
Infecção	5,6% (7/125)
Outras complicações pulmonares	5,6% (7/125)
Pneumonia	4,0% (5/125)
Arritmia cardíaca	3,2% (4/125)
Complicação no local de acesso	2,4% (3/125)
Infarto do miocárdio	2,4% (3/125)
Complicação vascular periférica	2,4% (3/125)
Disfunção/insuficiência renal	2,4% (3/125)
AVC em nova região	2,4% (3/125)

Categorização dos EA durante 90 dias segundo o sistema anatômico

Sistema anatômico	% (n/N)
Distúrbios do sistema nervoso	62,4% (78/125)
Infecções e infestações	44,0% (55/125)
Distúrbios cardíacos	28,8% (36/125)
Transtornos metabólicos e nutricionais	25,6% (32/125)
Transtornos gerais e problemas no local de administração	24,8% (31/125)
Distúrbios respiratórios, torácicos e do mediastino	24,8% (31/125)
Lesão, intoxicação e complicações do procedimento	18,4% (23/125)
Distúrbios gastrintestinais	16,0% (20/125)
Transtornos dos sistemas hematológico e linfático	14,4% (18/125)
Distúrbios vasculares	11,2% (14/125)
Transtornos psiquiátricos	10,4% (13/125)
Distúrbios renais e urinários	8,0% (10/125)
Distúrbios hepatobiliares	4,0% (5/125)
Investigações cirúrgicas caso seja necessário	3,2% (4/125)
Distúrbios cutâneos e dos tecidos subcutâneos	3,2% (4/125)
Neoplasias benignas, malignas e não especificadas (inclusive cistos e pólipos)	2,4% (3/125)
Transtornos musculosqueléticos e do tecido conectivo	0,8% (1/125)

GLOSSÁRIO DE SÍMBOLOS

		Atenção, ver Instruções de uso	
Rx Only		Somente com prescrição médica - A lei federal dos Estados Unidos restringe a utilização deste dispositivo aos médicos ou à sua solicitação	
		Não pirogênico	
STER LE EO		Esterilizado com óxido de etileno	
	Fabricante	EC REP	Representante da UE
LOT	Número de lote		Não reutilizar
	Prazo de validade	REF	Número de catálogo
STERILIZE	Não reesterilizar	LATEX	Sem látex

GARANTIA

A Penumbra, Inc. (Penumbra) garante que foram empregados cuidados razoáveis no projeto e na fabricação deste dispositivo. Esta garantia substitui e exclui todas as outras garantias, não expressamente previstas neste documento, explícitas ou implícitas, por força de lei ou de outra forma, incluindo quaisquer garantias implícitas de comercialização ou adequação para uso específico, sem contudo, a isso se limitar. O manuseio, a conservação, a limpeza e a esterilização deste dispositivo, bem como outros fatores relacionados com pacientes, diagnóstico, tratamento, procedimentos cirúrgicos e outras questões fora do controle da Penumbra afetam diretamente o dispositivo e os resultados decorrentes da sua utilização. A obrigação da Penumbra de acordo com a presente garantia limita-se à reparação ou substituição deste dispositivo, sendo que a Penumbra não será responsável por perdas acidentais ou consequentes nem por danos ou despesas, direta ou indiretamente decorrentes da utilização deste dispositivo. A Penumbra não assume nem autoriza qualquer pessoa a assumir em seu nome qualquer outra obrigação ou responsabilidade relacionada com este dispositivo. A Penumbra não assume qualquer responsabilidade referente a dispositivos reutilizados, reprocessados ou reesterilizados e não dá garantias, explícitas ou implícitas, incluindo, comercialização ou adequação ao uso pretendido deste dispositivo, sem contudo, a isso se limitar.

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Türkçe

Cihaz Tanımı

Penumbra System® birkaç cihazdan oluşur:

- Penumbra Reperfüzyon Kateteri
- Penumbra Aspirasyon Pompası
- Penumbra Pompa/Kutu Tüpü
- Penumbra Aspirasyon Tüp Sistemi
- Penumbra Separatörü

Penumbra System, sürekli aspirasyon yardımıyla damar yapısından pıhtıyı çıkarmak için tasarlanmıştır. Reperfüzyon Kateteri, pompadan doğrudan pıhtıya aspirasyon hedefler. Separatör, Reperfüzyon Kateterinin pıhtıyla tıkanması durumunda kateter lümenini temizlemek için kullanılabilir. İç çapı 1,37 mm (0,054 inç) veya daha büyük olan bir Reperfüzyon Kateteri kullanıldığında Separatör kullanılması gerekli olmayabilir. Reperfüzyon Kateteri, kılavuz bir kateter veya uzun femoral kılıf vasıtasıyla intrakranyal vaskülerin içine yerleştirilir ve birincil oklüzyon alanında nevrovasküler bir kılavuz tel vasıtasıyla rehberlik eder. Penumbra Reperfüzyon Kateteri, oklüde bir damardan pıhtıyı aspire etmek için Aspirasyon Pompası ile birlikte kullanılır. Gerekirse, Penumbra Separatörü, pıhtı çıkarma işlemine yardımcı olmak için Reperfüzyon Kateterinden yerleştirilebilir. Penumbra Separatörü, Reperfüzyon Kateteri ucundan pıhtının temizlenmesini kolaylaştırmak için Penumbra Reperfüzyon Kateteri içinden birincil oklüzyonun proksimal sınırında itilip geri çekilir. Aspirasyon kaynağı açısından Penumbra Reperfüzyon Kateteri, Penumbra Aspirasyon Tüp Sistemi ve Penumbra Pompa/Kutu Tüpü kullanılarak bağlanan Aspirasyon Pompası ile birlikte kullanılır. Penumbra Reperfüzyon Kateteri, buhar ile şekil verme mandreli, döner hemostaz valfi ve soyulabilen kılıf ile birlikte temin edilir. Penumbra Separatörü, bir introdüser ve bir tork cihazıyla birlikte temin edilir. Cihazlar floroskopi altında görülebilir.

Kullanım Endikasyonu

Penumbra System, semptom başlamasından itibaren 8 saat içinde intrakraniyal büyük damar oklüsif hastalığına (internal karotis, orta serebral - M1 ve M2 segmentler, bazilar ve vertebral arterler içinde) sekonder akut iskemik inme geçiren hastaların revaskülarizasyonunda kullanılmak içindir.

Kontrendikasyonları

Bilinen bir kontraendikasyonu yoktur.

Uyarılar

- Penumbra System sadece girişimsel nöro-endovasküler teknikler ve akut iskemik inme tedavisi ile ilgili uygun eğitim almış doktorlar tarafından kullanılmalıdır.
- Floroskopi yardımıyla sebebini dikkatlice değerlendirmeden Penumbra System'ın hiçbir bileşenini dirence karşı ilerletmeyin, geri çekmeyin veya kullanmayın. Sebebi belirlenemiyorsa cihazı veya sistemi bir ünite olarak geri çekin. Kontrolsüz torklama veya dirence karşı kateterin ya da separatörün kuvvet harcanmak suretiyle insersiyonu, cihaz veya damar hasarıyla sonuçlanabilir.
- Penumbra System'ı Penumbra Aspirasyon Pompası haricindeki bir pompa ile kullanmayın.

Önlemler

- Cihaz sadece tek kullanım için amaçlanmıştır. Tekrar sterilize etmeyin veya tekrar kullanmayın. Tekrar sterilizasyon ve/veya tekrar kullanım, kateter kaplama lubrikasyonunun etkisiz olmasıyla sonuçlanabilir. Bu durum ise, yüksek sürtünmeye ve hedeflenen nöro vaskülatür konumuna ulaşamamaya neden olabilir.
- Bükülmüş veya hasarlı cihazları kullanmayın. Açık veya hasarlı ambalajları kullanmayın. Tüm hasarlı cihazları ve ambalajı üreticiye/distribütöre geri gönderin.
- "Son Kullanma Tarihi"nden önce kullanın.
- Penumbra System'ı floroskopik görüntüleme ile birlikte kullanın.
- Aspirasyon gerçekleştirirken Penumbra Aspirasyon Tüp Sistemi valfinin pıhtıyı çıkarmak üzere gerekli minimum süre için açık olduğundan emin olun. Aşırı düzeyde aspirasyon ya da aspirasyon tamamlandığı halde Penumbra Aspirasyon Tüp Sistemi valfinin kapatılmaması önerilmez.
- Penumbra Separatörün nörovasküler kılavuz tel olarak kullanılması amaçlanmamıştır. Revaskülarizasyon işlemi sırasında Penumbra Reperfüzyon Kateterinin tekrar konumlandırılması gerekiyorsa, söz konusu konumlandırma standart mikrokateter ve kılavuz tel teknikleri kullanılarak uygun bir nörovasküler kılavuz tel üzerinden gerçekleştirilmelidir.
- Cihaza hasar verebileceği için Penumbra Reperfüzyon Kateteri ile birlikte otomatik yüksek basınçlı kontrast madde enjeksiyon ekipmanı kullanmayın.
- Tedaviden sonra 24 saat geçene kadar antikoagülant ve antitrombosit uygulamasına ara verilmelidir. Tıbbi kontrol ve akut inme sonrası bakım, ASA kılavuz ilkelerine uygun olmalıdır.[1] Nörolojik açıdan herhangi bir kötüleşme, acil bir BT taraması ile ve araştırmacının/hastanenin uygun gördüğü en iyi uygulama çerçevesinde diğer değerlendirmeler yoluyla değerlendirilmelidir.
- Hastada revaskülarizasyon elde etmek için izin verilen toplam süre, Penumbra System kullanılarak 120 dakikadır.

Olası Ters Olaylar

Olası komplikasyonlar arasında aşağıdakiler yer alır, fakat bunlarla kısıtlı değildir:

- akut oklüzyon
- arteriyovenöz fistül
- cihaz arızası
- damar spazmı, trombozu, diseksiyonu veya perforasyonu
- distal embolizasyon
- emboli
- enfeksiyon
- erişim bölgesinde hematom veya kanama
- hava embolisi
- inme dahil nörolojik bozukluklar
- intrakraniyal kanama
- iskemi
- kontrast madde nedeniyle alerjik reaksiyon ve anafilaksi
- kontrast maddeden kaynaklanan böbrek hasarı
- ölüm
- pıhtının tamamen çıkarılamaması
- yalancı anevrizma oluşumu

İşlem

1. Kullanmadan önce **Uyarılar, Önlemler** ve **Olası Ters Olaylar** bölümlerine başvurun.
2. Penumbra System'ın her bir cihazı kullanıldığında cihazı ambalajından çıkarın ve hasar veya kıvrılma olup olmadığını inceleyin.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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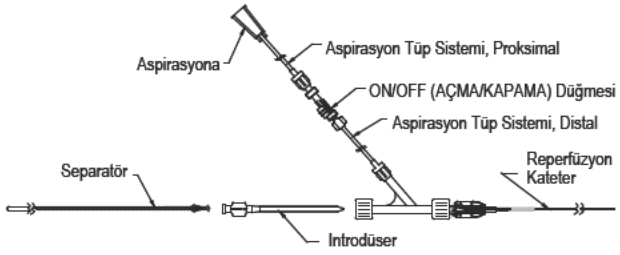
3. Ambalaj halkasından ve cihazdan heparinize salin geçirerek Penumbra System cihazlarını kullanıma hazırlayın (sadece Penumbra Reperfüzyon Kateterini ve Penumbra Separatörünü içerir).
4. Üreticinin *Kullanma Talimatına* uygun olarak bir kılavuz kateter veya uzun femoral kılıf hazırlayın.
5. Kılavuz kateteri veya uzun femoral kılıfı, pıhtı oklüzyon bölgesine proksimal uygun serebral arter içine yerleştirin.

Penumbra Reperfüzyon Kateterinin Hazırlanması ve Kullanılması

1. Damar çapını doğrulayın ve uygun büyüklükte bir Penumbra Reperfüzyon Kateteri seçin (Bkz. **Tablo 1**).
2. Penumbra Reperfüzyon Kateterinin ucu, buhar ile şekil verme mandreli (cihazla birlikte sağlanır) kullanılarak şekillendirilebilir.
3. Döner hemostaz valfini (cihazla birlikte sağlanır) Penumbra Reperfüzyon Kateterine takın.
4. Penumbra Aspirasyon Tüp Sistemini Aspirasyon Pompasına takın ve Aspirasyon Pompasını çalıştırın (Aspirasyon Pompası *Çalıştırma Kılavuzuna* başvurun). Kullanım öncesinde Aspirasyon Pompasının en az bir dakika çalışmasını sağlayın ve Aspirasyon göstergesinde −508 mmHg (−20 inçHg) ibaresinin okunduğundan emin olun. Penumbra Aspirasyon Tüp Sisteminin üzerinde bulunan valfin OFF (KAPALI) pozisyonunda olduğundan emin olun.
5. Aspirasyon Tüp Sistemini, **Şekil 1**'de gösterildiği gibi döner hemostaz valfinin yan portuna bağlayın.

Şekil 1 – Penumbra Separatörlü Monte Edilmiş Aspirasyon Sistemi



6. Penumbra Reperfüzyon Kateterini bir kılavuz telin proksimal göbeğine takılı olan döner hemostaz valfinin içinden geçirin. Bir kılavuz kateter kullanılmıyorsa Penumbra Reperfüzyon Kateterini soyulabilir kılıf yardımıyla uzun femoral kılıfın valfi içinden yerleştirin. Penumbra Reperfüzyon Kateterinin insersiyonundan sonra soyulabilir kılıfı vasküler kılıftan çıkarın ve Penumbra Reperfüzyon Kateteri şaftından soyarak çıkarın.
7. Floroskopi kılavuzluğu altında geleneksel kateterizasyon teknikleri kullanarak Penumbra Reperfüzyon Kateterini uygun bir nörovasküler kılavuz tel üzerinden hedef damarın içine ilerletin. Penumbra Reperfüzyon Kateterini pıhtının proksimaline konumlandırın. Kılavuz teli Penumbra Reperfüzyon Kateterinden çıkarın.
8. Aspirasyona başlamak için Penumbra Aspirasyon Tüp Sistemi üzerindeki valfi ON (AÇIK) pozisyonuna getirerek açın. Aspirasyonu durdurmak için Penumbra Aspirasyon Tüp Sistemi üzerindeki valfi OFF (KAPALI) pozisyonuna getirin ve Aspirasyon Pompasını kapatın.
9. 5 ml ya da 10 ml'lik bir şırınga kullanarak, kateter içinde kalmış olabilecek pıhtıları temizlemek amacıyla yaklaşık olarak 5 ml kanı Penumbra Reperfüzyon Kateterinden aspire edin.
10. Kılavuz kateterden kontrast madde enjekte etmek suretiyle bir tedavi sonrası anjiyo elde edin.

Penumbra Separatörünün Hazırlanması ve Kullanılması

1. Gerekirse, Penumbra Reperfüzyon Kateterine karşılık gelen uygun büyüklükte bir Penumbra Separatörü seçin (Bkz. **Tablo 1**).

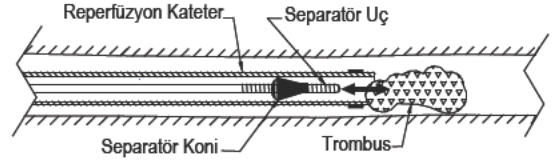
Tablo 1 – Separatör/Reperfüzyon Kateteri Cihaz Büyüklüğü Seçimi

Damar Boyutu (mm)	Penumbra Reperfüzyon Kateteri	Penumbra Separatörü
< 2,0	026	026
2,0 - 3,0	032 / 3MAX	032 / 3MAX
3,0 - 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX / ACE	054 / 5MAX

NOT: Oklüzyon alanına erişim, uygun bir iç mikrokateterin üç açılı kullanımı ile desteklenebilir.

2. Temin edilen introdüser kılıfını kullanarak Penumbra Separatörünü, döner hemostaz valfı içinden ve Penumbra Reperfüzyon Kateterinin proksimal göbeğin içine yerleştirin.
3. Aspirasyona başlamak için Penumbra Aspirasyon Tüp Sistemi üzerinde bulunan valfi ON (AÇIK) pozisyonuna getirin ve **Şekil 2**'de gösterildiği şekilde pıhtının aspirasyonuna ve temizlenmesine yardımcı olması için Penumbra Separatörünü Penumbra Reperfüzyon Kateterinden ilerletin/geri çekin.

Şekil 2 – Penumbra Separatörü Kullanılarak Pıhtı Aspirasyonu



4. Aspirasyonu durdurmak için Penumbra Aspirasyon Tüp Sistemi üzerindeki valfi OFF (KAPALI) pozisyonuna getirin ve Aspirasyon Pompasını kapatın.
5. Kullanıldıysa Penumbra Separatörünü çıkartın.
6. Gerekli olması durumunda, ek Penumbra Separatörleri ve Reperfüzyon Kateterleri doktorun kararına bağlı olarak ilave pıhtının temizlenmesinde kullanılabilir.

Klinik Veri Özeti

Penumbra Pivot çalışması, Penumbra System'ın güvenliğini ve etkinliğini değerlendirmek için prospektif, tek kollu bir çalışmaydı. Uluslararası 24 merkezde toplam 125 hasta çalışmaya katıldı. Ana giriş kriterleri şunlardır: NIH İnme Ölçeği (NIHSS) puanının 8 veya üstünde olması, semptom görülmesinden itibaren 8 saat içinde kendini gösterme ve tedavi edilebilir bir intrakraniyal damar oklüzyonu (TIMI 0 veya 1). Semptom başlangıcından itibaren 3 saat içinde kendisini gösteren hastalar rtPA tedavisi için uygun olmayan ya da tedaviye cevap vermeyen hastalar olması gerekiyordu. Primer uç noktalar, hedef damarın revaskülarizasyonu (TIMI 2 veya 3) ve işleme özgü ciddi ters olay vakasıdır (CTO). Tüm hastalar, işlemden itibaren 90 güne kadar takip edilmiş ve değerlendirilmiştir.

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İstatistiksel Analiz
En az 115 değerlendirilebilir hasta elde etmek amacıyla bu çalışma için örnek büyüklüğü 125 olarak seçildi. Hasta, primer uç nokta değerlendirmesi için uygunluk gereksinimlerini karşılamışsa ve Penumbra System ile tedavi edilmişse, değerlendirilebilir olarak dikkate alındı. Bu, kontrolsüz bir çalışma olduğundan, TIMI derecesi 2 veya 3 elde etmek amacıyla genel yanıt oranı için formel bir hipotez testi planlanmadı. Kategorik uç noktalar için standart tanımlayıcı istatistikler, uç noktasının her düzeyi için hasta sayısı ve yüzdesiydi. Sayısal uç noktalar için standart tanımlayıcı istatistikler şunları içeriyordu: Eksik olmayan gözlemlerin sayısı (n), ortalama, medyan, standart sapma, minimum değer ve maksimum değer.

Çalışmayla İlgili İşlemler
Hedef damara arteriyal erişim standart perkütan teknik kullanılarak elde edildi ve oklüde vasküler segmentin anjiyomimarisini tanımlamak için dört damarlı dijital çıkarmalı anjiyografi gerçekleştirildi. Her hasta için serebral büyük damar oklüzyonunun anjiyografi ile doğrulanması ve araştırmacı tarafından önceden primer oklüzyon bölgesinin belirlenmiş olması gerekliydi. Oklüzyonun tedavi edilebilir bir damarda olması durumunda uygun bir kılavuz kateter konumlandırıldı ve Penumbra Reperfüzyon Kateteri oklüde hedef damarın proksimal ucuna ilerletildi. Reperfüzyon Kateteri kılavuz kateterden yerleştirilince hasta çalışmaya kaydolmuş olarak dikkate alındı.

Temel Dahil Olma Kriterleri
- Aşağıdakiler de dahil olmak üzere akut iskemik inme ile tutarlı klinik bulgular:
  - Yüzde veya uzuvlarda ani uyuşma veya zayıflık
  - Ani konfüzyon, konuşma veya konuşmayı anlama güçlüğü
  - Ani yürüme zorluğu, baş dönmesi veya denge kaybı
- 18 - 79 yaş aralığı
- NIH İnme Ölçeği (NIHSS) puanı ≥ 8'e yol açan nörolojik bozukluk
- İnmeye yönelik Penumbra System tarafından erişilebilir intrakraniyal damarlarda komple oklüzyon (TIMI Derecesi 0) veya distal dal doldurma olmadan minimal perfüzyon ile kontrast madde penetrasyonu (TIMI Derecesi I)
- İmzalı bilgilendirme amaçlı olur formu
- İnme semptomu başlangıcından itibaren 8 saat içinde kendini gösterme
- Hasta semptom başlangıcından itibaren 3 saat içinde kendisini gösteriyorsa intravenöz rtPA tedavisi için uygun değildi ya da tedaviye cevap vermiyordu

Temel Hariç Olma Kriterleri
- Çalışmaya kaydolma sırasında hızla iyileşen nörolojik inme bulguları kanıtı
- NIHSS > 30 veya koma
- Hamile kadınlar
- Damar yapısının endovasküler erişimi imkansız kılacak kadar kıvrımlı olması
- Bilinen kanama diyatezi, koagülasyon yetersizliği veya INR > 3,0 ile oral antikoagülasyon tedavisi görüyor olması
- PTT'nin laboratuvar normal değerinin 2 katından büyük olması
- Çalışmaya katılma sırasında trombosit sayısı < 30.000
- Çalışma sonuçlarını karıştırabilecek önceden mevcut nörolojik veya psikiyatrik hastalık
- Kontrast maddeye karşı bilinen ciddi alerji
- Kontrol edilmeyen hipertansiyon (sistolik kan basıncı > 185 mmHg veya diastolik kan basıncı > 110 mmHg olarak tanımlanır)
- Kendini gösterme sırasında aşağıdaki durumların varlığının BT ile kanıtlanması:
  - Orta hat kaymasıyla önemli ölçüde kütle etkisi
  - Orta serebral arter bölgesinin 1/3'ünden büyük, geniş hipodansite bölgesi
  - İntrakraniyal kanama bulgusu
- Pıhtının çıkarılmasını engelleyebilecek, oklüzyona proksimal bir arteriyal stenozun anjiyografik kanıtı
- Önceden mevcut arteriyal hasarın anjiyografik kanıtı
- 90 günden az ömür beklentisi
- Çalışma cihazının değerlendirilmesini karıştırabilecek başka bir klinik araştırmaya katılma

Çalışmaya katılan deneklerin özellikle anjiyografik kriterler esas alınarak çalışmadan hariç tutulma sebeplerinin özeti
Çalışmaya kayıtlı hastalardan hiçbiri anjiyografik sebeplerle hariç tutulmamıştır.

Primer Etkinlik Uç Noktası
Primer Etkinlik Uç Noktası, oklüde hedef damarın revaskülarizasyonuydu. Revaskülarizasyon sadece Penumbra System'ın kullanılmasının ardından ve herhangi bir ek veya tamamlayıcı cihaz ya da tedavi kullanılmadan önce TIMI puanı II veya III ile tanımlandı. Anjiyografik sonuçlara bağımsız bir Merkez Laboratuvar tarafından hüküm verildi.

Etkinlik	% (n/N) [%95 GA]†
Primer Etkinlik Uç Noktası (TIMI puanı II veya III) *Tamamlayıcı tedaviler kullanılmadan önce TIMI puanları*	%81,6 (102/125) [%73,7; %88,0]
Cihaz Sonrası Revaskülarizasyon Başarısı (TIMI ≥ 2) *Kullanılan Tüm Tamamlayıcı Tedaviler, Tedavi Başarısızlığı Olarak Dikkate Alındı*	%81,6 (102/125) [%73,7; %88,0]
Cihaz Sonrası Revaskülarizasyon Başarısı (TIMI ≥ 2) *Kullanılan Tüm IA Litik Tedaviler, Tedavi Başarısızlığı Olarak Dikkate Alındı*	%81,6 (102/125) [%73,7; %88,0]

†Hassas Clopper-Pearson güven aralıkları

Primer Güvenlik Uç Noktası
Primer Güvenlik Uç Noktası, araştırmacı tarafından raporlandığı gibi, işlem sırasında ortaya çıkmış, cihaz ve/veya işlemle ilgili ciddi ters olay vakasıydı. 16 hastada işlemle ilgili 18 olay rapor edildi (%12,8). Bunların içinde, 3 hastada görülen 4 olay, Klinik Olay Komisyonu tarafından ciddi olarak değerlendirildi (%2,4).

İşlem sırasında Kompozit Ters Olaylar	% (n/N) [%95 GA]†
İşlem sırasında Kompozit CTO	%2,4 (3/125)
Primer Güvenlik Uç Noktası: İşlem sırasında İşlem/Cihaz ile ilgili Kompozit CTO	%2,4 (3/125)

†Hassas Clopper-Pearson güven aralıkları

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90 gün boyunca hastaların %2'sinden fazlasında ortaya çıkan her spesifik CTO

CTO	% (n/N)
Kompozit CTO'lar	%52,0 (65/125)
Serebral Ödem	%11,2 (14/125)
İntraserebral Kanama	%8,0 (10/125)
Solunum Bozukluğu/Yetmezliği	%8,0 (10/125)
Niteleyici İnme Semptomlarının Kötüleşmesi	%7,2 (9/125)
Enfeksiyon	%5,6 (7/125)
Diğer Pulmoner Kompl kasyonlar	%5,6 (7/125)
Zatürree	%4,0 (5/125)
Kardiyak Aritmi	%3,2 (4/125)
Erişim Bölgesi Komplikasyonu	%2,4 (3/125)
Miyokard Enfarktüsü	%2,4 (3/125)
Periferal Vasküler Kompl kasyon	%2,4 (3/125)
Böbrek Bozukluğu/Yetmezliği	%2,4 (3/125)
Yeni Bölgede İnme	%2,4 (3/125)

90 Gün Boyunca Anatomik Sistem Altında TO'ların Kategorizasyonu

Anatomik Sistem	% (n/N)
Sinir Sistemi Bozuklukları	%62,4 (78/125)
Enfeksiyonlar ve enfestasyonlar	%44,0 (55/125)
Kardiyak bozukluklar	%28,8 (36/125)
Metabolizma ve beslenme bozuklukları	%25,6 (32/125)
Genel bozukluklar ve uygulama sahası rahatsızlıkları	%24,8 (31/125)
Respiratuvar, torasik ve mediastinal bozukluklar	%24,8 (31/125)
Yaralanma, zehirlenme ve işlemle ilgili komplikasyonlar	%18,4 (23/125)
Gastrointestinal bozukluklar	%16,0 (20/125)
Kan ve lenf sistemi bozuklukları	%14,4 (18/125)
Vasküler bozukluk	%11,2 (14/125)
Ps kiyatrik bozukluklar	%10,4 (13/125)
Böbrek ve idrar yolu bozuklukları	%8,0 (10/125)
Hepatobiliyer bozukluklar	%4,0 (5/125)
Araştırmalar	%3,2 (4/125)
Cilt ve subkütan doku bozuklukları	%3,2 (4/125)
Benign, malign ve belirtilmemiş neoplazmalar (kistler ve polipler dahil)	%2,4 (3/125)
Kas-iskelet sistemi ve bağdoku bozuklukları	%0,8 (1/125)

SEMBOL SÖZLÜĞÜ

			D kkat, kullanma talimatına bakınız
Rx Only			Sadece reçete ile – ABD Federal Yasası, bu aygıtın satışını bir doktor tarafından ve bir doktorun isteği ile yapılacak şekilde kısıtlamaktadır
			Pirojen k değildir
STER LE EO			Etilen oksitle sterilize edilmiştir
	İmalatçı	EC REP	AB Temsilcisi
LOT	Lot numarası		Tekrar kullanmayın
	Son kullanma tarihi	REF	Katalog numarası
STERILIZE	Tekrar sterilize etmeyin	LATEX	Lateks içermez

GARANTI

Penumbra, Inc. (Penumbra), bu cihazın tasarımı ve üretiminde makul bir özen gösterildiğini garanti eder. Bu garanti, burada açıkça belirtilmeyen, yasaların işleyişiyle veya diğer şekilde açıkça veya zımnen ifade edilen, ticarete uygunluk veya belirli bir kullanıma uygunluk ile ilgili zımni garantiler de dahil olmak üzere fakat bunlarla kısıtlı olmamak kaydıyla diğer tüm garantilerin yerine geçer ve onları muaf tutar. Bu cihazın kullanılması, saklanması, temizliği ve sterilizasyonunun yanı s ra, hasta, tanı, tedavi ve cerrahi işlemlerle ilgili diğer faktörler ve Penumbra'nın kontrolü dış ndaki diğer konular cihazı ve cihaz kullanımından elde edilen sonuçları doğrudan etkiler. Bu garanti çerçevesinde Penumbra'nın yükümlülüğü, bu cihazın onar mı veya değiştirilmesiyle sınırlı olup, bu cihazının kullanımından doğrudan veya dolaylı olarak kaynaklanan her türlü arızi veya sonuçsal kayıplar, hasar veya masraflar için Penumbra sorumlu tutulamaz. Penumbra, bu cihazla bağlantılı herhangi diğer veya ilave yükümlülük veya sorumluluk kabul etmez ve bunları kendi yerine kabul etmeye herhangi bir kişiyi yetkilendirmez. Penumbra, tekrar kullanılan, tekrar işlemden geçirilen veya tekrar sterilize edilen cihazlarla ilgili sorumluluk kabul etmez ve söz konusu cihazlarla ilgili ticarete veya amaçlanan kullanıma uygunluk da dahil olmak üzere ancak bunlarla kısıtlı olmamak kaydıyla açıkça veya zımnen herhangi bir garantide bulunmaz.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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简体中文

器械描述

Penumbra System® 由以下几种器械组成：

- Penumbra 再灌注导管
- Penumbra 抽吸泵
- Penumbra 泵/滤器管
- Penumbra 抽吸管
- Penumbra 分离器

Penumbra System 旨在通过持续抽吸从血管中取出血栓。使用再灌注导管直接从泵抽吸血栓。如果再灌注导管被血栓堵塞，可以使用分离器清理再灌注导管管腔。使用内径为 1.37 mm（0.054 英寸）及以上的再灌注导管时可能不需要使用分离器。将再灌注导管通过导引导管或长股鞘置入颅内血管，然后沿着神经血管导丝上面引导至主要闭塞部位。Penumbra 再灌注导管与抽吸泵配合使用从闭塞血管抽吸血栓。如有必要，可以从再灌注导管置入 Penumbra 分离器以协助取出血栓。Penumbra 分离器在主要阻塞部位近处通过 Penumbra 再灌注导管推进和撤回，以协助将血栓从再灌注导管尖端清除。对于抽吸源，Penumbra 再灌注导管与抽吸泵通过 Penumbra 抽吸管和 Penumbra 泵/滤器管连接后使用。Penumbra 再灌注导管附带一个蒸汽成形芯棒和旋转止血阀，和一条可撕裂鞘。此外，Penumbra 分离器也附带一个导引器和转矩装置。这些装置在 X 线透视下可见。

适用范围

Penumbra System 适用于继发于颅内大血管闭塞性疾病（颈内动脉、大脑中动脉 – M1 和 M2 段、基底动脉和椎动脉内）的急性缺血性卒中患者，出现症状 8 小时内进行血管再通。

禁忌症

目前尚无已知禁忌症。

警告

- Penumbra System 应只能由受过适当神经血管内介入技术和急性缺血性卒中治疗培训的医师使用。
- 如果遇到阻力，在未利用 X 线透视仔细评估原因的情况下，请勿推进、撤回或使用 Penumbra System 的任何部件。如果无法确定原因，请撤出整个器械。遇到阻力时，过度扭转或用力插入导管或分离器可能导致器械受压，而损伤血管或器械。
- 请勿在 Penumbra System 中使用除了 Penumbra 抽吸泵之外的泵。

注意事项

- 本器械仅供一次性使用。请勿重复灭菌或重复使用。重新灭菌和/或重使用将会导致导管涂敷的润滑剂失去作用，从而导致摩擦力加大而不能将导管输送至目标神经血管位置。
- 如果器械弯结或损坏，请勿使用。如果器械包装已拆封或损坏，请勿使用。将所有有损坏的器械连同包装退回制造商/分销商。
- 请在 “使用期限” 日期前使用。
- 请结合 X 线透视显影技术使用本 Penumbra System。
- 进行抽吸时，确保 Penumbra 抽吸管阀尽可能开放取出血栓所需的最短时间。不建议过度抽吸或抽吸完成时不能闭合 Penumbra 抽吸管。
- Penumbra 分离器不能作为神经血管导丝使用。如果在血管再通操作中需要重新定位 Penumbra 再灌注导管，应当使用标准微导管和导丝技术通过适当的神经血管导丝进行重新定位。
- 请勿将自动高压对比剂注射器装置和 Penumbra 再灌注导管配合使用，因其可能损坏该器械。
- 应停止服用抗凝剂和抗血小板药物直至治疗后 24 小时。应按照 ASA 指南采取医疗措施以及进行急性卒中后治疗。[1] 任何神经系统的病情恶化均应按照研究者/医院的最佳实践的指征由急诊 CT 进行评估或进行其他评估。
- 使用 Penumbra System 对患者进行血管再通的允许总操作时间为 120 分钟。

潜在不良事件

可能会发生的并发症，包括但不限于以下事件：

- 包括中风的神经功能障碍
- 不能完全取出血栓
- 穿刺部位血肿或出血
- 动静脉瘘
- 对比剂导致的肾损伤
- 感染
- 假性动脉瘤形成
- 急性阻塞
- 空气栓塞
- 颅内出血
- 器械故障
- 缺血
- 栓子
- 死亡
- 血管痉挛、血栓形成、夹层或穿孔
- 因对比剂造成的过敏反应和过敏症
- 远端栓塞

操作步骤

1. 使用前请参阅《**警告、注意事项**和**潜在不良事件**》。
2. 使用 Penumbra System 的任意器械时，从包装中取出器械，检查是否有损坏或扭结。
3. 使用肝素化生理盐水冲洗包装环和器械，以准备 Penumbra System 器械（仅包括 Penumbra 再灌注导管和 Penumbra 分离器）供使用。
4. 按照制造商的《使用说明》准备导引导管或长股鞘。
5. 将导引导管或长股鞘放入接近血栓栓塞部位的适当的脑动脉中。

Penumbra 再灌注导管的准备和使用

1. 确认血管直径，选择适当尺寸的 Penumbra 再灌注导管（见**表 1**）。
2. 可以使用提供的蒸汽成形芯棒使 Penumbra 再灌注导管尖部成形。
3. 将提供的旋转止血阀连接至 Penumbra 再灌注导管。
4. 将 Penumbra 抽吸管连接至抽吸泵，并打开抽吸泵（请参阅《抽吸泵操作手册》）。在使用前，应使抽吸泵至少运行 1 分钟，并确认抽吸计的读数为 -508 mmHg(-20 英寸汞柱)。确保 Penumbra 抽吸管上的阀门处于 OFF（关）位置。

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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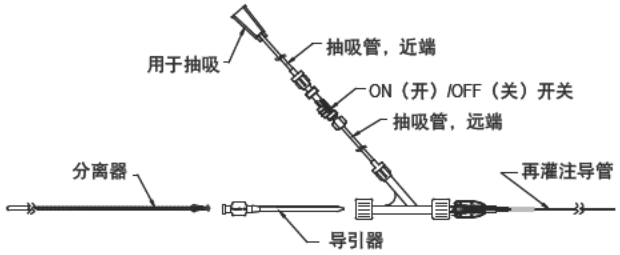
5. 将抽吸管连接至旋转止血阀的侧孔，如**图 1** 所示。

图 1 – 已装好 Penumbra 分离器的抽吸系统



6. 将 Penumbra 再灌注导管插入与导引导管近端接头相连的旋转止血阀。如果未使用导引导管，使用可撕裂鞘将 Penumbra 再灌注导管穿过长股鞘的阀门。插入 Penumbra 再灌注导管后，从血管鞘中取出可撕裂鞘，从 Penumbra 再灌注导管轴芯上撕下。
7. 在 X 线透视导引下使用传统导管技术，将 Penumbra 再灌注导管通过一个合适的神经血管导丝推进至靶血管。将 Penumbra 再灌注导管放置于血栓附近。从 Penumbra 再灌注导管上取下导丝。
8. 要开始抽吸，请将 Penumbra 抽吸管上的阀门打开至 ON（开）位置。要停止抽吸，请将 Penumbra 抽吸管上的阀门切换到 OFF（关）位置，然后关闭抽吸泵。
9. 使用 5 ml 或 10 ml 的注射器，从 Penumbra 再灌注导管中抽吸大约 5 ml 的血液，以取出可能残留在导管中的任何血栓。
10. 通过导引导管注射对比剂，以获取治疗后的血管造影片。

Penumbra 分离器准备和使用

1. 如有必要，选择与再灌注导管对应的适当尺寸的 Penumbra 分离器（见**表 1**）。

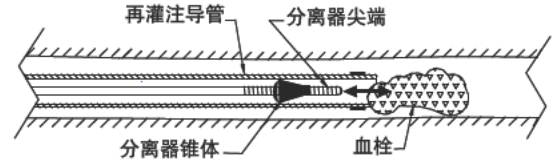
表 1 – 分离器/再灌注导管装置尺寸

血管尺寸（mm）	Penumbra 再灌注导管	Penumbra 分离器
< 2.0	026	026
2.0-3.0	032 / 3MAX	032 / 3MAX
3.0-4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX / ACE	054 / 5MAX

注意：可通过使用一条相容的内部微导管，借助于三轴方式进入闭塞部位。

2. 利用随附的导引鞘，将 Penumbra 分离器通过旋转止血阀插入 Penumbra 再灌注导管的近端接头中。
3. 要开始抽吸，请将 Penumbra 抽吸管上的阀门打开至 ON（开）位置，推进/撤回 Penumbra 分离器，以协助从再灌注导管抽吸和取出血栓，如**图 2** 所示。

图 2 – 使用 Penumbra 分离器抽吸血栓



4. 要停止抽吸，请将 Penumbra 抽吸管上的阀门切换到 OFF（关）位置，然后关闭抽吸泵。
5. 取出 Penumbra 分离器（如果使用的话）。
6. 如有必要，医生可酌情决定使用其他 Penumbra 分离器和再灌注导管进一步取栓。

临床数据概要

Penumbra 关键试验是一项评估 Penumbra System 的安全性和有效性的前瞻性单组试验。共有 125 例患者纳入 24 个国际研究中心。主要纳入标准为出现症状后 8 小时内 NIH 卒中量表 (NIHSS) 评分 ≥ 8，且为可治疗颅内血管闭塞（TIMI 0 或 1）。出现症状后 3 小时内切忌 rtPA 治疗或 rtPA 治疗效果不佳的患者。主要终点为靶血管的血管再通（TIMI 2 或 3）和操作相关严重不良事件 (SAE) 发生率。随访所有患者并进行评估直至手术后 90 天。

统计分析

选择 125 例患者的样本量以获得至少 115 例可评估患者。如果经 Penumbra System 治疗的患者符合主要终点评估的资格要求，则被认为是可评估患者。由于这是一项非对照研究，先前的假设检验并未计划评估达到 TIMI 2 或 3 级的总体应答率。各类终点的标准描述性统计为各终点水平的患者数量和百分比。对于数值型终点，标准描述性统计包括无丢失观察值受试者数量 (n)、平均值、中位值、标准差、最小值和最大值。

研究程序

使用标准经皮技术进入通向靶血管的动脉，并进行四血管数字减影血管造影术以确定闭塞血管段的血管结构。研究者事先确定每例患者存在主要闭塞部位且存在经血管造影术证实的大脑大血管闭塞。如果闭塞处为可治疗血管，将放置适当的导引导管，推进 Penumbra 再灌注导管至闭塞靶血管近端。再灌注导管从导引导管释放的患者被认为是纳入了试验。

主要纳入标准

- 临床体征符合急性缺血性卒中表现，包括：
  - 面部或四肢突然麻木或无力
  - 突发意识障碍、言语困难或语言理解能力障碍
  - 突发行走困难、头晕或丧失平衡
- 年龄为 18-79 岁
- 神经功能障碍导致NIH 卒中量表 (NIHSS) 评分≥ 8
- 可插入 Penumbra 卒中系统的颅内血管完全闭塞（TIMI 0 级）或 (Grade 0) 或对比剂可从微小血管孔通过但远端分支血管无填充（TIMI 1 级）或 (Grade I)
- 签署了知情同意书
- 出现中风症状后 8 小时内
- 出现症状后 3 小时内，但不适于 rtPA 治疗或 rtPA 治疗效果不佳

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主要排除标准

- 纳入时有卒中迅速进展性神经系统体征的证据
- NIHSS > 30 或昏迷
- 妊娠期女性
- 血管扭曲严重不能进行血管内操作
- 已知为出血体质、凝血功能障碍或口服抗凝剂治疗且 INR > 3.0
- PTT 高于实验室正常值 2 倍
- 入院时血小板计数 < 30000
- 可能混淆研究结果的先前存在的神经疾病或精神疾病
- 已知对对比剂严重过敏
- 未控制的高血压（定义为收缩压> 185 mmHg或舒张压> 110 mmHg）
- 出现以下情况的 CT 表现：
  - 显著质量效应伴中线偏移
  - 大脑中动脉区域低密度范围> 1/3
  - 颅内出血表现
- 闭塞部位附近动脉血管狭窄阻碍血栓取出的血管造影表现
- 先前已有动脉损伤的血管造影表现
- 预期寿命短于 90 天
- 参与了另一项可能混淆研究器械评估的临床试验

已纳入受试者退出研究原因汇总（尤其是基于血管造影标准）

已纳入患者均未因血管造影原因退出。

主要有效性终点

主要有效性终点为闭塞靶血管的血管再通。血管再通定义为未使用任何其他或辅助性器械或治疗，仅使用 Penumbra System 后获得 TIMI 2 或 3 级血流。血管造影结果由独立的核心实验室进行评估。

有效性	% (n/N) [95% 置信区间]†
主要有效性终点（TIMI 2 或 3 级） 使用了辅助治疗前的 TIMI 评分	81.6% (102/125) [73.7%, 88.0%]
使用器械后血管再通成功 (TIMI ≥ 2) 任何辅助治疗的使用均被视为治疗失败	81.6% (102/125) [73.7%, 88.0%]
使用器械后血管再通成功 (TIMI ≥ 2) 任何动脉内溶栓剂的使用均被视为治疗失败	81.6% (102/125) [73.7%, 88.0%]

†精确 Clopper-Pearson 置信区间

主要安全性终点

主要安全性终点为研究者报告的手术过程中与设备和/或手术相关的严重不良事件发生率。报告 16 例患者发生了 18 个手术相关事件 (12.8%)。其中，3 例患者的 4 个事件被临床事件委员会 (CEC) 评估为严重事件 (2.4%)。

手术过程中的复合不良事件	% (n/N) [95% 置信区间]†
手术过程中的复合 SAE	2.4% (3/125)
主要安全性终点： 手术过程中的复合手术/器械相关 SAE	2.4% (3/125)

†精确 Clopper-Pearson 置信区间

90 天内在超过 2% 患者中发生的各种特定 SAE

SAE	% (n/N)
复合 SAE	52.0% (65/125)
脑水肿	11.2% (14/125)
ICH（脑内出血）	8.0% (10/125)
呼吸功能障碍/呼吸衰竭	8.0% (10/125)
符合卒中症状加重	7.2% (9/125)
感染	5.6% (7/125)
其他肺部并发症	5.6% (7/125)
肺炎	4.0% (5/125)
心律失常	3.2% (4/125)
穿刺部位并发症	2.4% (3/125)
心肌梗死	2.4% (3/125)
外周血管并发症	2.4% (3/125)
肾功能障碍/肾衰竭	2.4% (3/125)
新部位卒中	2.4% (3/125)

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90 天内按照解剖系统的不良事件分类

解剖系统	% (n/N)
中枢神经系统疾病	62.4% (78/125)
感染和寄生虫病	44.0% (55/125)
心脏疾病	28.8% (36/125)
代谢和营养疾病	25.6% (32/125)
一般疾病和给药部位疾病	24.8% (31/125)
呼吸系统、胸部和纵膈疾病	24.8% (31/125)
损伤、中毒和手术并发症	18.4% (23/125)
胃肠疾病	16.0% (20/125)
血液和淋巴系统疾病	14.4% (18/125)
血管疾病	11.2% (14/125)
精神病	10.4% (13/125)
肾脏和尿路疾病	8.0% (10/125)
肝胆疾病	4.0% (5/125)
辅助检查	3.2% (4/125)
皮肤和皮下组织疾病	3.2% (4/125)
良性、恶性和性质不明的肿瘤(包括囊肿和息肉)	2.4% (3/125)
肌肉骨骼和结缔组织疾病	0.8% (1/125)

符号词汇表

	注意,请参阅使用说明		
Rx Only	仅凭处方使用 – 美国联邦法律规定本器械只能由医师使用或遵照医嘱使用		
	无热原		
STERILE EO	利用环氧乙烷灭菌		
	制造商	EC REP	欧盟授权代表
LOT	批号		请勿重复使用
	使用期限	REF	目录号
STERILIZE	请勿重新灭菌	LATEX	不含乳胶

质量保证

Penumbra, Inc. (Penumbra) 保证,本器械在设计和生产中均使用合理的保护措施。本保证代替并排除其他所有本文未明确陈述的保证,不管是依法所作的明示或暗示保证,或其他包括但不限于任何特定用途的适销性或适用性保证。本器械的操作、储存、清洁、灭菌处理,以及其他与患者、诊断、治疗、外科手术和其他超过 Penumbra 可控范围的相关因素会直接影响器械使用以及其使用结果。因而在本质量保证之下,Penumbra 的义务仅限于修理或更换本器械,而对于直接或间接由于使用本器械而导致的任何意外的或结果性损失、损坏或费用,Penumbra 概不负责。Penumbra 不承担,也未授权其他任何人士代其承担与本器械有关的其他任何法律责任或义务。若本器械经重复使用、再加工,或者重复灭菌,Penumbra 将不承担任何责任,也未作出任何有关本器械明示或暗示的保证,包括但不限于适销性或预定用途的适用性的保证。

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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繁體中文

裝置描述

Penumbra System® 包含數種裝置：

- Penumbra 再灌流導管
- Penumbra 抽吸幫浦
- Penumbra 幫浦/濾管
- Penumbra 抽吸管
- Penumbra 分離器

Penumbra System 旨在透過連續抽吸清除血管內的血栓。再灌流導管讓幫浦能夠直接對準血栓進行抽吸。分離器可用於在血栓堵塞再灌流導管的情況下疏通導管腔。在使用內徑大於 1.37 mm（0.054 英寸）的再灌流導管時，可能並沒有必要使用分離器。將再灌流導管穿過導引導管或長股鞘置入顱內血管，然後沿著神經血管導絲上面引導至主要閉塞部位。Penumbra 再灌流導管與抽吸幫浦一起配合使用，抽吸閉塞血管中的血栓。根據需要，可透過再灌流導管置入一個 Penumbra 分離器，輔助血栓清除。Penumbra 分離器經由位於主要閉塞部位近側邊緣的 Penumbra 再灌流導管內推進和縮回，這有利於從再灌流導管管尖清除血栓。Penumbra 再灌流導管與使用 Penumbra 抽吸管和 Penumbra 幫浦/濾管進行連接的抽吸幫浦一起作為抽吸源。Penumbra 再灌流導管配有一個蒸汽成形心軸和旋轉止血閥，以及一條可剝離式鞘。Penumbra 分離器配有一個導引器和轉矩裝置。使用螢光顯像檢查法可看見這些裝置。

適用範圍

Penumbra System 專用於以下患者的血管再造：因顱內大血管閉塞性疾病（頸內動脈、中動脈 – M1 和 M2 段、腦底部和椎動脈內）繼發急性缺血性腦中風，並且疾病發作後不超過 8 小時。

禁忌症

沒有已知的禁忌症。

警告事項

- 只有接受過適當的介入神經外科血管內技術和急性缺血性腦中風治療訓練的醫師才能使用 Penumbra System。
- 如果遇到阻力，在未利用螢光顯像檢查法仔細評估原因的情況下，請勿推進、縮回或使用 Penumbra System 的任何組件。如果無法確定原因，則將裝置或系統整體取出。遇到阻力時，過度扭轉或強行插入導管或分離器可能會導致裝置或血管損傷。
- 請勿將 Penumbra System 與 Penumbra 抽吸幫浦以外的幫浦配合使用。

防範措施

- 此裝置僅適於單次使用。請勿重複滅菌或重複使用。重複滅菌及/或重複使用可能會造成導管塗層潤滑效果不佳，從而導致摩擦力增大且無法進入目標神經血管部位。
- 請勿使用扭結或受損的裝置。請勿使用已打開或受損的包裝。請將所有受損的裝置連同包裝退回給製造商/分銷商。
- 請在「有效期限」之前使用。
- 請將 Penumbra System 與螢光顯像配合使用。
- 進行抽吸時，請確保 Penumbra 抽吸管閥門的開啟時間不超過取栓時所需的最短時間。不建議過度抽吸或在抽吸完成後仍讓 Penumbra 抽吸管閥門處於開啟狀態。
- 請勿將 Penumbra 分離器用作神經血管導絲。若在血管再造手術中需要重新放置 Penumbra 再灌流導管，則應採用標準的微導管和導絲技術並使用合適的神經血管導絲來進行放置。
- 切勿將自動高壓顯影劑注射裝置與 Penumbra 再灌流導管一起使用，否則可能會損壞裝置。
- 在治療後 24 小時內，請勿使用抗凝血藥物和抗血小板藥物。應遵循 ASA 指引進行醫療管理和急性中風後護理。[1]任何神經功能惡化都應根據研究員/醫院的最佳實踐，使用緊急 CT 掃描和其他評估方法進行評估。
- 按照規定，使用 Penumbra System 對患者進行血管再造的總時間為 120 分鐘。

潛在的不良事件

可能的併發症包括但不限於以下各項：

- 死亡
- 血管痙攣、血栓形成、剝離或穿孔
- 空氣栓塞
- 急性阻塞
- 栓塞
- 神經功能缺損，包括中風
- 缺血
- 假性動脈瘤形成
- 動靜脈瘻管
- 無法完全清除血栓
- 感染
- 腦出血
- 裝置故障
- 對顯影劑的過敏反應
- 遠端栓塞
- 導入部位血腫或出血
- 顯影劑使腎臟受損

程序

1. 使用之前，請仔細閱讀**警告事項**、**防範措施**和**潛在的不良事件**。
2. 使用 Penumbra System 的各個裝置時，應先從包裝中取出裝置並檢查是否有損壞或纏結現象。
3. 準備 Penumbra System 裝置時，應使用肝素生理鹽水沖洗包裝箍和裝置（僅限 Penumbra 再灌流導管和 Penumbra 分離器）。
4. 請遵循製造商的《使用說明》準備導引導管或長股鞘。
5. 將導引導管或長股鞘放入靠近血栓閉塞部位的適當腦動脈中。

PENUMBRA 再灌流導管的準備和使用

1. 確定血管直徑，選擇適當大小的 Penumbra 再灌流導管（參見**表 1**）。
2. 可使用隨附的蒸汽成形心軸對 Penumbra 再灌流導管的管尖進行定形。
3. 將隨附的旋轉止血閥連接至 Penumbra 再灌流導管。
4. 將 Penumbra 抽吸管連接至抽吸幫浦，並開啟抽吸幫浦（請參閱抽吸幫浦的《操作手冊》）。在使用前，應讓抽吸幫浦至少運行 1 分鐘，並確認抽吸壓力計的讀數為 −508 mmHg（−20 inHg）。確保 Penumbra 抽吸管上的閥門處於 OFF（關）位置。

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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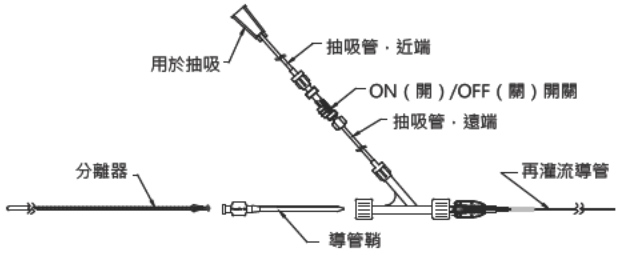
5. 將抽吸管連接至旋轉止血閥的側孔，如**圖 1** 所示。

圖 1 – 已裝好 Penumbra 分離器的抽吸系統



6. 將 Penumbra 再灌流導管插入已連接至導引導管近端接頭的旋轉止血閥。若未使用導引導管，使用可剝離式鞘透過長股鞘的閥門插入 Penumbra 再灌流導管。在插入 Penumbra 再灌流導管後，從血管鞘移除可剝離式鞘並從 Penumbra 再灌流導管軸剝離。
7. 在螢光顯像的指導下，使用常規的導管插入術，將 Penumbra 再灌流導管沿一 條適當的神經血管導絲推入靶血管。將 Penumbra 再灌流導管靠近血栓放置。 從 Penumbra 再灌流導管中取出導絲。
8. 要開始抽吸，請使 Penumbra 抽吸管上的閥門處於「ON」（開）位置。要停止抽吸，請將 Penumbra 抽吸管上的閥門切換到「OFF」（關）位置，然後關閉抽吸幫浦。
9. 使用 5 ml 或 10 ml 的注射器，從 Penumbra 再灌流導管中抽出大約 5 ml 血液，以清除導管中可能殘留的任何血栓。
10. 透過導引導管注射顯影劑，以取得治療後的血管造影圖像。

PENUMBRA 分離器的準備和使用

1. 選擇與再灌流導管相應大小的 Penumbra 分離器（參見**表 1**）。

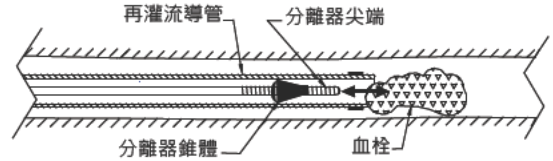
表 1 – 分離器/再灌流導管裝置大小選擇

血管尺寸（mm）	Penumbra 再灌流導管	Penumbra 分離器
< 2.0	026	026
2.0 至3.0	032 / 3MAX	032 / 3MAX
3.0 至 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX / ACE	054 / 5MAX

註：可透過一條相容的內部微導管，採用三軸方式進入閉塞部位。

2. 使用隨附的導引鞘，將 Penumbra 分離器透過旋轉止血閥插入 Penumbra 再灌流導管的近端接頭。
3. 要開始抽吸，請使 Penumbra 抽吸管上的閥門處於「ON」（開）位置，然後推進/縮回 Penumbra 分離器以協助從再灌流導管吸出和清除血栓，如**圖 2** 所示。

圖 2 – 使用 Penumbra 分離器抽吸血栓



4. 要停止抽吸，請使 Penumbra 抽吸管上的閥門處於「OFF」（關）位置，然後關閉抽吸幫浦。
5. 取出 Penumbra 分離器（如使用）。
6. 若有必要，醫師可酌情決定使用額外的 Penumbra 分離器和再灌流導管以進一步清除血栓。

臨床資料摘要

Penumbra 關鍵試驗是一項前瞻性單組臨床試驗，旨在評估 Penumbra System 的安全性和有效性。在 24 個國際中心總共招募 125 名患者。主要入選條件為 NIH 中風量表 (NIHSS) 評分 ≥ 8；症狀開始後 8 小時內入院；以及可治療的顱內血管閉塞（TIMI 0 或 1）。症狀開始後 3 小時內入院的患者必須不符合 rtPA 療法條件或對 rtPA 療法耐受性強。主要終點為靶血管的血管再造（TIMI 2 或 3）和程序性嚴重不良事件 (SAE) 的幾率。在程序結束後 90 天內，會對所有患者進行追蹤和評估。

統計分析

為產生至少 115 名可評估患者，本研究採用的樣本量為 125。如果一名患者滿足主要終點評估的合格要求，並且是使用 Penumbra System 治療的，則該患者即被視為可評估。由於這是一項非對照研究，因此沒有為總緩解率設計正式的假設檢驗，來確立 TIMI 2 級或 3 級。分類終點的標準描述性統計資料是每一級終點的患者數目和百分數。對於數值終點，標準描述性統計資料包括被觀察到的數量 (n)、平均值、中值、標準差、最小值和最大值。

研究程序

採用標準皮入技法經動脈進入靶血管；通過四血管數位減影血管造影確定閉塞血管段的血管構造。每名患者要透過血管造影確認腦大血管閉塞情況，並由研究人員事先指定一個主要閉塞部位。如果閉塞處於可治療血管內，則放入適當的導引導管，並將 Penumbra 再灌流導管推進到閉塞靶血管近端。當從導引導管置入再灌流導管時，一名患者即被視為已招募。

主要入圍條件

- 符合急性缺血性腦中風的臨床徵象，包括：
  - 突然發生面部或四肢發麻或無力
  - 突然發生意識障礙、言語表達或理解異常
  - 突然發生行走困難、頭暈或平衡感喪失
- 18 歲到 79 歲
- 神經功能缺損，導致 NIH 中風量表 (NIHSS) 評分 ≥ 8
- 用於腦中風的 Penumbra System 可進入的腦血管內完全閉塞（TIMI 0 級）或顯影劑滲透極少灌流但無遠端分支灌注（TIMI I 級）
- 已簽署知情同意書
- 中風症狀出現後 8 小時內入院
- 若在症狀出現後 3 小時內入院，不符合採用靜脈 rtPA 療法條件或對這種療法難受性強

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主要排除條件

- 在招募時中風有神經徵象迅速改善的臨床證據
- NIHSS >30 或昏迷
- 孕婦
- 血管扭曲，太難以在血管內通過
- 已知出血性素質、凝血缺陷或者在接受口服抗凝血治療且 INR >3.0
- PTT 大於實驗室正常值的 2 倍
- 入院時血小板 <30,000
- 原有神經或心理疾病，可能給研究結果造成混淆
- 已知對顯影劑嚴重過敏
- 控制不佳的高血壓（定義為收縮壓 >185 mmHg 或舒張壓 >110 mmHg）
- 入院時 CT 掃描表明存在以下疾病：
  - 嚴重巨塊效應，伴有中線偏移
  - 大塊高壓區大於大腦中動脈供血區的 1/3
  - 腦出血臨床證據
- 血管造影證據表明，閉塞部位近端一動脈狹窄可能妨礙血栓清除
- 血管造影證據表明，原來存在動脈損傷
- 預期存活期短於 90 天
- 參加另一項臨床研究試驗，可能會對研究裝置的評估造成混淆

已招募受試者排除原因一覽（尤其是那些基於血管造影條件的原因）

無已招募患者因血管造影原因被排除。

主要療效終點

主要療效終點是閉塞靶血管的血管再造。血管再造是在僅使用 Penumbra System 後、使用任何額外或輔助裝置或治療之前透過一個 II 級或 III 級的 TIMI 評分來定義的。血管造影結果由一個獨立核心實驗室裁定。

療效	% (n/N) [95% 置信區間]†
主要療效終點（TIMI 評分 II 或 III） 使用輔助療法之前的 TIMI 評分	81.6% (102/125) [73.7%, 88.0%]
使用裝置後血管再造成功 (TIMI ≥ 2) 任何輔助療法的使用均視為治療失敗	81.6% (102/125) [73.7%, 88.0%]
使用裝置後血管再造成功 (TIMI ≥ 2) 任何 IA 血栓溶解劑的使用均視為治療失敗	81.6% (102/125) [73.7%, 88.0%]

†Clopper-Pearson（精確）置信區間

主要安全性終點

主要安全性終點是根據研究人員報告在程序期間發生的、與裝置和/或程序有關的嚴重不良事件的發生率。報告有 16 名患者 (12.8%) 發生 18 個程序性事件。在這些事件中，有 3 名患者發生的 4 個事件被臨床事件委員會 (CEC) 評定為嚴重 (2.4%)。

程序期間發生的複合不良事件	% (n/N) [95% 置信區間]†
程序期間發生的複合嚴重不良事件	2.4% (3/125)
主要安全性終點： 程序期間發生的複合程序/裝置相關嚴重不良事件	2.4% (3/125)

†Clopper-Pearson（精確）置信區間

90 天期間曾經在 2% 以上患者中出現的嚴重不良事件一覽

嚴重不良事件	% (n/N)
複合嚴重不良事件	52.0% (65/125)
腦水腫	11.2% (14/125)
ICH（顱內出血）	8.0% (10/125)
呼吸功能障礙/衰竭	8.0% (10/125)
合格中風症狀惡化	7.2% (9/125)
感染	5.6% (7/125)
其他肺併發症	5.6% (7/125)
肺炎	4.0% (5/125)
心律失常	3.2% (4/125)
穿刺點併發症	2.4% (3/125)
心肌梗塞	2.4% (3/125)
外周血管併發症	2.4% (3/125)
腎功能障礙/衰竭	2.4% (3/125)
新供血區中風	2.4% (3/125)

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90 天期間各解剖系統出現的不良事件分類一覽

解剖系統	% (n/N)
神經系統紊亂	62.4% (78/125)
感染和蟲害侵染病	44.0% (55/125)
心臟疾患	28.8% (36/125)
新陳代謝和營養紊亂	25.6% (32/125)
一般疾患和處置部位狀況	24.8% (31/125)
呼吸、胸部和縱隔疾患	24.8% (31/125)
受傷、中毒和程序性併發症	18.4% (23/125)
胃腸紊亂	16.0% (20/125)
血液和淋巴系統疾患	14.4% (18/125)
血管疾患	11.2% (14/125)
精神失常	10.4% (13/125)
腎和泌尿功能紊亂	8.0% (10/125)
肝膽功能紊亂	4.0% (5/125)
試驗研究	3.2% (4/125)
皮膚或皮下組織疾患	3.2% (4/125)
良性、惡性和未指明腫瘤（包括囊腫和息肉）	2.4% (3/125)
肌肉骨骼和結締組織疾患	0.8% (1/125)

符號術語表

		注意，請參閱使用說明	
Rx Only		僅憑處方使用 – 美國聯邦法律規定本裝置只能由醫生使用或憑醫囑使用	
		無熱原	
STERILE EO		利用環氧乙烷滅菌	
	製造商	EC REP	歐盟授權代表
LOT	批號		切勿重複使用
	有效期限	REF	目錄編號
STERILIZE	切勿重新滅菌	LATEX	不含乳膠

保固

Penumbra, Inc. (Penumbra) 保證已對本裝置的設計和製造過程給予適當的謹慎管理。本保固替代並排除本文未載明之其他所有依法或以其他方式明示或默示的保證，包括但不限於對適銷性或特定用途之適用性的任何默示保證。本裝置的操作、儲存、清潔、滅菌，以及其他與患者、診斷、治療、外科手術和其他超過 Penumbra 可控範圍的相關因素會直接影響裝置使用的結果。因而在本保固之下，Penumbra 的義務僅限於修理或更換本裝置，而對於直接或間接由於使用本裝置而導致的任何偶然的或結果性損失、損壞或費用，Penumbra 概不負責。Penumbra 不承擔，也未授權其他任何人士代其承擔與本裝置有關的其他任何法律責任或一般責任。Penumbra 對於本裝置的重複使用、重新處理或重新滅菌不承擔任何法律責任，而且不作任何明示或默示的保證，包括但不限於對此類裝置的適銷性或預期用途之適用性的保證。

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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장치 설명

Penumbra System®은 다음의 여러 장치로 이루어져 있습니다:

- Penumbra 재관류 카테터
- Penumbra 흡인 펌프
- Penumbra 펌프/캐니스터 튜브
- Penumbra 흡인 튜브
- Penumbra 분리기

Penumbra System은 연속 흡인을 사용하여 혈관계에서 혈전을 제거하도록 설계되었습니다. 재관류 카테터는 펌프로 혈전을 직접 흡인하는 것을 목적으로 합니다. 분리기는 재관류 카테터가 혈전으로 막혔을 때 재관류 카테터의 내강을 비우는 데 사용할 수 있습니다. 내경이 1.37 mm(0.054 인치) 이상인 재관류 카테터를 사용할 때에는 분리기를 사용할 필요가 없을 수 있습니다. 재관류 카테터는 가이드 카테터 또는 긴 넙다리 유도관을 통과하여 두개내 혈관계로 삽입되고 신경혈관 가이드와이어를 통해 유도되어 주요 폐색 부위로 도달됩니다. Penumbra 재관류 카테터는 폐색된 혈관에서 혈전을 흡인하기 위해 흡인 펌프와 함께 사용됩니다. 필요에 따라 재관류 카테터에서 Penumbra 분리기를 전개하여 혈전 제거를 도울 수 있습니다. Penumbra 분리기는 Penumbra 재관류 카테터를 통해 주요 폐색 부위의 근위 가장자리에서 삽입하고 뒤로 당기며 재관류 카테터 팁에서 혈전을 원활히 제거할 수 있도록 합니다. 흡인원으로는 Penumbra 흡인 튜브 및 Penumbra 펌프/캐니스터 튜브를 사용하여 Penumbra 재관류 카테터를 흡인 펌프와 연결하여 사용합니다. Penumbra 재관류 카테터는 증기 쉐이핑 맨드렐, 회전 지혈 밸브, 박리 유도관과 함께 제공됩니다. Penumbra 분리기는 유도관 및 토크 장치와 함께 제공됩니다. 이 장치들은 형광 투시 검사를 통해 볼 수 있습니다.

적응증

Penumbra System은 증상이 나타난 지 8시간 내에 두개내 대혈관 폐색 질병(내경동맥, 중간 대뇌 – M1 및 M2 구역, 뇌저 및 척추 동맥)에 따른 급성 허혈성 뇌졸중이 있는 환자의 혈관재건술에 사용하도록 고안되었습니다.

금기 사항

알려진 금기 사항은 없습니다.

경고

- Penumbra System은 중재성 신경-혈관내 기법 및 급성 허혈성 뇌졸중의 치료에 관한 해당 교육을 이수한 의사만 이용해야 합니다.
- 저항이 있을 경우, 투시 검사를 사용하여 저항 원인을 조심스럽게 진단하지 않은 상태에서 저항에 대항하여 Penumbra System의 어느 구성 요소도 삽입하거나 뒤로 당기거나 사용하지 마십시오. 원인을 확인할 수 없는 경우, 장치 또는 시스템을 하나의 단위로 제거하십시오. 저항이 있는데도 무리하게 카테터 또는 분리기를 돌리거나 삽입하면 기기나 혈관 손상을 일으킬 수 있습니다.
- Penumbra System을 Penumbra 흡인 펌프가 아닌 다른 펌프와 함께 사용하지 마십시오.

주의 사항

- 본 장치는 1회용입니다. 재멸균하거나 재사용하지 마십시오. 재멸균하거나 재사용하면 카테터 코팅 윤활의 효과가 나빠져 마찰이 커지고 표적 신경혈관계 위치에 접근할 수 없게 됩니다.
- 장치가 비틀어져 있거나 손상된 경우 사용하지 마십시오. 포장이 개봉되어 있거나 손상된 경우 사용하지 마십시오. 장치 및 포장이 손상된 제품은 모두 제조업체/판매업체에 반품하십시오.
- "Use By(사용 기한)" 이전에 사용하십시오.
- Penumbra System을 투시 시각화 장치와 함께 사용하십시오.
- 흡인을 수행할 때, Penumbra 흡인 튜브 밸브가 혈전 제거에 필요한 최소 시간 동안만 열려 있도록 하십시오. 흡인을 완료한 후에 과도하게 흡인하거나 Penumbra 흡인 튜브 밸브를 닫지 않는 것은 좋지 않습니다.
- Penumbra 분리기는 신경혈관 가이드와이어로 사용하도록 고안되지 않았습니다. 혈관재건술을 시술하는 동안 Penumbra 재관류 카테터를 다시 배치해야 하는 경우 표준 마이크로카테터와 가이드와이어 기법을 사용하여 적절한 신경혈관 가이드와이어를 통해 수행해야 합니다.
- 자동 고압 조영제 주입 장비를 Penumbra 재관류 카테터와 함께 사용하지 마십시오. 장치가 손상될 수 있습니다.
- 항응고제와 항혈소판제의 투여는 시술 후 24 시간까지 중지해야 합니다. 의료 관리 및 급성 뇌졸중 사후 치료는 ASA 지침을 따라야 합니다.[1] 시험자/병원의 모범 사례에 따라 설명된 대로 응급 CT 스캔 및 기타 평가를 통해 모든 신경학적 악화를 평가해야 합니다.
- Penumbra System을 사용하여 환자의 혈관재건을 달성하는 데 허용되는 전체 시간은 120분입니다.

한국어

이상반응 가능성

가능한 합병증에는 다음과 같은 것들이 있지만 이에만 국한되지 않습니다:

- 가성 동맥류 형성
- 감염
- 공기 색전증
- 급성 폐색
- 뇌졸중을 비롯한 신경 결손
- 동정맥루
- 두개내 출혈
- 사망
- 색전증
- 원위 색전증
- 장치 오작동
- 조영제로 인한 신장 손상
- 조영제로 인한 알레르기 반응 및 과민증
- 허혈
- 혈관 연축, 혈전증, 절개 또는 천공
- 혈전 완전 제거 불가
- 혈종 또는 접근 부위의 출혈

시술

1. 사용하기 전에 **경고, 주의 사항, 이상반응 가능성**을 참조하십시오.
2. Penumbra System의 각 장치를 사용할 때, 장치를 포장재에서 꺼내어 손상되거나 꼬이지 않았는지 확인하십시오.
3. 포장 후프와 장치를 헤파린 첨가 식염수로 세척하여 Penumbra System 장치를 사용할 준비를 하십시오(Penumbra 재관류 카테터 및 Penumbra 분리기만 포함됨).
4. 제조업체의 사용 지침에 따라 가이드 카테터 또는 긴 넙다리 유도관을 준비하십시오.
5. 가이드 카테터 또는 긴 넙다리 유도관을 혈전 폐색 부위에서 가까운 적절한 대뇌 동맥에 삽입하십시오.

Penumbra 재관류 카테터 준비 및 사용

1. 혈관 직경을 확인하고 적절한 크기의 Penumbra 재관류 카테터를 선택하십시오(**표 1**참조).
2. Penumbra 재관류 카테터 팁은 제공된 증기 쉐이핑 맨드렐을 사용하여 형태를 만들 수 있습니다.
3. 제공된 회전 지혈 밸브를 Penumbra 재관류 카테터에 부착하십시오.
4. Penumbra 흡인 튜브를 흡인 펌프에 부착하고 흡인 펌프를 켜십시오(흡인 펌프 작동 설명서 참조). 사용하기 전에 최소 1 분 동안 흡인 펌프를 작동시키고 흡인 게이지가 –508 mmHg(–20 inHg)인지 확인하십시오. Penumbra 흡인 튜브의 밸브가 OFF 위치에 있는지 확인하십시오.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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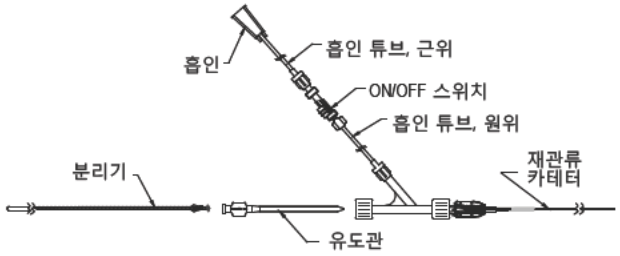
5. 그림 1과 같이 흡인 튜브를 회전 지혈 밸브의 측면 포트에 연결하십시오.

그림 1 – Penumbra 분리기와 조립된 흡인 시스템



6. 가이드 카테터의 근위 허브에 연결된 회전 지혈 밸브에 Penumbra 재관류 카테터를 삽입하십시오. 가이드 카테터를 사용하지 않을 경우 박리 유도관을 사용하여 긴 넙다리 유도관의 밸브를 통해 Penumbra 재관류 카테터를 끼우십시오. Penumbra 재관류 카테터를 끼운 후 혈관집에서 박리 유도관을 제거하고 Penumbra 재관류 카테터 샤프트에서 벗겨내십시오.
7. 투시 장치의 유도 하에 기존의 카테터 삽입 기법을 사용하여 Penumbra 재관류 카테터를 적절한 신경혈관 가이드와이어를 통해 표적 혈관에 삽입하십시오. Penumbra 재관류 카테터를 혈전에 가까이 배치하십시오. Penumbra 재관류 카테터에서 가이드와이어를 분리하십시오.
8. 흡인을 시작하려면 Penumbra 흡인 튜브의 밸브를 ON 위치로 여십시오. 흡인을 중지하려면, Penumbra 흡인 튜브의 밸브를 OFF 위치로 돌리고 흡인 펌프를 끄십시오.
9. 5 ml 또는 10 ml주사기를 사용하여 Penumbra 재관류 카테터로부터 약 5 ml의 혈액을 흡인하여 카테터에 남아있을 수 있는 혈전을 제거하십시오.
10. 조영제를 가이드 카테터를 통해 주입하여 치료 후 혈관조영상을 얻으십시오.

Penumbra 분리기 준비 및 사용

1. 필요할 경우 재관류 카테터에 해당하는 적절한 크기의 Penumbra 분리기를 선택하십시오(표 1 참조).

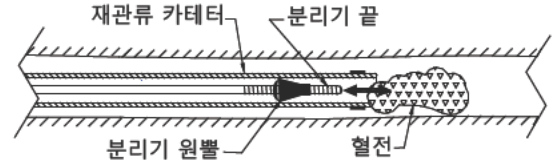
표 1 – 분리기/재관류 카테터 장치 크기 선택

혈관 크기(mm)	Penumbra 재관류 카테터	Penumbra 분리기
< 2.0	026	026
2.0 ~ 3.0	032 / 3MAX	032 / 3MAX
3.0 ~ 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX / ACE	054 / 5MAX

참고: 호환되는 내부 마이크로카테터의 삼중축을 사용하면 폐색 부위에 접근하는 데 도움이 될 수 있습니다.

2. 제공된 유도관을 사용하여, Penumbra 분리기를 회전 지혈 밸브를 통과하여 Penumbra 재관류 카테터의 근위 허브에 끼우십시오.
3. 흡인을 시작하려면 Penumbra 흡인 튜브의 밸브를 ON 위치로 열고 그림 2와 같이 재관류 카테터에서 흡인과 혈전 제거가 용이하게 되도록 Penumbra 분리기를 삽입하거나 뒤로 당기십시오.

그림 2 – Penumbra 분리기를 사용한 혈전 흡인



4. 흡인을 중지하려면, Penumbra 흡인 튜브의 밸브를 OFF 위치로 돌리고 흡인 펌프를 끄십시오.
5. 사용한 경우 Penumbra 분리기를 제거하십시오.
6. 필요한 경우, 의사의 판단 하에 혈전을 더 제거하기 위해 Penumbra 분리기 및 재관류 카테터를 추가로 사용할 수 있습니다.

임상 데이터 요약

중추적 Penumbra 임상시험은 Penumbra System의 안전성과 유효성을 평가하기 위한 전향적, 단일군 임상시험이었습니다. 24곳의 국제적인 시험기관에서 총 125명의 환자가 등록되었습니다. 주요 등록 기준은 NIH 뇌졸중 척도(NIHSS) 점수 ≥ 8, 증상 발생 후 8시간 내 내원, 치료 가능한 두개내 혈관의 폐색(TIMI 0 또는 1)이었습니다. 증상 발생 후 3시간 내에 내원한 환자는 rtPA 요법이 적합하지 않거나 이 요법에 반응하지 않아야 했습니다. 일차 평가변수는 표적 혈관의 혈관재건(TIMI 2 또는 3)과 시술 관련 중대한 이상반응(SAE)의 발생률이었습니다. 모든 환자들이 시술 후 최대 90일 동안 추적 관찰과 평가를 받았습니다.

통계 분석

이 연구에서는 적어도 115명의 평가 가능한 환자를 얻기 위해 125명의 표본 크기를 선택했습니다. 환자가 일차 평가변수 평가를 위한 자격 요건을 충족하고 Penumbra System으로 치료를 받았으면 해당 환자는 평가 가능한 것으로 간주되었습니다. 이 연구는 비대조 연구였으므로, TIMI 2등급 또는 3등급 확립을 위한 전체 반응률에 대한 공식적인 가설 검정은 계획되지 않았습니다. 범주형 평가변수에 대한 표준 기술 통계는 평가변수의 각 수준에 있는 환자의 수와 비율이었습니다. 수치적 평가변수에 대한 표준 기술 통계에는 비결측 관측수(n), 평균, 중앙값, 표준편차, 최소값, 최대값이 포함되었습니다.

연구 절차

표적 혈관에 대한 동맥 접근로는 표준 경피적 기법을 사용하여 확보했으며, 4혈관 디지털 감산 혈관조영술을 실시하여 폐색된 혈관 구역의 혈관구조를 정의했습니다. 각 환자는 혈관조영술을 통해 확인된 대뇌 대혈관 폐색과 시험자가 사전에 지정한 주요 폐색 부위가 있어야 했습니다. 치료 가능한 혈관에 폐색이 있는 경우, 적절한 가이드 카테터를 배치하고 폐색된 표적 혈관의 근위 단부로 Penumbra 재관류 카테터를 삽입했습니다. 환자는 재관류 카테터가 가이드 카테터로부터 전개되었을 때 등록된 것으로 간주되었습니다.

주요 선정 기준

- 다음을 비롯하여 급성 허혈성 뇌졸중과 일치하는 임상 징후:
  - 안면 또는 사지의 갑작스러운 무감각 또는 약화
  - 갑작스러운 혼동 또는 언어 장애
  - 갑작스러운 보행 곤란, 현기증 또는 균형 상실
- 18 ~ 79세
- NIH 뇌졸중 척도(NIHSS) 점수 ≥ 8
- 완전 폐색(TIMI 0등급) 또는 Penumbra 뇌졸중 시스템으로 접근 가능한 두개내 혈관에 최소 관류로 조영제가 침투하지만 원위 가지 충만은 일어나지 않음(TIMI I등급)
- 시험대상자 동의서에 서명
- 뇌졸중 증상 발생 후 8시간 내에 내원

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- 증상 발생 후 3시간 내에 내원한 경우 정맥 내 rtPA 요법에 적합하지 않거나 반응하지 않음

주요 제외 기준
- 등록 시점에 뇌졸중의 신경학적 징후가 급속히 호전되고 있다는 증거
- NIHSS >30 또는 혼수
- 임신한 여성
- 혈관이 너무 비틀어져 있어서 혈관 내 접근이 어려움
- 알려진 출혈성 소질, 응고 결함 또는 경구 항응고 요법 사용 및 INR > 3.0
- PTT가 검사실 정상치의 2배 초과
- 입원 시 혈소판 수 < 30,000
- 연구 결과에 혼란을 일으킬 수 있는 기존의 신경 질환 또는 정신 질환
- 조영제에 대한 알려진 중증 알레르기
- 비조절성 고혈압(수축기 혈압 > 185 mmHg 또는 확장기 혈압 > 110 mmHg으로 정의)
- 내원 당시 다음 질환을 보여주는 CT 상의 증거:
  - 유의한 종괴 효과 및 정중선 변위
  - 중간 대뇌동맥 영역의 > 1/3에 큰 저밀도 부위
  - 두개내 출혈의 증거
- 폐색 부위 근위에서 혈전 제거를 방해할 수 있는 동맥 협착의 혈관조영 증거
- 기존 동맥 손상의 혈관조영 증거
- 기대 여명 90일 미만
- 연구 장치의 평가에 혼란을 일으킬 수 있는 다른 임상시험에 참여

등록된 시험대상자의 제외 사유(특히 혈관조영 기준에 기반한 사유) 요약
등록된 환자 중 혈관조영 상의 이유로 제외된 환자는 없었습니다.

일차 유효성 평가변수
일차 유효성 평가변수는 폐색된 표적 혈관의 혈관재건이었습니다. 혈관재건은 Penumbra System만 사용한 후, 추가 또는 보강 장치 또는 요법을 사용하기 전에 TIMI 점수가 II 또는 III인 것으로 정의되었습니다. 혈관조영 결과는 독립 핵심 검사실에서 판정했습니다.

유효성	% (n/N) [95% 신뢰구간]†
일차 유효성 평가변수(TIMI 점수 II 또는 III) 보강 요법 사용 전 TIMI 점수	81.6%(102/125) [73.7%, 88.0%]
장치 사용 후 재건 성공(TIMI ≥ 2) 일체의 보강 요법 사용은 치료 실패로 간주	81.6%(102/125) [73.7%, 88.0%]
장치 사용 후 재건 성공(TIMI ≥ 2) 일체의 IA 용해제 사용은 치료 실패로 간주	81.6%(102/125) [73.7%, 88.0%]

†정확한 Clopper-Pearson 신뢰구간

일차 안전성 평가변수
일차 안전성 평가변수는 시험자가 보고한 시술 중에 발생한 장치 및/또는 시술 관련 중대한 이상반응의 발생률이었습니다. 16명의 환자에서 18건의 시술 관련 증례가 보고되었습니다(12.8%). 그 중 3명에서 발생한 4건(2.4%)은 임상사건위원회에 의해 중대한 것으로 평가되었습니다.

시술 중의 복합 이상반응	% (n/N) [95% 신뢰구간]†
시술 중의 복합 SAE	2.4%(3/125)
일차 안전성 평가변수: 시술 중의 복합 시술/장치 관련 SAE	2.4%(3/125)

†정확한 Clopper-Pearson 신뢰구간

90일까지 2%가 넘는 환자에서 발생한 각각의 특정 SAE

SAE	% (n/N)
복합 SAE	52.0%(65/125)
뇌부종	11.2%(14/125)
ICH	8.0%(10/125)
호흡 기능장애/부전	8.0%(10/125)
뇌졸중에 해당하는 증상 악화	7.2%(9/125)
감염	5.6%(7/125)
기타 폐 합병증	5.6%(7/125)
폐렴	4.0%(5/125)
심장 부정맥	3.2%(4/125)
접근 부위 합병증	2.4%(3/125)
심근 경색	2.4%(3/125)
말초 혈관 합병증	2.4%(3/125)
신장 기능장애/부전	2.4%(3/125)
새로운 부위의 뇌졸중	2.4%(3/125)

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90일까지 발생한 AE - 해부학적 기관계에 따른 분류

해부학적 기관계	% (n/N)
신경계 장애	62.4%(78/125)
감염 및 기생충감염	44.0%(55/125)
심장 장애	28.8%(36/125)
대사 및 영양 장애	25.6%(32/125)
전신 장애 및 투여 부위 장애	24.8%(31/125)
호흡기, 흉부 및 종격 장애	24.8%(31/125)
손상, 중독 및 시술 합병증	18.4%(23/125)
위장관 장애	16.0%(20/125)
혈액 및 림프계 장애	14.4%(18/125)
혈관 장애	11.2%(14/125)
정신과 장애	10.4%(13/125)
신장 및 비뇨 장애	8.0%(10/125)
간담도 장애	4.0%(5/125)
조사	3.2%(4/125)
피부 및 피하조직 장애	3.2%(4/125)
양성, 악성 및 상세불명의 종양(낭종 및 폴립 포함)	2.4%(3/125)
근골격 및 결합 조직 장애	0.8%(1/125)

기호 설명

		주의. 사용법 참조	
Rx Only		처방에 의해서만 사용 가능 – 미국 연방법에 따라 본 장치는 의사에 의해서만 또는 의사의 지시에 따라서만 사용할 수 있습니다	
		비발열성	
STERILE EO		산화 에틸렌으로 멸균 처리	
	제조업체	EC REP	유럽연합 대리점
LOT	로트 번호		재사용하지 마십시오
	사용 기한	REF	카탈로그 번호
STERILIZE	재멸균 금지	LATEX	무라텍스

보증

Penumbra, Inc. (Penumbra)는 본 장치의 설계 및 제조 과정에서 적절한 주의를 기울였음을 보증합니다. 본 보증은, 상품성이나 특정 용도 적합성에 대한 묵시적 보증을 비롯하여(하지만 이에 국한되지는 않음) 법적으로 또는 달리 명시적이든 묵시적이든 여기에 명시적으로 기술되지 않은 일체의 다른 보증을 대신하며 이들을 배제합니다. 환자, 진단, 치료, 수술 및 기타 Penumbra가 통제할 수 없는 요인들뿐만 아니라 본 장치의 취급, 보관, 세척 및 멸균이 본 장치와 그 사용으로 인한 결과에 직접적인 영향을 미칩니다. 본 보증에 따른 Penumbra의 의무는 본 장치의 수리 및 교체로 국한되며 Penumbra는 본 장치 사용으로 인해 직간접적으로 발생하는 일체의 부수적 또는 결과적 손실, 손상 또는 비용에 대해 책임을 지지 않습니다. Penumbra는 본 장치와 관련하여 기타 또는 추가의 의무나 책임을 일체 지지 않으며 또한 다른 어떤 사람도 이런 책임을 지도록 위임하지 않습니다. Penumbra는 재사용되거나, 재처리되거나, 재멸균된 장치에 대한 책임을 지지 않으며 본 장치와 관련하여 상품성이나 목적 용도 적합성을 비롯한(하지만 이에 국한되지는 않음) 명시적 또는 묵시적 보증을 하지 않습니다.

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Penumbra, Inc.
1351 Harbor Bay Pkwy
Alameda, CA 94502 USA

Tel: 1-888-BRAIN06 (1-888-272-4606)
1-510-748-3200
Fax: 1-510-748-3232

EC REP **EU Representative:**
MedPass International Ltd.
Windsor House, Bretforton
Evesham, Worcs. WR11 7JJ, UK

CE 0050

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K142458/S001

Penumbra

September 22, 2014

FDA CDRH DMC
SEP 23 2014
Received

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: K142458/S001 - Penumbra System ACE – Refuse to Accept Response – Supplement 1

Dear Mrs. Leigh Booth,

Penumbra, Inc. is submitting this response to the deficiencies identified in the FDA Refuse to Accept Letter e-mailed to Penumbra on September 17, 2014.

Penumbra Inc. requests that the information in this submission be considered confidential, and protected under 21 CFR 807.95, 18 USC 1905, 21 USC 331(j), 5 USC 552, and other applicable laws and provisions. Per the instructions accessed at http://www.fda.gov/cdrh/elecsub.html , an electronic copy is being provided with this submission and it is an exact duplicate of the response paper submission.

The FDA deficiencies are repeated below and followed by the Penumbra responses.

FDA Deficiency 1 (b)(4) [redacted]

(b)(4) Deficiencies [redacted]

Company Response:

(b)(4) Deficiencies [redacted]

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1 CD

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Alameda, Ca. 94502
U.S.A.

Regulatory Affairs
F 510.217.6414
www.penumbrainc.com

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Penumbra

FDA Deficiency 2 (b)(4) Deficiencies [redacted]

(b)(4) Deficiencies [redacted]

Company Response:

(b)(4) Deficiencies [redacted]

FDA Deficiency 3 (b)(4) Deficiencies [redacted]

(b)(4) Deficiencies [redacted]

Company Response:

(b)(4) Deficiencies [redacted]

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Penumbra

(b)(4) Deficiencies

[redacted]

(b)(4) Deficiencies

[redacted]

FDA Deficiency 4 (b)(4) Deficiencies

(b)(4) Deficiencies

[redacted]

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Penumbra

Company Response:

(b)(4) Deficiencies [redacted]

FDA Deficiency 5 (b)(4) Deficiencies [redacted]

(b)(4) Deficiencies [redacted]

Company Response:

(b)(4) Deficiencies [redacted]

FDA Deficiency 6 (b)(4) Deficiencies [redacted]

(b)(4) Deficiencies [redacted]

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Penumbra

Company Response:

(b)(4) Deficiencies

[redacted]

If there are any questions regarding this response submission, please contact Michaela Mahl, Senior Manager Regulatory Affairs, at 510-748-3288, or via e-mail at michaela.mahl@penumbrainc.com or alternate Mr. Seth Schulman, Director Regulatory Affairs, at 510-748-2223, or via e-mail at seth.schulman@penumbrainc.com.

Sincerely,

Michaela Mahl

Michaela Mahl, MSBE
Senior Manager Regulatory Affairs
Phone: (510)748-3288
e-mail: michaela.mahl@penumbrainc.com

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Penumbra

September 22, 2014

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Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: K142458/S001 - Penumbra System ACE – Refuse to Accept Response – Supplement 1

Dear Mrs. Leigh Booth,

Penumbra, Inc. is submitting this response to the deficiencies identified in the FDA Refuse to Accept Letter e-mailed to Penumbra on September 17, 2014.

Penumbra Inc. requests that the information in this submission be considered confidential, and protected under 21 CFR 807.95, 18 USC 1905, 21 USC 331(j), 5 USC 552, and other applicable laws and provisions. Per the instructions accessed at http://www.fda.gov/cdrh/elecsub.html , an electronic copy is being provided with this submission and it is an exact duplicate of the response paper submission.

The FDA deficiencies are repeated below and followed by the Penumbra responses.

FDA Deficiency 1 (b)(4) Deficiencies

(b)(4) Deficiencies

Company Response:

(b)(4) Deficiencies

Penumbra, Inc.
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Alameda, Ca. 94502
U.S.A.

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F 510.217.8414
www.penumbrainc.com

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Penumbra

FDA Deficiency 2 (b)(4) Deficiencies

(b)(4) Deficiencies

Company Response:

(b)(4) Deficiencies

FDA Deficiency 3 (b)(4) Deficiencies

(b)(4) Deficiencies

Company Response:

(b)(4) Deficiencies

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Penumbra

(b)(4) Deficiencies

[redacted]

FDA Deficiency 4 (b)(4) Deficiencies [redacted]

(b)(4) Deficiencies

[redacted]

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Penumbra

Company Response:

(b)(4) Deficiencies

[redacted]

FDA Deficiency 5 (b)(4) Deficiencies

(b)(4) Deficiencies

[redacted]

Company Response:

(b)(4) Deficiencies

[redacted]

FDA Deficiency 6 (b)(4) Deficiencies

(b)(4) Deficiencies

[redacted]

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Penumbra

Company Response:

(b)(4) Deficiencies

[redacted]

If there are any questions regarding this response submission, please contact Michaela Mahl, Senior Manager Regulatory Affairs, at 510-748-3288, or via e-mail at michaela.mahl@penumbrainc.com or alternate Mr. Seth Schulman, Director Regulatory Affairs, at 510-748-2223, or via e-mail at seth.schulman@penumbrainc.com.

Sincerely,

Michaela Mahl

Michaela Mahl, MSBE
Senior Manager Regulatory Affairs
Phone: (510)748-3288
e-mail: michaela.mahl@penumbrainc.com

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8 510(K) SUMMARY OF SAFETY & EFFECTIVENESS

(as required by 21 CFR 807.92)

Pursuant to Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, Penumbra Inc. is providing the summary of Substantial Equivalence for the Penumbra System ACE.

8.1 Sponsor/Applicant Name and Address

Penumbra, Inc.
1351 Harbor Bay Parkway
Alameda, CA 94502 USA

8.2 Sponsor Contact Information

Michaela Mahl
Senior Manager, Regulatory Affairs
Phone: (510) 748-3288
FAX: (510) 217-6414
Email: michaela.mahl@penumbrainc.com

8.3 Date of Preparation of 510(k) Summary

September 22, 2014

8.4 Device Trade or Proprietary Name

Penumbra System ACE

8.5 Device Classification

Regulatory Class:	II
Classification Panel:	Neurology
Classification Name:	Catheter, Thrombus Removal
Regulation Number:	21 CFR §870.1250
Product Code:	NRY

8.6 Predicate Devices

510(k) Number / Clearance Date	Name of Predicate Device	Name of Manufacturer
K072718 [28Dec2007], K090752 [21Sep2009], K100769 [21May2010], K113163 [28NOV2011], K133317 [13MAY2014]	Penumbra System / Penumbra System MAX®	Penumbra, Inc. 1351 Harbor Bay Parkway Alameda, CA 94502 USA

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.7 Predicate Comparison

System Name	**Penumbra System/Penumbra System MAX**	**Penumbra System ACE**
Device	**Predicate Device**	**Subject Device**
510(k) No.	K090752	K142458
Classification	Class II, NRY	SAME
Indication	The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.	SAME
Materials	Medical Grade Plastic, Stainless Steel/Nitinol & Pt/Ir Band	SAME with additional Blends of the Medical Grade Plastics and additional SS & NiTi round wires
Coating	Hydrophilic coating	SAME
Effective Length	Appropriately sized for the target vasculature	SAME plus two shorter lengths
Proximal OD & ID		SAME with larger diameters
Distal OD & ID		SAME with larger diameters
Packaging Materials		
Pouch	Polyester/Polyethylene/ Tyvek®	SAME
Hoop	Polyethylene	SAME
Display Carton	SBS Paperboard	SAME
Packaging Configuration	Individual	SAME
Sterilization	EtO	SAME
Shelf-Life	36 Months	SAME

8.8 Device Description

The Penumbra System ACE components are additional components to the currently available Penumbra System / Penumbra System MAX. The Penumbra System ACE components provide a larger lumen to assist in the efficient removal of thrombus from the neurovasculature. The devices are provided sterile, non-pyrogenic, and intended for single use only.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

8.9 Intended Use

The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.

8.10 Summary of Non-Clinical Data

As required under Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, a summary of any information regarding safety and effectiveness of the device follows.

Included in this section are summary descriptions of the testing, which substantiates the safe and effective performance of the subject Penumbra System ACE as well as its substantial equivalence to the predicate devices:

- Biocompatibility
- Design Verification (Bench-Top Testing)
- Design Validation (GLP Animal Testing)

The subject Penumbra System ACE devices met all established requirements.

8.10.1 Biocompatibility Testing

Biocompatibility tests conducted on the materials of the Penumbra System ACE devices were selected in accordance with EN ISO 10993 -1 guidelines (Biological Evaluation of Medical Devices) for limited duration (<24 hours), external communicating devices, contacting circulating blood. All studies were conducted pursuant to 21 CFR, Part 58, Good Laboratory Practices. In summary, non-clinical testing found the Penumbra System ACE devices to be biocompatible according to the requirements of EN ISO 10993 requirements. The following tests were performed and all tests passed successfully:

Test	Acceptance Criteria	Results	Pass / Fail
In Vitro Cytotoxicity	Sample extracts must yield cell lysis grade 2 or lower	Grade 1: Slight	Pass
Sensitization	Test Group shall yield Grade < 1 score on Magnusson and Kligman scale (provided control Grade < 1)	Grade 0: No visible change	Pass
Acute Intracutaneous Reactivity (Irritation)	The difference in the mean test article and mean control score must be grade 1.0 or lower	Grade ≤ 1.0 difference between mean test article and mean control score	Pass

Test	Acceptance Criteria	Results	Pass / Fail
Systemic Toxicity			
Acute Systemic Toxicity	Sample extracts must not cause the following: • > 10% weight loss in 3 or more test animals • Mortality of 2 or more test animals • Abnormal behavior in 2 or more test animals	No evidence of systemic toxicity from sample extracts • No weight loss (all gained weight) • No death • All test animals appeared normal	Pass
Rabbit Pyrogen Study	Sample Extracts must not cause a total rise in body temperature of ≥0.5°C	Non-pyrogenic: No evidence of material-mediated pyrogenicity; no single animal had a total body temperature rise of ≥0.5°C	Pass
Hemocompatibility			
In Vitro Hemolysis	Sample extracts must be non-hemolytic (≤ 2% hemolytic index)	Non-hemolytic: Hemolytic Index = 0.70% Corrected Hemolytic index = 0.00%	Pass
Complement Activation	The concentrations of C3a and SC5b-9 in the test samples are statistically similar to the predicate (Exposure Control & Ref Material) control and statistically lower than the positive control for all exposure times	The test sample concentrations of C3a and SC5b-9 were statistically similar or lower than the predicate control sample concentrations, and statistically lower than the positive control sample concentrations at all three exposure times	Pass
Dog Thrombogenicity	The device must be non-thrombogenic after 4 hours *in vivo* when compared to a control device (Boston Scientific Excelsior SL-10 microcatheter)	No significant thrombosis with a Grade of 0 was observed in 2 out 2 test site and 2 out of 2 control sites. Based on the evaluation criteria, the amount of thrombosis was not considered significant	Pass

In summary non-clinical testing substantiates that the Penumbra System ACE devices are non-cytotoxic, non-sensitizing, non-irritating, non-toxic, non-pyrogenic, non-hemolytic, and non-thrombogenic.

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

8.10.2 Bench-top Testing

The physical and mechanical properties of the Penumbra System ACE devices were assessed using standard test methods and pre-determined acceptance criteria. The following tests were performed and all tests passed successfully:

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Dimensional/ Visual Inspection	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Simulated Use [Intracranial Access & Vessel Access Entry Performance]	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Coating Integrity	(b) [redacted]	Coating has not delaminated, peeled, or flaked after simulated use	100% Must meet Specification	100% Pass
Particulate Testing (Reperfusion Catheter Hydrophilic Coating)	(b) [redacted]	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Particulate Testing (Reperfusion Catheter /Separator)	(b) [redacted]	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Coating Integrity	(b) [redacted]	Coating is not grossly damaged after undergoing particulate testing	100% Must meet Specification	100% Pass
Hub/Catheter Air Aspiration	(b) [redacted]	When negative pressure is pulled, no air may leak into hub	100% Must meet Specification	100% Pass
Pressure Test	(b) [redacted]	45 psi for 30 sec MIN	100% Must meet Specification	100% Pass
Reperfusion Catheter/Sheath or 8F Guide & 0.014" Guidewire compatibility (Friction Force)	(b)(4) [redacted]	Maximum value per specification	100% Must meet Specification	100% Pass
Markerband Section Bond Strength	(b) [redacted]	Minimum value per specification	100% Must meet Specification	100% Pass
Joint Sections Bond Strength	((b) [redacted] b	Minimum value per specification	100% Must meet Specification	100% Pass

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Hub to Shaft & Hub to Hypotube Bond Strength	(b)	Minimum value per specification	100% Must meet Specification	100% Pass
Elongation to Failure – Reperfusion Catheter	(b)	% Elongation ≥ 5%	100% Must meet Specification	100% Pass
Corrosion	(b)	No visible corrosion on Reperfusion Catheter immediately after Corrosion Testing procedure	100% Must meet Specification	100% Pass

The results of the tests appropriately address the physical and mechanical performance expectations of the device. This is further supported by the surgical handling and performance results reported in the *in vivo* study. Based on these overall results, the physical and mechanical properties of the subject Penumbra System ACE devices are acceptable for the intended use and substantially equivalent to the predicate device.

8.10.3 Animal Study

An animal study was conducted to evaluate the safe use of the Penumbra System ACE devices in a swine model. The study concluded that:

- No vessel injury was noted on the final angiograms following the vessel response procedure.
- No abnormal gross or histology findings were noted in test vessel segments.
- The use of the Penumbra System ACE devices resulted in no significant vascular response in these experimental conditions.

8.10.4 Summary of Substantial Equivalence

The subject Penumbra System ACE devices are substantially equivalent to the predicate device with regard to intended use, operating principle, design concept, materials, shelf-life, packaging and sterilization processes.

(b)(4) Schematic Drawings

(b)(4) Schematic Drawings

(b)(4) Schematic Drawings

(b)(4) Schematic Drawings

[redacted]

(b)(4) Schematic Drawings

[redacted]

(b)(4) Schematic Drawings

(b)(4) Specifications

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(b)(4) Specifications

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(b)(4) Specifications

[redacted]

(b)(4) Specifications

(b)(4) Specifications

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5.4 Expiration Dating (Stability)

Shelf-Life/Packaging validation testing was performed (b)(4) [redacted] (b)(4) [redacted]

Table 1: Shelf-life – Testing Results

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Dimensional/ Visual Inspection	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Simulated Use [Intracranial Access & Vessel Access Entry Performance]	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Pouch Leak Testing	(b) [redacted]	Pouch seals, pouch front, and pouch back material do not leak	100% Must meet Specification	100% Pass
Pouch Seals (Visual)	(b) [redacted]	No channels or voids are present on the pouch	100% Must meet Specification	100% Pass
Particulate Testing (Reperfusion Catheter (b)(4) [redacted] (b) [redacted] Hydrophilic Coating)	(b) [redacted]	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Particulate Testing (Reperfusion Catheter (b)(4) [redacted] (b)(4) [redacted] Separator)	(b) [redacted]	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Catheter Coating Integrity	(b) [redacted]	Coating has not delaminated, peeled, or flaked after simulated use	100% Must meet Specification	100% Pass
Hub / Catheter Air Aspiration	(b) [redacted]	No air may leak into hub	100% Must meet Specification	100% Pass
Pressure Test	(b) [redacted]	45 psi for 30 sec MIN	100% Must meet Specification	100% Pass
Markerband Section Bond Strength	(b) [redacted]	(b)(4) [redacted] Minimum	100% Must meet Specification	100% Pass

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Attribute	Sample Size	Specification	Acceptance Criteria	Results
(b)(4) [redacted]) Bond Strength	(b) [redacted]	(b)(4) [redacted] Minimum	100% Must meet Specification	100% Pass
(b)(4) [redacted] Bond Strength	(b) [redacted]	(b)(4) [redacted] Minimum	100% Must meet Specification	100% Pass
(b)(4) [redacted] Bond Strength	(b) [redacted]	(b)(4) [redacted] Minimum	100% Must meet Specification	100% Pass
(b)(4) [redacted] Bond Strength	(b) [redacted]	(b)(4) [redacted] Minimum	100% Must meet Specification	100% Pass
Hub to Shaft Bond Strength	(b) [redacted]	(b) [redacted] Minimum	100% Must meet Specification	100% Pass
Hub to Hypotube Bond Strength	(b) [redacted]	(b) [redacted] Minimum	100% Must meet Specification	100% Pass
Elongation to Failure – Reperfusion Catheter	(b) [redacted]	% Elongation ≥ 5%	100% Must meet Specification (b)(4) [redacted]	100% Pass

Based on these existing shelf-life test results the Reperfusion Catheters ACE 64 and ACE 68 will be labelled with a 36-month shelf-life.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

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(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b)(4)

[redacted]

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(b)(4)

[redacted]

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

Form Approved: OMB No. 0910-0120; Expiration Date: 1/31/2017

Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 10993-4:2009 (ISO 10993-4:2002/R2009) Bio eval of med devices -- Part 4: Selection of tests for interaction w/ blood

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☐	☒
FDA Recognition number [3]	#N/A	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☒	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: N/A

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

PSC Publishing Services (301) 443-6740 EF

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 10993-4:2009 (ISO 10993-4:2002/R2009) Bio eval of med devices -- Part 4: Selection of tests for interaction w/ blood

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
Annex B	Laboratory tests - Principles, scientific basis, and interpretation	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Test selection: complement activation - C3a and SC5b-9 through enzyme assay

DESCRIPTION
Test lab: Nelson Labs 6280 South Redwood Road, Salt Lake City, UT 84123

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
Annex C	Evaluation of hemolytic properties of medical devices and their components	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Test selection: direct contact and extract method.

DESCRIPTION
Test lab: Nelson Labs 6280 South Redwood Road, Salt Lake City, UT 84123

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

◆ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 1 hour per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Form Approved: OMB No. 0910-0120; Expiration Date: 1/31/2017

Department of Health and Human Services
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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 10993-5:2009 (ISO 10993-5:2009) Biological evaluation of medical devices -- Part 5: Tests for in vitro cytotoxicity

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#2-153	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☒	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: N/A

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 10993-5:2009 (ISO 10993-5:2009) Biological evaluation of medical devices -- Part 5: Tests for in vitro cytotoxicity

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
8	Test procedures	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Test selection: MEM Elution

DESCRIPTION
Test lab: Nelson Laboratories 6280 South Redwood Road, Salt Lake City, UT 84123

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 10993-10:2010 (ISO 10993-10:2010) Bio evaluation of medical devices -- Part 10: Tests for irritation & skin sensitization

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#2-174	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☒	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: N/A

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 10993-10:2010 (ISO 10993-10:2010) Bio evaluation of medical devices -- Part 10: Tests for irritation & skin sensitization

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
7	Skin sensitization tests	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Test selection: Guinea Pig Maximization Sensitization Test, Magnusson-Kligman Method

DESCRIPTION
Test lab: Sinclair Research, 562 State Road DD, Auxvase, MO 65231, USA

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 10993-11:2010 (ISO 10993-11:2010) Biological evaluation of medical devices -- Part 10: Tests for systemic toxicity

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#2-176	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
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Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: N/A

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EXTENT OF STANDARD CONFORMANCE
SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 10993-11:2010 (ISO 10993-11:2010) Biological evaluation of medical devices -- Part 10: Tests for systemic toxicity

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

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[1] Reference §6.1 and §6.2

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(b)(4) [redacted]

(b)(4) [redacted]

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[redacted]

[9] Reference §6.3

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Revision History

Rev	(b)(4)	Originator	Effective	Description of Change
(b)	(b)(4)	(b)(6)	08/13/14	(b)(4)
(b)	(b)(4)	(b)(6)	08/21/14	

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Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

EN 20594-1:1993 [=ISO594-1:1986] Conical fittings with a 6 % (Luer) taper for syringes, needles, ect. - Part 1

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#6-11	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☒
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN 20594-1:1993 [=ISO594-1:1986] Conical fittings with a 6 % (Luer) taper for syringes, needles, ect. - Part 1

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

❖ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ISO 594-2:1988 Conical fittings with a 6 % (Luer) taper for syringes, needles, ect. - Part 2

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#6-129	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☒
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☒	☐
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN 20594-1:1993 [=ISO594-1:1986] Conical fittings with a 6 % (Luer) taper for syringes, needles, ect. - Part 1

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ❖		
DESCRIPTION		
JUSTIFICATION		

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

USP<788> - Particle Size & Stability

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☐	☒
FDA Recognition number [3]	#N/A	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
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Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: N/A

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
USP<788> - Particle Size & Stability

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
N/A	PARTICULATE MATTER IN INJECTIONS	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖
Both methods of light obscuration particle count test and microscopic particle test count selected

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ❖

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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English

Device Description

The Penumbra System® is comprised of several devices:

- Penumbra Reperfusion Catheter
- Penumbra Separator
- Penumbra Aspiration Pump
- Penumbra Pump/Canister Tubing
- Penumbra Aspiration Tubing

The Reperfusion Catheter is introduced through a guide catheter or long femoral sheath and into the intracranial vasculature and guided over a neurovascular guidewire to the site of the primary occlusion. The Penumbra Reperfusion Catheter is used in parallel with the Penumbra Separator and an aspiration source to separate the thrombus and aspirate it from the occluded vessel. The Penumbra Separator is deployed from the Penumbra Reperfusion Catheter. The Penumbra Separator is advanced and retracted through the Penumbra Reperfusion Catheter at the proximal margin of the primary occlusion. This facilitates aspiration and debulking of the thrombus and reduces or eliminates the endovascular clot burden. For the aspiration source, the Penumbra Reperfusion Catheter is used in conjunction with the Aspiration Pump, which is connected using the Penumbra Aspiration Tubing and the Penumbra Pump/ Canister Tubing. The Penumbra Separator is provided with an introducer and torque device. The Penumbra Reperfusion Catheter is provided with a steam shaping mandrel and rotating hemostasis valve, and a peelable sheath. The devices are visible under fluoroscopy.

Indication for Use

The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.

Contraindications

There are no known contraindications.

Warnings

- The Penumbra System should only be used by physicians who have received appropriate training in interventional neuro-endovascular techniques and treatment of acute ischemic stroke.
- Do not use the Penumbra System with a pump other than the Penumbra Aspiration Pump.

Precautions

- The device is intended for single use only. Do not resterilize or reuse. Resterilization and/or Reuse may result in ineffective catheter coating lubrication, which may result in high friction and the inability to access the target neuro vasculature location.
- Do not use kinked or damaged devices. Do not use open or damaged packages.
- Use prior to the "Use By" date.
- Use the Penumbra System in conjunction with fluoroscopic visualization.
- Do not advance or use any component of the Penumbra System against resistance without careful assessment of the cause using fluoroscopy. If the cause cannot be determined, withdraw the device. Unrestrained torquing or forced insertion of the catheter or separator against resistance may result in compression of the device which may lead to vessel damage and/or tip breakage.
- Maintain a constant infusion of appropriate flush solution.
- When performing aspiration, ensure that the Penumbra Aspiration Tubing valve is open for only the minimum time needed to remove thrombus. Excessive aspiration or failure to close the Penumbra Aspiration Tubing valve when aspiration is complete is not recommended.
- The Penumbra Separator is not intended for use as a neurovascular guidewire. If repositioning of the Penumbra Reperfusion Catheter is necessary during the revascularization procedure, such reposition should be performed over an appropriate neurovascular guidewire using standard microcatheter and guidewire techniques.
- Do not use automated high-pressure contrast injection equipment with the Penumbra Reperfusion Catheter because it may damage the device.
- Administration of anticoagulants and antiplatelets should be suspended until 24 hours post-treatment. Medical management and acute post stroke care should follow the ASA guidelines.[1] Any neurological deterioration should be evaluated by urgent CT scan and other evaluations as indicated according to investigator/hospital best practice.
- The total time allowed to achieve patient revascularization is 120 minutes of using the Penumbra System.

Potential Adverse Events

Possible complications include, but are not limited to, the following:

- allergic reaction and anaphylaxis from contrast media
- acute occlusion
- air embolism
- arteriovenous fistula
- death
- device malfunction
- distal embolization
- emboli
- false aneurysm formation
- hematoma or hemorrhage at access site
- inability to completely remove thrombus
- infection
- intracranial hemorrhage
- ischemia
- kidney damage from contrast media
- neurological deficits including stroke
- vessel spasm, thrombosis, dissection, or perforation

Procedure

1. Refer to **Warnings**, **Precautions**, and **Potential Adverse Events** prior to use.
2. As each device of the Penumbra System is used, remove the device from the packaging, and inspect for damage or for kinks.
3. Prepare Penumbra System devices for use by flushing the packaging hoop and device with heparinized saline (includes Penumbra Reperfusion Catheter and Penumbra Separator only).
4. Prepare a guide catheter or long femoral sheath according to the manufacturer's *Instructions for Use*.
5. Place the guide catheter or long femoral sheath into the appropriate cerebral artery that is proximal to the thrombus occlusion site.

Penumbra Reperfusion Catheter Preparation and Use

1. Confirm vessel diameter, and select an appropriate size Penumbra Reperfusion Catheter (See **Table 1**).
2. The Penumbra Reperfusion Catheter tip may be shaped using the steam shaping mandrel provided.
3. Attach the rotating hemostasis valve provided to the Penumbra Reperfusion Catheter.
4. Insert the Penumbra Reperfusion Catheter into a rotating hemostasis valve connected to the proximal hub of a guide catheter. If a guide catheter is not used, insert the Penumbra Reperfusion Catheter through the valve of the long femoral sheath using the peelable sheath. After inserting the Penumbra Reperfusion Catheter, remove the peelable sheath from the vascular sheath, and peel from the Penumbra Reperfusion Catheter shaft.
5. Using conventional catheterization techniques under fluoroscopic guidance, advance the Penumbra Reperfusion Catheter into the target vessel over an appropriate neurovascular guidewire. Position the

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Penumbra Reperfusion Catheter proximal to the thrombus. Remove the guidewire from the Penumbra Reperfusion Catheter.

Penumbra Separator Preparation and Use

1. Attach the Penumbra Aspiration Tubing to the Aspiration Pump and turn on the Aspiration Pump (Refer to the Aspiration Pump *Operation Manual*). Allow the Aspiration Pump to run for at least one minute prior to use, and confirm that the Aspiration gauge reads −20inHg. Ensure the valve on the Penumbra Aspiration Tubing is switched to the OFF position.
2. Select an appropriate size Penumbra Separator corresponding to the Reperfusion Catheter (see **Table 1**).

Table 1 – Separator/Reperfusion Catheter Device Size Selection

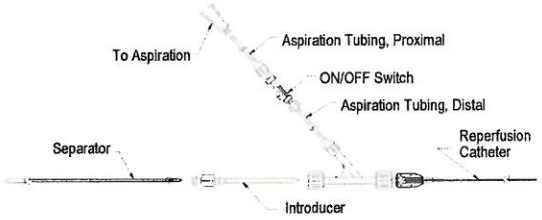
Vessel Size (mm)	Penumbra Reperfusion Catheter	Penumbra Separator
< 2.0	026	026
2.0 to 3.0	032 / 3MAX	032 / 3MAX
3.0 to 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX	054 / 5MAX

3. Advance the Penumbra Reperfusion Catheter to gently embed the distal tip into the thrombus.

NOTE: Access to the site of occlusion may be aided by the triaxial use of a compatible inner microcatheter.

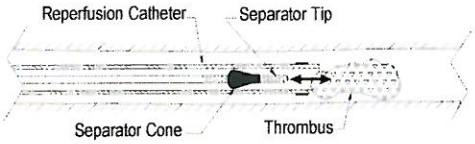
4. Using the introducer sheath provided, insert the Penumbra Separator through the rotating hemostasis valve and into the proximal hub of the Penumbra Reperfusion Catheter.
   Connect the Aspiration Tubing to the side port of the rotating hemostasis valve as shown in **Figure 1**.

Figure 1 – Assembled Aspiration System with Penumbra Separator



6. To begin aspiration, open the valve on the Penumbra Aspiration Tubing to the ON position, and advance/retract the Penumbra Separator to assist with aspiration and removal of the thrombus as shown in **Figure 2**.

Figure 2 – Thrombus Aspiration Using the Penumbra Separator



7. To stop aspiration, switch the valve on the Penumbra Aspiration Tubing to the OFF position, and turn off the Aspiration Pump.
8. Remove the Penumbra Separator.
9. If necessary, additional Penumbra Separators and Reperfusion Catheters may be used to further remove thrombus at the discretion of the physician.
10. Using a 5cc or 10cc syringe, aspirate approximately 5cc of blood from the Penumbra Reperfusion Catheter to remove any thrombus that may remain in the catheter.
11. Obtain a post-treatment angiogram by injecting contrast media through the guide catheter.

Symbols Glossary

	Attention, see instructions for use		
Rx Only	Prescription only – US Federal Law restricts this device to use by or on the order of a physician		
	Nonpyrogenic		
STERILE EO	Sterilized using ethylene oxide		
	Manufacturer	EC REP	EU Representative
LOT	Lot number		Do not reuse
	Use by	REF	Catalogue number
STERILIZE	Do not resterilize	LATEX	Latex free

Warranty

Penumbra Inc. (Penumbra) warrants that reasonable care has been used in the design and manufacture of this device. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular use. Handling, storage, cleaning, and sterilization of this device as well as other factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond Penumbra's control directly affect the device and the results obtained from its use. Penumbra's obligation under this warranty is limited to the repair or replacement of this device and Penumbra shall not be liable for any incidental or consequential loss, damage, or expense directly or indirectly arising from the use of this device. Penumbra neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this device. Penumbra assumes no liability with respect to devices reused, reprocessed, or resterilized and makes no warranties, expressed or implied, including but not limited to merchantability or fitness for intended use, with respect to such device.

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Beschreibung Der Vorrichtung

Das Penumbra System® besteht aus mehreren Vorrichtungen:

- Penumbra Reperfusionskatheter
- Penumbra Separator
- Penumbra Aspirationspumpe
- Penumbra Pumpen-/Behälterschlauchsystem
- Penumbra Aspirationsschlauchsystem

Der Reperfusionskatheter wird über einen Führungskatheter oder eine lange femorale Schleuse in die intrakranielle Vaskulatur eingeführt und mithilfe eines neurovaskulären Führungsdrahtes zur primären Okklusionsstelle geführt. Gleichzeitig mit dem Penumbra Reperfusionskatheter werden der Penumbra Separator und eine Aspirationsquelle eingesetzt, um den Thrombus abzutrennen und aus dem verschlossenen Gefäß abzusaugen. Der Penumbra Separator wird vom Penumbra Reperfusionskatheter freigesetzt. Der Penumbra Separator wird am proximalen Rand der primären Okklusion durch den Penumbra Reperfusionskatheter vorgeschoben und zurückgezogen. Dies vereinfacht die Aspiration und das Debulking des Thrombus und vermindert bzw. beseitigt die Belastung durch endovaskuläre Blutgerinnsel. Die Aspirationsquelle besteht aus dem Penumbra Reperfusionskatheter und der Aspirationspumpe, die an das Aspirationsschlauchsystem und das Penumbra Pumpen-/Behälter-schlauchsystem angeschlossen ist. Der Penumbra Separator wird zusammen mit einer Einführschleuse und einer Drehvorrichtung geliefert. Der Lieferumfang des Penumbra Reperfusionskatheters umfasst einen Dampfformmandrin und ein hämostatisches Drehventil sowie eine abziehbare Schleuse. Die Vorrichtungen sind unter Röntgendurchleuchtung sichtbar.

Indikationen

Das Penumbra System ist zur Revaskularisierung von Patienten mit akuten ischämischen Schlaganfällen als Folge von Verschlusskrankheiten in den großen intrakraniellen Blutgefäßen (innerhalb der inneren Herzschlagader, der mittleren Gehirnarterie – Abschnitte M1 und M2, der Basilararterie und der Arteria vertebralis) vorgesehen. Der Eingriff muss innerhalb von 8 Stunden nach Einsetzen der Symptome durchgeführt werden.

Kontraindikationen

Es sind keine Kontraindikationen bekannt.

Warnhinweise

- Das Penumbra System darf nur von Ärzten verwendet werden, die ausreichend in neuro-endovaskulären Interventionsverfahren und der Behandlung von akuten ischämischen Schlaganfällen geschult sind.
- Das Penumbra System darf nur mit der Penumbra Aspirationspumpe verwendet werden.

Vorsichtsmassnahmen

- Diese Vorrichtung ist nur zur einmaligen Verwendung geeignet. Nicht resterilisieren oder wieder verwenden. Resterilisierung und/oder Wiederverwendung kann zu unwirksamer Schmierung der Katheterbeschichtung führen, die wiederum hohe Reibung verursachen und den Zugang zur neurovaskulären Zielstelle verhindern kann.
- Geknickte bzw. beschädigte Vorrichtungen nicht verwenden. Geöffnete oder beschädigte Packungen nicht verwenden.
- Vor dem Verfallsdatum verwenden.
- Das Penumbra System unter Röntgendurchleuchtung verwenden.
- Das Penumbra System nicht verwenden oder vorschieben, wenn ein Widerstand zu spüren ist, ohne die Ursache hierfür zuerst unter Röntgendurchleuchtung zu prüfen. Die Vorrichtung zurückziehen, wenn keine Ursache gefunden werden kann. Übermäßiges Drehen oder ein erzwungenes Einführen des Katheters oder Separators bei auftretendem Widerstand kann zu einer Kompression der Vorrichtung und zu Gefäßschäden und/oder Brechen der Spitze führen.
- Eine kontinuierliche Infusion mit geeigneter Spüllösung aufrechterhalten.
- Bei der Aspiration sicherstellen, dass das Ventil des Penumbra Aspirationsschlauchsystems nur für den zur Thrombusentfernung erforderlichen Mindestzeitraum geöffnet ist. Eine übermäßig lange Aspirationszeit bzw. ein Fehler beim Verschließen des Penumbra Aspirationsschlauchventils nach Abschluss der Aspiration sollte vermieden werden.
- Der Penumbra Separator ist nicht für die Verwendung als neurovaskulärer Führungsdraht vorgesehen. Sollte der Penumbra Reperfusionskatheter während des Revaskularisierungseingriffs neu positioniert werden müssen, muss diese Umpositionierung mithilfe eines geeigneten neurovaskulären Führungsdrahtes und unter Anwendung von Standard-Techniken für Mikrokatheter und Führungsdrähte vorgenommen werden.
- Keinen automatisierten Hochdruckinjektor für Kontrastmittel mit dem Penumbra Reperfusionskatheter verwenden, da dies zu Schäden an der Vorrichtung führen könnte.
- Die Verabreichung von Thrombozytenaggregationshemmern und Antikoagulanzien sollte erst 24 Stunden nach dem Eingriff erfolgen. Das Medizin-Management und die akute Schlaganfallnachsorge sollten gemäß der ASA (American Stroke Association)-Richtlinien durchgeführt werden.[1] Neurologische Verschlechterungen jeder Art sollten umgehend mit einem computertomographischen oder einem anderen vom Arzt bzw. dem Krankenhaus hierfür üblicherweise verwendeten Verfahren untersucht werden.
- Bei der Verwendung des Penumbra Systems beträgt die max. Zeitdauer bis zum Erreichen der Patienten-Revaskularisierung 120 Minuten.

Deutsch

Potenzielle Nebenwirkungen

Zu den möglichen Komplikationen gehören u. a. folgende:

- Allergische Reaktion und Anaphylaxie durch Kontrastmittel
- Akute Okklusion
- Luftembolien
- Arteriovenöse Fisteln
- Tod
- Fehlfunktion der Vorrichtung
- Distale Embolisation
- Embolie
- Bildung von falschen Aneurysmen
- Hämatome oder Blutungen an der Zugangsstelle
- Unvollständige Entfernung des Thrombus
- Infektion
- Intrakranielle Blutungen
- Ischämie
- Nierenschäden durch Kontrastmittel
- Neurologische Störungen, einschließlich Schlaganfall
- Gefäßspasmus, Thrombose, Dissektion oder Perforation

Verfahren

1. Vor der Verwendung die Abschnitte **Warnhinweise**, **Vorsichtsmaßnahmen** und **Potenzielle Nebenwirkungen** durchlesen.
2. Jede Vorrichtung des Penumbra Systems vor Gebrauch aus der Verpackung nehmen und auf Schäden oder Knicke untersuchen.
3. Die Vorrichtungen des Penumbra Systems zur Verwendung vorbereiten, indem die Verpackungsschlaufe und die Vorrichtung mit heparinisierter Kochsalzlösung gespült werden (nur für Penumbra Reperfusionskatheter und Penumbra Separator).
4. Einen Führungskatheter bzw. eine lange femorale Schleuse entsprechend der *Gebrauchsanweisung* des Herstellers vorbereiten.
5. Den Führungskatheter bzw. die lange femorale Schleuse proximal zur Thrombusverschlussstelle in der entsprechenden Gehirnarterie positionieren.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Penumbra Reperfusionskatheter – Vorbereitung Und Verwendung

1. Den Gefäßdurchmesser bestimmen und den geeigneten Penumbra Reperfusionskatheter (siehe **Tabelle 1**) auswählen.
2. Die Spitze des Penumbra Reperfusionskatheters kann mit dem im Lieferumfang enthaltenen Dampfformmandrin geformt werden.
3. Das im Lieferumfang enthaltene hämostatische Drehventil an den Penumbra Reperfusionskatheter anschließen.
4. Den Penumbra Reperfusionskatheter in ein hämostatisches Drehventil einführen, das am proximalen Ansatz eines Führungskatheters angeschlossen ist. Wenn kein Führungskatheter verwendet wird, den Penumbra Reperfusionskatheter mithilfe der abziehbaren Schleuse durch das Ventil der langen femoralen Schleuse einführen. Nach dem Einführen des Penumbra Reperfusionskatheters die abziehbare Schleuse aus der Gefäßschleuse entfernen und vom Penumbra Reperfusionskatheterschaft abziehen.
5. Unter Röntgendurchleuchtung und gemäß den herkömmlichen Katheterisierungsmethoden den Penumbra Reperfusionskatheter mithilfe eines geeigneten neurovaskulären Führungsdrahtes in das Zielgefäß vorschieben. Den Penumbra Reperfusionskatheter proximal zum Thrombus positionieren. Den Führungsdraht aus dem Penumbra Reperfusionskatheter entfernen.

Penumbra Separator – Vorbereitung Und Verwendung

1. Das Penumbra Aspirationsschlauchsystem an die Aspirationspumpe anschließen und diese einschalten (siehe das *Betriebshandbuch* der Aspirationspumpe). Die Aspirationspumpe mindestens eine Minute vor Gebrauch laufen lassen und überprüfen, ob das Aspirationsmanometer –20 inHg anzeigt. Sicherstellen, dass das Ventil am Penumbra Aspirationsschlauchsystem in der Position OFF (AUS) steht.
2. Einen für die Verwendung mit dem gewählten Reperfusionskatheter geeigneten Penumbra Separator auswählen (siehe **Tabelle 1**).

Tabelle 1 – Auswahl der Separator-/Reperfusionskathetergröße

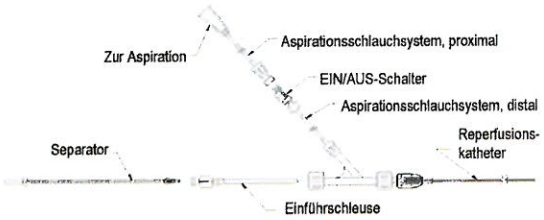
Gefäßgröße (mm)	Penumbra Reperfusionskatheter	Penumbra Separator
< 2,0	026	026
2,0 bis 3,0	032 / 3MAX	032 / 3MAX
3,0 bis 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Den Penumbra Reperfusionskatheter vorsichtig vorschieben, um die distale Spitze in den Thrombus einzubetten.

HINWEIS: Der Zugang zur Okklusionsstelle kann durch die triaxiale Verwendung eines kompatiblen inneren Mikrokatheters erleichtert werden.

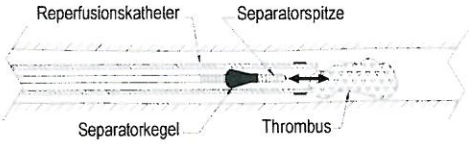
4. Den Penumbra Separator mithilfe der Einführschleuse in das hämostatische Drehventil und den proximalen Anschluss des Penumbra Reperfusionskatheters einführen.
5. Das Aspirationsschlauchsystem wie in **Abb. 1** gezeigt am Seitenanschluss des hämostatischen Drehventils anschließen.

Abb. 1 – Das zusammengebaute Aspirationssystem mit Penumbra Separator



6. Um mit der Aspiration zu beginnen, das Ventil am Penumbra Aspirations schlauchsystem in die Position ON (EIN) stellen und den Penumbra Separator vorschieben/zurückziehen, um die Aspiration und die Entfernung des Thrombus (wie in **Abb. 2** dargestellt) zu erleichtern.

Abb. 2 – Thrombus-Aspiration mithilfe des Penumbra Separators



7. Das Ventil am Penumbra Aspirationsschlauchsystem zum Beenden der Aspiration in die Position OFF (AUS) drehen und die Aspirationspumpe ausschalten.
8. Den Penumbra Separator entfernen.
9. Es können ggf. weitere Penumbra Separatoren und Reperfusionskatheter zur Entfernung des Thrombus eingesetzt werden, wenn dies vom Arzt als erforderlich erachtet wird.
10. Mit einer 5-ml- oder 10-ml-Spritze ca. 5 ml Blut aus dem Penumbra Reperfusionskatheter aspirieren, um einen eventuell im Katheter verbliebenen Thrombus zu entfernen.
11. Ein postoperatives Angiogramm erstellen, indem Kontrastmittel durch den Führungskatheter injiziert wird.

Erläuterung Der Symbole

		Achtung! Siehe Gebrauchsanweisung	
Rx Only		Verschreibungspflichtig – Laut Bundesgesetz der USA darf diese Vorrichtung ausschließlich von einem Arzt oder auf Anordnung eines Arztes verwendet werden.	
		Pyrogenfrei	
STERILE EO		Steril (Ethylenoxid)	
	Hersteller	EC REP	Bevollmächtigter in der EU
LOT	Chargennummer		Nicht wieder verwenden
	Zu verwenden bis	REF	Katalognummer
STERILIZE	Nicht resterilisieren	LATEX	Latexfrei

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Descrizione del dispositivo

Il sistema Penumbra System® comprende diversi componenti:

- Catetere di riperfusione Penumbra
- Separatore Penumbra
- Pompa di aspirazione Penumbra
- Tubo contenitore/pompa Penumbra
- Tubo di aspirazione Penumbra

Il catetere di riperfusione viene introdotto in un catetere guida o una guaina femorale lunga e all'interno dell'albero vascolare del sistema nervoso centrale e, tramite una guida neurovascolare viene condotto fino al sito dell'occlusione primaria. Il catetere di riperfusione Penumbra deve essere usato insieme al separatore Penumbra e a una fonte di aspirazione, in modo da ottenere la separazione del trombo e poterlo aspirare dal vaso occluso. Il separatore Penumbra viene rilasciato dal catetere di riperfusione Penumbra. Il separatore Penumbra viene fatto avanzare e viene retratto all'interno del catetere di riperfusione Penumbra in corrispondenza del margine prossimale dell'occlusione primaria. Questo processo facilita l'aspirazione e la riduzione del trombo e consente di diminuire o eliminare il rischio di coagulo endovascolare. Per quanto riguarda la fonte di aspirazione, il catetere di riperfusione Penumbra viene usato insieme alla pompa di aspirazione, la quale può essere collegata tramite il tubo di aspirazione Penumbra e il tubo contenitore/pompa Penumbra. Il separatore Penumbra è dotato di un introduttore e di un dispositivo di torsione. Il catetere di riperfusione è dotato di un mandrino di sagomatura a vapore, una valvola emostatica girevole e una guaina distaccabile. I dispositivi sono visibili in fluoroscopia.

Indicazioni per l'uso

Il sistema Penumbra System è indicato per la rivascolarizzazione di pazienti ...tti da ictus ischemico acuto secondario a malattie vascolari occlusive dei ...ndi vasi intracranici (arterie carotide interna, cerebrale media – segmenti ...I e M2, basilare e vertebrale) entro 8 ore dall'insorgenza dei sintomi.

Controindicazioni

Nessuna nota.

Avvertenze

- Il sistema Penumbra System deve essere utilizzato esclusivamente da medici specializzati in tecniche interventistiche neuro-endovascolari e nel trattamento di ictus ischemico acuto.
- Usare il sistema Penumbra System esclusivamente con la pompa di aspirazione Penumbra.

Precauzioni

- Il dispositivo è monouso. Non risterilizzare o riutilizzare. La risterilizzazione e/o lo riutilizzo del dispositivo possono compromettere la lubrificazione del rivestimento del catetere, con conseguente aumento dell'attrito e impossibilità di raggiungere la posizione desiderata nell'albero vascolare del sistema nervoso.
- Non utilizzare dispositivi deformati o danneggiati. Non usare confezioni aperte o danneggiate.
- Usare prima della data di scadenza.
- Usare il sistema Penumbra System in fluoroscopia.
- Qualora si riscontri resistenza non fare avanzare o usare nessun componente del sistema Penumbra System senza aver prima determinato la causa di tale resistenza tramite fluoroscopia. Se non è possibile determinare la causa, rimuovere il dispositivo. Una torsione eccessiva o l'introduzione forzata del catetere o separatore qualora si riscontri resistenza possono comprimere il dispositivo, causando lesioni vascolari e/o la rottura della punta.
- Mantenere un'infusione costante della soluzione di irrigazione adeguata.
- Durante l'aspirazione, controllare che la valvola del tubo di aspirazione Penumbra rimanga aperta solo per il tempo minimo necessario per la rimozione del trombo. L'aspirazione eccessiva o la mancata chiusura della valvola del tubo di aspirazione Penumbra al termine dell'aspirazione sono condizioni non raccomandabili.
- Il separatore Penumbra è controindicato per l'uso come guida neurovascolare. Se durante la procedura di rivascolarizzazione fosse necessario il riposizionamento del catetere di riperfusione Penumbra, eseguire il riposizionamento usando una guida neurovascolare adeguata, secondo le tecniche che prevedono l'uso di una guida e di un microcatetere standard.
- Non usare attrezzature automatiche per l'iniezione di mezzo di contrasto ad alta pressione con il catetere di riperfusione Penumbra in quanto potrebbero danneggiare il dispositivo.
- La somministrazione di anticoagulanti e antipiastrinici deve essere sospesa fino a 24 ore dopo l'intervento. La gestione medica e la cura successive all'ictus acuto devono essere conformi alle linee guida dell'ASA.[1] Qualsiasi deterioramento neurologico deve essere valutato tramite una scansione TAC d'urgenza e altre valutazioni in accordo con le migliori pratiche ospedaliere.
- Il tempo totale concesso per la rivascolarizzazione è di 120 minuti con il sistema Penumbra System.

Italiano

Effetti collaterali potenziali

Possibili complicazioni includono, in modo non limitativo, le seguenti:

- Reazione allergica e anafilassi da mezzo di contrasto
- Occlusione acuta
- Embolia gassosa
- Fistola arterovenosa
- Morte
- Malfunzionamento del dispositivo
- Embolizzazione distale
- Emboli
- Falso aneurisma
- Ematoma o emorragia al sito di accesso
- Impossibilità di rimozione completa del trombo
- Infezione
- Emorragia intracranica
- Ischemia
- Danni renali causati dal mezzo di contrasto
- Deficienze neurologiche, incluso ictus
- Vasospasmo, trombosi, dissezione o perforazione del vaso

Procedura

1. Prima dell'uso, fare riferimento a **Avvertenze**, **Precauzioni** ed **Effetti collaterali**.
2. Prima dell'uso dei dispositivi del sistema Penumbra System, rimuovere i dispositivi dalla confezione e controllare che non presentino danni o deformazioni.
3. Preparare per l'uso i dispositivi del sistema Penumbra System irrigando la guaina della confezione e il dispositivo con soluzione fisiologica eparinizzata (inclusi solo il catetere di riperfusione Penumbra e il separatore Penumbra).
4. Preparare un catetere guida o una guaina femorale lunga in base alle *istruzioni per l'uso* del produttore.
5. Posizionare il catetere guida o la guaina femorale lunga in corrispondenza dell'arteria cerebrale adeguata, prossimale al sito dell'occlusione trombotica.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Preparazione e uso del catetere di riperfusione Penumbra

1. Confermare il diametro del vaso e selezionare un catetere di riperfusione Penumbra di dimensioni adeguate (**Tabella 1**).
2. La punta del catetere di riperfusione Penumbra può essere modificata usando il mandrino di sagomatura a vapore in dotazione.
3. Collegare la valvola emostatica girevole in dotazione al catetere di riperfusione Penumbra.
4. Introdurre il catetere di riperfusione Penumbra nella valvola emostatica girevole collegata al raccordo prossimale di un catetere guida. Qualora non si utilizzi un catetere guida, inserire il catetere di riperfusione Penumbra attraverso la valvola della guaina femorale lunga utilizzando la guaina distaccabile. Dopo aver inserito il catetere di riperfusione Penumbra, rimuovere la guaina distaccabile dalla guaina vascolare e distaccarla dal corpo del catetere di riperfusione Penumbra.
5. Facendo uso delle tecniche convenzionali di cateterismo in fluoroscopia, fare avanzare il catetere di riperfusione Penumbra nel vaso target lungo una guida neurovascolare adeguata. Posizionare il catetere di riperfusione Penumbra in posizione prossimale rispetto al trombo. Rimuovere la guida dal catetere di riperfusione Penumbra.

Preparazione e uso del separatore Penumbra

1. Collegare il tubo di aspirazione Penumbra alla pompa di aspirazione e accendere la pompa di aspirazione (fare riferimento al *Manuale di funzionamento* della pompa di aspirazione). Lasciare funzionare la pompa per almeno un minuto prima dell'uso, quindi controllare che la lettura dell'indicatore di aspirazione corrisponda a –20inHg. Controllare che la valvola sul tubo di aspirazione Penumbra si trovi nella posizione OFF (spento).
2. Selezionare un separatore Penumbra di dimensioni adeguate al catetere di riperfusione (**Tabella 1**).

Tabella 1 – Selezione delle dimensioni del catetere di riperfusione/separatore

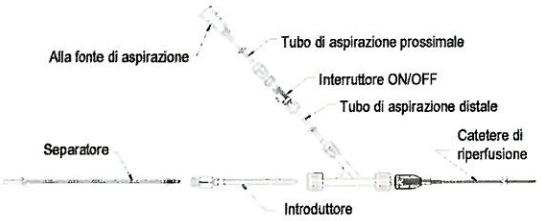
Dimensioni vaso (mm)	Catetere di riperfusione Penumbra	Separatore Penumbra
< 2,0	026	026
da 2,0 a 3,0	032 / 3MAX	032 / 3MAX
da 3,0 a 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Fare avanzare il catetere di riperfusione Penumbra in modo che la punta distale si infili delicatamente nel trombo.

NOTA: per agevolare l'accesso al sito dell'occlusione è possibile servirsi di un microcatetere interno compatibile in posizione triassale.

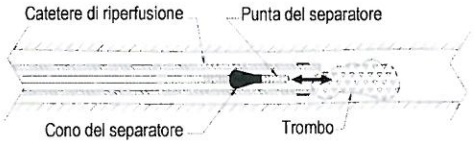
4. Usando l'introduttore in dotazione, introdurre il separatore Penumbra nella valvola emostatica girevole e nel raccordo prossimale del catetere di riperfusione Penumbra.
5. Collegare il tubo di aspirazione all'attacco laterale della valvola emostatica girevole, come illustrato nella **Figura 1**.

Figura 1 – Sistema di aspirazione montato con il separatore Penumbra



6. Per avviare l'aspirazione, aprire la valvola sul tubo di aspirazione Penumbra sulla posizione ON (acceso), e fare avanzare/retrarre il separatore Penumbra per favorire l'aspirazione e la rimozione del trombo, come illustrato nella **Figura 2**.

Figura 2 – Aspirazione del trombo tramite il separatore Penumbra



7. Per interrompere l'aspirazione, portare la valvola sul tubo di aspirazione Penumbra sulla posizione OFF (spento) e spegnere la pompa di aspirazione.
8. Rimuovere il separatore Penumbra.
9. Se necessario, a discrezione del medico è possibile usare separatori e cateteri di riperfusione Penumbra aggiuntivi per l'ulteriore rimozione di materiale trombotico.
10. Con una siringa da 5 cc o da 10 cc, aspirare circa 5 cc di sangue dal catetere di riperfusione Penumbra in modo da eliminare eventuali residui trombotici dal catetere.
11. Ottenere un angiogramma post-trattamento iniettando mezzo di contrasto attraverso il catetere guida.

Legenda dei simboli

	Attenzione, vedere le istruzioni per l'uso.		
Rx Only	Solo su prescrizione – La legge federale degli Stati Uniti autorizza l'uso di questo prodotto esclusivamente su prescrizione medica		
	Apirogeno		
STERILE EO	Sterilizzato con ossido di etilene		
	Fabbricante	EC REP	Rappresentante nell'UE
LOT	Numero di lotto		Non riutilizzare
	Usare entro	REF	Numero di catalogo
STERILIZE	Non risterilizzare	LATEX	Non contiene lattice

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Descripción del dispositivo

El sistema Penumbra System® consta de varios componentes:

- Catéter de reperfusión de Penumbra
- Separador de Penumbra
- Bomba de aspiración de Penumbra
- Tubo de bomba/recipiente de Penumbra
- Tubo de aspiración de Penumbra

El catéter de reperfusión se introduce mediante un catéter guía o una vaina femoral larga dentro de la vasculatura intracraneal y se conduce a través de una guía neurovascular hasta el lugar de la oclusión primaria. El catéter de reperfusión de Penumbra se desplaza en paralelo con el separador de Penumbra y una fuente de aspiración para separar el trombo y aspirarlo del vaso ocluido. El separador de Penumbra se despliega desde el catéter de reperfusión de Penumbra. El separador de Penumbra se hace avanzar y se retrae a través del catéter de reperfusión de Penumbra en el margen proximal de la oclusión primaria. Esto facilita la aspiración y la reducción del trombo y reduce o elimina la carga endovascular de coágulos. Para la fuente de aspiración, el catéter de reperfusión de Penumbra se utiliza junto con la bomba de aspiración, que se conecta utilizando el tubo de aspiración y el tubo de bomba/recipiente de Penumbra. El separador de Penumbra cuenta con un dispositivo introductor y de torsión. El catéter de reperfusión de Penumbra cuenta con un mandril de modelado al vapor, una válvula rotativa de hemostasia y una vaina extraíble. Los dispositivos son visibles con fluoroscopia.

Indicaciones de uso

Penumbra System está destinado para el uso en la revascularización de pacientes con accidente cerebrovascular isquémico agudo secundario a enfermedad oclusiva intracraneal de vasos grandes (dentro de las arterias carótida interna, cerebral media (segmentos M1 y M2), basilar y vertebral) dentro de las primeras 8 horas de la aparición de los síntomas.

Contraindicaciones

No existen contraindicaciones conocidas.

Advertencias

- El Penumbra System sólo deben utilizarlo médicos que hayan recibido una formación adecuada en técnicas de intervención neuroendovascular y en tratamiento de accidentes cerebrovasculares isquémicos agudos.
- No utilice el Penumbra System con otra bomba que no sea la bomba de aspiración de Penumbra.

Precauciones

- Este dispositivo está indicado para un solo uso. No reesterilizar ni reutilizar. La resterilización o reutilización puede producir la lubricación incorrecta del revestimiento del catéter, lo cual, a su vez, puede ocasionar una alta fricción e impedir el acceso a la ubicación del sistema vascular neural de destino.
- No usar dispositivos torcidos o dañados. No usar si los envases están abiertos o dañados.
- Utilizar antes de la fecha de caducidad.
- Utilizar Penumbra System junto con visualización fluoroscópica.
- No hacer avanzar ni utilizar ningún componente de Penumbra System, si se encuentra resistencia, sin antes realizar una evaluación cuidadosa de la causa mediante fluoroscopia. Si no se puede determinar la causa, retirar el dispositivo. Si la torsión es ilimitada o si el catéter o el separador se insertan de manera forzada cuando haya resistencia, es posible que el dispositivo se comprima y, en consecuencia, puede ocasionar daños en el vaso sanguíneo y/o la ruptura de la punta.
- Mantener una infusión constante de solución de lavado apropiada.
- Al aspirar, asegurarse de que la válvula del tubo de aspiración de Penumbra esté abierta sólo el tiempo mínimo necesario para la extracción del trombo. No se recomienda aspirar más de lo necesario ni cerrar incorrectamente la válvula del tubo de aspiración de Penumbra al terminar el proceso de aspiración.
- El separador de Penumbra no está destinado al uso como guía neurovascular. Si es necesario volver a colocar el catéter de reperfusión de Penumbra durante el proceso de revascularización, dicha recolocación se debe llevar a cabo con una guía neurovascular adecuada mediante técnicas estándar de microcatéter y de guía.
- No utilizar equipos automatizados de inyección de contraste de alta presión con el catéter de reperfusión de Penumbra, ya que podría dañar el dispositivo.
- Se debe suspender la administración de anticoagulantes y antiplaquetarios hasta 24 horas después del tratamiento. El control médico y los cuidados después del accidente cerebrovascular agudo deben seguir las directrices de ASA.[1] Cualquier deterioro neurológico se debe evaluar mediante TC urgente y otros sistemas de evaluación según las mejores prácticas del investigador o el hospital.
- El tiempo total permitido para lograr la revascularización del paciente es de 120 minutos de uso de Penumbra System.

Posibles reacciones adversas

Entre las posibles complicaciones se incluyen las siguientes:

- reacción alérgica y anafilaxis debida a los medios de contraste
- oclusión aguda
- embolia gaseosa
- fístula arteriovenosa
- muerte
- funcionamiento incorrecto del dispositivo
- embolización distal
- émbolos
- formación de un falso aneurisma
- hematoma o hemorragia en el lugar del acceso
- imposibilidad de extraer completamente el trombo
- infección
- hemorragia intracraneal
- isquemia
- daño en el riñón debido a los medios de contraste
- déficit neurológicos, incluido accidente cerebrovascular
- espasmos de vasos, trombosis, disección o perforación

Español

Procedimiento

1. Consulte las **advertencias**, **precauciones** y **posibles reacciones adversas** antes del uso.
2. Cuando vaya a utilizar los dispositivos de Penumbra System, extraiga el dispositivo del embalaje e inspecciónelo para comprobar que no existen daños ni defectos.
3. Prepare los dispositivos de Penumbra System para su uso, enjuagando el embalaje y el dispositivo con solución salina heparinizada (incluye únicamente el catéter de reperfusión y el separador de Penumbra).
4. Prepare un catéter guía o la vaina femoral larga según las *Instrucciones de uso* del fabricante.
5. Coloque el catéter guía o la vaina femoral larga en la arteria cerebral adecuada proximal al lugar de oclusión del trombo.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Preparación y uso del catéter de reperfusión de Penumbra

1. Confirme el diámetro del vaso y seleccione un tamaño apropiado para el catéter de reperfusión de Penumbra (consulte la **Tabla 1**).
2. La punta del catéter de reperfusión de Penumbra se debe moldear con el mandril de modelado al vapor suministrado.
3. Conecte la válvula rotativa de hemostasia que se proporciona al catéter de reperfusión de Penumbra.
4. Inserte el catéter de reperfusión de Penumbra en una válvula rotativa de hemostasia conectada a la conexión proximal de un catéter guía. Si no se utiliza un catéter guía, inserte el catéter de reperfusión Penumbra a través de la válvula de la vaina femoral larga por medio de la vaina extraíble. Después de colocar el catéter de repercusión de Penumbra, extraiga la vaina extraíble de la vaina femoral y retírela del cuerpo del catéter de reperfusión de Penumbra.
5. Mediante técnicas de cateterismo convencional con guía fluoroscópica, haga avanzar el catéter de reperfusión de Penumbra hacia el vaso de destino sobre una guía neurovascular adecuada. Coloque el catéter de reperfusión de Penumbra proximal al trombo. Retire la guía del catéter de reperfusión de Penumbra.

Preparación y uso del separador de Penumbra

1. Conecte el tubo de aspiración de Penumbra a la bomba de aspiración y actívela (consulte el *Manual de funcionamiento* de la bomba de aspiración). Haga funcionar la bomba de aspiración durante al menos un minuto antes de utilizarla y confirme que el indicador de aspiración se encuentre en –20 inHg. Asegúrese de que la válvula del tubo de aspiración de Penumbra esté en la posición de APAGADO (OFF).
2. Seleccione un separador de Penumbra de tamaño adecuado correspondiente al catéter de reperfusión (consulte la **Tabla 1**).

Tabla 1 – Selección de tamaño del dispositivo separador/catéter de reperfusión

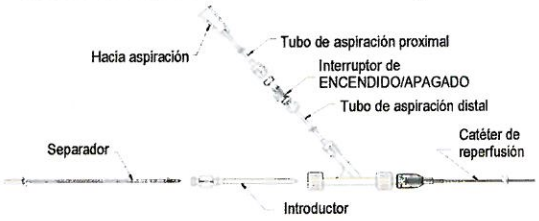
Tamaño del vaso (mm)	Catéter de reperfusión de Penumbra	Separador de Penumbra
< 2,0	026	026
De 2,0 a 3,0	032 / 3MAX	032 / 3MAX
De 3,0 a 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Haga avanzar el catéter de reperfusión de Penumbra hasta introducir con cuidado el extremo distal en el trombo.

NOTA: es posible facilitar el acceso al sitio de la oclusión mediante el uso triaxial de un microcatéter interno compatible.

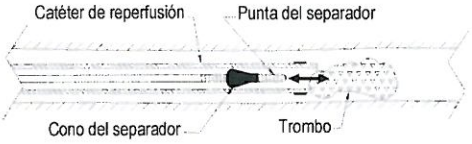
4. Mediante la vaina introductora proporcionada, inserte el separador de Penumbra a través de la válvula rotativa de hemostasia en la conexión proximal del catéter de reperfusión de Penumbra.
5. Conecte el tubo de aspiración al orificio lateral de la válvula rotativa de hemostasia como se muestra en la **Figura 1**.

Figura 1 – Sistema de aspiración ensamblado con separador de Penumbra



6. Para comenzar la aspiración, lleve la válvula del tubo de aspiración de Penumbra a la posición de ENCENDIDO (ON) y haga avanzar/retraiga el separador de Penumbra para facilitar la aspiración y la extracción del trombo como se muestra en la **Figura 2**.

Figura 2 – Aspiración de trombo mediante el separador de Penumbra



7. Para detener la aspiración, lleve la válvula del tubo de aspiración de Penumbra a la posición de APAGADO (OFF) y apague la bomba de aspiración.
8. Extraiga el separador de Penumbra.
9. Si resulta necesario, y a criterio del médico, es posible usar separadores y catéteres de reperfusión, de Penumbra, adicionales para seguir extrayendo trombos.
10. Con ayuda de una jeringa de 5 ó 10 cc, aspire aproximadamente 5 cc de sangre del catéter de reperfusión de Penumbra para extraer cualquier trombo que pudiera quedar en el catéter.
11. Obtenga un angiograma posterior al tratamiento inyectando medio de contraste a través del catéter guía.

Glosario de símbolos

		Atención, consultar las instrucciones de uso	
Rx Only		Sólo bajo prescripción: las leyes federales de Estados Unidos restringen el uso de este dispositivo a un médico o a su petición	
		Apirogénico	
STERILE EO		Esterilizado usando óxido de etileno	
	Fabricante	EC REP	Representante en UE
LOT	Número de lote		De un solo uso
	Fecha de caducidad	REF	N.º de referencia
	No reesterilizar	LATEX	Sin látex

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Az eszköz leírása

A Penumbra System® több készülékből áll:

- Penumbra reperfúziós katéter
- Penumbra szeparátor
- Penumbra szívópumpa
- Penumbra csövek a pumpához/tartályhoz
- Penumbra szívócső

A reperfúziós katétert egy vezetőkatéteren vagy egy hosszú, femorális hüvelyen keresztül vezesse be az intrakraniális érrendszerbe, és neurovaszkuláris vezetődróton vigye a primer okklúzió helyére. A Penumbra reperfúziós katétert használja együtt a Penumbra szeparátorral és egy szívóeszközzel, hogy szeparálja a trombust, és kiszívja azt az elzáródott érből. A Penumbra szeparátort a Penumbra reperfúziós katéterből kell kinyitni. A Penumbra szeparátort a Penumbra reperfúziós katéteren keresztül vigye fel és húzza vissza a primer okklúzió proximális szélénél. Ez megkönnyíti a trombus kiszívását és megkisebbítését, továbbá csökkenti, vagy kiküszöböli az alvadás okozta endovaszkuláris megterhelést. Szívóeszközként a Penumbra reperfúziós katétert használja a szívópumpával összekötve, amelyhez a Penumbra szívócsöveket és a Penumbra pumpához/tartályhoz való csöveket használja. A Penumbra szeparátort ellátták egy bevezető és forgató eszközzel. A Penumbra reperfúziós katéteren található egy hőhatásra alakítható mandrin és egy forgatható vérzésgátló szelep és egy leválasztható hüvely. Az eszközök képerősítő alatt láthatók.

Alkalmazási javallatok

A Penumbra System olyan betegek revaszkularizációjára tervezték a tünetek jelentkezésétől számított 8 órán belül, akiknél agyi nagyér-elzáródásos betegség következtében (a. carotis interna, cerebri media – M1- és M2-szegmentumok, valapi és gerincvelői artériák) akut iszkémiás stroke lépett fel.

Ellenjavallatok

Nincsenek ismert ellenjavallatok.

Figyelmeztetés

- A Penumbra Systemet kizárólag olyan orvosok használhatják, akik megfelelő kiképzést kaptak az intervencionális neuro-endovaszkuláris technikák és az akut iszkémiás stroke kezelésének területén.
- Ne használja a Penumbra System eszközeit másfajta pumpával, mint a Penumbra aspirációs pumpával.

Óvintézkedések

- Az eszköz kizárólag egyszeri használatra készült. Ne sterilizálja vagy használja újra! Az eszköz ismételt sterilizálása és/vagy felhasználása a katéter bevonatának nem megfelelő síkosítását eredményezheti, ami nagy surlódáshoz vezethet és a neuro-vaszkuláris célhely elérését akadályozhatja.
- Ne használjon megtört vagy sérült eszközöket! Ne használjon nyitott vagy sérült csomagolású terméket!
- Használja fel a lejárati idő előtt!
- A Penumbra System képerősítő ellenőrzése alatt használja!
- Soha ne vezesse be vagy használja fel a Penumbra System egyik elemét sem, ha az ellenállásba ütközik, és ennek okát a képerősítővel való gondos követés mellett nem tudja meghatározni. Ha az okot nem lehet meghatározni, akkor vegye ki az eszközt. Amennyiben a katéter vagy a szeparátor feszül csavarás közben, vagy ellenállással szemben próbálja a bevezetést erőltetni, az eszköz összenyomódhat, ami érsérüléshez és/vagy a csúcs töréséhez vezethet.
- Megfelelő öblítő oldattal tartson fenn folyamatos infúziót.
- A szívás végzésekor győződjön meg róla, hogy a Penumbra szívócsövek szelepe csak annyi időre van kinyitva, amennyi minimálisan szükséges a trombus eltávolításához. Nem ajánlott, hogy túlzott mértékben végezze a szívást, vagy hogy a trombus kiszívásának befejeztével elmulassza lezárni a Penumbra szívócsöveinek szelepét.
- A Penumbra szeparátort nem neurovaszkuláris vezetődrótnak tervezték. Ha a revaszkularizációs eljárás során a Pneumbra reperfúziós katéter áthelyezése válik szükségessé, akkor az ilyen áthelyezést megfelelő neurovaszkuláris vezetődrót felett kell elvégezni a szokásos mikrokatéteres és vezetődrótos technikák alkalmazásával.
- Ne használjon automatikus, magas nyomású kontrasztanyag-befecskendező berendezést a Penumbra reperfúziós katéterhez, mert az károsíthatja az eszközt.
- A kezelést követően 24 órára fel kell függeszteni a véralvadásgátlók és a trombocitaellenes szerek adagolását. Az orvosi kezelést és az akut stroke-ot követő ápolást az ASA-irányelveknek megfelelően kell végezni.[1] Mindenfajta neurológiai kiesést akut CT-vizsgálattal kell követni, és további vizsgálatokat kell elvégezni a vizsgáló orvos, ill. a kórház legjobb tudása/lehetőségei szerint.
- A beteg revaszkularizációjának elérésére összesen legfeljebb 120 perc engedélyezett a szeparátor vagy a trombuseltávolító gyűrű, ill. mindkettő használata esetén.

Lehetséges mellékhatások

A lehetséges szövődmények többek között az alábbiak lehetnek:

- allergiás és anafilaxiás reakció a kontrasztanyagra
- akut elzáródás
- légembólia
- arteriovenózus fisztula
- halál
- az eszköz hibás működése
- disztális embolizáció
- embóliák
- álaneurizma kialakulása
- vérömleny vagy vérzés a behatolás helyén
- nem sikerül a trombust teljes mértékben eltávolítani
- fertőzés
- intrakraniális vérzés
- iszkémia
- kontrasztanyag okozta vesekárosodás
- neurológiai kiesések, beleértve a stroke-ot is
- érgörcs, trombózis, ér-disszekció vagy érperforáció

Magyar

Eljárás

1. Használat előtt nézze át a **Figyelmeztetések**, **Óvintézkedések** és a **Lehetséges mellékhatások** c. szakaszokat.
2. A Penumbra System valamennyi eszközének használatakor vegye ki az eszközt a csomagolásból, és szemrevételezéssel ellenőrizze, hogy nincs-e rajta sérülés vagy megtörés.
3. Készítse elő használatra a Penumbra System eszközeit oly módon, hogy heparinozott fiziológiás sóoldattal átöblíti a csomagológyűrűt és az eszközt (csak a Penumbra reperfúziós katéterre és a Penumbra szeparátorra értendő).
4. A gyártó *Használati utasításának* megfelelően készítsen elő egy vezetőkatétert vagy egy hosszú femorális hüvelyt.
5. Jutassa fel a vezetőkatétert vagy a hosszú femorális hüvelyt a megfelelő agyi artériába, amely proximálisan helyezkedik el a trombus által elzárt területtől.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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A Penumbra Reperfúziós Katéter Előkészítése És Használata

1. Határozza meg az ér átmérőjét, és válassza ki a megfelelő méretű Penumbra reperfúziós katétert (lásd az **1. táblázatot**).
2. A mellékelt hőhatásra alakítható mandrin használatával formálhatja a Penumbra reperfúziós katéter hegyét.
3. Csatlakoztassa a mellékelt forgatható vérzésgátló szelepet a Penumbra reperfúziós katéterhez.
4. Helyezze be a Penumbra reperfúziós katétert a vezetőkatéter kónuszához illesztett forgatható vérzésgátló szelepbe. Ha nem használ vezetőkatétert, vezesse be a Penumbra reperfúziós katétert a hosszú femorális hüvely szelepén keresztül a leválasztható hüvely segítségével. A Penumbra reperfúziós katéter bevezetése után távolítsa el a leválasztható hüvelyt a vaszkuláris hüvelyből, és válassza le a Penumbra reperfúziós katéter hüvelyéről.
5. Képerősítő alatt végzett szokványos katéterezési technikák alkalmazásával, megfelelő neurovaszkuláris vezetődrót segítségével vezesse fel a Penumbra reperfúziós katétert a kezelendő érbe. Helyezze el a Penumbra reperfúziós katétert a trombustól proximálisan. Távolítsa el a vezetődrótot a Penumbra reperfúziós katéterből.

A Penumbra Szeparátor Előkészítése És Használata

1. Csatlakoztassa a Penumbra szívócsöveket a szívópumpához, és kapcsolja be a szívópumpát (a szívópumpa *Felhasználói kézikönyvében* írottaknak megfelelően). Használat előtt legalább egy percig járassa a szívópumpát, és győződjön meg róla, hogy a szívásmérő –20 inHg-t mutat. Győződjön meg róla, hogy a Penumbra szívócsöveinek szelepe kikapcsolt „OFF" állásban van-e!
2. Válasszon ki egy alkalmas méretű Penumbra szeparátort, amely megfelel a reperfúziós katéternek (lásd az **1. táblázatot**).

1. táblázat – Szeparátor/reperfúziós katéter eszközök méreteinek megválasztása

Az ér mérete (mm)	Penumbra reperfúziós katéter	Penumbra szeparátor
< 2,0	026	026
2,0-tól 3,0-ig	032 / 3MAX	032 / 3MAX
3,0-tól 4,0-ig	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Vezesse fel a Penumbra reperfúziós katétert annyira, hogy annak disztális hegye finoman beleérjen a trombusba.

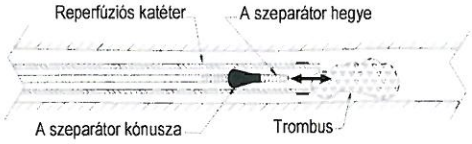
FIGYELEM: az elzáródás helyének megközelítése megkönnyíthető kompatibilis belső mikrokatéter triaxiális alkalmazásával.

4. A mellékelt bevezető hüvely segítségével helyezze be a Penumbra-szeparátort a forgatható vérzésgátló szelepen át a Penumbra reperfúziós katéter proximális kónuszába.
5. Csatlakoztassa a szívócsöveket a forgatható vérzésgátló szelep oldalsó portjához, amint azt az **1. ábra** mutatja.

1. ábra – A Penumbra szeparátorral összeszerelt szívórendszer

6. A szívás megkezdéséhez nyissa ki a Penumbra szívócsövön lévő szelepet „ON" állásba forgatással, majd tolja előre/húzza vissza a Penumbra szeparátort, így elősegítve a trombus beszívását és eltávolítását, amint azt a **2. ábra** mutatja.

2. ábra – A trombus beszívása a Penumbra szeparátor használatával



7. A szívás befejezéséhez kapcsolja a Penumbra szívócsövön lévő szelepet „OFF" állásba, és kapcsolja le a szívópumpát.
8. Távolítsa el a Penumbra szeparátort.
9. Ha szükséges, akkor az orvos döntése alapján újabb Penumbra szeparátorok és reperfúziós katéterek használhatóak a trombus további eltávolításához.
10. 5 vagy 10 ml-es fecskendő használatával szívjon ki kb. 5 ml vért a Penumbra reperfúziós katéterből, hogy eltávolítson minden trombust, ami esetlegesen a katéterben maradt.
11. A műtét után készítsen angiogramot olymódon, hogy a kontrasztanyagot a vezetőkatéteren keresztül fecskendezi be.

Jelölések jegyzéke

		Figyelem, lásd a használati utasítást	
Rx Only		Vényköteles – az Egyesült Államok szövetségi törvénye alapján ez az eszköz csak orvos által vagy orvosi rendelvényre használható	
		Pirogénmentes	
STERILE EO		Etilén-oxiddal sterilizált	
	Gyártó	EC REP	Képviselő az EU-ban
LOT	Tételszám		Tilos újrafelhasználni
	Felhasználható	REF	Katalógusszám
STERILIZE	Tilos újrasterilizálni	LATEX	Latex-mentes

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Description du dispositif

Le Penumbra System® est composé de plusieurs dispositifs :

- un cathéter de reperfusion Penumbra
- un séparateur Penumbra
- une pompe d'aspiration Penumbra
- un tube pompe/boîtier Penumbra
- un tube d'aspiration Penumbra

Le cathéter de reperfusion est introduit par un cathéter guide ou une gaine fémorale longue dans le réseau vasculaire intracrânien et guidé sur un guide neuro-vasculaire vers le site de l'occlusion principale. Le cathéter de reperfusion Penumbra est utilisé en conjonction avec un séparateur Penumbra et une source d'aspiration en vue de séparer le thrombus et de l'extraire du vaisseau occlus. Le séparateur Penumbra est déployé du cathéter de reperfusion Penumbra. La progression et la rétraction du séparateur Penumbra s'effectuent par le cathéter de reperfusion Penumbra, au niveau du bord proximal de l'occlusion principale. Ceci facilite l'aspiration et la réduction du thrombus et réduit ou élimine la charge endovas-culaire du caillot. La source d'aspiration est assurée par le cathéter de reper-fusion Penumbra, en conjonction avec la pompe d'aspiration raccordée au moyen du tube d'aspiration Penumbra et du tube pompe/boîtier Penumbra. Le cathéter de reperfusion Penumbra est fourni avec un mandrin de modelage à la vapeur et une valve hémostatique rotative et une gaine pelable. Les dispositifs sont visibles sous radioscopie.

Indication

Le Penumbra System est destiné à être utilisé dans la revascularisation de patients souffrant d'un accident vasculaire cérébral ischémique consécutif à une affection occlusive d'un gros vaisseau intracrânien (dans l'artère carotide interne, les segments M1 et M2 de l'artère cérébrale moyenne, les artères [illegible]ilaire et vertébrale) dans les 8 heures suivant l'apparition des symptômes.

[illegible]ntre indications

Aucune contre-indication connue.

Mises en garde

- Le Penumbra System doit être utilisé uniquement par des médecins ayant reçu une formation adéquate dans le domaine des techniques interventionnelles neuro-endovasculaires et du traitement d'un accident vasculaire cérébral ischémique aigu.
- Ne pas utiliser le Penumbra System avec une pompe autre que la pompe d'aspiration Penumbra.

Précautions

- Ce dispositif est à usage unique. Ne pas réutiliser, ni re-stériliser. Toute restérilisation et/ou réutilisation risquerait de rendre inefficace la lubrification du revêtement du cathéter, ce qui pourrait augmenter les frictions et empêcher d'accéder à l'emplacement neurovasculaire cible.
- Ne pas utiliser de dispositifs pliés ou endommagés. Ne pas utiliser si l'emballage est ouvert ou endommagé.
- Utiliser avant la date de péremption (« À utiliser avant »).
- Utiliser le Penumbra System conjointement à une visualisation radioscopique.
- En cas de résistance, ne pas faire progresser ou utiliser un quelconque composant du Penumbra System avant d'en avoir déterminé la cause sous radioscopie. Retirer le dispositif si la cause de la résistance ne peut pas être déterminée. Un serrage non contrôlé ou une insertion forcée du cathéter ou du séparateur contre la résistance peut entraîner une compression du dispositif et provoquer une lésion du vaisseau et/ou une rupture de l'embout.
- Maintenir une perfusion constante de solution de rinçage adaptée.
- Lors de l'aspiration, s'assurer que la valve du tube d'aspiration Penumbra n'est ouverte que pendant la durée minimale nécessaire à l'élimination du thrombus. Une aspiration excessive ou le fait de ne pas fermer la valve du tube d'aspiration Penumbra lorsque l'aspiration est terminée est déconseillé.
- Le séparateur Penumbra n'est pas destiné à servir de guide neuro-vasculaire. En cas de repositionnement nécessaire du cathéter de reperfusion Penumbra lors de la procédure de revascularisation, l'effectuer sur un guide neuro-vasculaire adapté en appliquant des techniques par microcathéter et guide standard.
- Ne pas utiliser d'équipement automatisé d'injection à haute pression de produit de contraste avec le cathéter de reperfusion Penumbra au risque d'endommager ce dernier.
- L'administration d'anticoagulants et d'antiplaquettaires doit être suspendue pendant les 24 heures suivant le traitement. La prise en charge médicale et les soins post-accident vasculaire cérébral aigu doivent se conformer aux directives de l'ASA.[1] Toute dégradation neurologique doit être évaluée au moyen d'un tomodensitogramme d'urgence et d'autres moyens d'évaluation tels qu'indiqués par les pratiques exemplaires définies par l'investigateur ou l'hôpital.
- La durée totale allouée pour parvenir à la revascularisation d'un patient et de 120 minutes en utilisant le Penumbra System.

Reactions potentielles indesirables

Les complications possibles incluent notamment :

- réaction allergique et anaphylaxie au produit de contraste
- occlusion aiguë
- embolie gazeuse
- fistule artérioveineuse
- décès
- dysfonctionnement du dispositif
- embolisation distale
- embolie
- formation d'un faux anévrisme
- hématome ou hémorragie au niveau du site d'accès
- incapacité d'éliminer complètement le thrombus
- infection
- hémorragie intracrânienne
- ischémie
- lésion rénale causée par le produit de contraste
- déficits neurologiques incluant l'accident vasculaire cérébral
- spasme, thrombose, dissection ou perforation vasculaires

Procedure

1. Consulter les **Mises en garde**, **Précautions** et **Réactions potentielles indésirables** avant toute utilisation.
2. Au moment de l'utilisation de chaque dispositif du Penumbra System, retirer ledit dispositif du conditionnement et vérifier qu'il ne présente ni dommages ni pliures.
3. Préparer les dispositifs du Penumbra System en rinçant la boucle d'emballage et le dispositif avec du sérum physiologique hépariné (cette instruction ne concerne que le cathéter de reperfusion Penumbra, et le séparateur Penumbra).
4. Préparer un cathéter guide ou une gaine fémorale longue conformément au *Mode d'emploi* du fabricant.
5. Placer le cathéter guide ou la gaine fémorale longue dans l'artère cérébrale correcte, proximale au site d'occlusion du thrombus.

Français

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Preparation et utilisation du catheter de reperfusion Penumbra

1. Confirmer le diamètre du vaisseau et sélectionner un cathéter de reperfusion Penumbra de taille correcte (voir le **Tableau 1**).
2. L'extrémité du cathéter de reperfusion Penumbra peut être modelée à l'aide du mandrin de modelage à la vapeur fourni.
3. Fixer la valve hémostatique rotative fournie au cathéter de reperfusion Penumbra.
4. Insérer le cathéter de reperfusion Penumbra dans une valve hémostatique rotative raccordée à l'embase proximale du cathéter guide. Dans le cas où un cathéter guide ne serait pas utilisé, insérer le cathéter de reperfusion Penombra dans la valve de la gaine fémorale longue à l'aide de la gaine pelable. Après avoir inséré le cathéter de reperfusion Penumbra, retirer la gaine pelable de la gaine vasculaire et la peler du corps de catéher de reperfusion Penumbra.
5. Selon des techniques de cathétérisme conventionnelles sous radioscopie, faire progresser le cathéter de reperfusion Penumbra dans le vaisseau cible sur un guide neuro-vasculaire adapté. Placer le cathéter de reperfusion Penumbra proximalement par rapport au thrombus. Retirer le guide du cathéter de reperfusion Penumbra.

Preparation et utilisation du separateur Penumbra

1. Fixer le tube d'aspiration Penumbra à la pompe d'aspiration et activer cette dernière (consulter le *Manuel d'utilisation* de la pompe d'aspiration). Permettre à la pompe d'aspiration de fonctionner pendant au moins une minute avant toute utilisation et confirmer que la jauge d'aspiration indique -20 inHg. S'assurer que la valve du tube d'aspiration Penumbra est mise sur arrêt.
2. Sélectionner un séparateur Penumbra de taille correcte, correspondant au cathéter de reperfusion (voir le **Tableau 1**).

Tableau 1 – Sélection de la taille du séparateur/cathéter de reperfusion

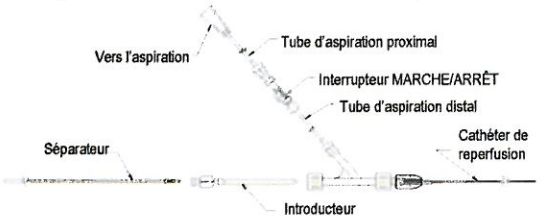
Taille du vaisseau (mm)	Cathéter de reperfusion Penumbra	Séparateur Penumbra
< 2,0	026	026
2,0 à 3,0	032 / 3MAX	032 / 3MAX
3,0 à 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Faire progresser le cathéter de reperfusion Penumbra pour ancrer délicatement son extrémité distale dans le thrombus.

REMARQUE : L'accès au site d'occlusion peut être facilité par l'utilisation triaxiale d'un microcathéter interne compatible.

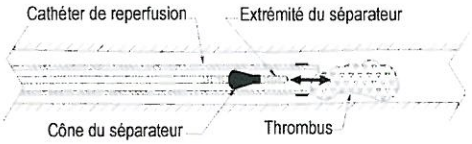
4. À l'aide de la gaine d'introduction fournie, insérer le séparateur Penumbra par la valve hémostatique rotative dans l'embase proximale du cathéter de reperfusion Penumbra.
5. Raccorder le tube d'aspiration à l'orifice latéral de la valve hémostatique rotative, comme illustré à la **Figure 1**.

Figure 1 – Système d'aspiration assemblé avec séparateur Penumbra



6. Pour commencer l'aspiration, ouvrir la valve du tube d'aspiration Penumbra en la mettant en position de fonctionnement et faire progresser/rétracter le séparateur Penumbra pour faciliter l'aspiration et l'élimination du thrombus, comme illustré à la **Figure 2**.

Figure 2 – Aspiration d'un thrombus à l'aide du séparateur Penumbra



7. Pour arrêter l'aspiration, mettre la valve du tube d'aspiration Penumbra en position d'arrêt et arrêter la pompe d'aspiration.
8. Retirer le séparateur Penumbra.
9. Si nécessaire, des séparateurs et des cathéters de reperfusion Penumbra supplémentaires peuvent être utilisés pour une élimination de thrombus plus poussée, à la discrétion du médecin.
10. À l'aide d'une seringue de 5 ou 10 cc, aspirer environ 5 cc de sang du cathéter de reperfusion Penumbra pour éliminer tout thrombus susceptible de rester dans le cathéter.
11. Réaliser une angiographie post-traitement en injectant un produit de contraste par le cathéter guide.

Glossaire des symboles

	Attention, consulter le mode d'emploi		
Rx Only	Sur ordonnance uniquement – Conformément à la législation fédérale des États-Unis, ce dispositif ne peut être utilisé que par un médecin ou sur ordonnance médicale.		
	Non pyrogène		
STERILE EO	Stérilisé à l'oxyde d'éthylène		
	Fabricant	EC REP	Mandataire pour l'UE
LOT	Numéro du lot		Ne pas réutiliser
	Date de péremption	REF	N° de référence
	Ne pas restériliser		Sans latex

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Περιγραφη του οργανου

Το Penumbra System® αποτελείται από αρκετά όργανα:

- Καθετήρα επαναιμάτωσης Penumbra
- Διαχωριστή Penumbra
- Αντλία αναρρόφησης Penumbra
- Σωλήνα αντλίας/δοχείου Penumbra
- Σωλήνα αναρρόφησης Penumbra

Ο καθετήρας επαναιμάτωσης εισάγεται μέσω οδηγού καθετήρα ή μηριαίου θηκαριού μεγάλου μήκους στο ενδοκρανιακό αγγειακό σύστημα και κατευθύνεται πάνω από νευροαγγειακό οδηγό σύρμα προς τη θέση της πρωτογενούς απόφραξης. Ο καθετήρας επαναιμάτωσης Penumbra χρησιμοποιείται παράλληλα με το διαχωριστή Penumbra και μια πηγή αναρρόφησης ώστε να διαχωρίσει το θρόμβο και να τον αναρροφήσει από το αποφραγμένο αγγείο. Ο διαχωριστής Penumbra αναπτύσσεται από τον καθετήρα επαναιμάτωσης Penumbra. Ο διαχωριστής Penumbra προωθείται και μαζεύεται μέσω του καθετήρα επαναιμάτωσης Penumbra στο εγγύς όριο της πρωτογενούς απόφραξης. Αυτό διευκολύνει την αναρρόφηση και τον καθαρισμό (debulking) του θρόμβου και μειώνει ή εξαλείφει την επιβάρυνση λόγω του ενδοαγγειακού θρόμβου. Ως πηγή αναρρόφησης, χρησιμοποιείται ο καθετήρας επαναιμάτωσης Penumbra σε συνδυασμό με την αντλία αναρρόφησης, η οποία συνδέεται με τη χρήση του σωλήνα αναρρόφησης Penumbra και του σωλήνα αντλίας/δοχείου Penumbra. Ο διαχωριστής Penumbra παρέχεται με εισαγωγέα και συσκευή στρέψης. Ο καθετήρας επαναιμάτωσης Penumbra παρέχεται με αξονίσκο διαμόρφωσης με ατμό, περιστροφική αιμοστατική βαλβίδα και αποφλειούμενο θηκάρι. Τα όργανα είναι ορατά υπό ακτινοσκόπηση.

Ενδειξεις Χρησης

Το Penumbra System προορίζεται για χρήση στην επαναγγείωση των ασθενών με οξύ ισχαιμικό εγκεφαλικό επεισόδιο μετά από ενδοκρανιακή αποφρακτική θρόμβο μεγάλου αγγείου (εντός της εσωτερικής καρωτιδικής, έσω εγκεφαλικής – τμήματα M1 και M2, βασικής και σπονδυλικής αρτηρίας) εντός 8 ωρών από την έναρξη των συμπτωμάτων.

Αντενδειξεις

Δεν υπάρχουν γνωστές αντενδείξεις.

Προειδοποιησεις

- Το Penumbra System πρέπει να χρησιμοποιείται μόνο από ιατρούς άρτια καταρτισμένους στις επεμβατικές νευρο-ενδοαγγειακές τεχνικές και τη θεραπεία του οξέος ισχαιμικού εγκεφαλικού επεισοδίου.
- Μη χρησιμοποιείτε το Penumbra System με αντλία διαφορετική από την αντλία αναρρόφησης Penumbra.

Προφυλαξεις

- Το όργανο αυτό προορίζεται για μία μόνο χρήση. Μην επαναποστειρώνετε ούτε να επαναχρησιμοποιείτε. Η επαναποστείρωση και/ή η επαναχρησιμοποίηση μπορεί να έχουν ως αποτέλεσμα ανεπαρκή λίπανση της επικάλυψης του καθετήρα, πράγμα που μπορεί να προκαλέσει υψηλή τριβή και αδυναμία πρόσβασης στη στοχευόμενη νευραγγειακή θέση.
- Μη χρησιμοποιείτε όργανα που έχουν υποστεί στρεβλώσεις ή ζημιά. Μη χρησιμοποιείτε το προϊόν αν οι συσκευασίες έχουν ανοιχτεί ή υποστεί ζημιά.
- Χρησιμοποιήστε το προϊόν πριν την ημερομηνία λήξης.
- Χρησιμοποιήστε το Penumbra System σε συνδυασμό με ακτινοσκοπική απεικόνιση.
- Μην προωθείτε ούτε να χρησιμοποιείτε οποιοδήποτε συστατικό μέρος του Penumbra System εάν αισθανθείτε αντίσταση, πριν αξιολογήσετε προσεκτικά την αιτία με ακτινοσκόπηση. Αν δεν μπορείτε να προσδιορίσετε την αιτία της αντίστασης, αποσύρετε το όργανο. Η ανεξέλεγκτη συστροφή ή βίαιη εισαγωγή του καθετήρα ή του διαχωριστή υπό αντίσταση μπορεί να προκαλέσει συμπίεση του οργάνου, πράγμα που μπορεί να οδηγήσει σε αγγειακή κάκωση και/ή θραύση του άκρου.
- Διατηρήστε σταθερή έγχυση του κατάλληλου διαλύματος έκπλυσης.
- Κατά τη διενέργεια της αναρρόφησης, βεβαιωθείτε ότι η βαλβίδα του σωλήνα αναρρόφησης Penumbra είναι ανοικτή μόνο για τον ελάχιστο χρόνο που απαιτείται για την αφαίρεση του θρόμβου. Δεν συνιστάται η υπερβολική αναρρόφηση ή το μη κλείσιμο της βαλβίδας του σωλήνα αναρρόφησης Penumbra όταν ολοκληρωθεί η αναρρόφηση.
- Ο διαχωριστής Penumbra δεν προορίζεται για χρήση ως νευροαγγειακό οδηγό σύρμα. Αν απαιτείται επανατοποθέτηση του καθετήρα επαναιμάτωσης Penumbra κατά τη διάρκεια της διαδικασίας επαναγγείωσης, αυτή η επανατοποθέτηση θα πρέπει να διενεργηθεί περνώντας τον καθετήρα πάνω από κατάλληλο νευροαγγειακό οδηγό σύρμα με τη χρήση τυπικών τεχνικών μικροκαθετήρα και οδηγού σύρματος.
- Μη χρησιμοποιείτε αυτοματοποιημένο εξοπλισμό έγχυσης σκιαγραφικής ουσίας με υψηλή πίεση σε συνδυασμό με τον καθετήρα επαναιμάτωσης Penumbra διότι μπορεί να προκληθεί ζημιά στο όργανο.
- Η χορήγηση αντιπηκτικής και αντιαιμοπεταλιακής αγωγής πρέπει να αναστέλλεται μέχρι 24 ώρες μετά τη θεραπεία. Κατά την ιατρική αντιμετώπιση και τη φροντίδα μετά από οξύ εγκεφαλικό επεισόδιο πρέπει να τηρούνται οι κατευθυντήριες οδηγίες του ASA.[1] Τυχόν νευρολογική επιδείνωση πρέπει να αξιολογείται με επείγουσα αξονική τομογραφία και άλλες αξιολογήσεις όπως ενδείκνυται σύμφωνα με τη βέλτιστη πρακτική του ερευνητή/νοσοκομείου.
- Ο συνολικός χρόνος που επιτρέπεται για την επίτευξη της επαναγγείωσης του ασθενούς είναι 120 λεπτά χρήσης του Penumbra System.

Πιθανα ανεπιθυμητα συμβαντα

Ανάμεσα στις πιθανές επιπλοκές, και χωρίς να περιορίζονται σε αυτές, περιλαμβάνονται και οι εξής:

- αλλεργική αντίδραση και αναφυλαξία από τη σκιαγραφική ουσία
- οξεία απόφραξη
- εμβολή αέρα
- σχηματισμός αρτηριοφλεβώδους συριγγίου
- θάνατος
- δυσλειτουργία του οργάνου
- περιφερική εμβολή
- έμβολα
- σχηματισμός ψευδούς ανευρύσματος
- αιμάτωμα ή αιμορραγία στη θέση πρόσβασης
- αδυναμία πλήρους αφαίρεσης του θρόμβου
- λοίμωξη
- ενδοκρανιακή αιμορραγία
- ισχαιμία
- βλάβη στα νεφρά από τη σκιαγραφική ουσία
- νευρολογικές διαταραχές συμπεριλαμβανομένου του εγκεφαλικού επεισοδίου
- αγγειόσπασμος, θρόμβωση, διαχωρισμός ή διάτρηση

Διαδικασια

1. Ανατρέξτε στις ενότητες **Προειδοποιήσεις**, **Προφυλάξεις** και **Πιθανά Ανεπιθύμητα Συμβάντα** πριν από τη χρήση.
2. Καθώς χρησιμοποιούνται όλα τα όργανα του Penumbra System, αφαιρέστε το κάθε όργανο από τη συσκευασία και επιθεωρήστε το για ζημιά ή στρεβλώσεις.
3. Προετοιμάστε τα όργανα του συστήματος Penumbra για χρήση, εκπλένοντας τη στεφάνη συσκευασίας και το όργανο με ηπαρινισμένο αλατούχο διάλυμα (περιλαμβάνει τον καθετήρα επαναιμάτωσης Penumbra και το διαχωριστή Penumbra μόνο).
4. Προετοιμάστε έναν οδηγό καθετήρα ή μηριαίο θηκάρι μεγάλου μήκους σύμφωνα με τις *Οδηγίες Χρήσης* του κατασκευαστή.
5. Τοποθετήστε τον οδηγό καθετήρα ή το μηριαίο θηκάρι μεγάλου μήκους στην κατάλληλη εγκεφαλική αρτηρία που βρίσκεται εγγύς της θέσης απόφραξης από το θρόμβο.

Ελληνικά

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Προετοιμασια και Χρηση του Καθετηρα Επαναιματωσης Penumbra

1. Επιβεβαιώστε τη διάμετρο του αγγείου και επιλέξτε έναν καθετήρα επαναιμάτωσης Penumbra κατάλληλου μεγέθους (Βλ. **Πίνακας 1**).
2. Το άκρο του καθετήρα επαναιμάτωσης Penumbra μπορεί να διαμορφωθεί χρησιμοποιώντας τον άξονα διαμόρφωσης με ατμό που παρέχεται.
3. Συνδέστε την παρεχόμενη περιστροφική αιμοστατική βαλβίδα στον καθετήρα επαναιμάτωσης Penumbra.
4. Εισαγάγετε τον καθετήρα επαναιμάτωσης Penumbra σε μια περιστροφική αιμοστατική βαλβίδα συνδεδεμένη με την εγγύς πλήμνη του οδηγού καθετήρα. Αν δεν χρησιμοποιηθεί οδηγός καθετήρας, εισαγάγετε τον καθετήρα επαναιμάτωσης Penumbra μέσω της βαλβίδας του μηριαίου θηκαριού μεγάλου μήκους χρησιμοποιώντας το αποφλειούμενο θηκάρι. Αφού εισάγετε τον καθετήρα επαναιμάτωσης Penumbra, αφαιρέστε το αποφλειούμενο θηκάρι από το αγγειακό θηκάρι και αποκολλήστε το από τον άξονα του καθετήρα επαναιμάτωσης Penumbra.
5. Με τη χρήση συμβατικών τεχνικών καθετηριασμού υπό ακτινοσκοπική καθοδήγηση, προωθήστε τον καθετήρα επαναιμάτωσης Penumbra πάνω από κατάλληλο νευροαγγειακό οδηγό σύρμα και εισαγάγετέ τον στο στοχευόμενο αγγείο. Τοποθετήστε τον καθετήρα επαναιμάτωσης Penumbra εγγύς του θρόμβου. Αφαιρέστε το οδηγό σύρμα από τον καθετήρα επαναιμάτωσης Penumbra.

Προετοιμασια και Χρηση του Διαχωριστη Penumbra

1. Συνδέστε το σωλήνα αναρρόφησης Penumbra με την αντλία αναρρόφησης και ενεργοποιήστε την αντλία αναρρόφησης (Ανατρέξτε στο *Εγχειρίδιο Λειτουργίας* της αντλίας αναρρόφησης). Αφήστε την αντλία αναρρόφησης να λειτουργήσει για τουλάχιστον ένα λεπτό πριν από τη χρήση και επιβεβαιώστε ότι το μανόμετρο της αντλίας αναρρόφησης δείχνει –20inHg. Βεβαιωθείτε ότι η βαλβίδα στο σωλήνα αναρρόφησης Penumbra είναι γυρισμένη στη θέση απενεργοποίησης.
   Επιλέξτε ένα διαχωριστή Penumbra κατάλληλου μεγέθους ο οποίος ταιριάζει με τον καθετήρα επαναιμάτωσης (Βλ. **Πίνακας 1**).

Πίνακας 1 – Επιλογή μεγέθους διαχωριστή/καθετήρα επαναιμάτωσης

Μέγεθος αγγείου (mm)	Καθετήρας επαναιμάτωσης Penumbra	Διαχωριστής Penumbra
< 2,0	026	026
2,0 έως 3,0	032 / 3MAX	032 / 3MAX
3,0 έως 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Προωθήστε τον καθετήρα επαναιμάτωσης Penumbra ώστε το περιφερικό άκρο να σφηνωθεί απαλά μέσα στο θρόμβο.

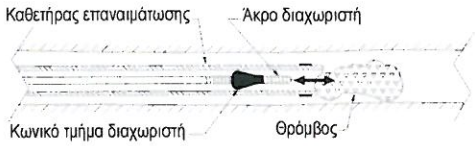
ΣΗΜΕΙΩΣΗ: Η πρόσβαση στη θέση της απόφραξης μπορεί να διευκολυνθεί μέσω τριαξονικής χρήσης ενός συμβατού εσωτερικού μικροκαθετήρα.

4. Με το παρεχόμενο θηκάρι εισαγωγής, εισαγάγετε το διαχωριστή Penumbra μέσω της περιστροφικής αιμοστατικής βαλβίδας και προωθήστε τον μέσα στην εγγύς πλήμνη του καθετήρα επαναιμάτωσης Penumbra.
5. Συνδέστε το σωλήνα αναρρόφησης με την πλευρική θύρα της περιστροφικής αιμοστατικής βαλβίδας όπως φαίνεται στο **Σχήμα 1**.

Σχήμα 1 – Συναρμολογημένο σύστημα αναρρόφησης με διαχωριστή Penumbra

6. Για να αρχίσει η αναρρόφηση, ανοίξτε τη βαλβίδα του σωλήνα αναρρόφησης Penumbra στη θέση ενεργοποίησης και προωθήστε/μαζέψτε το διαχωριστή Penumbra ώστε να διευκολύνετε την αναρρόφηση και την αφαίρεση του θρόμβου όπως φαίνεται στο **Σχήμα 2**.

Σχήμα 2 – Αναρρόφηση θρόμβου με τη χρήση του διαχωριστή Penumbra



7. Για να σταματήσει η αναρρόφηση, τοποθετήστε τη βαλβίδα του σωλήνα αναρρόφησης Penumbra στη θέση απενεργοποίησης και απενεργοποιήστε την αντλία αναρρόφησης.
8. Αφαιρέστε το διαχωριστή Penumbra.
9. Αν χρειαστεί, μπορεί να χρησιμοποιηθούν πρόσθετοι διαχωριστές και καθετήρες επαναιμάτωσης Penumbra, ώστε να γίνει περαιτέρω αφαίρεση θρόμβου κατά την κρίση του ιατρού.
10. Με τη χρήση σύριγγας των 5 cc ή 10 cc, αναρροφήστε περίπου 5 cc αίματος από τον καθετήρα επαναιμάτωσης Penumbra ώστε να αφαιρεθεί τυχόν θρόμβος που ενδέχεται να παραμένει εντός του καθετήρα.
11. Διενεργήστε αγγειογράφημα μετά τη θεραπεία με έγχυση σκιαγραφικής ουσίας μέσω του οδηγού καθετήρα.

Γλωσσαρι συμβολων

		Προσοχή, βλ. οδηγίες χρήσης.	
Rx Only		Χορηγείται μόνο με ιατρική συνταγή – Η ομοσπονδιακή νομοθεσία των Η.Π.Α. επιτρέπει τη χρήση της συσκευής αυτής μόνο από ιατρό ή κατόπιν εντολής ιατρού	
		Μη πυρετογόνο	
STERILE EO		Αποστειρωμένο με χρήση οξειδίου του αιθυλενίου	
	Κατασκευαστής	EC REP	Αντιπρόσωπος στην Ε.Ε.
LOT	Κωδικός παρτίδας		Μην επαναχρησιμοποιείτε
	Ημερομηνία λήξης	REF	Αριθμός καταλόγου
	Μην επαναποστειρώνετε	LATEX	Χωρίς λάτεξ

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Popis zařízení

Systém Penumbra System® se skládá z několika zařízení:

- reperfuzní katétr Penumbra,
- separátor Penumbra,
- odsávací čerpadlo Penumbra,
- hadička čerpadla/kanistru Penumbra,
- odsávací hadička Penumbra.

Reperfuzní katétr se zavádí přes vodicí katétr nebo pomocí dlouhého femorálního pláště do intrakraniálních cév a je naváděn přes neurovaskulární vodicí drát do místa primární okluze. Reperfuzní katétr Penumbra se používá spolu se separátorem Penumbra a zdrojem odsávání pro oddělení trombu a jeho odsátí z uzavřené cévy. Separátor Penumbra se implantuje z reperfuzního katétru Penumbra. Separátor Penumbra se poté posune a vytáhne přes reperfuzní katétr Penumbra na proximálním okraji místa primární okluze. Toto usnadňuje odsátí a zmenšení objemu trombu a snižuje nebo eliminuje zátěž způsobenou endovaskulární sraženinou. Jako zdroj odsávání se reperfuzní katétr Penumbra používá ve spojení s odsávacím čerpadlem, které je připojeno pomocí odsávacích hadiček Penumbra a hadiček čerpadla/kanistru Penumbra. Separátor Penumbra se dodává se zavaděčem a torzním zařízením. Reperfuzní katétr Penumbra se dodává s mandrénem pro tvarování parou a rotačním hemostatickým ventilem a plášťovým zavaděčem. Zařízení jsou viditelná pomocí fluoroskopie.

Indikace k použití

Systém Penumbra System je určen k použití při revaskularizaci u pacientů s akutní ischemickou mozkovou příhodou následkem okluzního onemocnění velkých intrakraniálních cév (v řečišti a. carotis interna, a. cerebri media – segmenty M1 a M2, a. basillaris a aa. vertebrales) v průběhu 8 hodin od nástupu symptomů.

Kontraindikace

Kontraindikace nejsou známy.

Varování

- Systém Penumbra System mohou používat pouze lékaři, kteří byli náležitě proškoleni v intervenčních neuroendovaskulárních technikách a léčbě akutní ischemické mozkové příhody.
- Systém Penumbra System používejte pouze s odsávacím čerpadlem Penumbra.

Bezpečnostní opatření

- Zařízení je určeno pouze pro jedno použití. Neresterilizujte ani opakovaně nepoužívejte. Resterilizace anebo opětovné použití může vést k neefiktivitě povrchového lubrikantu katétru, což může následně způsobit vysoké tření a neschopnost přistoupit k cílovému neurovaskulárnímu místu.
- Nepoužívejte ohnuté nebo poškozené zařízení. Nepoužívejte otevřená nebo poškozená balení.
- Použijte před uplynutím data spotřeby.
- Systém Penumbra System používejte v kombinaci s fluoroskopickým zobrazováním.
- Neposunujte a nepoužívejte jakoukoli součást systému Penumbra System proti odporu bez předchozího pečlivého stanovení důvodu rezistence pomocí fluoroskopie. Pokud příčinu nelze zjistit, zařízení vyjměte. Kroucení nebo násilné zavádění katétru nebo oddělovače proti odporu může vést ke kompresi zařízení, která může mít za následek poškození zařízení nebo zlomení hrotu.
- Udržujte konstantní infuzi vhodného proplachovacího roztoku.
- Při odsávání se ujistěte, že ventil odsávací hadičky Penumbra je otevřený pouze po minimální dobu nutnou k odstranění trombu. Nedoporučujeme nadměrné odsávání nebo neuzavření ventilu odsávací hadičky Penumbra po dokončení odsávání.
- Separátor Penumbra není určen k použití jako neurovaskulární vodicí drát. V případě nutnosti úpravy polohy reperfuzního katétru Penumbra v průběhu revaskularizačního zákroku je nutné tuto úpravu provést po vhodném neurovaskulárním vodicím drátu pomocí standardních technik využívajících mikrokatétr a vodicí drát.
- Nepoužívejte automatizované vysokotlaké injektory kontrastní látky spolu s reperfuzním katétrem Penumbra, neboť by mohlo dojít k poškození zařízení.
- Podávání antikoagulačních a protidestičkových látek musí být pozastaveno na 24 hodin po zákroku. Lékařská péče a akutní péče po mozkové příhodě musí být provedena dle pokynů ASA.[1] Jakékoli neurologické poruchy je nutné vyhodnotit pomocí emergentního skenu CT a dalšími metodami, jak je indikováno dle nejlepší možné praxe vyšetřujícího/nemocnice.
- Celková povolená doba pro dosažení revaskularizace u pacienta je 120 minut používání systému Penumbra.

Možné nežádoucí účinky

K možným komplikacím mimo jiné patří:

- alergická a anafylaktická reakce na kontrastní látky,
- akutní okluze,
- vzduchová embolie,
- arteriovenózní píštěl,
- úmrtí,
- selhání zařízení,
- distální embolizace,
- embolie,
- tvorba nepravého aneuryzmatu,
- hematom nebo krvácení v místě přístupu,
- nemožnost úplného odstranění trombu,
- infekce,
- intrakraniální krvácení,
- ischemie,
- poškození ledvin kontrastní látkou,
- neurologické deficity včetně mrtvice,
- vazospazmus, trombóza, disekce nebo perforace.

Postup

1. Před použitím si přečtěte části **Varování**, **Bezpečnostní opatření** a **Možné nežádoucí účinky**.
2. Při použití jakéhokoli zařízení systému Penumbra System vyjměte zařízení z obalu a zkontrolujte, zda není poškozené nebo ohnuté.
3. Připravte zařízení systému Penumbra System k použití propláchnutím obalu a zařízení heparinizovaným fyziologickým roztokem (týká se pouze reperfuzního katétru Penumbra a separátoru Penumbra).
4. Připravte si vodicí katétr nebo dlouhý femorální plášť dle *Návodu k použití* výrobce.
5. Zaveďte vodicí katétr nebo dlouhý femorální plášť do příslušné mozkové artérie, která leží proximálně od místa uzávěru trombem.

Příprava a použití reperfuzního katétru Penumbra

1. Potvrďte průměr cévy a vyberte vhodnou velikost reperfuzního katétru Penumbra (viz **Tabulka 1**).
2. Hrot reperfuzního katétru Penumbra je možné vytvarovat pomocí dodaného mandrénu pro tvarování parou.
3. Připojte dodaný rotační hemostatický ventil k reperfuznímu katétru Penumbra.
4. Vložte reperfuzní katétr Penumbra do rotačního hemostatického ventilu, který je připojen k proximální hlavě vodicího katétru. Pokud není vodicí katétr použit, zasuňte pomocí plášťového zavaděče reperfuzní katétr Penumbra do ventilu dlouhého femorálního pláště. Po zasunutí reperfuzního katétru Penumbra odstraňte plášťový zavaděč z vaskulárního pláště a sloupněte jej z dříku reperfuzního katétru Penumbra.
5. Konvenčními katetrizačními technikami pod fluoroskopickým vedením postupujte reperfuzním katétrem Penumbra do cílové cévy přes vhodný neurovaskulární vodicí drát. Reperfuzní katétr Penumbra umístěte proximálně od trombu. Vyjměte vodicí drát z reperfuzního katétru Penumbra.

Čeština

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Příprava a použití separátoru Penumbra

1. Připojte odsávací hadičku Penumbra k odsávacímu čerpadlu a čerpadlo zapněte (viz *Provozní příručka* odsávacího čerpadla). Před použitím nechte odsávací čerpadlo alespoň jednu minutu běžet a zkontrolujte, zda ukazatel odsávání ukazuje –20 palců Hg. Zkontrolujte, zda je ventil na odsávací hadičce Penumbra přepnutý do polohy OFF (VYPNUTO).
2. Vyberte vhodnou velikost separátoru Penumbra, která odpovídá reperfuznímu katétru (viz **Tabulka 1**).

Tabulka 1 – Volba velikosti separátoru/reperfuzního katétru

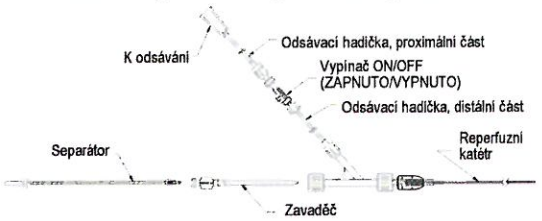
Průměr cévy (mm)	Reperfuzní katétr Penumbra	Separátor Penumbra
<2,0	026	026
2,0 až 3,0	032 / 3MAX	032 / 3MAX
3,0 až 4,0	041 / 4MAX	041 / 4MAX
>4,0	054 / 5MAX	054 / 5MAX

3. Posuňte reperfuzní katétr Penumbra tak, abyste opatrně usadili distální hrot do trombu.

POZNÁMKA: Přístup k místu okluze je možné usnadnit triaxiálním použitím kompatibilního vnitřní mikrokatétru.

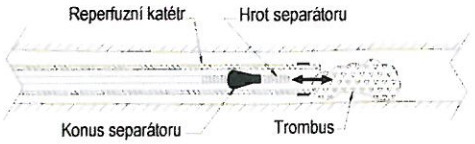
4. Pomocí dodaného plášťového zavaděče zaveďte separátor Penumbra přes rotační hemostatický ventil do proximální hlavy reperfuzního katétru Penumbra.
5. Připojte odsávací hadičku k bočnímu portu rotačního hemostatického ventilu, jak je zobrazeno na **Obrázku 1**.

Obrázek 1 – Sestavený odsávací systém se separátorem Penumbra



6. Odsávání zahájíte tak, že otevřete ventil na odsávací hadičce Penumbra do polohy ON (ZAPNUTO) a posunete/vytáhnete separátor Penumbra tak, abyste si usnadnili odsávání a odstranění trombu, viz **Obrázek 2**.

Obrázek 2 – Odsátí trombu pomocí separátoru Penumbra



7. Odsávání zastavíte přepnutím ventilu na odsávací hadičce Penumbra do polohy OFF (VYPNUTO) a vypnutím odsávacího čerpadla.
8. Vyjměte separátor Penumbra.
9. Je-li to nutné, je možné, dle rozhodnutí lékaře, použít další separátory a reperfuzní katétry Penumbra k dalšímu odstranění trombu.
10. Pomocí 5ml nebo 10ml stříkačky odsajte přibližně 5 ml krve z reperfuzního katétru Penumbra pro odstranění trombu, který mohl zůstat v katétru.
11. Po zákroku zhotovte angiogram aplikací kontrastní látky přes vodicí katétr.

Vysvětlení symbolů

		Pozor, prostudujte návod k použití	
Rx Only		Pouze na lékařský předpis – federální zákony USA omezují použití tohoto prostředku jen na lékaře nebo na lékařský předpis	
		Nepyrogenní	
STERILE EO		Sterilizováno ethylenoxidem	
	Výrobce	EC REP	Pověřený zástupce pro EU
LOT	Číslo šarže		Nepoužívejte opakovaně
	Použitelné do	REF	Katalogové číslo
	Neprovádějte resterilizaci		Neobsahuje latex

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Dansk

Beskrivelse af anordningen

Penumbra System® består af flere anordninger:

- Penumbra-reperfusionskateter
- Penumbra-separator
- Penumbra-aspirationspumpe
- Penumbra-pumpe/cylinderrør
- Penumbra-aspirationsslange

Reperfusionskatetret indføres gennem et ledekateter eller et langt femoralt hylster ind i den intrakraniale vaskulatur og føres over en neurovaskulær guidewire til det sted, hvor den primære okklusion er. Penumbra-reperfusionskatetret bruges sammen med Penumbra-separatoren og en aspirationskilde til at separere tromben og aspirere den ud af det okkluderede kar. Penumbra-separatoren anlægges fra Penumbra-reperfusionskatetret. Penumbra-separatoren fremføres og trækkes tilbage gennem Penumbra-reperfusionskatetret ved den proksimale kant af den primære okklusion. Det gør aspiration og separation af tromben nemmere, og reducerer eller eliminerer det endovaskulære blodkoagel. Som aspirationskilde anvendes Penumbra-reperfusionskatetret sammen med aspirationspumpen, som tilsluttes ved hjælp af Penumbra-aspirations-slangen og Penumbra-pumpen/cylinderrøret. Penumbra-separatoren leveres sammen med en indførings- og vridningsanordning. Penumbra-reperfusionskatetret leveres med en dorn til dampformning og en drejelig hæmostatisk ventil samt et aftageligt hylster. Anordningerne er synlige under røntgengennemlysning.

Indikationer for brug

Penumbra-systemet er beregnet til revaskularisering af patienter med akut iskæmisk slagtilfælde sekundært til intrakranial okklusionssygdom af store kar (arteria corotis interna, arteria cerebri media - M1 og M2-segmenter, arteria basilaris og arteria vertebralis) inden for 8 timer af symptombegyndelse.

Kontraindikationer

Der er ingen kendte kontraindikationer.

Advarsler

- Penumbra System må kun anvendes af læger, der har modtaget behørig oplæring i interventionelle neurovaskulære teknikker og behandling af akut iskæmisk slagtilfælde.
- Penumbra System må ikke bruges sammen med andre pumper end Penumbra-aspirationspumpen.

Forholdsregler

- Anordningen er kun beregnet til engangsbrug. Må ikke resteriliseres eller genbruges. Resterilisering og/eller genbrug kan gøre katetrets smørende belægning ineffektiv, hvilket kan medføre en høj gnidningsmodstand og gøre det umuligt at få adgang til det neurovaskulære målsted.
- Brug ikke bøjede eller beskadigede anordninger. Brug ikke åbnede eller beskadigede pakker.
- Bruges inden "Anvendes inden"-datoen.
- Brug Penumbra System sammen med fluoroskopi.
- Hvis der mødes modstand under fremføring eller tilbagetrækning af et af Penumbra System's komponenter, skal der foretages en omhyggelig vurdering af årsagen vha. fluoroskopi, før der fortsættes. Hvis årsagen ikke kan findes, skal anordningen trækkes tilbage. Ubegrænset vridning eller tvunget indføring af katetret eller separatoren mod modstand kan medføre komprimering af anordningen, hvilket kan beskadige karret og/eller brække spidsen.
- Der skal opretholdes konstant infusion med en passende skylleopløsning.
- Når der udføres aspiration, må Penumbra-aspirationsslangeventilen kun være åbnet i maksimalt det tidsrum, det tager at fjerne tromben. Der må ikke anvendes overdreven aspiration, og Penumbra-aspirations-slangeventilen skal lukkes, når aspirationen er gennemført.
- Penumbra-separatoren er beregnet til at blive brugt som en neurovaskulær guidewire. Hvis det er nødvendigt at genplacere Penumbra-reperfusionskatetret under revaskulariseringsindgrebet, skal genplaceringen foretages over en passende neurovaskulær guidewire ved hjælp af standard mikrokateter- og guidewireteknikker.
- Der må ikke bruges udstyr med automatisk højtryk til at injicere kontraststof sammen med Penumbra-reperfusionskatetret, da det kan beskadige anordningen.
- Indgift af antikoagulanter og anitrombocytter må ikke foretages, før 24 timer efter indgrebet. Medicinsk behandling og efterbehandling af akut slagtilfælde skal følge retningslinjerne fra ASA.[1] En eventuel neurologisk forværring skal straks evalueres ved hjælp af CT-scanning og anden evaluering i henhold til investigators/hospitalets protokol.
- Der må i alt kun bruges 120 minutter til revaskularisering af patienten ved hjælp af Penumbra System.

Mulige komplikationer

Mulige komplikationer omfatter, men er ikke begrænset til, følgende:

- allergisk reaktion og anafylaksi pga. kontraststof
- akut okklusion
- luftemboli
- arteriovenøs fistel
- død
- funktionsfejl i anordningen
- distal embolisering
- emboli
- dannelse af falsk aneurisme
- hæmatom eller hæmoragi ved adgangsstedet
- manglende evne til helt at fjerne tromben
- infektion
- intrakranial hæmoragi
- iskæmi
- nyreskader pga. kontraststof
- neurologiske deficits, inklusive slagtilfælde
- karspasme, trombose, dissektion eller perforation

Indgreb

1. Læs **Advarsler**, **Forholdsregler** og **Mulige komplikationer** før brug af anordningerne.
2. Tag anordningerne i Penumbra System ud af emballagen i takt med, at de skal bruges, og efterse dem for beskadigelser og knæk.
3. Klargør Penumbra System-anordningerne til brug ved at skylle emballageringen og anordningen med hepariniseret saltvand (det gælder kun Penumbra-reperfusionskatetret og Penumbra-separatoren).
4. Klargør et ledekateter eller et langt femoralt hylster ifølge producentens *Brugsanvisning*.
5. Anbring ledekatetret eller det lange femorale hylster i den korrekte arteria cerebralis proksimalt i forhold til trombeokklusionsstedet.

Klargøring og brug af Penumbra-reperfusionskateter

1. Bekræft kardiameteren og vælg et Penumbra-reperfusionskateter i den korrekte størrelse (Se **tabel 1**).
2. Penumbra-reperfusionskatetrets spids kan dampformes med den medfølgende dorn.
3. Fastgør den drejelige hæmostatiske ventil, der følger med Penumbra-reperfusionskatetret.
4. Indsæt Penumbra-reperfusionskatetret i den drejelige hæmostatiske ventil, der er tilsluttet den proksimale muffe på et ledekateter. Hvis der ikke anvendes et ledekateter, indsættes Penumbra-reperfusionskatetret gennem ventilen på det lange femorale hylster vha. det aftagelige hylster. Når Penumbra-reperfusionskatetret er indsat, fjernes det aftagelige hylster fra det vaskulære hylster og tages af Penumbra-reperfusionskatetrets skaft.
5. Ved hjælp af traditionelle kateteriseringsteknikker føres Penumbra-reperfusionskatetret under røntgengennemlysning ind i målkarret over en passende neurovaskulær guidewire. Placer Penumbra-reperfusionskatetret proksimalt for tromben. Fjern guidewiren fra Penumbra-reperfusionskatetret.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Klargøring og brug af Penumbra-separator

1. Fastgør Penumbra-aspirationsslangen til aspirationspumpen, og tænd for aspirationspumpen (der henvises til aspirationspumpens *Brugerhåndbog*). Lad aspirationspumpen køre i mindst et minut før brug og bekræft, at aspirationsmåleren står på –20 tommers Hg. Sørg for, at ventilen på Penumbra-aspirationsslangen er slukket (OFF).
2. Vælg en Penumbra-separator i en størrelse, der passer til reperfusionskatetret (se **tabel 1**).

Tabel 1 – Størrelser på separator/reperfusionskateteranordning

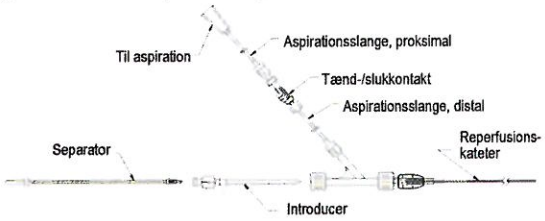
Karstørrelse (mm)	Penumbra-reperfusionskateter	Penumbra-separator
< 2,0	026	026
2,0 til 3,0	032 / 3MAX	032 / 3MAX
3,0 til 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Fremfør Penumbra-reperfusionskatetret for forsigtigt at indlejre den distale spids i tromben.

BEMÆRK: Adgang til okklusionsstedet kan lettes ved triaksial brug af et kompatibelt indvendigt mikrokateter.

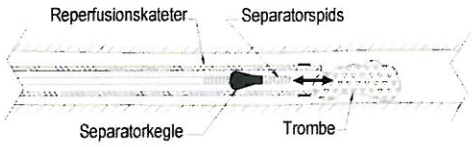
4. Anvend den vedlagte introducersheath til at indsætte Penumbra-separatoren gennem den drejelige hæmostatiske ventil og ind i den proksimale muffe på Penumbra-reperfusionskatetret.
5. Slut aspirationsslangen til sideporten på den drejelige hæmostatiske ventil som vist på **figur 1**.

Figur 1 – Samlet aspirationssystem med Penumbra-separator



6. Åbn ventilen på Penumbra-aspirationsslangen, så den er tændt (ON) for at påbegynde aspiration, og fremfør/tilbagetræk Penumbra-separatoren som en hjælp til aspiration og fjernelse af tromben, som vist på **figur 2**.

Figur 2 – Trombeaspiration med Penumbra-separator



7. Sæt ventilen på Penumbra-aspirationsslangen på slukket (OFF) for at standse aspiration, og sluk for aspirationspumpen.
8. Fjern Penumra-separatoren.
9. Hvis nødvendigt, kan der efter lægens skøn bruges yderligere Penumbra-separatorer og reperfusionskatetre til yderligere at fjerne tromben.
10. Aspirer ca. 5 ml blod fra Penumbra-reperfusionskatetret med en 5 eller 10 ml sprøjte for at fjerne eventuel trombe, der stadig er i katetret.
11. Tag et angiogram efter indgrebet ved at injicere kontraststof gennem ledekatetret.

Ordliste med symboler

	Bemærk: Se brugsanvisning		
Rx Only	Receptpligtig – Ifølge amerikansk lovgivning må anordningen kun bruges af en læge eller på dennes anvisning		
	Ikke-pyrogen		
STERILE EO	Steril (ethylenoxid)		
	Producent	EC REP	Forhandler i EU
LOT	Lotnr.		Kun til engangsbrug
	Anvendes inden	REF	Katalognummer
	Må ikke resteriliseres		Latexfri

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Beskrivning av enhet

Penumbra System® består av flera enheter:

- Penumbra Reperfusionskateter
- Penumbra Avskiljare
- Penumbra Aspirationspump
- Penumbra Pump-/Behållarslang
- Penumbra Aspirationsslang

Reperfusionskatetern förs genom en styrkateter eller en lång femoralishylsa in i den intrakraniala vaskulaturen och över en neurovaskulär ledare till det primära ocklusionsstället. Penumbra Reperfusionskateter används parallellt med Penumbra Avskiljare och en aspirationskälla för att skilja ut tromben och suga ut den ur det ockluderade kärlet. Avskiljaren sätts in från reperfusionskatetern. Avskiljaren förs fram och dras tillbaka genom reperfusionskatetern vid den primära ocklusionens proximala periferi. Detta underlättar aspiration och reduktion av tromben och reducerar eller eliminerar den endovaskulära proppbelastningen. Som aspirationskälla används Penumbra Reperfusionskateter i kombination med aspirationspumpen som ansluts med hjälp av Penumbra Aspirationsslang och Penumbra Pump-/Behållarslang. Penumbra Avskiljare levereras med en introducer och en åtdragningsanordning. Penumbra Reperfusionskateter tillhandahålls med en ångformningsmandrin och roterande hemostasventil och en avskalbar hylsa. Enheterna är synliga under fluoroskopi.

Indikationer för användning

Penumbra System är avsett för användning vid revaskularisering av patienter med akut ischemisk stroke till följd av ocklusiv sjukdom i de stora intrakraniala kärlen (i inre halspulsådern, mellersta arteriae cerebri – segment M1 och M2, arteria basilaris och arteriae vertebrales) inom 8 timmar från det att de första symptomen uppträder.

Kontraindikationer

Det finns inga kända kontraindikationer.

Varningar

- Penumbra System får endast användas av läkare som har genomgått lämplig utbildning i tekniker för neuro-endovaskulära ingrepp och behandling av akut ischemisk stroke.
- Använd inte Penumbra System med en annan pump än Penumbra Aspirationspump.

Försiktighetsåtgärder

- Anordningen är endast avsedd för engångsbruk. Får ej omsteriliseras eller återanvändas. Omsterilisering och/eller återanvändning kan resultera i ineffektiv smörjning av kateterns beläggning, vilket kan resultera i hög friktion och oförmåga få åtkomst till neurovaskulaturens målområde.
- Använd inte böjda eller skadade anordningar. Använd ej skadade eller redan öppnade förpackningar.
- Använd före bäst före-datumet.
- Använd Penumbra System i kombination med visualisering genom fluoroskopi.
- För inte fram och använd inte komponenterna i Penumbra System om det uppstår motstånd utan att först ha fastställt orsaken till det med hjälp av fluoroskopi. Dra ut anordningen igen om orsaken inte kan fastställas. Allt för hård vridning eller forcerad införsel av katetern eller avskiljaren mot motstånd kan resultera i hoptryckning av enheten vilket kan leda till kärlskada och/eller spetsbrott.
- Upprätthåll en konstant infusion av lämplig spolningslösning.
- Vid aspiration ska ventilen till Penumbra Aspirationsslang endast vara öppen under kortast möjliga tid som behövs för att avlägsna tromben. Undvik att aspirera för kraftigt och glöm inte att stänga ventilen till aspirationsslangen när utsugningsprocessen har slutförts.
- Penumbra Avskiljare är inte avsedd att användas som en neurovaskulär ledare. Om det blir nödvändigt att placera om Penumbra Reperfusions-katetern under revaskulariseringsproceduren ska omplaceringen utföras över tillämplig neurovaskulär ledare med hjälp av standardiserad mikrokateter- och ledarteknik.
- Använd inte utrustning för automatisk högtrycksinjicering av kontrastmedel tillsammans med Penumbra Reperfusionskateter eftersom det kan skada enheten.
- Tillförsel av antikoagulanter och trombocythämmande medel bör avbrytas i 24 timmar efter behandlingen. Medicinsk behandling och akut poststrokebehandling bör följa ASA:s riktlinjer.[1] Eventuell neurologisk försämring ska omedelbart utvärderas genom datortomografi och andra undersökningar som indikeras av utredande läkare/sjukhusets rådande praxis.
- Den totala tillåtna tiden för patientrevaskularisering är 120 minuter med hjälp av Penumbra System.

Potentiella biverkningar

Möjliga komplikationer omfattar, men är inte begränsade till, följande:

- allergiska reaktioner och anafylaxi orsakade av kontrastmedel
- akut ocklusion
- luftemboli
- arteriovenös fistel
- dödsfall
- enheten slutar fungera
- distal embolisering
- emboli
- falsk aneurysmbildning
- hematom eller hemorragi vid platsen för ingreppet
- oförmåga att helt avlägsna tromben
- infektion
- intrakranial hemorragi
- ischemi
- njurskador från kontrastmedel
- neurologiska brister, inklusive stroke
- kärlspasmer, trombos, dissektion eller perforation

Svenska

Ingrepp

1. Se avsnitten **Varningar**, **Försiktighetsåtgärder** och **Potentiella biverkningar** innan du använder produkten.
2. Allt eftersom de enskilda enheterna i Penumbra System används ska de tas ut ur förpackningen och kontrolleras så att de inte uppvisar skador eller veck.
3. Förbered enheterna i Penumbra System för användning genom att spola förpackningsöglan och enheten med heparinisserad saltlösning (gäller endast Penumbra Reperfusionskateter och Penumbra Avskiljare).
4. Förbered en styrkateter eller en lång femoralishylsa enligt tillverkarens *bruksanvisning*.
5. Placera styrkatetern eller den långa femoralishylsan i lämplig hjärnartär proximalt i förhållande till tromben och ocklusionsstället.

Förberedelse och bruk av Penumbra Reperfusionskateter

1. Fastställ kärldiametern och välj en Penumbra Reperfusionskateter av lämplig storlek (se **tabell 1**).
2. Reperfusionskateterns spets kan formas med hjälp av den medföljande ångformningsmandrinen.
3. Anslut den medföljande roterande hemostasventilen till Penumbra Reperfusionskateter.
4. Sätt in Penumbra Reperfusionskatetern i en roterande hemostasventil som är ansluten till den proximala fattningen på en styrkateter. Om en styrkateter inte används, ska du föra in Penumbra Reperfusionskatetern genom ventilen i den långa femoralishylsan med hjälp av den avskalbara hylsan. Efter införseln av Penumbra Reperfusionskatetern ska du avlägsna den avskalbara hylsan från den vaskulära hylsan och skala av från Penumbra Reperfusionskateterns skaft.
5. Använd konventionell kateterinsättningsteknik under fluoroskopi och för in Penumbra Reperfusionskateter i målkärlet över en tillämplig neurovaskulär ledare. Placera reperfusionskatetern proximalt i förhållande till tromben. Avlägsna ledaren från reperfusionskatetern.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Förberedelse och bruk av Penumbra Avskiljare

1. Anslut Penumbra Aspirationsslang till aspirationspumpen och starta pumpen (se *användarhandboken* till aspirationspumpen). Låt aspirationspumpen gå i minst en minut innan den används. Kontrollera att det står "–20inHg" på aspirationsmätaren. Kontrollera att ventilen på aspirationsslangen står i läge OFF (AV).
2. Välj en Penumbra Avskiljare av en storlek som motsvarar reperfusionskateterns (se **tabell 1**).

Tabell 1. Välja storlek på avskiljare och reperfusionskateter

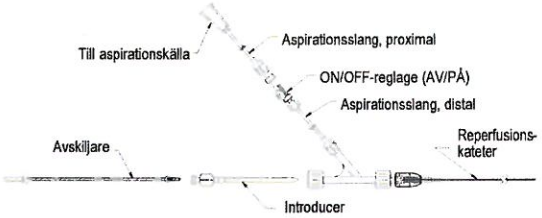
Kärlstorlek (mm)	Penumbra Reperfusionskateter	Penumbra Avskiljare
< 2,0	026	026
2,0–3,0	032 / 3MAX	032 / 3MAX
3,0–4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. För försiktigt fram Penumbra Reperfusionskateter tills den distala spetsen tränger in i tromben.

OBS! Det kan vara lättare att komma åt ocklusionsstället genom triaxial användning av en kompatibel innermikrokateter.

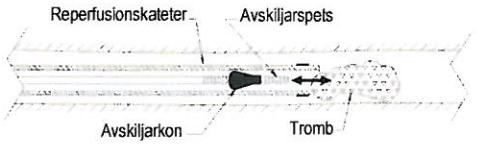
4. Använd den medföljande introducern och för Penumbra Avskiljare genom den roterande hemostasventilen och in i reperfusionskateterns proximala fattning.
5. Anslut aspirationsslangen till sidoporten på den roterande hemostasventilen såsom visas i **figur 1**.

Figur 1. Monterat aspirationssystem med Penumbra Avskiljare



6. Påbörja aspirationen genom att öppna ventilen på Penumbra Aspirationsslang (ställ om den till läge ON [PÅ]) och för fram/dra tillbaka Penumbra Avskiljare för att underlätta aspirationen och avlägsnandet av tromben såsom visas i **figur 2**.

Figur 2. Trombaspiration med hjälp av Penumbra Avskiljare



7. Stäng av aspirationen genom att ställa om ventilen på Penumbra Aspirationsslang till läge OFF (AV) och stäng av aspirationspumpen.
8. Avlägsna Penumbra Avskiljare.
9. Vid behov kan ytterligare avskiljare och reperfusionskatetrar användas efter läkarens gottfinnande i syfte att ytterligare reducera tromben.
10. Använd en 5 ml- (5 cc) eller 10 ml-spruta (10 cc) och sug upp ca 5 ml (5 cc) blod från Penumbra Reperfusionskateter för att avlägsna eventuella trombrester från katetern.
11. Ta ett angiogram efter behandlingen genom att injicera kontrastmedel genom styrkatetern.

Symbolförklaring

		Obs! Läs bruksanvisningen	
Rx Only		Endast receptbelagt – USA:s federala lagstiftning begränsar användningen av denna produkt som endast får användas av läkare eller på läkares ordination	
		Ej feberframkallande	
STERILE EO		Steriliserad med etylenoxid	
	Tillverkare	EC REP	EU-representant
LOT	Partinummer		Får ej återanvändas
	Bäst före	REF	Katalognummer
	Får ej omsteriliseras		Latexfri

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Beschrijving van het instrument

Het Penumbra System® bestaat uit verschillende apparaten:

- Penumbra-reperfusiekatheter
- Penumbra-separator
- Penumbra-aspiratiepomp
- Penumbra-pomp/busslang
- Penumbra-aspiratieslang

De reperfusiekatheter wordt door een geleidekatheter of lange femorale schacht in de intracraniale vasculatuur ingebracht en over een neurovasculaire voerdraad opgevoerd naar de plaats van de primaire occlusie. De Penumbra-reperfusiekatheter wordt parallel gebruikt met de Penumbra-separator en een aspiratiebron, om de trombus af te scheiden en uit het geoccludeerde vat te aspireren. De Penumbra-separator wordt uitgevouwen vanuit de Penumbra-reperfusie-katheter. De Penumbra-separator wordt bij de proximale rand van de primaire occlusie opgevoerd en teruggetrokken door de Penumbra-reperfusiekatheter. Dit vergemakkelijkt aspiratie en losmaking van de trombus en reduceert of elimineert tevens de endovasculaire belasting door het stolsel. Als aspiratiebron wordt de Penumbra-reperfusiekatheter gebruikt in combinatie met de aspiratiepomp, die wordt aangesloten met de Penumbra-aspiratieslang en de Penumbra-pomp/busslang. De Penumbra-separator wordt geleverd met een inbrenger en een torsie-instrument. De Penumbra-reperfusiekatheter wordt geleverd met een stoomvormmandrijn en een roterende hemostaseklep alsmede een pelbare schacht. De instrumenten zijn zichtbaar onder fluoroscopie.

Indicaties voor gebruik

Het Penumbra System is bedoeld voor gebruik bij de revascularisatie van patiënten met acute ischemische beroerte, secundair aan occlusie van grote intracraniale vaten (in de aa. carotis interna, cerebri media – segmenten M1 M2, basilaris en vertebralis) binnen 8 uur nadat de eerste symptomen zijn getreden.

Contra-indicaties

Er zijn geen contra-indicaties bekend.

Waarschuwingen

- Het Penumbra System mag alleen worden gebruikt door artsen die een relevante opleiding hebben genoten in neuro-endovasculaire interventietechnieken en de behandeling van acute ischemische beroerten.
- Gebruik het Penumbra System niet met een andere pomp dan de Penumbra-aspiratiepomp.

Voorzorgsmaatregelen

- Het instrument is uitsluitend bedoeld voor eenmalig gebruik. Gebruik of steriliseer het instrument niet opnieuw. Hersterilisatie en/of hergebruik kan ertoe dat de laag glijmiddel op de katheter niet werkzaam is, met als mogelijk gevolg hoge wrijving en het niet kunnen toegang krijgen tot de beoogde locatie in de neurovasculatuur.
- Geknikte of beschadigde instrumenten niet gebruiken. Geopende of beschadigde verpakkingen niet gebruiken.
- Gebruiken vóór het verstrijken van de uiterste gebruiksdatum.
- Gebruik het Penumbra System in combinatie met fluoroscopische visualisatie.
- Geen van de onderdelen van het Penumbra System mag tegen weerstand in worden opgevoerd of gebruikt zonder dat eerst zorgvuldig de oorzaak van de weerstand is onderzocht met behulp van fluoroscopie. Als de oorzaak niet kan worden vastgesteld, dient u het instrument terug te trekken. Het onbeperkt aanhalen of het gedwongen inbrengen van de katheter of separator tegen de weerstand in kan leiden tot samendrukking van het hulpmiddel, waardoor het bloedvat kan worden beschadigd en/of de tip kan breken.
- Houd een constante infusie van geschikte spoelvloeistof in stand.
- Zorg er bij het aspireren voor dat de klep van de Penumbra-aspiratieslang niet langer wordt opengehouden dan nodig om de trombus te verwijderen. Overmatige aspiratie of het openhouden van de klep van de Penumbra-aspiratieslang wanneer de aspiratie is voltooid, wordt afgeraden.
- De Penumbra-separator is niet bedoeld voor gebruik als neurovasculaire voerdraad. Als het tijdens de revascularisatieprocedure nodig is om de Penumbra-reperfusiekatheter te herpositioneren, dan moet dit worden gedaan over een geschikte neurovasculaire voerdraad, met gebruikmaking van standaardtechnieken voor microkatheters en voerdraden.
- Met de Penumbra-reperfusiekatheter mag geen geautomatiseerde apparatuur voor het onder hoge druk injecteren van contrastmiddel worden gebruikt, aangezien deze het instrument kan beschadigen.
- De toediening van anticoagulantia en plaatjesremmers moet worden uitgesteld tot 24 uur na de behandeling. Medische behandeling en acute zorg na een beroerte moeten voldoen aan de richtlijnen van de ASA.[1] Elke neurologische verslechtering moet met spoed worden onderzocht door middel van een CT-scan en andere methoden, op basis van de ervaring van de onderzoeker/het ziekenhuis.
- De totaal toegestane tijd voor het bereiken van revascularisatie bij de patiënt bedraagt 120 minuten gebruik van het Penumbra System.

Nederlands

Mogelijke bijwerkingen

Mogelijke complicaties omvatten, maar zijn niet beperkt tot:

- allergische reactie en anafylaxie door contrastmiddel
- acute occlusie
- luchtembolie
- arterioveneuze fistel
- overlijden
- defect aan het instrument
- distale embolisatie
- embolie
- vorming van pseudo-aneurysma
- hematoom of bloeding op de toegangsplaats
- het niet volledig kunnen verwijderen van de trombus
- infectie
- intracraniale bloeding
- ischemie
- nierschade door contrastmiddel
- neurologische stoornissen, waaronder beroerte
- vaatspasme, trombose, dissectie of perforatie

Procedure

1. Lees vóór gebruik de hoofdstukken **Waarschuwingen**, **Voorzorgsmaatregelen** en **Mogelijke bijwerkingen**.
2. Verwijder elk instrument van het Penumbra System voor gebruik uit de verpakking en inspecteer het op schade en knikken.
3. Prepareer instrumenten van het Penumbra System vóór gebruik door de verpakkingsring en het instrument met gehepariniseerde zoutoplossing te spoelen (alleen voor de Penumbra-reperfusiekatheter en Penumbra-separator).
4. Prepareer een geleidekatheter of lange femorale schacht volgens de *Gebruiksaanwijzing* van de fabrikant.
5. Plaats de geleidekatheter of lange femorale schacht in de geschikte cerebrale arterie die zich proximaal van de occlusieplaats met de trombus bevindt.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Preparatie en gebruik van de Penumbra-reperfusiekatheter

1. Controleer de vaatdiameter en kies een Penumbra-reperfusiekatheter van een geschikte maat (zie **tabel 1**).
2. De tip van de Penumbra-reperfusiekatheter kan worden gevormd met behulp van de meegeleverde stoomvormmandrijn.
3. Bevestig de meegeleverde roterende hemostaseklep aan de Penumbra-reperfusiekatheter.
4. Steek de Penumbra-reperfusiekatheter in een roterende hemostaseklep die is bevestigd aan de proximale connector van een geleidekatheter. Als er geen geleidekatheter wordt gebruikt, brengt u de Penumbra-reperfusiekatheter in via de klep van de lange femorale schacht met behulp van de pelbare schacht. Nadat u de Penumbra-perfusiekatheter hebt ingebracht, verwijdert u de pelbare schacht uit de vasculaire schacht en pelt u hem los van de schacht van de Penumbra-perfusiekatheter.
5. Gebruik conventionele katheterisatietechnieken en fluoroscopie om de Penumbra-reperfusiekatheter over een geschikte neurovasculaire voerdraad op te voeren in het doelvat. Positioneer de Penumbra-reperfusiekatheter proximaal van de trombus. Verwijder de voerdraad uit de Penumbra-reperfusiekatheter.

Preparatie en gebruik van de Penumbra-separator

1. Bevestig de Penumbra-aspiratieslang aan de aspiratiepomp en zet de aspiratiepomp aan (zie de *Gebruikshandleiding* van de aspiratiepomp). Laat de aspiratiepomp vóór gebruik minstens één minuut werken en controleer of de aspiratiemeter -20 inch Hg aangeeft. Zorg ervoor dat de klep op de Penumbra-aspiratieslang in de UIT-stand staat.
2. Kies aan de hand van de reperfusiekatheter een geschikte maat Penumbra-separator (zie **tabel 1**).

Tabel 1 – Keuze instrumentmaat separator/reperfusiekatheter

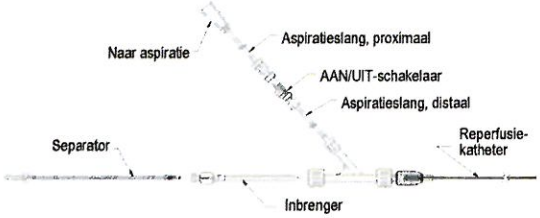
Vaatafmeting (mm)	Penumbra-reperfusiekatheter	Penumbra-separator
< 2,0	026	026
2,0 tot 3,0	032 / 3MAX	032 / 3MAX
3,0 tot 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Voer de Penumbra-reperfusiekatheter op om voorzichtig de distale tip in de trombus vast te zetten.

OPMERKING: De toegang tot de occlusieplaats kan worden vergemakkelijkt door triaxiaal gebruik van een compatibele inwendige microkatheter.

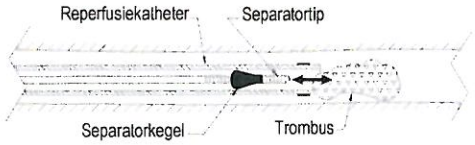
4. Steek met behulp van de meegeleverde inbrengschacht de Penumbra-separator door de roterende hemostaseklep in de proximale connector van de Penumbra-reperfusiekatheter.
5. Sluit de aspiratieslang aan op de zijpoort van de roterende hemostaseklep; zie **afbeelding 1**.

Afbeelding 1 – Opgebouwd aspiratiesysteem met Penumbra-separator



6. U kunt de aspiratie beginnen door de klep op de Penumbra-aspiratieslang in de AAN-stand te zetten en de Penumbra-separator op te voeren/terug te trekken ter ondersteuning bij de aspiratie en de verwijdering van de trombus; zie **afbeelding 2**.

Afbeelding 2 – Aspiratie van trombus met de Penumbra-separator



7. U stopt de aspiratie door de klep op de Penumbra-aspiratieslang in de UIT-stand te zetten en de aspiratiepomp uit te schakelen.
8. Verwijder de Penumbra-separator.
9. Indien nodig kunnen meerdere Penumbra-separators en reperfusiekatheters worden gebruikt om de trombus verder te verwijderen. Dit is ter beoordeling van de arts.
10. Aspireer met een spuit van 5 cc (ml) of 10 cc (ml) ongeveer 5 cc (ml) bloed uit de Penumbra-reperfusiekatheter om eventueel trombusmateriaal dat is achtergebleven in de katheter te verwijderen.
11. Maak na de behandeling een angiogram door contrastmiddel door de geleidekatheter te injecteren.

Verklaring van de symbolen

		Opgelet, zie gebruiksaanwijzing	
Rx Only		Uitsluitend op voorschrift – In de Verenigde Staten mag dit product uitsluitend worden gebruikt door of in opdracht van een arts	
		Niet-pyrogeen	
STERILE EO		Gesteriliseerd met ethyleenoxide	
	Fabrikant	EC REP	Vertegenwoordiger voor de EU
LOT	Partijnummer		Niet opnieuw gebruiken
	Te gebruiken vóór	REF	Catalogusnummer
	Niet opnieuw steriliseren	LATEX	Latexvrij

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Opis urządzenia

W skład systemu Penumbra® wchodzi kilka urządzeń:

- cewnik reperfuzyjny Penumbra,
- separator Penumbra,
- pompa aspiracyjna Penumbra,
- rurki do pompy/pojemnika Penumbra,
- rurki do aspiracji Penumbra.

Cewnik reperfuzyjny jest wprowadzany przez cewnik prowadzący lub długą koszulkę udową do wewnątrzczaszkowego układu naczyniowego i kierowany wzdłuż prowadnika nerwowo-naczyniowego do miejsca pierwotnie niedrożnego. Cewnik reperfuzyjny Penumbra jest wykorzystywany równolegle z separatorem Penumbra oraz źródłem aspiracji do oddzielenia skrzepliny i jej aspiracji z zatkanego naczynia. Separator Penumbra wprowadzany jest przy pomocy cewnika reperfuzyjnego Penumbra. Separator Penumbra jest wysuwany i chowany poprzez cewnik reperfuzyjny Penumbra na proksymalnym obrzeżu miejsca pierwotnie niedrożnego. Ułatwia to aspirację oraz usuwanie masy skrzepliny, a także zmniejsza lub eliminuje występowanie skrzepu wewnątrz-naczyniowego. Co do źródła aspiracji, cewnik reperfuzyjny Penumbra jest wykorzystywany w połączeniu z pompą aspiracyjną, która jest podłączana za pomocą rurek do aspiracji Penumbra oraz rurek do pompy/pojemnika Penumbra. Separator Penumbra dostarczany jest wraz z urządzeniem wpro-wadzającym oraz urządzeniem skręcającym. Cewnik reperfuzyjny Penumbra dostarczany jest wraz z mandrynem kształtowanym za pomocą pary oraz obrotową zastawką hemostatyczną i zdejmowaną koszulką. Urządzenia te widoczne są we fluoroskopii.

Wskazania

System Penumbra przeznaczony jest do użytku w celu rewaskularyzacji u pacjentów z ostrym udarem niedokrwiennym mózgu spowodowanym zatorobą zarostową dużych naczyń wewnątrzczaszkowych (wewnątrz-czaszkowic szyjnych wewnętrznych, środkowych mózgu — segmentów M1 i M2, podstawnej i kręgowych) w ciągu 8 godzin od wystąpienia objawów.

Przeciwwskazania

Nie są znane żadne przeciwwskazania.

Ostrzeżenia

- System Penumbra powinien być używany wyłącznie przez lekarzy odpowiednio przeszkolonych w technikach interwencyjnych nerwowo-naczyniowych, a także w leczeniu ostrego udaru niedokrwiennego mózgu.
- Systemu Penumbra nie wolno używać z pompą inną niż pompa aspiracyjna Penumbra.

Środki ostrożności

- Urządzenie jest przeznaczone wyłącznie do jednorazowego użytku. Nie używać i nie sterylizować powtórnie. Powtórna sterylizacja i/lub powtórne użycie mogą być przyczyną nieskutecznego nawilżania powłoki cewnika, co z kolei może powodować duże tarcie i uniemożliwiać dostęp do docelowej lokalizacji nerwowo-naczyniowej.
- Nie używać urządzeń zagiętych lub uszkodzonych. Nie używać urządzenia, jeśli opakowanie było otwarte lub uszkodzone.
- Nie używać po upływie daty ważności.
- Korzystać z systemu Penumbra w połączeniu z obrazowaniem fluoroskopowym.
- W przypadku wystąpienia oporu nie wsuwać ani nie korzystać z żadnego składnika systemu Penumbra bez dokładnego wyjaśnienia przyczyny wystąpienia oporu za pomocą fluoroskopii. Jeśli nie można określić przyczyny, należy wycofać urządzenie. Nieostrożne skręcanie i wprowadzanie cewnika oraz separatora na siłę mimo oporu może spowodować ściśnięcie przyrządu, co z kolei może spowodować uszkodzenie naczynia i/lub złamanie końcówki.
- Należy utrzymywać stały przepływ odpowiedniego roztworu do przepłukiwania.
- W trakcie wykonywania aspiracji otwierać zastawkę rurek do aspiracji Penumbra wyłącznie na jak najkrótszy czas potrzebny do usunięcia skrzepliny. Nie zaleca się nadmiernej aspiracji ani nie zamknięcia zastawki rurek do aspiracji Penumbra po zakończeniu aspiracji.
- Separator Penumbra nie jest przeznaczony do użytku jako prowadnik nerwowo-naczyniowy. Jeżeli w czasie trwania zabiegu rewaskularyzacji wymagana jest zmiana położenia cewnika reperfuzyjnego Penumbra, powinna ona zostać przeprowadzona na odpowiednim prowadniku nerwowo-naczyniowym, za pomocą standardowych technik dotyczących mikrocewnika i prowadnika.
- Nie należy używać automatycznych urządzeń do wysokociśnieniowych iniekcji kontrastowych wraz z cewnikiem reperfuzyjnym Penumbra, ponieważ może to spowodować uszkodzenie urządzenia.
- Podawanie środków przeciwkrzepliwych oraz przeciwpłytkowych należy zawiesić na okres do 24 godzin po zakończeniu leczenia. Opieka medyczna w fazie ostrej po udarze mózgu powinna być prowadzona zgodnie z wytycznymi Amerykańskiego Stowarzyszenia Udaru Mózgu.[1] Jakiekolwiek pogorszenie się stanu neurologicznego pacjenta powinno zostać ocenione za pomocą pilnego badania TK oraz innych badań zgodnych ze standardami postępowania danego lekarza/szpitala.
- Całkowity dopuszczalny czas do uzyskania rewaskularyzacji pacjenta za pomocą systemu Penumbra wynosi 120 minut.

Potencjalne działania niepożądane

Do możliwych powikłań należą między innymi:

- reakcja alergiczna oraz anafilaktyczna na środki kontrastowe
- ostre zamknięcie naczynia
- zator powietrzny
- przetoka tętniczo-żylna
- zgon
- wadliwe działanie urządzenia
- embolizacja obwodowa
- zatory
- powstanie tętniaka rzekomego
- krwiak lub krwotok w miejscu wkłucia
- brak możliwości całkowitego usunięcia skrzepliny
- zakażenie
- krwotok wewnątrzczaszkowy
- niedokrwienie
- uszkodzenie nerek środkami kontrastowymi
- deficyty neurologiczne, w tym udar
- skurcz naczynia, zakrzepica, rozwarstwienie ściany naczynia lub perforacja

Polski

Procedura

1. Przed użyciem zapoznać się z **Ostrzeżeniami**, **Środkami ostrożności** oraz **Potencjalnymi działaniami niepożądanymi**.
2. Przed użyciem każdego urządzenia systemu Penumbra usunąć je z opakowania, a następnie obejrzeć pod kątem uszkodzenia lub zagięć.
3. Przygotować urządzenia systemu Penumbra do użytku, przepłukując obręcz opakowania oraz urządzenia heparynizowanym roztworem soli fizjologicznej (dotyczy tylko cewnika reperfuzyjnego Penumbra oraz separatora Penumbra).
4. Przygotować cewnik prowadzący lub długą koszulkę udową zgodnie z *Instrukcją użycia* producenta.
5. Umieścić cewnik prowadzący lub długą koszulkę udową w odpowiedniej tętnicy mózgowej, proksymalnej względem miejsca zatkania skrzepliną.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Przygotowanie oraz korzystanie z cewnika reperfuzyjnego Penumbra

1. Potwierdzić średnicę naczynia i wybrać odpowiedni rozmiar cewnika reperfuzyjnego Penumbra (patrz **Tabela 1**).
2. Końcówkę cewnika reperfuzyjnego Penumbra można ukształtować za pomocą dostarczonego mandrynu kształtowanego za pomocą pary.
3. Przymocować dostarczoną obrotową zastawkę hemostatyczną do cewnika reperfuzyjnego Penumbra.
4. Wprowadzić cewnik reperfuzyjny Penumbra do obrotowej zastawki hemostatycznej połączonej z proksymalnym portem cewnika prowadzącego. Jeśli cewnik prowadzący nie jest używany, wprowadzić cewnik reperfuzyjny Penumbra przez zawór długiej koszulki udowej, używając zdejmowanej koszulki. Po wprowadzeniu cewnika reperfuzyjnego Penumbra zdjąć zdejmowaną koszulkę z koszulki naczyniowej i z trzonu cewnika reperfuzyjnego Penumbra.
5. Korzystając ze standardowych technik cewnikowania wspomaganego fluoroskopią, wprowadzić cewnik reperfuzyjny Penumbra do naczynia docelowego po odpowiednim prowadniku nerwowo-naczyniowym. Umieścić cewnik reperfuzyjny Penumbra proksymalnie względem skrzepliny. Usunąć prowadnik z cewnika reperfuzyjnego Penumbra.

Przygotowanie oraz używanie separatora Penumbra

1. Przymocować rurki do aspiracji Penumbra do pompy aspiracyjnej, a następnie włączyć pompę aspiracyjną (patrz *Podręcznik użytkownika* pompy aspiracyjnej). Przed użyciem pompy aspiracyjnej odczekać około minutę przy włączonej pompie, a następnie sprawdzić, czy wskaźnik aspiracji pokazuje -20 inHg (-20 cali słupa rtęci; -508 mmHg). Upewnić się, że zastawka na rurkach do aspiracji Penumbra jest przełączona w pozycję OFF (wył.).
2. Wybrać odpowiedni rozmiar separatora Penumbra odpowiadający cewnikowi reperfuzyjnemu (patrz **Tabela 1**).

Tabela 1 — Wybór rozmiaru separatora/cewnika reperfuzyjnego

Rozmiar naczynia (mm)	Cewnik reperfuzyjny Penumbra	Separator Penumbra
< 2,0	026	026
2,0 do 3,0	032 / 3MAX	032 / 3MAX
3,0 do 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Wprowadzić cewnik reperfuzyjny Penumbra aż do delikatnego umieszczenia końcówki dystalnej w skrzeplinie.

UWAGA: Można ułatwić dostęp do miejsca niedrożności poprzez trójosiowe użycie kompatybilnego mikrocewnika wewnętrznego.

4. Korzystając z dostarczonej koszulki naczyniowej, przeprowadzić separator Penumbra przez obrotową zastawkę hemostatyczną, a następnie przez proksymalny port cewnika reperfuzyjnego Penumbra.
5. Przymocować rurki aspiracyjne do portu bocznego obrotowej zastawki hemostatycznej, jak pokazano na **Rysunku 1**.

Rysunek 1 — Złożony system aspiracji wraz z separatorem Penumbra

6. Aby rozpocząć aspirację, otworzyć zastawkę na rurkach do aspiracji Penumbra, przekręcając ją w pozycję ON (wł.), a następnie wsunąć/wycofać separator Penumbra w taki sposób, aby wspomóc aspirację i usuwanie skrzepliny, jak pokazano na **Rysunku 2**.

Rysunek 2 — Aspiracja skrzepliny za pomocą separatora Penumbra

7. Aby przerwać aspirację, przełączyć zastawkę na rurkach do aspiracji Penumbra w pozycję OFF (wył.), a następnie wyłączyć pompę aspiracyjną.
8. Usunąć separator Penumbra.
9. Jeżeli zachodzi taka konieczność, można skorzystać z dodatkowych separatorów i cewników reperfuzyjnych Penumbra, w celu dalszego usunięcia skrzepliny, zgodnie z postanowieniem lekarza.
10. Korzystając z 5 ml lub 10 ml strzykawki, pobrać około 5 ml krwi z cewnika reperfuzyjnego Penumbra w celu usunięcia resztek skrzepliny, które mogą znajdować się w cewniku.
11. Wstrzyknąć środki kontrastowe przez cewnik prowadzący w celu uzyskania angiogramu pozabiegowego.

Słownik symboli

	Uwaga, sprawdzić w instrukcji użycia		
Rx Only	Tylko na receptę – prawo federalne USA zezwala na sprzedaż tego urządzenia wyłącznie przez lekarza lub na jego zlecenie		
	Produkt niepirogenny		
STERILE EO	Sterylizowano tlenkiem etylenu		
	Producent	EC REP	Przedstawiciel w UE
LOT	Numer serii		Nie używać ponownie
	Termin ważności	REF	Numer katalogowy
STERILIZE	Nie sterylizować ponownie	LATEX	Nie zawiera lateksu

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Descrição do Dispositivo

O Penumbra System® é constituído por vários dispositivos:

- Cateter de Reperfusão Penumbra
- Separador Penumbra
- Bomba de Aspiração Penumbra
- Tubagem da Bomba/Recipiente Penumbra
- Tubagem de Aspiração Penumbra

O Cateter de Reperfusão é introduzido através de um cateter-guia ou de uma bainha femoral comprida e para dentro da vasculatura intracraniana e é guiado sobre um fio-guia neurovascular até ao local da oclusão primária. O Cateter de Reperfusão Penumbra é utilizado em paralelo com o Separador Penumbra e com uma fonte de aspiração para separar o trombo e aspirá-lo do vaso obstruído. O Separador Penumbra é desdobrado através do Cateter de Reperfusão Penumbra. O Separador Penumbra é avançado e retraído através do Cateter de Reperfusão Penumbra na margem proximal da oclusão primária. Isto facilita a aspiração e a remoção do trombo e reduz ou elimina o problema do coágulo endovascular. Para a fonte de aspiração, o Cateter de Reperfusão Penumbra é utilizado com a Bomba de Aspiração, que é ligada utilizando a Tubagem de Aspiração Penumbra e a Tubagem da Bomba/ Recipiente Penumbra. O Separador Penumbra é fornecido com um introdutor e um dispositivo de torção. O Cateter de Reperfusão Penumbra é fornecido com um mandril para moldagem a vapor e uma válvula hemostática rotativa e uma bainha destacável. Os dispositivos são visíveis sob fluoroscopia.

Indicação para Utilização

O Penumbra System destina-se a ser utilizado na revascularização de pacientes com ataque isquémico agudo secundário a doenças obstrutivas dos grandes vasos intracranianos (dentro das artérias carótida interna, cerebral média – segmentos M1 e M2, basilar e vertebral) até 8 horas após o início dos sintomas.

Contra-indicações

Não existem contra-indicações conhecidas.

Advertências

- O Penumbra System só deve ser utilizado por médicos que tenham recebido a devida formação em técnicas intervencionais neuro-endovasculares e no tratamento de ataque isquémico agudo.
- Não utilize o Penumbra System com uma bomba que não seja a Bomba de Aspiração Penumbra.

Precauções

- O dispositivo foi concebido para uma única utilização apenas. Não reesterelize nem reutilize. A resterilização e/ou reutilização pode resultar numa lubrificação do revestimento do cateter ineficaz, o que pode resultar em alta fricção e na incapacidade de se obter acesso ao local alvo na neurovasculatura.
- Não utilize dispositivos dobrados nem danificados. Não utilize se as embalagens estiverem abertas ou danificadas.
- Utilize antes do vencimento do prazo de validade.
- Utilize o Penumbra System com visualização fluoroscópica.
- Não faca avançar nem utilize nenhum componente do Penumbra System contra resistência sem efectuar uma avaliação cuidadosa da causa por meio de fluoroscopia. Retire o dispositivo se não conseguir determinar a causa da resistência. A torção livre ou a inserção forçada do cateter ou separador contra resistência pode causar a compressão do dispositivo, o que pode causar danos no vaso e/ou a quebra da ponta.
- Mantenha uma infusão constante com uma solução de irrigação apropriada.
- Ao efectuar a aspiração, certifique-se de que a válvula da Tubagem de Aspiração Penumbra está aberta durante apenas o tempo mínimo necessário para retirar o trombo. Aspiração excessiva ou a falha do fechamento da válvula da Tubagem de Aspiração Penumbra depois da aspiração ser concluída não são recomendadas.
- O Separador Penumbra não foi concebido para ser utilizado como um fio-guia neurovascular. Se for necessário reposicionar o Cateter de Reperfusão Penumbra durante o procedimento de revascularização, tal reposicionamento deve ser efectuado sobre um fio-guia neurovascular apropriado utilizando técnicas padrão de microcateter e fio-guia.
- Não utilize equipamento de injecção de meio de contraste de alta pressão automática com o Cateter de Reperfusão Penumbra porque isso pode danificar o dispositivo.
- A administração de anticoagulantes e antiplaquetários deve ser suspensa até 24 horas pós-tratamento. A gestão médica e cuidados pós-trombose devem seguir as directrizes da ASA.[1] Qualquer deterioração neurológica deve ser avaliada através de um exame imagiológico TC urgente e outras avaliações, conforme indicado de acordo com a melhor prática investigadora/hospitalar.
- O tempo total permitido para alcançar a revascularização do paciente é de 120 minutos de utilização do Penumbra System.

Efeitos Indesejáveis Possíveis

As complicações possíveis incluem, mas não se limitam às seguintes:

- reacção alérgica e anafiláctica ao meio de contraste
- oclusão aguda
- embolia gasosa
- fístula arteriovenosa
- morte
- avaria do dispositivo
- embolização distal
- êmbolos
- formação de falso aneurisma
- hematoma ou hemorragia no local de acesso
- incapacidade de retirar completamente o trombo
- infecção
- hemorragia intracraniana
- isquemia
- lesões renais devido ao meio de contraste
- deficiência neurológica incluindo derrame
- espasmo, trombose, dissecção ou perfuração do vaso

Procedimento

1. Consulte as **Advertências**, **Precauções** e **Efeitos Indesejáveis Possíveis** antes da utilização.
2. À medida que utiliza cada dispositivo do Penumbra System, retire o dispositivo da embalagem, e inspeccione-o para detectar danos ou dobras.
3. Prepare os dispositivos do Penumbra System para serem utilizados irrigando o laço da embalagem e o dispositivo com solução salina heparinizada (inclui apenas o Cateter de Reperfusão Penumbra e o Separador Penumbra).
4. Prepare um cateter-guia ou uma bainha femoral comprida de acordo com as *Instruções para Utilização* do fabricante.
5. Coloque o cateter-guia ou a bainha femoral comprida na artéria cerebral apropriada que se encontra proximal ao local de oclusão do trombo.

Português

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Preparação e Utilização do Cateter de Reperfusão Penumbra

1. Confirme o diâmetro do vaso, e seleccione um Cateter de Reperfusão Penumbra com o tamanho apropriado (Consulte o **Quadro 1**).
2. A ponta do Cateter de Reperfusão Penumbra pode ser moldada utilizando o mandril para moldagem a vapor fornecido.
3. Ligue a válvula hemostática rotativa fornecida ao Cateter de Reperfusão Penumbra.
4. Introduza o Cateter de Reperfusão Penumbra dentro de uma válvula hemostática rotativa ligada ao cubo proximal de um cateter-guia. Se não for utilizado um cateter-guia, insira o Cateter de Reperfusão Penumbra através da válvula da bainha femoral comprida usando a bainha destacável. Depois de inserir o Cateter de Reperfusão Penumbra, retire a bainha destacável da bainha vascular e destaque do corpo do Cateter de Reperfusão Penumbra.
5. Utilizando técnicas de cateterização convencionais sob orientação fluoroscópica, faça avançar o Cateter de Reperfusão Penumbra para dentro do vaso alvo através de um fio-guia neurovascular apropriado. Posicione o Cateter de Reperfusão Penumbra proximal ao trombo. Retire o fio-guia do Cateter de Reperfusão Penumbra.

Preparação e Utilização do Separador Penumbra

1. Ligue a Tubagem de Aspiração Penumbra à Bomba de Aspiração e ligue a Bomba de Aspiração (Consulte o *Manual de Utilização* da Bomba de Aspiração). Deixe a Bomba de Aspiração funcionar durante pelo menos um minuto antes de a utilizar, e certifique-se de que o indicador da Aspiração indica -20 inHg. Certifique-se de que a válvula na Tubagem de Aspiração Penumbra se encontra na posição OFF (Desligada).
2. Seleccione um Separador Penumbra de tamanho apropriado correspondente ao Cateter de Reperfusão (consulte o **Quadro 1**).

Quadro 1 – Selecção do Tamanho do Dispositivo Separador/Cateter de Reperfusão

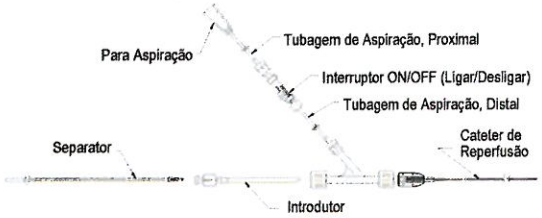
Tamanho do Vaso (mm)	Cateter de Reperfusão Penumbra	Separador Penumbra
< 2,0	026	026
2,0 a 3,0	032 / 3MAX	032 / 3MAX
3,0 a 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Faça avançar o Cateter de Reperfusão Penumbra para prender suavemente a ponta distal dentro do trombo.

NOTA: O acesso ao local da oclusão pode ser auxiliado pela utilização triaxial de um microcateter interno compatível.

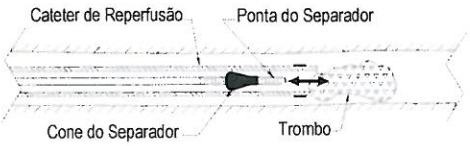
4. Utilizando a bainha introdutora fornecida, introduza o Separador Penumbra através da válvula hemostática rotativa e para dentro do cubo proximal do Cateter de Reperfusão Penumbra.
5. Ligue a Tubagem de Aspiração à porta lateral da válvula hemostática rotativa, conforme ilustrado na **Figura 1**.

Figura 1 – Sistema de Aspiração Montado com o Separador Penumbra



6. Para iniciar a aspiração, coloque a válvula na Tubagem de Aspiração Penumbra na posição ON (Ligada), e faca avançar/retraia o Separador Penumbra para ajudar a aspiração e remoção do trombo, conforme ilustrado na **Figura 2**.

Figura 2 – Aspiração do Trombo Utilizando o Separador Penumbra



7. Para interromper a aspiração, coloque a válvula da Tubagem de Aspiração Penumbra na posição OFF (Desligada), e desligue a Bomba de Aspiração.
8. Retire o Separador Penumbra.
9. Se necessário, podem ser utilizados Separadores e Cateteres de Reperfusão Penumbra para retirar mais trombos, à discrição do médico.
10. Utilizando uma seringa de 5 cc ou de 10 cc, aspire cerca de 5 cc de sangue do Cateter de Reperfusão Penumbra para retirar qualquer trombo que ainda possa estar dentro do cateter.
11. Efectue um angiograma pós-tratamento injectando o meio de contraste através do cateter-guia.

Glossário de Símbolos

		Atenção, consulte as Instruções para Utilização	
Rx Only		Apenas com receita médica - A lei federal (E.U.A.) só permite a utilização deste dispositivo por médicos ou mediante receita médica	
		Não pirogénico	
STERILE EO		Esterilizado utilizando óxido de etileno	
	Fabricante	EC REP	Representante da UE
LOT	Número de lote		Não reutilize
	Utilize até	REF	Número de catálogo
STERILIZE	Não reesterilize	LATEX	Sem látex

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Cihaz açıklaması

Penumbra System® birçok bileşenden oluşmaktadır:

- Penumbra Reperfüzyon Kateteri
- Penumbra Separatör
- Penumbra Aspirasyon Pompası
- Penumbra Pompa/Kap Boru Sistemi
- Penumbra Aspirasyon Boru Sistemi

Reperfüzyon Kateteri, kılavuz bir kateter veya uzun femoral kılıf vasıtasıyla intrakranyal vaskülerin içine yerleştirilir ve birincil oklüzyon alanında nevrovasküler bir kılavuz tel vasıtasıyla rehberlik eder. Penumbra Reperfüzyon Kateteri, Penumbra Separatör ile ve pıhtıyı ayırmak ve pıhtıyı oklüz damardan aspire etmek için kullanılan bir aspirasyon kaynağı ile paralel kullanılır. Penumbra Separatör, Penumbra Reperfüzyon Kateterinden açılır. Penumbra Separatörü, ileri itilip Penumbra Reperfüzyon Kateteri üzerinden birincil oklüzyonun proksimal sınırına kadar geri çekilir. Bu durum pıhtının aspirasyonunu ve toplaşmamasını sağlarken endovasküler pıhtı riskini azaltır ya da yok eder. Aspirasyon kaynağı için Penumbra Reperfüzyon Kateteri, Penumbra Aspirasyon Tüp Sistemi ve Penumbra Pompa/Kap Tüp Sistemi kullanımı vasıtasıyla bağlanan Aspirasyon Pompası ile birlikte kullanılır. Penumbra Separatör, bir adet introdüser ve tork cihazıyla birlikte temin edilir. Penumbra Reperfüzyon Kateteri, buhar ile şekil verme mandreli, döner hemostaz valfi ve soyulabilen kılıf ile birlikte temin edilir. Cihazlar, floroskopi altında görülebilir.

Kullanım endikasyonları

Penumbra System, semptomların görülmesinden itibaren 8 saat içerisinde intrakranyal geniş damar oklüzyonu hastalığına (İnternal carotid içinde selebral ortasında – M1 ve M2 segmentleri, baziler ve vertebral arterler) ikincil olarak gelişen akut istemik strok hastalarının revaskülerizasyonunda kullanılmak için [illegible]arlanmıştır.

[illegible]da göre

Bilinen herhangi bir kontraendikasyonu yoktur.

Uyarılar

- Penumbra System yalnızca, müdahalesel nevro-endovasküler teknikleri ve akur istemik strokların tedavisi alanında gerekli eğitimi almış doktorların kullanımı içindir.
- Penumbra System'i Penumbra Aspirasyon Pompası'ndan başka bir pompayla kullanmayın.

Önlemler

- Aygıt tek kullanımlıktır. Tekrar kullanmayın ya da sterilize etmeyin. Yeniden sterilizasyon ve/veya yeniden kullanım kateter kaplamasındaki lubrikasyonun etkisini kaybetmesine neden olabilir, bu da yüksek derecede sürtünmeye ve hedef nöro vaskülatür konuma erişilememesine yol açabilir.
- Dolanmış veya hasarlı bileşenleri kullanmayın. Açık veya hasarlı ambalajları kullanmayın.
- Son kullanma tarihinden önce kullanın.
- Penumbra System'i floroskopik vizüalizasyon ile birlikte kullanın.
- Direncin nedeni floroskopi ile saptanmadıkça Penumbra System'i dirence karşı hiçbir zaman ilerletmeyin ya da çekmeyin. Eğer direncin nedeni belirlenemiyorsa cihazı çekin. Kateterin ya da separatörün dirence karşı kontrolsüz bir şekilde bükülmesi ya da zorlanarak takılması cihazın sıkıştırılmasına neden olabilir; bu da damar hasarına ve/veya uç kırılmasına yol açabilir.
- Uygun bir yıkama solüsyonunun devamlı infüzyonunu sağlayın.
- Aspirasyon yaparken Penumbra Aspirasyon Tüp Sistemi valfinin, pıhtıyı temizleyebilecek minimum sure için açık olduğundan emin olun. Uzun süreli aspirasyon ya da aspirasyon sona erdiği zaman Penumbra Aspirasyon Tüp Sistemi valfinin kapatılmaması tavsiye edilmemektedir.
- Penumbra Separatör, nevrovasküler kılavuz teli amacıyla hazırlanmamıştır. Eğer revaskülerizasyon prosedürü süresince Penumbra Reperfüzyon Kateterinin yeniden yerleştirilmesi gerekirse, söz konusu yeniden yerleştirme standart mikrokateter ve kılavuz teli tekniklerinin kullanımıyla uygun bir nevrovasküler kılavuz teli üzerinde yapılmalıdır.
- Penumbra Reperfüzyon Kateteri ile birlikte otomatik yüksek basınçlı contrast enjeksiyonu kullanmayın; cihaza hasara neden olabilir.
- Antikoagulanların ve antiplateletlerin yönetimi, Müdahaleden 24 saat öncesine kadar ertelenmelidir. Medikal yönetim ve akut post strok bakımı ASA rehberi doğrultusunda olmalıdır.[1] Herhangi bir nörolojik bozunum CT taraması ve diğer değerlendirme yöntemleri içinde en kısa zamanda incelenmelidir.
- Hastaya uygulanabilecek toplam revaskülerizasyon süresi Penumbra System'in 120 dakikalık kullanımıdır.

Olası yan etkiler

Olası yan etkilere aşağıda sayılanlar dahildir ancak bunlarla sınırlı değildir:

- Kontrast maddeye karşı alerjik reaksiyon
- Akut oklüzyon
- Hava embolisi
- Arteriovenöz fistül
- Ölüm
- Cihaz Arızaları
- Distal embolizasyon
- Emboli
- Hatalı Anevrizmal Oluşum
- Erişim bölgesinde kanama
- Pıhtının tümüyle temizlenmesine sorun
- Enfeksiyon
- İntrakranyal Kanama
- İskemi
- Kontrast madde nedeniyle böbrek hasarı
- Strok dahil nörolojik defisit
- Damar spazmı, diseksiyon, perforasyon, yırtılma veya yaralanma

Prosedür

1. Kullanmadan once **Uyarılar**, **Önlemler** ve **Olası Yan Etkiler Bölümlerini** inceleyiniz.
2. Penumbra System'in her bir Cihazının kullanılması için cihazı ambalajından çıkarın ve eğilme, burkulma ve diğer hasarları kontrol edin.
3. Penumbra System cihazlarını, ambalajlama çemberini ve cihazı steril salin kullanarak yıkamak vasıtasıyla kullanıma hazırlayın (Sadece Penumbra Reperfüzyon Kateteri ve Penumbra Separatörünü kapsar).
4. Üreticinin *Kullanım Talimatlarına* uygun olarak bir kılavuz kateteri veya uzun femoral kılıf hazırlayın.
5. Kılavuz kateterini ya da uzun femoral kılıfı, pıhtı oklüzyon alanına proksimal olan uygun serebral artere yerleştirin.

Penumbra reperfüzyon kataterinin hazırlanması ve kullanılması

1. Damar çapını doğrulayın ve uygun boyutlu bir Penumbra Reperfüzyon Kateteri seçin (Bakınız **Tablo 1**).
2. Penumbra Reperfüzyon Kateterinin ucu, tedarik edilen buhar ile şekillendirme mandrelinin kullanımı vasıtasıyla şekillendirilebilir.
3. Penumbra Reperfüzyon Kateteri ile birlikte temin edilen döner hemostaz valfini takın.
4. Penumbra Reperfüzyon Kateterini, kılavuz kateterin proksimal göbeğine bağlı bulunan döner hemostaz valfinin içine takın. Bir kılavuz kateteri kullanılmamışsa, soyulabilen kılıfı kullanarak Penumbra Reperfüzyon Kateterini uzun femoral kılıftan sokun. Penumbra Reperfüzyon Kateterini yerleştirdikten sonra, soyulabilen kılıfı vasküler kılıftan çıkartın ve Penumbra Reperfüzyon Kateteri milinden soyun.
5. Konvansiyonal kateterizasyon tekniklerini kullanarak floroskopik kılavuzluk dahilinde, Penumbra Reperfüzyon Kateterini, uygun bir nevrovasküler kılavuz teli üzerinden hedef damara doğru ilerletin. Penumbra Reperfüzyon Kateterini pıhtıya proksimal olacak şekilde yerleştirin. Kılavuz teli Penumbra Reperfüzyon Kateterinden çıkartın.

Türkçe

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Penumbra separatörünün hazırlanması ve kullanılması

1. Penumbra Aspirasyon Tüp Sistemini, Aspirasyon Pompasına takın ve Aspirasyon Pompasını çalıştırın (Bakınız: Aspirasyon Pompası *Çalıştırma Talimatları*). Kullanım öncesinde Aspirasyon Pompasının en az bir dakika çalışmasını sağlayın ve Aspirasyon Göstergesinde –20inHg ibaresinin okunduğundan emin olun. Penumbra Aspirasyon Tüp Sisteminin üzerinde bulunan valfin OFF (KAPALI) pozisyonunda olduğundan emin olun.
2. Reperfüzyon Kateterine karşılık gelen uygun boyutlu bir Penumbra Seperatör seçin (Bakınız **Tablo 1**).

Tablo 1 – Separatör/Reperfüzyon Cihazı Boyut Seçimi

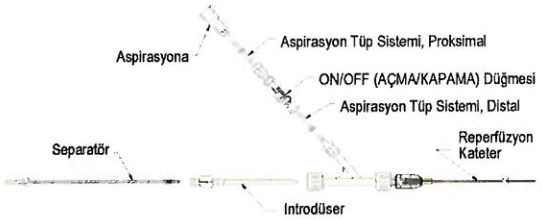
Damar Boyutu (mm)	Penumbra Reperfüzyon Kateteri	Penumbra Separatör
< 2,0	026	026
2,0 ila 3,0	032 / 3MAX	032 / 3MAX
3,0 ila 4,0	041 / 4MAX	041 / 4MAX
> 4,0	054 / 5MAX	054 / 5MAX

3. Penumbra Reperfüzyon Kateterini yerleşen pıhtının distal ucuna doğru yavaşça ilerletin.

NOT: Oklüzyon alanına erişim, uygun bir iç mikrokateterin üç açılı kullanımı ile desteklenebilir.

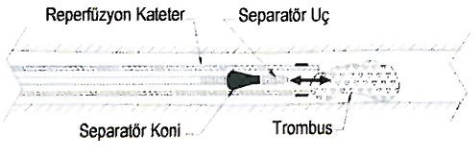
4. Temin edilen introdüser kılıfını kullanarak Penumbra Separatörü, döner hemostaz valfı üzerinden ve Penumbra Reperfüzyon Kateterinin proksimal göbeğine doğru takın.
5. Aspirasyon Tüp Sistemini, **Şekil 1**'de gösterildiği gibi döner hemostaz valfinin yan kısmına bağlayın.

Şekil 1 – Kurulmuş Penumbra Separatörlü Aspirasyon Sistemi



6. Aspirasyona başlamak için Penumbra Aspirasyon Tüp Sistemi üzerinde bulunan valfi ON (AÇIK) pozisyonuna getirin ve **Şekil 2**'de belirtildiği şekilde pıhtının aspirasyonuna ve temizlenmesine yardımcı olması için Penumbra Separatörü ilerletin ya da geri çekin.

Şekil 2 – Penumbra Separatör Kullanımıyla Pıhtı Aspirasyonu



7. Aspirasyonu durdurmak için Penumbra Aspirasyon Tüp Sistemi üzerindeki valfi OFF (KAPALI) pozisyonuna getirin ve Aspirasyon Pompasını kapatın.
8. Penumbra Separatörü çıkartın.
9. Gerekli olması durumunda, ek Penumbra Separatörleri ve Reperfüzyon Kateterleri doktorun kararına bağlı olarak ileri pıhtının temizlenmesinde kullanılabilir.
10. 5 cc ya da 10 cc'lik bir şırınga kullanarak, kateter içinde kalan pıhtıları temizlemek amacıyla yaklaşık olarak 5 cc kanı Penumbra Reperfüzyon Kateterinden aspire edin.
11. Kılavuz kateterden contrast madde enjekte etmek suretiyle bir müdahale öncesi anjiyo hazırlayın.

Sembol Sözlüğü

	Dikkat, kullanım talimatlarına bakınız		
Rx Only	Sadece reçete ile – ABD Federal Yasası, bu aygıtın satışını bir doktor tarafından ve bir doktorun isteği ile yapılacak şekilde kısıtlamaktadır		
	Pirojenik değildir		
STERILE EO	Etilen oksitle sterilize edilmiştir		
	İmalatçı	EC REP	AB Temsilcisi
LOT	Kafile numarası		Yeniden kullanmayın
	Son kullanma tarihi	REF	Katalog numarası
	Tekrar sterilize etmeyin	LATEX	Lateks içermez

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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器材說明

Penumbra System® 包含數種裝置：

- Penumbra 再灌流導管
- Penumbra 分離器
- Penumbra 抽吸幫浦
- Penumbra 幫浦/濾管
- Penumbra 抽吸管

將再灌流導管透過導引導管或長股鞘置入顱內血管，然後沿神經血管導絲到達主要閉塞部位。將 Penumbra 再灌流導管與 Penumbra 分離器和抽吸源平行放置，以分離血栓並將其從閉塞血管中吸出。Penumbra 分離器是透過 Penumbra 再灌流導管置入的。Penumbra 分離器可在位於主要閉塞部位近側邊緣的 Penumbra 再灌流導管中推進和縮回。這有利於吸出和消融血栓，並減少或消除血管內凝塊造成的負擔。Penumbra 再灌流導管可與使用 Penumbra 抽吸管和 Penumbra 幫浦/濾管進行連接的抽吸幫浦一起用作抽吸源。Penumbra 分離器配有一個導引器和轉矩裝置以及可剝離式鞘。Penumbra 再灌流導管配有一個蒸汽成形心軸和旋轉止血閥。使用螢光顯像檢查法可看見這些裝置。

使用指示

Penumbra System 專用於以下病員的血管再造：患有顱內大血管閉塞性疾病（頸內動脈、中動脈 – M1 和 M2 段、腦底部和椎動脈內），並且在疾病發作後 8 小時內繼發急性缺血性腦中風。

禁忌症

沒有已知的禁忌症。

警告

- 只有接受過適當的介入神經外科血管內技術和急性缺血性腦中風治療訓練的醫師才能使用 Penumbra System。
- 請勿將 Penumbra System 與 Penumbra 抽吸幫浦以外的幫浦配合使用。

注意事項

- 該器材僅供一次性使用。切勿重新滅菌或重複使用。重新滅菌及/或重複使用可能會造成導管塗層潤滑無效，從而導致摩擦力增大且無法進入靶神經血管部位。
- 切勿使用纏結或損壞的器材。切勿使用已開啟或損壞的包裝。
- 在「有效日期」所示日期之前使用。
- 請將 Penumbra System 與螢光顯像配合使用。
- 在遇到阻力時，若沒有使用螢光顯像檢查法仔細評估原因，切勿推進或使用 Penumbra System 的任何組件。若無法確定原因，請取出器材。過度扭轉或遇到阻力時強行插入導管或分離器會使裝置受壓，進而導致血管損傷和/或導管尖端破裂。
- 持續穩定地輸入合適的沖洗液。
- 進行抽吸時，請確保 Penumbra 抽吸管閥門的開啟時間不超過取栓時所需的最短時間。不建議過度抽吸或在抽吸完成後仍讓 Penumbra 抽吸管閥門處於開啟狀態。
- 請勿將 Penumbra 分離器用作神經血管導絲。若在血管再造手術中需要重新放置 Penumbra 再灌流導管，則應採用標準的微導管和導絲技術並使用合適的神經血管導絲來進行放置。
- 切勿將自動高壓顯影劑注射器材與 Penumbra 再灌流導管一起使用，否則可能會損壞器材。
- 在治療後 24 小時內，請勿使用抗凝血藥物和抗血小板藥物。應遵循 ASA 指引進行醫療管理和急性中風後護理。[1] 任何神經功能惡化都應根據研究員/醫院的最佳實踐，使用緊急 CT 掃描和其他評估方法進行評估。
- 按照規定，使用 Penumbra System 對病員進行血管再造的總時間為 120 分鐘。

可能的副作用

可能的併發症包括但不限於：

- 對顯影劑的過敏反應
- 急性阻塞
- 空氣栓塞
- 動靜脈瘻管
- 死亡
- 器材故障
- 遠端栓塞
- 栓塞
- 形成假性動脈瘤
- 導入部位血腫或出血
- 無法完全清除血栓
- 感染
- 腦出血
- 缺血
- 顯影劑使腎臟受損
- 神經功能缺損，包括中風
- 血管痙攣、血栓、剝離或穿孔

程序

1. 使用之前，請仔細閱讀**警告**、**注意事項**和**可能的副作用**。
2. 使用 Penumbra System 的各個器材時，應先從包裝中取出器材並檢查是否有損壞或纏結現象。
3. 準備 Penumbra System 器材時，應使用肝素生理鹽水沖洗包裝箍和器材（僅限 Penumbra 再灌流導管和 Penumbra 分離器）。
4. 請遵循製造商的《使用說明》準備導引導管或長股鞘。
5. 將導引導管或長股鞘放入靠近血栓閉塞部位的適當腦動脈中。

Penumbra 再灌流導管的準備和使用

1. 確定血管直徑，選擇適當大小的 Penumbra 再灌流導管（參見**表 1**）。
2. 可使用隨附的蒸汽成形心軸對 Penumbra 再灌流導管的管尖進行定形。
3. 將隨附的旋轉止血閥連接至 Penumbra 再灌流導管。
4. 將 Penumbra 再灌流導管插入已連接至導引導管近端接頭的旋轉止血閥。若未使用導引導管，使用可剝離式鞘透過長股鞘的閥門插入 Penumbra 再灌流導管。在插入 Penumbra 再灌流導管後，從血管鞘移除可剝離式鞘並從 Penumbra 再灌流導管桿剝離。
5. 在螢光顯像的指導下，使用常規的導管插入術，將 Penumbra 再灌流導管沿一條適當的神經血管導絲推入靶血管。將 Penumbra 再灌流導管靠近血栓放置。從 Penumbra 再灌流導管中取出導絲。

Penumbra 分離器的準備和使用

1. 將 Penumbra 抽吸管連接至抽吸幫浦，並開啟抽吸幫浦（請參閱抽吸幫浦的操作手冊）。在使用之前，應讓抽吸幫浦運行至少一分鐘，並確認抽吸壓力計的讀數為 –20inHg。確保 Penumbra 抽吸管上的閥門處於「OFF」（關）位置。
2. 選擇與再灌流導管相應大小的 Penumbra 分離器（參見**表 1**）。

表 1 – 分離器/再灌流導管器材大小選擇

血管大小 (mm)	Penumbra 再灌流導管	Penumbra 分離器
< 2.0	026	026
2.0 至 3.0	032 / 3MAX	032 / 3MAX
3.0 至 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX	054 / 5MAX

3. 推進 Penumbra 再灌流導管，使其末端輕輕嵌入血栓。

註：可透過一條相容的內部微導管，採用三軸方式進入閉塞部位。

4. 使用隨附的導管鞘，將 Penumbra 分離器透過旋轉止血閥插入 Penumbra 再灌流導管的近端接頭。
5. 將抽吸管連接至旋轉止血閥的側孔，如**圖 1** 所示。

中文

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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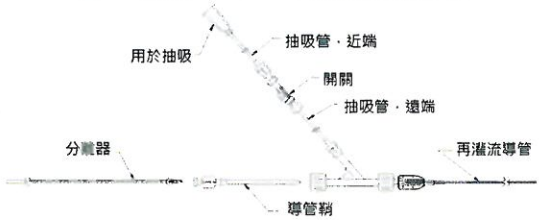
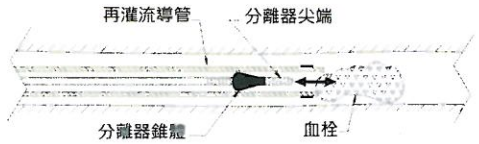
圖 1 – 已裝好 Penumbra 分離器的抽吸系統



6. 要開始抽吸，請使 Penumbra 抽吸管上的閥門處於「ON」（開）位置，然後推進/縮回 Penumbra 分離器以協助吸出和清除血栓，如**圖 2** 所示。

圖 2 – 使用 Penumbra 分離器吸出血栓



7. 要停止抽吸，請使 Penumbra 抽吸管上的閥門處於「OFF」（關）位置，然後關閉抽吸幫浦。
8. 取出 Penumbra 分離器。
9. 若有必要，醫師可酌情決定使用額外的 Penumbra 分離器和再灌流導管以進一步清除血栓。

使用 5cc 或 10cc 的注射器，從 Penumbra 再灌流導管中抽出大約 5cc 血液，以清除導管中可能殘留的任何血栓。

11. 透過導引導管注射顯影劑，以取得治療後的血管造影圖像。

符號術語表

		注意，請參閱使用說明	
Rx Only		僅憑處方使用 – 美國聯邦法律規定本裝置只能由醫生使用或憑醫囑使用	
		無熱原	
STERILE EO		利用環氧乙烷滅菌	
	製造商	EC REP	歐盟授權代表
LOT	批號		切勿重複使用
	使用期限	REF	目錄編號
	切勿重新滅菌	LATEX	不含乳膠

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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器械描述

Penumbra System® 包括以下若干器械：

- Penumbra 再灌注导管
- Penumbra 分离器
- Penumbra 抽吸泵
- Penumbra 泵/过滤管
- Penumbra 抽吸管

将再灌注导管通过导引导管或长股鞘置入颅内血管，然后通过神经血管导丝引导至主要闭塞部位。将 Penumbra 再灌注导管与 Penumbra 分离器和抽吸源平行放置，以便分离血栓并将其从闭塞血管中吸出。Penumbra 分离器是通过 Penumbra 再灌注导管置入的。Penumbra 分离器可在主要闭塞部位的近边缘处通过 Penumbra 再灌注导管推进和收缩。这有助于抽吸血栓和减小血栓块，并可减轻或消除血管内凝块造成的负担。Penumbra 再灌注导管与使用 Penumbra 抽吸管和 Penumbra 泵/过滤管连接的抽吸泵一起用作抽吸源。Penumbra 分离器附带一个导引器和转矩装置。Penumbra 再灌注导管附带一个蒸汽成形芯棒和旋转止血阀，和一条可撕裂鞘。使用荧光透视法可以看见这些装置。

用途

Penumbra System 适用于对颅内大血管阻塞（颈内动脉、大脑中动脉 – M1 和 M2 段、基底动脉和椎动脉内）继发急性缺血性脑中风的患者进行血管再造，而且必须在症状发作的 8 小时内。

禁忌症

没有已知的禁忌症。

警告

- 只有经过适当的介入神经外科血管内治疗技术和急性缺血性脑中风治疗培训的医生，才可以使用 Penumbra System。
- 切勿在 Penumbra System 中使用除 Penumbra 抽吸泵以外的其他泵。

注意事项

- 本器械仅供一次性使用。请勿反复消毒或重复使用。反复消毒和/或重复使用可能会使导管涂层的润滑作用失效，从而产生较大的摩擦力，使器械无法进入目标神经脉管部位。
- 请勿使用扭曲或者受损的器材。不要使用已开启或损坏的包装。
- 请在“有效期”截止之前使用。
- 将 Penumbra System 与荧光成像系统配合使用。
- 在使用 Penumbra System 的任何组件遇到阻力时，必须先使用荧光透视法仔细评估阻力原因，再决定是否要推进。如果无法确定原因，应退出器械。迎着阻力无限制地扭曲或用力插入导管或分离器，可能会导致器械受到挤压，进而造成血管损伤和/或尖端破裂。
- 持续稳定地输入正确的冲洗液。
- 进行抽吸时，请确保 Penumbra 抽吸管阀门的打开时间不超过取栓所需的最短时间。请勿过度抽吸或在抽吸完成后不关闭 Penumbra 抽吸管的阀门。
- 不应将 Penumbra 分离器用作神经血管导丝。如果在血管再造手术期间需要调整 Penumbra 再灌注导管的位置，应使用标准的微导管和导丝技术通过适当的神经血管导丝来进行调整。
- 不要将 Penumbra 再灌注导管与自动高压造影剂注射器配合使用，否则可能会损坏器械。
- 应在完成治疗后的 24 小时之内使用抗凝血剂和抗血小板药物。应严格遵循 ASA 治疗指导原则实施医疗处理和急性脑中风后的护理。[1] 如果出现任何神经功能的恶化现象，应根据研究员/医院最佳实践中的说明，通过紧急 CT 扫描和其他评估方法进行评估。
- 使用 Penumbra System 为患者完成血管再造的总时间限制为 120 分钟。

可能发生的不良事件

可能出现的并发症包括但不限于：

- 由造影剂引起的过敏反应
- 急性梗塞
- 气体栓塞
- 动静脉瘘
- 死亡
- 器械故障
- 末端栓塞
- 栓塞
- 形成假性动脉瘤
- 导入部位血肿或出血
- 无法完全去除血栓
- 感染
- 颅内出血
- 局部缺血
- 由造影剂引起的肾脏损伤
- 神经功能缺损，包括中风
- 血管痉挛、血栓、撕裂或穿孔

步骤

1. 使用器械前，请仔细阅读**警告**、**注意事项**和**可能发生的不良事件**。
2. 在使用 Penumbra System 的各种器械时，应先从包装中取出器械并检查是否存在损坏或扭结现象。
3. 准备使用 Penumbra System 中的器械时，应使用肝素化生理盐水冲洗捆扎束和器械（仅包括 Penumbra 再灌注导管和 Penumbra 分离器）。
4. 按照制造商提供的《使用说明》准备导引导管或长股鞘。
5. 将导引导管或长股鞘置入最接近血栓闭塞部位的脑动脉中。

Penumbra 再灌注导管的准备和使用

1. 确定血管直径，并选择适当尺寸的 Penumbra 再灌注导管（参见**表 1**）。
2. 可使用附带的蒸汽成形芯棒来改变 Penumbra 再灌注导管尖端的形状。
3. 将随附的旋转止血阀连接至 Penumbra 再灌注导管。
4. 将 Penumbra 再灌注导管插入已连接至导引导管近端接头上的旋转止血阀。如果未使用导引导管，则使用可撕裂鞘将 Penumbra 再灌注导管插入长股鞘的阀。插入 Penumbra 再灌注导管后，将可撕裂鞘从血管鞘中取出，并从 Penumbra 再灌注导管轴进行撕裂。
5. 在荧光透视的引导下利用常规导管插入技术，利用适当的神经与血管导丝，将 Penumbra 再灌注导管推入靶血管。将 Penumbra 再灌注导管置于血栓近侧。从 Penumbra 再灌注导管中取出导丝。

Penumbra 分离器的准备和使用

1. 将 Penumbra 抽吸管连接至抽吸泵，并打开抽吸泵（请参阅《抽吸泵操作手册》）。在使用前，应使抽吸泵至少运行 1 分钟，并确认抽吸计的读数为 -20inHg。确保 Penumbra 抽吸管上的阀门处于 OFF（关）位置。
2. 选择与再灌注导管相应的适当尺寸的 Penumbra 分离器（参见**表 1**）。

表 1 - 分离器/再灌注导管器械的尺寸选择

血管尺寸 (mm)	Penumbra 再灌注导管	Penumbra 分离器
< 2.0	026	026
2.0 至 3.0	032 / 3MAX	032 / 3MAX
3.0 至 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX	054 / 5MAX

3. 推进 Penumbra 再灌注导管，使其远端轻轻地插入血栓中。

注：可通过一条相容的内部微导管，采用三轴方式进入闭塞部位。

4. 利用随附的导引器鞘，将 Penumbra 分离器通过旋转止血阀插入 Penumbra 再灌注导管的近端接头中。
5. 将抽吸管连接至旋转止血阀的侧孔，如**图 1** 所示。

简体中文

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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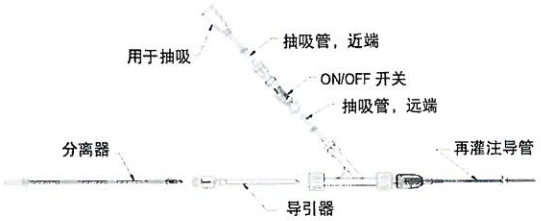
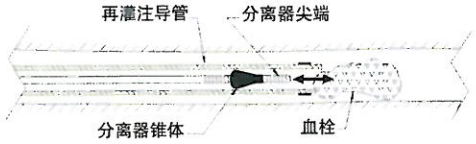
图 1 – 已装好 Penumbra 分离器的抽吸系统



6. 要开始抽吸，请将 Penumbra 抽吸管上的阀门打开至 ON（开）位置，然后推进/缩回 Penumbra 分离器，以协助抽吸和取出血栓，如**图 2** 所示。

图 2 – 使用 Penumbra 分离器抽吸血栓



7. 要停止抽吸，请将 Penumbra 抽吸管上的阀门转换到 OFF（关）位置，然后关闭抽吸泵。
8. 取出 Penumbra 分离器。
9. 如有必要，医生可酌情决定使用其他 Penumbra 分离器和再灌注导管进一步取栓。
   使用 5cc 或 10cc 的注射器，从 Penumbra 再灌注导管中抽吸大约 5cc 的血液，以取出可能残留在导管中的任何血栓。
11. 通过导引导管注射造影剂，以获取治疗后的血管造影片。

符号词汇表

	注意，请参阅使用说明		
Rx Only	仅凭处方 – 美国联邦法律规定本装置只能由医生使用或遵照医嘱使用		
	无热原		
STERILE EO	利用环氧乙烷灭菌		
	制造商	EC REP	欧盟授权代表
LOT	批号		切勿重复使用
	使用期限	REF	目录号
STERILIZE	切勿重新灭菌	LATEX	不含乳胶

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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한국어

장치 설명
Penumbra System®은 다음과 같은 여러 장치들로 이루어져 있습니다.
- Penumbra 재관류 카테터
- Penumbra 분리기
- Penumbra 흡인 펌프
- Penumbra 펌프/캐니스터 튜브
- Penumbra 흡인 튜브

재관류 카테터는 가이드 카테터 또는 긴 넙다리 유도관을 통과하여 두개내 혈관계로 삽입되고 신경혈관 가이드와이어를 통과하여 주요 폐색 부위로 유도됩니다. Penumbra 재관류 카테터는 혈전을 분리하여 폐색된 혈관에서 흡입하기 위해 Penumbra 분리기 및 흡인 소스와 함께 사용됩니다. Penumbra 분리기는 Penumbra 재관류 카테터에서 배치됩니다. Penumbra 분리기는 주요 폐색의 근위 가장자리에서 Penumbra 재관류 카테터를 통해 삽입되고 뒤로 당겨집니다. 이렇게 하면 혈전을 쉽게 흡입하고 혈전의 용적을 축소할 수 있으며 혈관내 응괴를 줄이거나 제거합니다. 흡입 소스를 위해, Penumbra 재관류 카테터는 Penumbra 흡인 튜브와 Penumbra 펌프/캐니스터 튜브를 사용하여 연결되는 흡인 펌프와 연결하여 사용됩니다. Penumbra 분리기는 유도관 및 회전 장치와 함께 제공됩니다. Penumbra 재관류 카테터는 증기 쉐이핑 맨드렐 및 회전 지혈 밸브, 박리 유도관과 함께 제공됩니다. 이 장치들은 투시 검사를 통해 볼 수 있습니다.

사용 지침
Penumbra System 은 증상이 나타난 지 8시간 내에 두개내 대형 혈관의 폐색 질병(내경 동맥, 중간 대뇌 – M1 및 M2 구역, 뇌저 및 척추 동맥)에 대한 속발성의 급성 허혈 뇌졸증이 있는 환자의 혈관재건술에 사용하도록 고안되었습니다.

금기 사항
알려진 금기 사항이 없습니다.

경고
- Penumbra System 은 중재성 신경방사선 기술 및 급성 허혈 뇌졸증의 치료에 관한 해당 교육을 이수한 의사만 이용하는 것이 좋습니다.
- Penumbra System 을 Penumbra 흡인 펌프가 아닌 다른 펌프와 함께 사용하지 마십시오.

주의 사항
- 장치는 한 환자에게 한 번만 사용하십시오. 재살균하거나 재사용하지 마십시오. 재살균 및/또는 재사용할 경우 카테터 코팅 윤활의 효과를 없애서 마찰이 커지고 목표 신경 혈관 위치에 접근할 수 없게 됩니다.
- 장치가 비틀어져 있거나 손상된 경우 사용하지 마십시오. 포장이 개봉되어 있거나 손상된 경우 사용하지 마십시오.
- "유통 일자(Use by)" 이전에 사용하십시오.
- Penumbra System 을 투시 가시화 장치와 연결하여 사용하십시오.
- 투시 검사를 사용하여 저항 원인을 조심스럽게 진단하지 않은 상태에서 저항에 대항하여 Penumbra System 의 어느 구성 요소도 삽입 또는 사용하지 마십시오. 원인을 확인할 수 없는 경우 장치를 제거하십시오. 저항이 있는데도 카테터 또는 분리기를 함부로 회전하거나 억지로 삽입하면 장치가 압착되어 혈관 손상 및/또는 팁 파손을 일으킬 수 있습니다.
- 적절한 세척 용액의 지속적인 유입을 유지하십시오.
- 흡인을 수행할 때, Penumbra 흡인 튜브 밸브가 혈전 제거에 필요한 최소 시간 동안만 열려 있는지 확인하십시오. 흡인을 완료한 후에 과도하게 흡인하거나 Penumbra 흡인 튜브 밸브를 닫지 않는 것은 좋지 않습니다.
- Penumbra 분리기는 신경혈관 가이드와이어로 사용하도록 고안되지 않았습니다. 혈관재건술을 시술하는 동안 Penumbra 재관류 카테터를 다시 배치해야 하는 경우 표준 마이크로카테터와 가이드와이어 기술을 사용하여 적절한 신경혈관 가이드와이어를 통해 수행되어야 합니다.
- 자동 고압 조영제 주입 장비를 Penumbra 재관류 카테터와 함께 사용하지 마십시오. 장치가 손상될 수 있습니다.
- 항응고제와 항혈소판제의 투여는 시술 후 24 시간까지 중지되어야 합니다. 의료 관리 및 급성 뇌졸증 사후 치료는 ASA 지침[1]을 따라야 합니다. 모든 신경계 장애는 조사관/병원 사례에 따라 설명된 대로 응급 CT 스캔 및 기타 평가에 의해 평가되어야 합니다.
- Penumbra System 을 사용하여 환자의 혈관재건술에 허용되는 전체 시간은 120 분입니다.

부작용 가능성
다음과 같은 합병증이 있을 수 있습니다.
- 조영제로 인한 알레르기 반응 및 과민증
- 급성 폐색
- 공기 색전증
- 동정맥루
- 사망
- 장치 고장
- 원위 색전증
- 색전증
- 가성 동맥류 형성
- 혈종 또는 접근 부위의 출혈
- 혈전 완전 제거 불가
- 감염
- 두개내 출혈
- 허혈
- 조영제로 인한 신장 손상
- 중풍 등의 신경 결함
- 혈관 연축, 혈전증, 절개, 또는 천공

시술
1. 사용하기 전에 **경고**, **주의 사항** 및 **부작용 가능성을** 참조하십시오.
2. Penumbra System 의 각 장치를 사용할 때, 장치를 포장재에서 꺼내고 손상되었거나 꼬였는지 확인하십시오.
3. 포장 후프와 장치를 헤파린 첨가 식염수로 세척하여 Penumbra System 장치를 사용할 준비를 하십시오(Penumbra 재관류 카테터 및 Penumbra 분리기만 포함됨).
4. 제조업체의 사용 지침에 따라 가이드 카테터 또는 긴 넙다리 유도관을 준비하십시오.
5. 가이드 카테터 또는 긴 넙다리 유도관을 혈전 폐색 부위에서 가까운적절한 대뇌 동맥에 놓으십시오.

Penumbra 재관류 카테터 준비 및 사용
1. 혈관 직경을 확인하고 적절한 크기의 Penumbra 재관류 카테터를 선택하십시오(**표 1** 참조).
2. Penumbra 재관류 카테터 끝은 제공된 증기 쉐이핑 맨드렐을 사용하여 만들 수 있습니다.
3. 제공된 회전 지혈 밸브를 Penumbra 재관류 카테터에 부착하십시오.
4. Penumbra 재관류 카테터를 가이드 카테터의 근위 허브에 연결된 회전 지혈 밸브에 끼우십시오. 가이드 카테터를 사용하지 않을 경우 박리 유도관을 사용하여 긴 넙다리 유도관의 밸브를 통해 Penumbra 재관류 카테터를 끼우십시오. Penumbra 재관류 카테터를 끼운 후 혈관집에서 박리 유도관을 제거하고 Penumbra 재관류 카테터 샤프트에서 벗겨내십시오.
5. 투시 장치의 유도 아래 기존의 카테터 삽입 기술을 사용하여 Penumbra 재관류 카테터를 적절한 신경혈관 가이드와이어를 통해 목표 혈관에 삽입하십시오. Penumbra 재관류 카테터를 혈전에 가까이 배치하십시오. Penumbra 재관류 카테터에서 가이드와이어를 분리하십시오.

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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Penumbra 분리기 준비 및 사용

1. Penumbra 흡인 튜브를 흡인 펌프에 부착하고 흡인 펌프의 전원을 켜십시오 (흡인 펌프 작동 설명서 참조). 사용하기 전에 최소 1 분 동안 흡인 펌프를 실행하고 흡인 게이지가 –20inHg인지 확인하십시오. Penumbra 흡인 튜브의 밸브가 OFF 위치에 있는지 확인하십시오.
2. 재관류 카테터에 해당하는 적절한 크기의 Penumbra 분리기를 선택하십시오 (**표 1** 참조).

표 1 – 분리기/재관류 카테터 장치 크기 선택

혈관 크기 (mm)	Penumbra 재관류 카테터	Penumbra 분리기
< 2.0	026	026
2.0 ~ 3.0	032 / 3MAX	032 / 3MAX
3.0 ~ 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX	054 / 5MAX

3. Penumbra 재관류 카테터를 삽입하여 원위 끝을 혈전 부위에 부드럽게 삽입하십시오.

참고: 호환되는 내부 마이크로카테터의 삼중축을 사용하면 폐색 부위에 접근하는 데 도움이 될 수 있습니다.

4. 제공된 유도관을 사용하여, Penumbra 분리기를 회전 지혈 밸브에 통과하도록 Penumbra 재관류 카테터의 근위 허브에 끼우십시오.
5. **그림 1** 과 같이 흡인 튜브를 회전 지혈 밸브의 옆면 포트에 연결하십시오.

그림 1 – Penumbra 분리기와 조립된 흡인 시스템

6. 흡인을 시작하려면 Penumbra 흡인 튜브의 밸브를 ON 위치로 열고 **그림 2** 와 같이 흡인과 혈전의 제거를 돕기 위해 Penumbra 분리기를 삽입하고 뒤로 당기십시오.

그림 2 – Penumbra 분리기를 사용하는 혈전 흡인

7. 흡인을 정지하려면 Penumbra 흡인 튜브의 밸브를 OFF 위치로 전환하고 흡인 펌프의 전원을 끄십시오.
8. Penumbra 분리기를 분리하십시오.
9. 필요한 경우, 의사의 판단 하에 혈전을 더 많이 제거하기 위해 Penumbra 분리기 및 재관류 카테터 시술을 추가로 사용할 수 있습니다.
10. 5cc 또는 10cc 주사기를 사용하여, Penumbra 재관류 카테터에서 약 5cc의 혈액을 흡인하여 카테터에 남아 있을 수 있는 혈전을 제거하십시오.
11. 조영제를 가이드 카테터를 통해 주입하여 치료 후 혈관조영상을 얻으십시오.

기호 설명

		주의. 사용법 참조	
Rx Only		처방에 의해서만 사용 가능 – 미국 연방 법에 따라 본 장치는 의사에 의해서만 또는 의사의 지시에 따라서만 사용할 수 있습니다.	
		비발열성	
STERILE EO		산화 에틸렌으로 멸균 처리	
	제조업체	EC REP	유럽연합 대리점
LOT	로트 번호		재사용하지 마십시오
	사용 기한	REF	카탈로그 번호
STERILIZE	재멸균 금지	LATEX	무라텍스

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Penumbra, Inc.
1351 Harbor Bay Pkwy
Alameda, CA 94502 USA

Tel: 1-888-BRAIN06 (1-888-272-4606)
1-510-748-3200
Fax: 1-510-748-3232

EC REP **EU Representative:**
MedPass International Ltd.
Windsor House Barnett Way
Barnwood, Gloucester GL4 3RT, UK

CE 0050

Penumbra Neuro Australia PTY LTD
Level 10, 1 Margaret Street
Sydney NSW 2000 Australia
Tel: 1300 817 025
Fax: 1300 817 026

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Received

October 09, 2014

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Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

K142458/S2

RE: K142458/S002 - Penumbra System ACE – Refuse to Accept Response – Supplement 2

Dear Mrs. Leigh Booth,

Penumbra, Inc. is submitting this response to the deficiencies identified in the FDA Refuse to Accept Letter e-mailed to Penumbra on October 08, 2014.

Penumbra Inc. requests that the information in this submission be considered confidential, and protected under 21 CFR 807.95, 18 USC 1905, 21 USC 331(j), 5 USC 552, and other applicable laws and provisions. Per the instructions accessed at http://www.fda.gov/cdrh/elecsub.html , an electronic copy is being provided with this submission and it is an exact duplicate of the response paper submission.

The FDA deficiency is repeated below and followed by the Penumbra response.

FDA Deficiency 1 (b)(4)

(b)(4)

[redacted]

Company Response:

(b)(4)

[redacted]

Penumbra, Inc.
1351 Harbor Bay Parkway
Alameda, Ca. 94502
U.S.A.

Regulatory Affairs
F 510.217.6414
www.penumbrainc.com

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Penumbra

(b)(4)

Attachment 1: [redacted]
Attachment 2:
Attachment 3:
Attachment 4:
Attachment 5:
Attachment 6:
Attachment 7:
Attachment 8:
Attachment 9:
Attachment 10
Attachment 11

If there are any questions regarding this response submission, please contact Michaela Mahl, Senior Manager Regulatory Affairs, at 510-748-3288, or via e-mail at michaela.mahl@penumbrainc.com or alternate Mr. Seth Schulman, VP Regulatory Affairs, at 510-748-2223, or via e-mail at seth.schulman@penumbrainc.com.

Sincerely,

Michaela Mahl

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Senior Manager Regulatory Affairs
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e-mail: michaela.mahl@penumbrainc.com

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October 09, 2014

U.S. Food and Drug Administration
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Document Mail Center – WO66-G609
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Silver Spring, MD 20993-0002

RE: K142458/S002 - Penumbra System ACE – Refuse to Accept Response – Supplement 2

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The FDA deficiency is repeated below and followed by the Penumbra response.

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Company Response:

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Sincerely,

Michaela Mahl

Michaela Mahl, MSBE
Senior Manager Regulatory Affairs
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e-mail: michaela.mahl@penumbrainc.com

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. RESPONSIBILITY

(b)(4) [redacted]

4. REFERENCE DOCUMENTS

(b)(4) [redacted]

(b)(4) [redacted]

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[2] Reference Section 10.

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Revision History

Rev	(b)(4)	Originator	Effective	Description of Change
(b)	(b)(4)	(b)(6)	07/15/14	(b)(4)
(b)	(b)(4)	(b)(6)	08/21/14	

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

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Revision History

Rev	(b)(4) [redacted]	Originator	Effective	Description of Change
(b)(4) [redacted]		(b)(6) [redacted]	08/30/12	(b)(4) [redacted]
		(b)(6) [redacted]	08/31/12	
		(b)(6) [redacted]	09/12/12	
		(b)(6) [redacted]	05/20/13	
		(b)(6) [redacted]	02/19/14	
		(b)(6) [redacted]	07/10/14	
		(b)(6) [redacted]	08/01/14	

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

(b)(4) [redacted]

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(b)(4) [redacted]

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

Revision History				
Rev	(b)(4) [redacted]	Originator	Effective	Description of Change
(b) [redacted]	(b)(4) [redacted]	(b)(6) [redacted]	07/15/14	(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

(b)(4) [redacted]

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

(b)(4)

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

Revision History

Rev	(b)(4) [redacted]	Originator	Effective	Description of Change
(b)(4) [redacted]		(b)(6) [redacted]	03/03/05	(b)(4) [redacted]
			05/18/07	
			07/25/07	
			11/30/07	
(b)(4) [redacted]			08/05/08	
			12/18/08	

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Revision History

Rev	(b)(4) [redacted]	Originator	Effective	Description of Change
(b)(4) [redacted]		(b)(6) [redacted]	02/19/09	(b)(4) [redacted]
			03/09/09	
			08/21/09	
			01/25/10	
			05/12/10	
			03/16/11	
			04/19/11	
			05/19/11	
			02 Aug 2011	
			09/21/11	

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

Revision History

Rev	ECO #	Originator	Effective	Description of Change
(b)(4) [redacted]		(b)(6) [redacted]	04/02/12	(b)(4) [redacted]
			05/17/12	
			05/10/13	
			09/09/13	
			10/02/13	
			12/11/13	
			12/16/13	
(b)(4) [redacted]		[redacted]	02/19/14	

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Revision History

Rev	(b)(4) [redacted]	Originator	Effective	Description of Change
(b) [redacted]	[redacted]	(b)(6) [redacted]	08/01/14	(b)(4) [redacted]

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

(b)(4)

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

Appendix A

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Revision History

Rev	(b)(4) [redacted]	Originator	Effective	Description of Change
(b)(4) [redacted]		(b)(6) [redacted]	03/29/12	(b)(4) [redacted]
			04/18/12	
			05/18/12	
			10/23/12	
			02/26/13	
			05/10/13	
			02/19/14	
			08/01/14	

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

(b)(4) [redacted]

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Revision History

Rev	ECO #	Originator	Effective	Description of Change
(b)(4) [redacted]		(b)(6) [redacted]	06/19/14	(b)(4) [redacted]
			07/16/14	
			07/23/14	

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

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Revision History

Rev	(b)(4) [redacted]	Originator	Effective	Description of Change
(b [redacted]	[redacted]	(b)(6) [redacted]	03/21/14	(b)(4) [redacted]
(b [redacted]	[redacted]	(b)(6) [redacted]	06/10/14	

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

(b)(4)

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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(b)(4) [redacted] [redacted] Test

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

(b)(4)

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Revision History

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(b)(4) [redacted]		(b)(6) [redacted]	07/11/14	(b)(4) [redacted]
			08/01/14	
			08/12/14	
				(b)(4) [redacted]

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

(b)(4) [redacted] **Test**

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

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[redacted]

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Revision History

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(b) [redacted]	[redacted]	(b)(6) [redacted]	07/11/14	(b)(4) [redacted]

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1. PURPOSE

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2. REFERENCE DOCUMENTS

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Revision History

Rev	(b)(4) [redacted]	*Originator*	*Effective*	*Description of Change*
(b)(4) [redacted]		(b)(6) [redacted]	02/04/05	(b)(4) [redacted]
		(b)(6) [redacted]	03/03/05	
		(b)(6) [redacted]	06/07/05	
		(b)(6) [redacted] try	04/12/10	
		(b)(6) [redacted]	02/08/12	

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REFERENCE

Annex A

(b)(4) [redacted]

Test (b)(4) [redacted]

(b)(4) [redacted]

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Penumbra

K142458/S003

FDA CDRH DMC
APR 13 2015
Received

April 10, 2015

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: K142458/S003 - Penumbra System ACE – Additional information request - Response to Queries 1 to 16 – Supplement 3

Dear Mrs. Leigh Booth,

Penumbra, Inc. is submitting this response to the deficiencies identified in the FDA Letter e-mailed to Penumbra on November 30, 2014.

Penumbra Inc. requests that the information in this submission be considered confidential, and protected under 21 CFR 807.95, 18 USC 1905, 21 USC 331(j), 5 USC 552, and other applicable laws and provisions. Per the instructions accessed at http://www.fda.gov/cdrh/elecsub.html , an electronic copy is being provided with this submission and it is an exact duplicate of the response paper submission.

The FDA deficiencies are repeated below and followed by the Penumbra responses in bold.

FDA: (b)(4) [redacted]

(b)(4) [redacted]

Penumbra, Inc.
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Alameda, Ca. 94502
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Regulatory Affairs
F 510.217.6414
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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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Penumbra

(b)(4)

[redacted]

Penumbra:

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[redacted]

If there are any questions regarding this response submission, please contact Michaela Mahl, Senior Manager Regulatory Affairs, at 510-748-3288, or via e-mail at michaela.mahl@penumbrainc.com or alternate Mr. Seth Schulman, VP Regulatory Affairs, at 510-748-2223, or via e-mail at seth.schulman@penumbrainc.com.

Sincerely,

Michaela Mahl

Michaela Mahl, MSBE
Senior Manager Regulatory Affairs
Phone: (510)748-3288
e-mail: michaela.mahl@penumbrainc.com

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Penumbra

April 10, 2015

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: K142458/S003 - Penumbra System ACE – Additional information request - Response to Queries 1 to 16 – Supplement 3

Dear Mrs. Leigh Booth,

Penumbra, Inc. is submitting this response to the deficiencies identified in the FDA Letter e-mailed to Penumbra on November 30, 2014.

Penumbra Inc. requests that the information in this submission be considered confidential, and protected under 21 CFR 807.95, 18 USC 1905, 21 USC 331(j), 5 USC 552, and other applicable laws and provisions. Per the instructions accessed at http://www.fda.gov/cdrh/elecsub.html , an electronic copy is being provided with this submission and it is an exact duplicate of the response paper submission.

The FDA deficiencies are repeated below and followed by the Penumbra responses in bold.

FDA: (b)(4) [redacted]

(b)(4) [redacted]

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Penumbra

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If there are any questions regarding this response submission, please contact Michaela Mahl, Senior Manager Regulatory Affairs, at 510-748-3288, or via e-mail at michaela.mahl@penumbrainc.com or alternate Mr. Seth Schulman, VP Regulatory Affairs, at 510-748-2223, or via e-mail at seth.schulman@penumbrainc.com.

Sincerely,

Michaela Mahl

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Attachment Table

Attachment #	Document #	Description
0	N/A	List of Attachments
1	N/A	(b)(4) Manufacturing Information [redacted]
2	(b)(4) [redacted]	(b)(4) Manufacturing Information [redacted]
3	N/A	(b)(4) Manufacturing [redacted]
4a	(b)(4) [redacted]	Additional Testing for ACE 64 and ACE 68 ([redacted] (b)(4) testing)
4b		Protocol to [redacted] (b)(4) Manufacturing Information)
5a		Shelf Life – Penumbra System ACE Reperfusion Catheters [redacted] (b)(4) Manufactur testing)
5b		Protocol to [redacted] (b)(4) Manufacturing Information testing)
6a		Design Verification, Reperfusion Catheters ACE 64 and ACE 68
6b		Protocol to [redacted] (b)(4) 0
7a		[redacted] (b)(4) Manufacturing Information Testing
7b		Protocol to [redacted] (b)(4) 4) Manufactur
8a		Instructions for Use – Penumbra System [ACE] - Clean
8b		Instructions for Use – Penumbra System [ACE] - Redline
9a		[redacted] (b)(4) Manufacturing Information Tests for Penumbra System
9b		Protocol to [redacted] (b)(4)
10		[redacted] (b)(4) Manufacturing Information ACE 64
11a		Shelf Life – Reperfusion Catheters ACE [redacted] (b)(4) Manufac cturin [redacted] (b)(4) Manufactur
11b		Protocol to [redacted] (b)(4) Manufacturing Information [redacted]
12a	N/A	ACE 64 and ACE 68 Pouch Labels - Clean
12b	N/A	ACE 64 and ACE 68 Pouch Labels - Redline
13	N/A	Section 8 - 510k Summary – updated
14	N/A	Section 9 - Indication for Use - updated
15	NA	The SPEED study: initial clinical evaluation of the Penumbra novel 054 Reperfusion Catheter
16	N/A	FDA Form 3654 – 6 Standards

(b)(4) Schematic Drawings

[redacted]

(b)(4) Schematic Drawings

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015
Surg Radiol Anat (2013) 35:385 394
DOI 10.1007/s00276 012 1042 8

ORIGINAL ARTICLE

Geometric classification of the carotid siphon: association between geometry and stenoses

Chi Zhang · Fang Pu · Shuyu Li · Sheng Xie · Yubo Fan · Deyu Li

Received: 12 September 2012 / Accepted: 8 November 2012 / Published online: 27 November 2012
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Abstract
Purpose The development of intracranial internal carotid artery (ICA) stenoses may be associated with the morphology of the siphon. The aim is to quantitatively characterize the geometry of ICA, and develop a classifier of the ICA shape in relation to the location and incidence of stenoses.
Methods The ICA geometry from 74 subjects was analyzed by means of image-based computational techniques. The siphon was split into two bends, and was described in terms of curvature radius, radius of vessel, angle of bending, and length. Differences of geometry between ICA classes were assessed in control group, consisted of 30 subjects without stenoses. In stenosed group, the association between the ICA classes and the incidence of stenoses were investigated and validated by hemodynamic simulation.
Results The curvature radius and angle of the posterior bend were significantly different between ICA classes, as well as the angle between the two bends. An innovative classifier was developed with the three geometric parameters. The ICA classification was found associated with the incidence of stenoses at the siphon.
Conclusions Geometric factors relative to the ICA were correlated with the location and incidence of stenoses at the siphon. The present work has potential implications in the quest for hemodynamic factors contributing to the initiation and progression of intracranial ICA stenoses.

Keywords Geometry · Internal carotid artery · Carotid siphon · Stenosis · Hemodynamics

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Introduction

Evidence gathered in the last decades supports the hypothesis that the formation and development of arterial stenoses are the result of a complex interplay between systemic factors, changes in the biomechanical properties of vessel walls, and local hemodynamic factors such as low and oscillatory wall shear stress (WSS) [14, 29]. In particular, the involvement of hemodynamics in arterial stenoses is supported by the circumstantial evidence that stenoses tend to develop in areas generally associated with altered hemodynamic forces such as bends and bifurcations [4, 5]. One of the most susceptible sites for vascular lesions lays at the siphon of internal carotid artery (ICA), which is famous for the tortuous shape [25]. Unfortunately, the ICA stenosis has been proven to be correlated to stroke and transient cerebral ischemia [3, 15].

Recent image-based computational studies have shown how a hemodynamic pattern is represented by the morphology of blood vessels, and that geometry can constitute a simple surrogate for complex hemodynamic behaviors [6, 11]. In that context, the study on 3D geometry of cerebral vasculature in vivo may contribute to elucidate the

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key hemodynamic factors correlating to the initiation and progression of the vascular disease. In additional, the concept of ICA classes has also been found to be correlated to hemodynamic patterns [28, 30]. Actually, the classification of the ICA shape has been proposed for decades [8] (Fig. 1). But the clinical application for the ICA classification was realized recently [7]. The investigation on the association between the classification and the stenosis of ICA may contribute to the risk prediction for stenoses at the siphon.

To date, the majority of works dealing with ICA geometry have focused on the correlation between the morphological features and the development of vascular lesions located in or after the ICA [20, 21, 24]. Although the importance of 3D geometric characterization of ICA has been realized in cerebrovascular diseases, the significance of ICA classification in exploring the hemodynamic mechanism of stenoses remains inexplicit [16, 17]. In additional, robust and objective approaches for the ICA classification based on the measurement of 3D geometric quantities have been seldom considered [1].

In this work, the geometry of each class of ICA is quantitatively characterized. An innovative method for the ICA classification is proposed. The correlation between the ICA classes, the incidence of stenoses, and the hemodynamic factors in ICA are also investigated. This work suggests the significance of the ICA classification for the hemodynamic investigations linked to stenoses in the siphon.

Materials and methods

Patient population, image acquisition, and model reconstruction

The study population consisted of the inpatients at Peking University First Hospital between 2006 and 2008, who met the following inclusion criteria: (1) Over 40 years old, (2) Anterior cerebral arteries, middle cerebral arteries and basilar artery remained patent, (3) Systemic vascular diseases like vasculitis were not found clinically, and (4) No evidence of ICA stenosis or common carotid artery on transcranial Doppler (TCD), carotid duplex ultrasound or MRA. Accordingly, 74 subjects namely 148 branches of ICA were chosen for the study. 44 patients were found to have unilateral or bilateral ICA stenoses at the siphon section, composing the stenotic group. The others formed the control group. Patient demographic data are summarized in Table 1. The study was approved by the Ethics Committees of both Beihang University and Peking University First Hospital.

All MRA images were acquired on a 1.5T magnetic resonance (MR) scanner (GE HD, Milwaukee) with an 8-channel head coil in the cross-sectional direction. A 3D TOF sequence was used for the image acquisition. The settings were: TR/TE 22/6.9 ms, flip angle 20°, field of view 220 × 180 mm^2, matrix 288 × 192, slice thickness 1.4 mm. The raw data of MRA was reconstructed with the technique of maximal intensity projection. All images were reviewed by a senior radiologist, who also classified the ICA according to the anatomical shape.

The 3D reconstruction of the ICA was performed with the Mimics software (Materialise, Belgium) [12, 13]. The ICA lumen images were segmented with the threshold method and reconstructed into the 3D models. The ICA, including its bifurcation into anterior cerebral artery (ACA) and middle cerebral artery (MCA), were reconstructed for every subject (Fig. 2). The centerlines were generated for each model from the intracranial ICA to the ACA and MCA by joining the center of maximal spheres locally inscribed within the vessel. Two bends were defined as B1 and B2 along the centerline at the siphon section.

Geometric characterization

The geometry of ICA was measured based on the measurement of the centerline. As two obvious bends were found at the siphon section, the geometry of the bends was measured. The curvature radius of the bend (CR) is defined

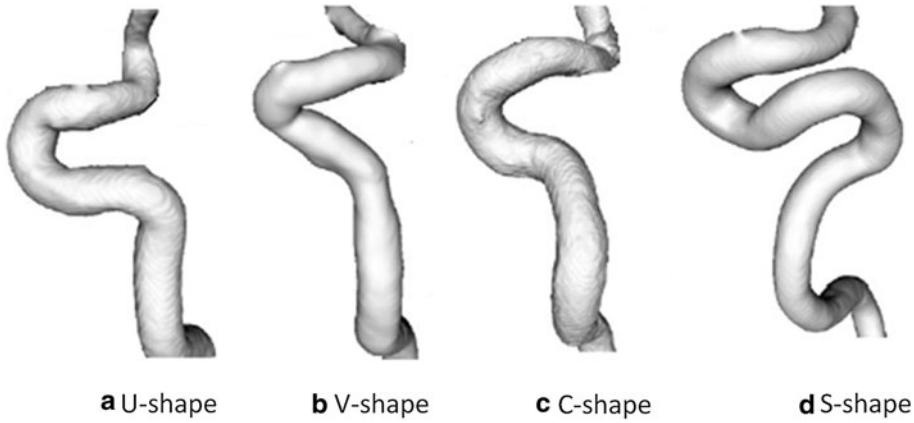

Fig. 1 Examples of carotid siphon shape classes

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Table 1 Patients' demographics data

	Subjects	Age	Gender		Hypertension	Diabetes	Smoker
	N	years	Male	Female	*N*	*N*	*N*
Control group	30	68 ± 10	16	14	26	16	5
Stenosed group	44	59 ± 9	30	14	41	21	9

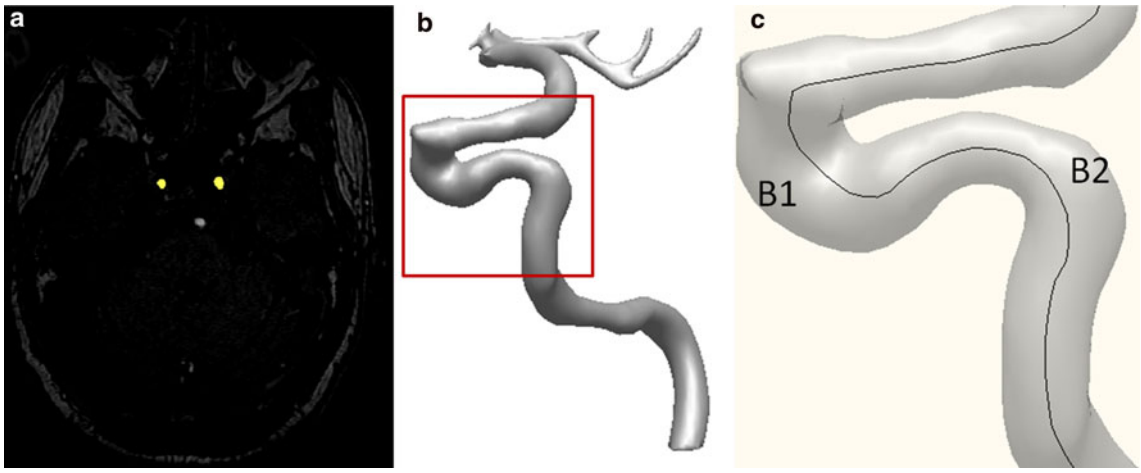

Fig. 2 **a** MRA image for internal carotid arteries (ICA). The *yellow parts* denote the horizontal sections of ICAs. **b** 3D model of an ICA reconstructed from the MRA images. The *red rectangle* covers the siphon section. **c** Centerline extracted from the artery. B1 and B2 are the anterior and posterior siphon bends, respectively

as the radius of the osculating circle (OC) fitting to the centerline in the osculating plane (OP), using least squares optimization method (Fig. 3). The first and last overlapped point between OC and the centerline were defined as P1 and P2, respectively, which were referred as the beginning and end of the bend. The midpoint between P1 and P2 along the centerline was defined as P3. Vessel cross-section area is considered related to hemodynamic properties [2]. Thus, we defined local vessel radius at P1, P2, and P3 (R1, R2, R3) as the radius of a circle perpendicular to the centerline at these three points, respectively.

The vectors tangent to the centerline at P1 and P2 in OP were defined as V1 and V2, respectively. The angle of the bend was characterized in terms of the angle from V1 to V2. The distance from the end of B2 to the beginning of B1 was defined as the distance of the two bends (D). The angle between the two bends was characterized as the angle between the two OPs (orientation of OP was defined as V_{OP}).

All the geometric parameters described above are summarized in Table 2.

Statistical analysis

For all geometric parameters listed in Table 2, mean, SD (in the following reported as mean ± SD), and range were computed.

Control group was divided into three types according to the anatomical shape, as clinically reported. Means and SDs of each parameter were calculated separately for each type. The statistical significance of the differences in the distribution of the geometric parameters between the three types was assessed by means of a Student *t* test.

To identify the performance of individual geometric parameters as classifiers of ICA shape, receiver-operating characteristics (ROC) analysis was performed on each of them. The area under the curve (AUC) was taken as a global figure of classifier performance. Optimal thresholds for the classifiers were obtained by maximizing the Matthews correlation coefficient which aims at finding the levels that maximize the sensitivity and specificity.

Multivariate logistic regression analysis was performed to assess the potential for a combination of geometric parameters in discriminating ICA shapes. Multivariate logistic regression models built from different combinations of geometric parameters, taken as independent variables, underwent a selection process based on the minimization of the Akaike information criterion. The geometric parameters with larger AUC (AUC > 0.75) in the ROC analysis were selected for the model. Estimates of coefficients and P values were reported for the obtained optimal model. The optimal model was expressed as:

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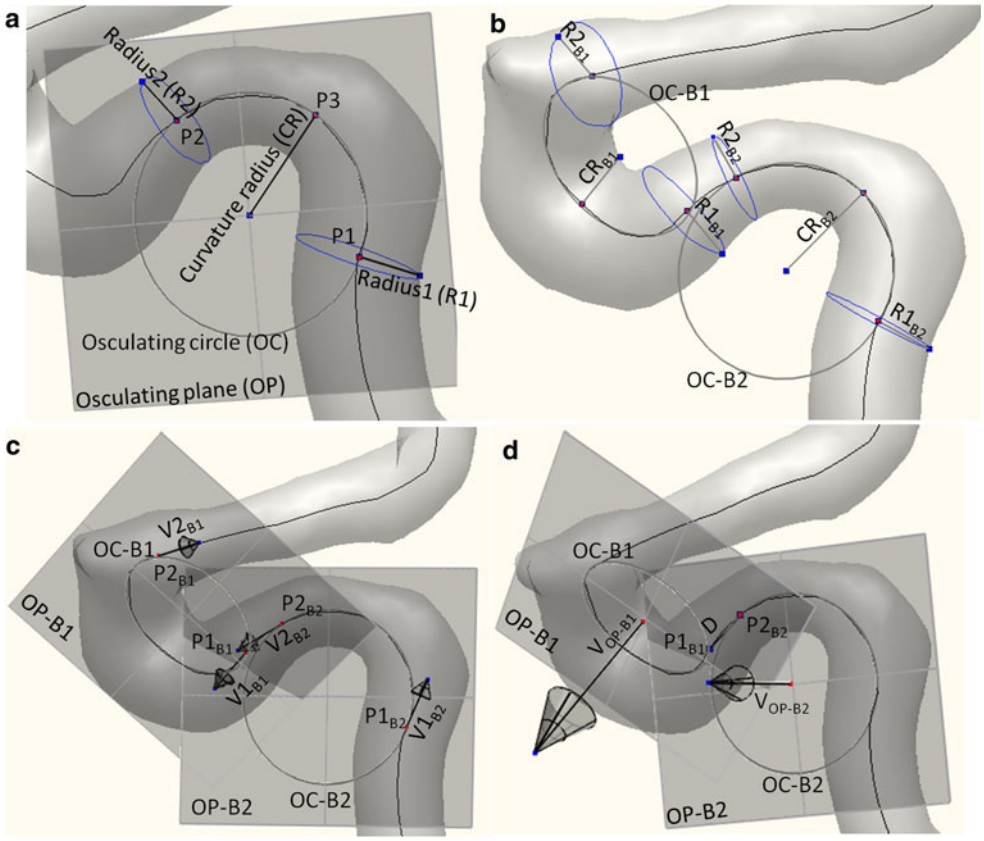

Fig. 3 Geometric characterization of internal carotid artery (ICA). **a** Representation of the local osculating circle (*OC*) fitting to the bend of the centerline and the osculating plane (*OP*). The curvature radius (*CR*) of the bend is defined as the radius of OC. The first and last overlap point between OC and the centerline are defined as P1 and P2. The midpoint between P1 and P2 is P3. The radius of the artery at P1, P2, and P3 are defined as R1, R2, and R3, respectively. **b** Measurement of CR, R1, R2, and R3 at B1 and B2. **c** The vectors tangent to the centerline at $P1_{B2}$, $P2_{B2}$, $P1_{B1}$, and $P2_{B1}$ are defined as $V1_{B2}$, $V2_{B2}$, $V1_{B1}$, and $V2_{B1}$, respectively. **d** The vectors normal to OP B2 and OP B1 are defined as $V_{OP\ B2}$ and $V_{OP\ B1}$, respectively. *D* denotes the distance from $P2_{B2}$ to $P1_{B1}$

$$\ln\frac{P_v}{P_u} = Const1 + \sum_i B1_i G_i \quad (1)$$

$$\ln\frac{P_c}{P_u} = Const2 + \sum_i B2_i G_i \quad (2)$$

where P_u, P_v, and P_c are the odds of finding a U, V, and C-shaped ICA, respectively; G_i means the geometric parameters selected by the multivariate logistic regression analysis; $B1_i$ and $B2_i$ are the coefficients. The model means that if the siphon of ICA is U-shaped, then the ratio of $\frac{P_u}{P_v}$ and $\frac{P_u}{P_c}$ would be much larger than 1. ICAs in control group were reclassified according to the multivariate logistic regression models. The results were compared with the classification clinically reported. The average geometric parameters were calculated for each type of ICA that was same, classified by the multivariate logistic regression model and the radiologist. Hemodynamic analysis was performed for the ICA models with the average geometric parameters.

The incidence of stenoses in the stenotic group was compared between each type of ICAs with Chi-square test. The difference of the incidence was compared with the results of hemodynamic simulation.

Table 2 Symbols and descriptions of geometric parameters

Symbol	Description
Geometric parameters for B1	
$R1_{B1}$, $R2_{B1}$, $R3_{B1}$	Radius of ICA at P1, P2, P3 in B1, respectively
$R_{av\ B1}$	Average of $R1_{B1}$, $R2_{B1}$, $R3_{B1}$
CR_{B1}	Curvature radius of B1
$CR_{std\ B1}$	Ratio of CR_{B1} to $R_{av\ B1}$
α_{B1}	Angle between $V1_{B1}$ and $V2_{B1}$
Geometric parameters for B2	
$R1_{B2}$, $R2_{B2}$, $R3_{B2}$	Radius of ICA at P1, P2, P3 in B2, respectively
$R_{av\ B2}$	Average of $R1_{B2}$, $R2_{B2}$, $R3_{B2}$
CR_{B2}	Curvature radius of B2
$CR_{std\ B2}$	Ratio of CR_{B2} to $R_{av\ B2}$
α_{B2}	Angle between $V1_{B2}$ and $V2_{B2}$
Geometric parameters between two bends	
D	Distance between $P2_{B2}$ and $P1_{B1}$
β	Angle between $V_{OP\ B2}$ and $V_{OP\ B1}$

Hemodynamic validation

According to the average geometric parameters of each types of ICA, three models of ICA were designed for the hemodynamic analysis. The models of ICAs were meshed in Gambit software (ANSYS, US). The tetrahedral meshes were used for the interior of the blood vessel, while more detailed hexahedral meshes were used near the wall of the blood vessel, to acquire precise results of WSS.

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The inlet and outlet were set perpendicular to the centerline for ICA models. The inflow boundary condition was a time-dependent velocity inlet, described as:

$$v = \begin{cases} 0.3 + 0.1[\cos 8\pi(t - 0.125)] & t \in [0, 0.125) \\ 0.35 + 0.05[\cos 8\pi(t - 0.125)] & t \in [0.125, 0.25) \\ -\frac{2}{15}(t - 2.5) & t \in [0.25, 1) \end{cases} \quad (3)$$

The outlet was set to be a free outflow without any mass loss. The blood was considered as incompressible Newtonian fluid with the density $\rho = 1056$ kg/m^3 and the dynamic viscosity $\mu = 4 \times 10^{-3}$ kg/ms [10]. Flow in ICA was simulated with the finite volume-based software Fluent (ANSYS, US) and using a second-order unsteady solver. The time step was set to 0.001 s to get time step independent results. The calculation was performed for six cycles. And the data of the last cycle were considered as the simulation results to make sure the convergence of the solution.

Results

Although four types of ICA shape had been clinically reported before, S-shaped ICA was not found in the present study. The shape of ICA was classified into three types by a senior radiologist for the cases in control group. The number and proportion of the ICAs with different shapes are reported in Table 3.

ICA geometry

Geometry reconstruction was performed successfully for all cases in control and stenosed groups in the study (Fig. 4). In each model, centerlines were successfully computed for all the branches. Means, SDs, and range of all geometric parameters computed for control group are reported in Table 4.

The curvature radii of the two bends along the carotid siphon (CR_{B1} and CR_{B2}) were measured, and ranged from 1.71 to 6.56 mm (mean 3.44 ± 0.82) and 2.74 to 12.83 mm (mean 4.82 ± 2.19) for B1 and B2, respectively. The mean radius of the siphon ($R_{av\text{-}B1}$ and $R_{av\text{-}B2}$) was 2.22 ± 0.32 and 2.49 ± 0.36 mm at B1 and B2, respectively, in accordance with a value of about 2 mm commonly found in the literature [18]. Because of anatomic differences in the course of ICA among subjects, the mean radius of blood vessel and the curvature radius at B2 were found significantly different between three types of ICA ($R_{av\text{-}B2}$: $p_{uv} = 0.001$; CR_{B2}: $p_{uv} = 0.000$, $p_{uc} = 0.000$) (Fig. 5). The effect of curvature is normally assessed by the ratio of the curvature to the radius of vessel [23]. Therefore, the curvature radius is standardized by the local radius of blood vessel ($CR_{std\text{-}B1}$ and $CR_{std\text{-}B2}$). The difference between ICA classes was even larger when the standardized curvature was analyzed ($p_{uv} = 0.000$, $p_{uc} = 0.000$). Consequently, the standardized curvature radius was used for further analysis in the study.

The angles of the two bends along the siphon (α_{B1} and α_{B2}) were 155.2 ± 24.4 and 110.6 ± 38.8° for B1 and B2, respectively. The angle of B1 was found significantly different between U and C-shaped ICAs ($p = 0.011$). The difference was also significant between the angles of B2 in the three types of ICA ($p_{uv} = 0.000$, $p_{uc} = 0.000$). For the distance between the two bends (D), the value was 4.02 ± 1.32 mm which was significantly different between U and C-shaped ICAs ($p_{uc} = 0.007$). The angle between the two bends (β) was 45.5 ± 17.4°, which was also significantly different between the three ICA classes ($p_{uc} = 0.000$, $p_{vc} = 0.000$).

For all the geometric parameters that were found significantly different between ICA classes, ROC analysis was performed to select the optimal threshold for the classification of ICA. As a result, the parameters with that AUC larger than 0.75 were highlighted in Table 5 because they demonstrate some effectiveness in discriminating ICA shapes, and were also selected for the multivariate logistic regression model. Of all quantities, $CR_{std\text{-}B2}$ and β were associated with the highest AUC (0.95) reflecting the fact that the shape of ICA mainly depends on the curvature of B2 and the angle between B1 and B2. α_{B2} had the second-largest AUC (0.94) indicating that the angle of B2 also played an important role in the ICA classification. Optimal thresholds were computed for these parameters based on the Matthews correlation coefficient.

Multivariate logistic analysis led to an optimal model including only $CR_{std\text{-}B2}$, α_{B2}, and β as independent variables. The multivariate logistic model takes the form:

$$\ln\frac{P_v}{P_u} = -12.704 + 5.259CR_{std\ B2} - 0.833\beta + 3.206\alpha_{B2} \quad (4)$$

$$\ln\frac{P_c}{P_u} = -16.788 + 1.82CR_{std\ B2} + 5.035\beta + 3.878\alpha_{B2} \quad (5)$$

A summary of the coefficients and P values reported in Table 6. To classify the anatomic shape of ICA, the

Table 3 The number and proportion of the ICAs with different shapes

	U shape	V shape	C shape
Number	33	17	10
Proportion (%)	55.0	28.3	16.7

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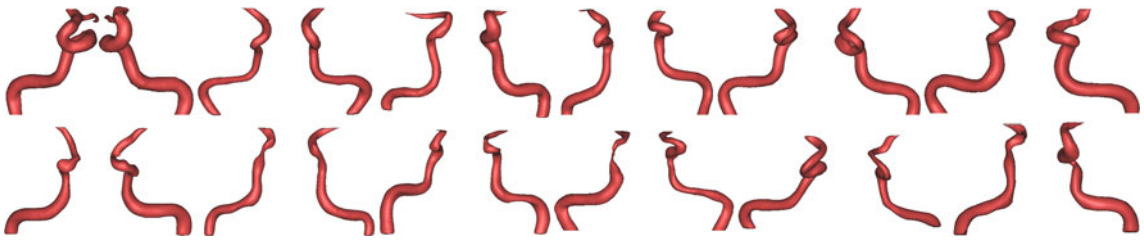

Fig. 4 Surface models reconstructed from MRA images. *The upper raw* control group, *the lower raw* stenosed group

Table 4 Mean ± SD, minimum, and maximum values for geometric parameters

Geometric parameter	Mean ± SD	Minimum	Maximum
$R_{av\ B1}$ (mm)	2.22 ± 0.32	1.62	3.00
CR_{B1} (mm)	3.44 ± 0.82	1.71	6.56
$CR_{std\ B1}$	1.56 ± 0.37	1.04	2.85
α_{B1} (°)	155.2 ± 24.4	110.3	211.8
$R_{av\ B2}$ (mm)	2.49 ± 0.36	1.45	3.24
CR_{B2} (mm)	4.82 ± 2.19	2.74	12.83
$CR_{std\ B2}$	2.02 ± 1.07	1.04	5.35
α_{B2} (°)	110.6 ± 38.8	32.1	204.4
D (mm)	4.02 ± 1.32	1.28	6.76
β (°)	45.5 ± 17.4	9.8	84.7

average accurate rate of the model was 88.5 %, which was computed by comparing the classification results of control group with the clinical report.

Stenosed group was classified by the multivariate logistic model. The incidence of stenoses was compared between the three types. According to the clinical reports, the stenosis usually occurs at C2 (the latter half of B1) and C4 (the whole B2) sections [16, 22]. Therefore, the incidences of stenoses at C2, C4 were also analyzed individually. The results show that the incidence in the U-shaped ICA is higher than the other two types (Fig. 6). At C2 section, the incidence has no significant differences. But at C4 section, the incidence is significantly higher in the U-shaped ICA.

In order to reconstruct the typical shapes of ICAs, the average geometric parameters of each type of ICA were computed for ICAs that were same, classified by the multivariate logistic model and the clinical report in control group (Table 7). R_{av} is the mean of $R_{av\text{-}B1}$ and $R_{av\text{-}B2}$. Typically, the U-shaped ICA has a larger angle and smaller curvature radius at B2 than the other two types; the C-shaped ICA has the largest angle between the two bends.

Hemodynamic validation

According to the average geometric parameters of each type of ICA, three typical models were reconstructed. The cross-section was simplified as a circle with a uniform radius. All the bifurcations along the ICA were removed. The shapes of the three models are obviously different because of the significant differences between CR_{B2}, α_{B2}, and β. The hemodynamic results also show obvious differences between three types of ICA, reflecting the fact that the shape plays a significant role in the hemodynamics in ICAs (Fig. 7). The time-averaged WSS contour shows that there are three low WSS regions along the carotid siphon in all types of ICA. The three low WSS regions are at the outer wall of the former half of B2, the inner wall of the latter half of B2, and the inner wall of the latter half of B1, respectively. But in the former two regions, the magnitude of WSS in the U-shaped ICA is even lower than the other two types. The oscillation shear index (OSI, the measurement of oscillatory WSS) contour shows that the value is only high at the third region in the V and C-shaped ICAs. But in the U-shaped, the value is high in the three regions indicating that the U-shaped ICA may have more locations preferred to stenoses, and have high risk for atherosclerotic stenoses.

Discussion

In this study, the complex geometry of ICA was quantitatively investigated between three types of ICAs. For each case, a 3D model of the ICA was reconstructed, and the centerline was automatically generated along the carotid siphon. Geometry of the bends along the siphon was characterized in relation to the ICA classification. Statistical analysis and hemodynamic simulation were both performed to assess the effect of ICA geometry on the incidence of stenoses.

Geometric parameters

In light of present results, the ICA is described as two near-planar bends concatenated in a nonplanar fashion. As a result, the anatomic shape of ICA is mainly characterized by the geometric parameters in and between the local planes of curvatures.

Among the geometric parameters studied in this paper, $CR_{std\text{-}B2}$ and α_{B2} basically quantifies the intensity of

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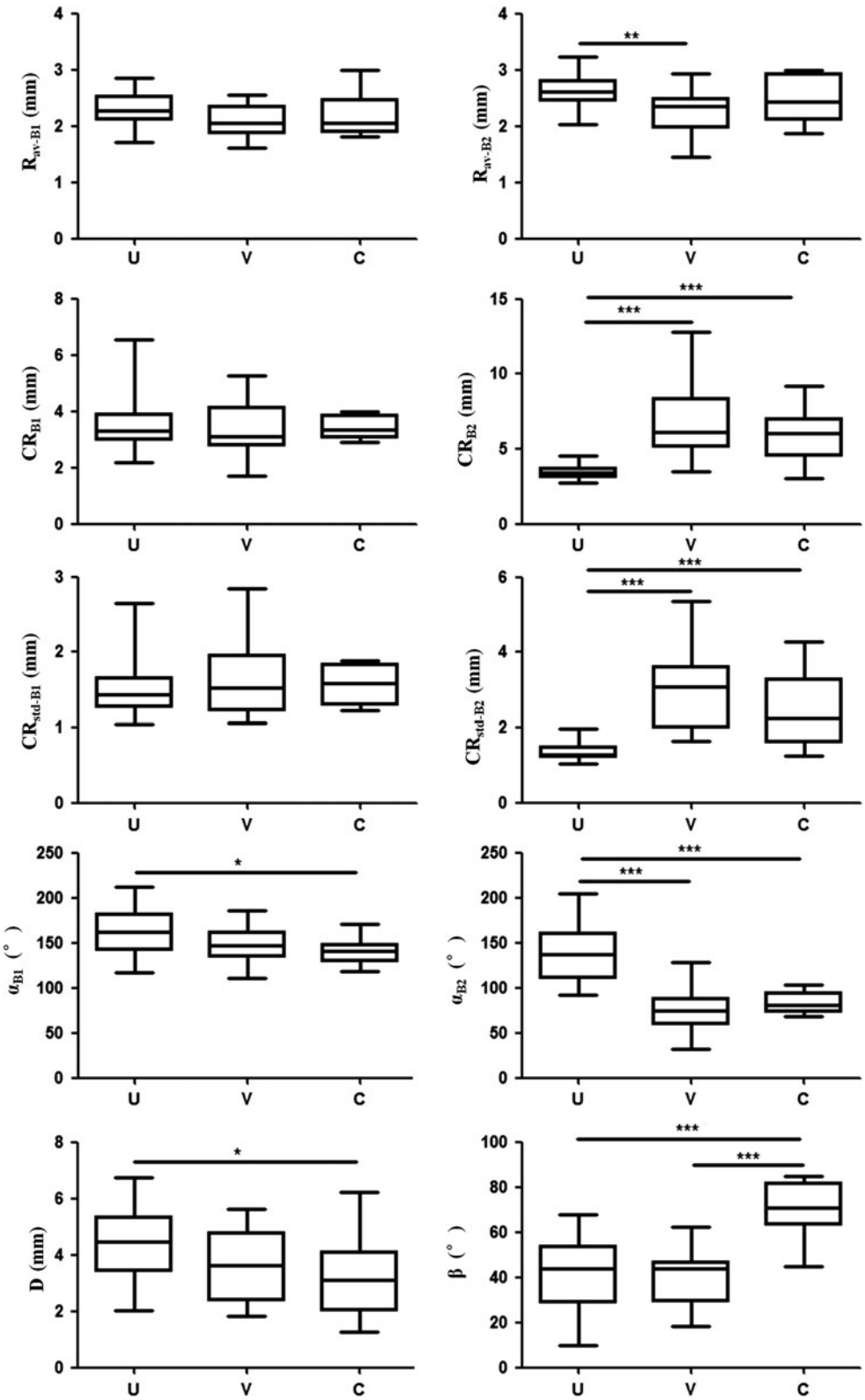

Fig. 5 Box plot showing the distribution of the geometric parameters between different shapes. *Top raw* Rav B1 and Rav B2, *second raw* CRB1 and CRB2, *third raw* CRstd B1 and CRstdB2, *forth raw* αB1 and αB2, *bottom raw* D and β. Statistically significant difference: *($p < 0.05$), **($p < 0.01$), ***($p < 0.001$)

curvature at B2. Therefore, the differences of the two parameters between ICA classes cause different distribution of hemodynamic factors along the arterial wall at B2. The hemodynamic simulation validates that small $CR_{\text{std-B2}}$, but large α_{B2} would result in disadvantageous hemodynamic factors such as low WSS and high OSI, at both the inner wall and outer wall of B2. β denotes the angle between the two bends along the siphon which also plays

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Table 5 Receiver operating characteristics curve analysis of the geometrical parameters

Geometric parameter	AUC	Optimal threshold	Odds ratio
$CR_{std\ B2}$	0.95	1.655	82.67
$R_{av\ B2}$	0.74	2.455	6.40
β	0.95	56.35	82.80
D	0.70	4.21	3.23
α_{B1}	0.70	149	4.18
α_{B2}	0.94	101.35	20.53

Table 6 Multivariate logistic regression model selected through minimization of the Akaike information criterion with three covariates

Geometric parameter	*p*	B1*	B2
Intercept	0.000	12.704	16.788
$CR_{std\ B2}$	0.000	5.259	1.82
β	0.000	0.833	5.035
α_{B2}	0.008	3.206	3.878

* B1 and B2 denote the coefficients in formula (1) and (2), respectively

an important role in the ICA classification. Lee et al. [9] recently studied fluid dynamics in double bends paying particular attention to the effect of their nonplanar concatenation. In their simulations, the terminal bend influences the out flow pattern to a different extent depending on the orientation of its upstream bend. However, in the present study, the angle between the two bends may influence the hemodynamic factors between B1 and B2, but not at B1 and the downstream.

Shape classification

The geometric description of the ICA siphon confirmed the heterogeneity of the anatomic shape reflected by the inter- and intra-individual variability in the geometric parameters in the study. Nevertheless, common patterns could be indentified within each type of ICAs. Significant differences exist between the three ICA classes regarding the geometric parameters of $CR_{std\text{-}B2}$, α_{B2}, and β. The distribution of the geometric parameters tends to cluster to several classes, which is the basis for developing a classifier for the anatomic shape of ICAs.

Table 7 The average geometrical parameters of each ICA class

Geometric parameter	U	V	C
R_{av} (mm)	2.5	2.2	2.4
CR_{B1} (mm)	3.6	3.4	3.5
CR_{B2} (mm)	3.4	7.3	6.8
α_{B1} (°)	164	143	142
α_{B2} (°)	139	77	82
β (°)	42	37	74
D (mm)	4.4	3.7	3.0

To the best of our knowledge, with the exception of selected works, the methods and significance of the classification for the ICA shape has not been thoroughly investigated[19, 26]. Recently, Bogunovic [1] developed a classifier for the ICA shape with a computer-based automatic method. But the accurate rate (63 84 %) is lower than that achieved in this study. In additional, the three geometric parameters correlated to the ICA classification were firstly abstracted from the shape feature of ICA by the multivariate logistic regression, facilitating the clinical application of the measurement.

The significance of the ICA classification was realized recently. The ICA classification was found correlated to different settings of aneurysm development [27]. Sangalli et al. studied 65 subjects and found that in the ICAs with aneurysms at or after the terminal bifurcation, 70 % of them are V-shaped. Moreover, all the ICAs without aneurysm are U-shaped. Therefore, the ICA classification was considered as an important factor correlated to the hemodynamics and pathological mechanism of intracavernous aneurysms. Besides the correlation between the ICA classes and the presence of aneurysm or its rupture status, the direct clinical relevance of the shape classes in selecting

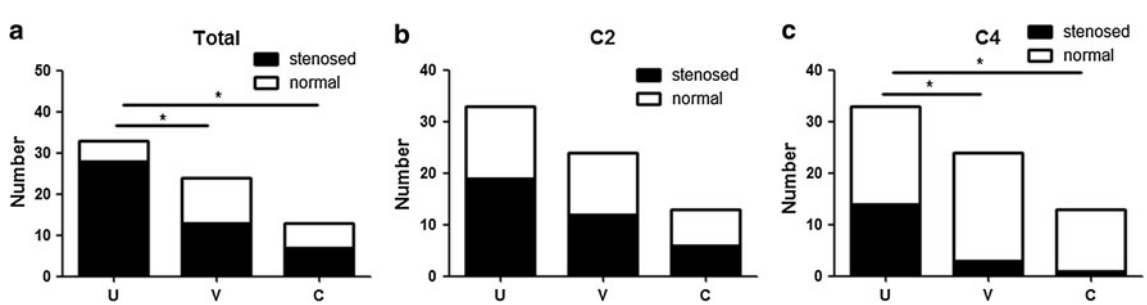

Fig. 6 Comparison of the incidence of stenoses between three types of ICAs. **a** Total incidence at C2 and C4. **b** Incidence at C2. **c** Incidence at C4

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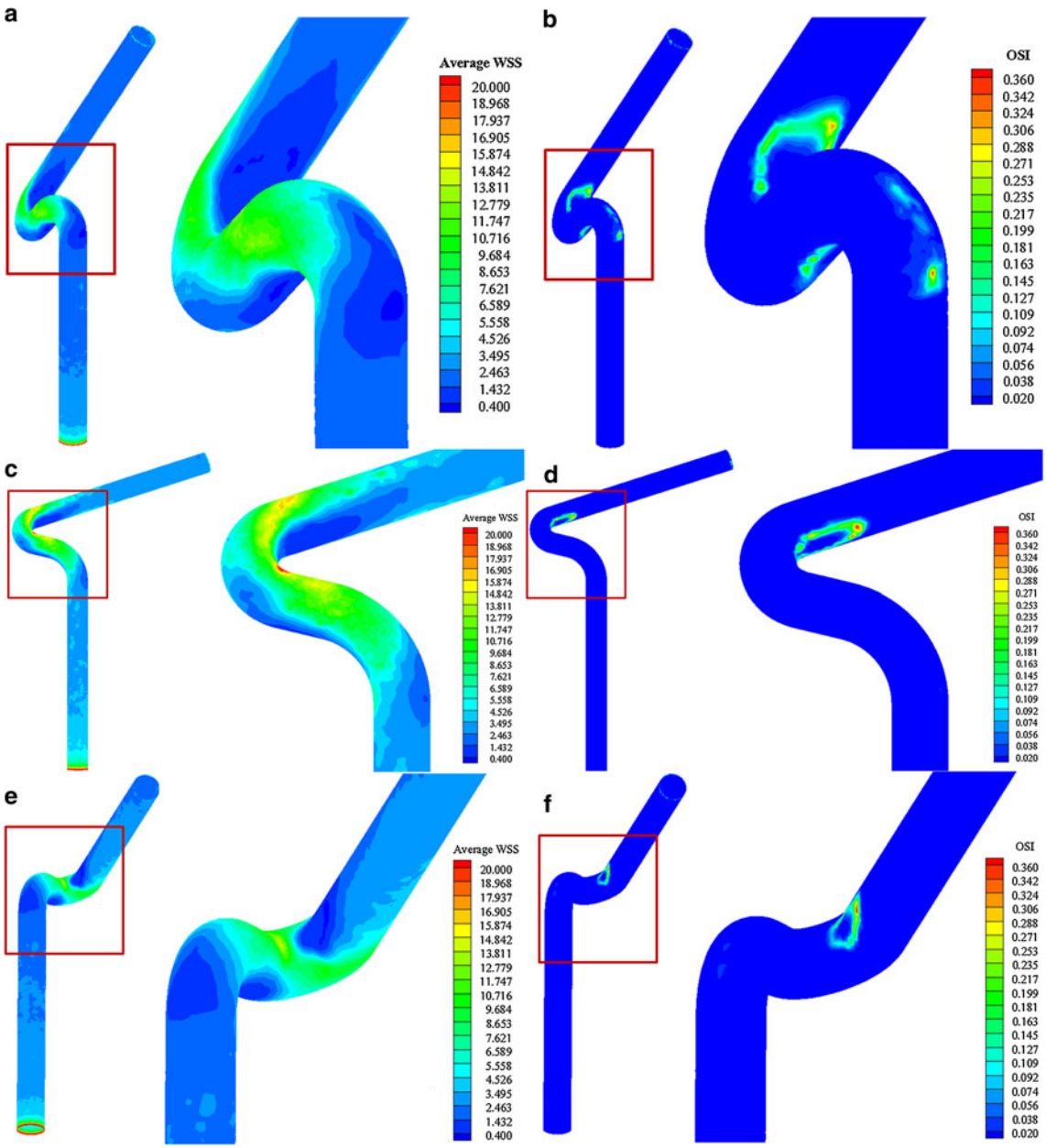

Fig. 7 The magnitude of time averaged WSS and OSI at the siphon for three types of ICA. **a**, **b** U shaped; **c, d** V shaped; **e, f** C shaped. The color scale is in Pa in average WSS contours

the endovascular treatment strategy has also been proposed in 2008.

However, the potential association between the ICA classification and stenoses was firstly mentioned by us in 2012 [30]. In the present study, the association was proved by the statistic results and validated by the hemodynamic simulation. The different incidence of ICA stenoses between the three types indicates that the geometry of ICA plays a significant role in the development of stenoses. Hemodynamic simulation shows that the hemodynamic factors have different distribution pattern between ICA classes, validating the effect of ICA geometry on the hemodynamics and stenoses. Therefore, the significance of the study on the geometry and classification of ICA is obvious, because it has potential implication in predicting the risk for stenoses in the siphon.

Study limitation

The first limitation is related to the imaging modality used in the present study. The accuracy of the geometry measurement heavily depends on the imaging quality.

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Therefore, subjects were firstly selected according to the quality of MRA images. The increasing availability of high-resolution computed tomography and MR scanners will make it possible to extend a 3D arterial study to a larger number of subjects and to decrease the bias in the selection of the population in future studies.

The geometric measurement was simplified to several parameters along the siphon, which were selected according to the anatomical description for the shape classification. The parameters selected in the study represent the main characteristics of the ICA shape. The classifier developed with the three of the parameters shows an ability to classify the ICA shape effectively. However, the simplification may influence the ICA classification. More detailed measurement could achieve a better classifier for ICA.

Conclusion

In the present study, the potential of 3D geometric analysis for highlighting ICA classes associated with the location and incidences of stenoses has been demonstrated. Our results indicate the quantitative differences between three ICA classes, and provide an innovative classifier for the ICA shapes. The typical geometry of the three classes were modeled and hemodynamically simulated. The results suggest the association between the ICA classes, the hemodynamic factors, and the incidence of stenoses in the siphon, thus implying the potential significance in the risk prediction for intracranial ICA stenoses.

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Conflict of interest This study has no conflict of interest to report.

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

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[6] Reference §5.3

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[8] Reference §5.2

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(b	(b)(4)	(b)(6)	03/30/15	(b)(4)

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. BACKGROUND

(b)(4) [redacted]

4. REFERENCE DOCUMENTS

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APPENDIX A

Reperfusion Catheter ACE 64 (b)(4) [redacted] Test Flow Diagram

(b)(4) [redacted]

(b)(4) [redacted]

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APPENDIX B

Reperfusion Catheter ACE 68 (b)(4)) Test Flow Diagram

(b)(4)

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Revision History				
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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

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(b)(4)

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(b [redacted] **TEST SUMMARY**

(b)(4) [redacted]

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(b)(4)

[redacted]

6.1.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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(b)(4) [redacted]

6.2.1. Reperfusion Catheter ACE 64

(b)(4) [redacted]

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6.2.2. Reperfusion Catheter ACE 68

(b)(4)

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6.3. (b)(4) Testing (b)(4)

6.3.1. Reperfusion Catheter ACE 64

(b)(4)

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6.3.2. Reperfusion Catheter ACE 68

(b)(4)

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6.4. (b)(4) Test

6.4.1. Reperfusion Catheter ACE 64

(b)(4) [redacted]

6.4.2. Reperfusion Catheter ACE 68

(b)(4) [redacted]

6.5. Reperfusion Catheter / (b)(4) [redacted]

6.5.1. Reperfusion Catheter ACE 64

(b)(4) [redacted]

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6.5.2. Reperfusion Catheter ACE 68

(b)(4)

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6.6. Reperfusion Catheter Safety (b)(4) Testing)

6.6.1. Reperfusion Catheter ACE 64

(b)(4)

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6.6.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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(b)(4)

[redacted]

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6.7. (b)(4) Test

6.7.1. Reperfusion Catheter ACE 64

(b)(4)

6.7.2. Reperfusion Catheter ACE 68

(b)(4)

6.8. (b)(4)

6.8.1. Reperfusion Catheter ACE 64

(b)(4)

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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6.8.2. Reperfusion Catheter ACE 68

(b)(4) [redacted]

6.9. (b)(4) [redacted] Test

6.9.1. Reperfusion Catheter ACE 64

(b)(4) [redacted]

6.9.2. Reperfusion Catheter ACE 68

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b)(4) [redacted]

6.10.1. Reperfusion Catheter ACE 64

(b)(4) [redacted]

6.10.2. Reperfusion Catheter ACE 68

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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7. DATA

7.1. (b)(4)

7.1.1. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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7.1.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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7.2. (b)(4) Testing

7.2.1. Reperfusion Catheter ACE 64 (b)(4)

(b)(4)

[redacted]

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(b)(4)

[redacted]

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7.2.2. Reperfusion Catheter ACE 64/(b)(4)

(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4)

[redacted]

7.2.3. Reperfusion Catheter ACE 68 (b)(4) [redacted]

(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4) [redacted]

7.2.4. Reperfusion Catheter ACE 68/(b) [redacted]

(b)(4) [redacted]

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[redacted]

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(b)(4)

[redacted]

7.3. (b)(4) Testing

7.3.1. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b)(4)

[redacted]

7 3 2 Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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(b)(4)

[redacted]

7.4. (b)(4) Testing

7.4.1. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

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(b)(4)

[redacted]

7.4.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

(b)(4)

[redacted]

7.5. (b)(4) Testing

7.5.1. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

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(b)(4)

[redacted]

7.5.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

7.6. (b)(4) [redacted] Testing

7.6.1. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

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(b)(4)

[redacted]

7.6.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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Revision History				
Rev	(b)(4)	**Originator**	**Effective**	**Description of Change**
(	(b)(4)	(b)(6)	04/08/15	(b)(4)

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. BACKGROUND

(b)(4) [redacted]

4. REFERENCE DOCUMENTS

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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[redacted]

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9.4. (b)(4) Testing (b)(4)

(b)(4)

[redacted]

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(b)(4) [redacted]

9.5. (b)(4) [redacted] Test

(b)(4) [redacted]

(b)(4) [redacted]

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(b)(4)

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[redacted]

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(b)(4)

[redacted]

9.7.2. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

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(b)(4) [redacted]

9.8 [redacted] Test

(b)(4) [redacted]

(b)(4) [redacted]

9.2. (b)(4) [redacted] Test

(b)(4) [redacted]

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(b)(4)

[redacted]

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APPENDIX A

ACE Reperfusion Catheter Packaging and Shelf Life Test Flow Diagram

(b)(4)

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Revision History

Rev	(b)(4)	Originator	Effective	Description of Change
(	[redacted]	(b)(6) [redacted]	11/24/14	(b)(4) [redacted]
(	[redacted]	(b)(6) [redacted]	03/13/15	

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Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

(b)(4)

[redacted]

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4.5. (b)(4) Test

(b)(4)

[redacted]

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(b)(4)

4.8. (b)(4) Testing (b)(4)

(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4) [redacted] (b)(4)

7. TEST (b)(4) [redacted]

(b)(4) [redacted]

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[redacted]

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(b)(4)

[redacted]

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(b)(4)

[redacted]

7.1.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4)

[redacted]

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7.2. (b)(4) Testing (b)(4)

7.2.1. Reperfusion Catheter ACE 64

(b)(4)

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7.2.2. Reperfusion Catheter ACE 68

(b)(4) [redacted]

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(b)(4) [redacted]

(b)(4) [redacted]

(b)(4) [redacted]

(b)(4) [redacted]

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7.4.2. Reperfusion Catheter ACE 68

(b)(4) [redacted]

7.5. (b)(4) [redacted] Testing

7.5.1. Reperfusion Catheter ACE 64

(b)(4) [redacted]

7.5.2. Reperfusion Catheter ACE 68

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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7.6. Reperfusion Catheter (b)(4)

7.6.1. Reperfusion Catheter ACE 64

(b)(4)

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(b)(4)

[redacted]

7.6.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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(b)(4)

[redacted]

[redacted]

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8.2.2. Reperfusion Catheter ACE 68

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[redacted]

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8.6.1. Reperfusion Catheter ACE 68 (b)(4)

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8.7.1. Reperfusion Catheter ACE (b)(4)

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.9 ([redacted] Testing

b

8.9.1. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.9.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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8.10. (b)(4)

8.10.1. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

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8.10.2. Reperfusion Catheter ACE 68

(b)(4)

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8.11. (b)(4) Testing

8.11.1. Reperfusion Catheter ACE 64

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.11.2. Reperfusion Catheter ACE 68

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.12. (b)(4) Testing

8.12.1. Reperfusion Catheter ACE 64

(b)(4)

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8.12.2. Reperfusion Catheter ACE 68

(b)(4)

[redacted]

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[redacted]

[9] Reference §6.3

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[10] Reference §6.4

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8.13.2. Reperfusion Catheter ACE 68

8.13.2.1. (b)(4) Testing

(b)(4)

[redacted]

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(b)(4)

(b)(4)

[redacted]

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8.13.2.1.3. Reperfusion Catheter ACE 68/(b)(4) [redacted]

(b)(4) [redacted]

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.13.2.1.4. Reperfusion Catheter ACE 68/(b)(4)

(b)(4)

[redacted]

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8.13.2.2. (b)(4) [redacted] Testing

8.13.2.2.1. Reperfusion Catheter ACE 68 (b)(4) [redacted]

(b)(4) [redacted]

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.13.2.2.2. Reperfusion Catheter ACE 68 (b)(4) [redacted]

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.13.2.2.3. Reperfusion Catheter ACE 68 (b)(4) [redacted]

(b)(4) [redacted]

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8.13.2.2.4. Reperfusion Catheter ACE 68 (b)(4) [redacted]

(b)(4) [redacted]

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8.13.2.2.5. Reperfusion Catheter ACE 68 (b)(4)

(b)(4)

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8.13.2.2.6. Reperfusion Catheter ACE 68 (b)(4)

(b)(4)

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8.13.2.2.7. Reperfusion Catheter ACE 68 (b) (4)

(b)

(b)(4)

[redacted]

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Revision History				
Rev	**ECO #**	**Originator**	**Effective**	**Description of Change**
(	[redacted]	(b)(6)	08/13/14	(b)(4)
(	[redacted]	(b)(6)	08/21/14	

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. RESPONSIBILITY

(b)(4) [redacted]

4. REFERENCE DOCUMENTS

(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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[redacted]

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8.12. (b)(4) **Test**

(b)(4)

[redacted]

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[redacted]

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[redacted]

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[redacted]

[1] Test Method is based on ISO10555-1: 2013, Annex A

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9.1.2. Reperfusion Catheter ACE 68

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[redacted]

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[redacted]

[2] Reference Section 10.

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[redacted]

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(b)(4)

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[redacted]

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[redacted]

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APPENDIX A

Reperfusion Catheter ACE 64 ((b)(4) Test Flow Diagram

(b)(4)

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APPENDIX B

Reperfusion Catheter ACE 68 (b)(4) Test Flow Diagram

(b)(4)

[redacted]

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Revision History

Rev	(b)(4)	Originator	Effective	Description of Change
(	(b)(4)	(b)(6)	07/15/14	(b)(4)
(	(b)(4)	(b)(6)	08/21/14	

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

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[redacted]

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[redacted]

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(b)(4)

[redacted]

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Revision History				
Rev	(b)(4)	**Originator**	**Effective**	**Description of Change**
(b	(b)(4) [redacted]	(b)(6) [redacted]	[redacted]/03/15	(b)(4) [redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

1. PURPOSE

(b)(4)

2. SCOPE

(b)(4)

3. BACKGROUND

(b)(4)

4. REFERENCE DOCUMENTS

(b)(4)

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(b)(4)

[redacted]

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Revision History

Rev	ECO #	Originator	Effective	Description of Change
(b	[redacted]	(b)(6)	03/19/15	(b)(4) [redacted]
(b	[redacted]	(b)(6)	03/19/15	

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English

Device Description

The Penumbra System® is comprised of several devices:

- Penumbra Reperfusion Catheter
- Penumbra Aspiration Pump
- Penumbra Pump/Canister Tubing
- Penumbra Aspiration Tubing
- Penumbra Separator

The Penumbra System is designed to remove thrombus from the vasculature using continuous aspiration. The Reperfusion Catheter targets aspiration from the pump directly to the thrombus. The Separator may be used to clear the lumen of the Reperfusion Catheter should it become blocked with thrombus. The use of the Separator may not be necessary when using a Reperfusion Catheter with an I.D. of 0.054in or larger. The Reperfusion Catheter is introduced through a guide catheter or long femoral sheath and into the intracranial vasculature and guided over a neurovascular guidewire to the site of the primary occlusion. The Penumbra Reperfusion Catheter is used with the Aspiration Pump to aspirate thrombus from an occluded vessel. As needed, a Penumbra Separator may be deployed from the Reperfusion Catheter to assist with thrombus removal. The Penumbra Separator is advanced and retracted through the Penumbra Reperfusion Catheter at the proximal margin of the primary occlusion to facilitate clearing of the thrombus from the Reperfusion Catheter tip. For the aspiration source, the Penumbra Reperfusion Catheter is used in conjunction with the Aspiration Pump, which is connected using the Penumbra Aspiration Tubing and the Penumbra Pump/Canister Tubing. The Penumbra Reperfusion Catheter is provided with a steam shaping mandrel and rotating hemostasis valve, and a peelable sheath. The Penumbra Separator is provided with an introducer and torque device. The devices are visible under fluoroscopy.

Indication for Use

The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. The Reperfusion Catheters ACE 64 and ACE 68 are intended for use in revascularization within the Internal Carotid Artery (ICA) within 8 hours of symptom onset.

Contraindications

There are no known contraindications.

Warnings

- The Penumbra System should only be used by physicians who have received appropriate training in interventional neuro-endovascular techniques and treatment of acute ischemic stroke.
- Do not advance, retract or use any component of the Penumbra System against resistance without careful assessment of the cause using fluoroscopy. If the cause cannot be determined, withdraw the device or system as a unit. Unrestrained torquing or forced insertion of the catheter or separator against resistance may result in damage to the device or vessel.
- Do not use the Penumbra System with a pump other than the Penumbra Aspiration Pump.

Precautions

- The device is intended for single use only. Do not resterilize or reuse. Resterilization and/or Reuse may result in ineffective catheter coating lubrication, which may result in high friction and the inability to access the target neuro vasculature location.
- Do not use kinked or damaged devices. Do not use open or damaged packages. Return all damaged devices and packaging to the manufacturer/ distributor.
- Use prior to the “Use By” date.
- Use the Penumbra System in conjunction with fluoroscopic visualization.
- Maintain a constant infusion of appropriate flush solution.
- When performing aspiration, ensure that the Penumbra Aspiration Tubing valve is open for only the minimum time needed to remove thrombus. Excessive aspiration or failure to close the Penumbra Aspiration Tubing valve when aspiration is complete is not recommended.
- The Penumbra Separator is not intended for use as a neurovascular guidewire. If repositioning of the Penumbra Reperfusion Catheter is necessary during the revascularization procedure, such reposition should be performed over an appropriate neurovascular guidewire using standard microcatheter and guidewire techniques.
- Do not use automated high-pressure contrast injection equipment with the Penumbra Reperfusion Catheter because it may damage the device.
- Administration of anticoagulants and antiplatelets should be suspended until 24 hours post-treatment. Medical management and acute post stroke care should follow the ASA guidelines.[1] Any neurological deterioration should be evaluated by urgent CT scan and other evaluations as indicated according to investigator/hospital best practice.
- The total time allowed to achieve patient revascularization is 120 minutes of using the Penumbra System.

Potential Adverse Events

Possible complications include, but are not limited to, the following:

- allergic reaction and anaphylaxis from contrast media
- acute occlusion
- air embolism
- arteriovenous fistula
- death
- device malfunction
- distal embolization
- emboli
- false aneurysm formation
- hematoma or hemorrhage at access site
- inability to completely remove thrombus
- infection
- intracranial hemorrhage
- ischemia
- kidney damage from contrast media
- neurological deficits including stroke
- vessel spasm, thrombosis, dissection, or perforation

Procedure

1. Refer to **Warnings, Precautions**, and **Potential Adverse Events** prior to use.
2. As each device of the Penumbra System is used, remove the device from the packaging, and inspect for damage or for kinks.
3. Prepare Penumbra System devices for use by flushing the packaging hoop and device with heparinized saline (includes Penumbra Reperfusion Catheter and Penumbra Separator only).
4. Prepare a guide catheter or long femoral sheath according to the manufacturer’s *Instructions for Use*.
5. Place the guide catheter or long femoral sheath into the appropriate cerebral artery that is proximal to the thrombus occlusion site.

Penumbra Reperfusion Catheter Preparation and Use

1. Confirm vessel diameter, and select an appropriate size Penumbra Reperfusion Catheter (See **Table 1**).
2. The Penumbra Reperfusion Catheter tip may be shaped using the steam shaping mandrel provided.
3. Attach the rotating hemostasis valve provided to the Penumbra Reperfusion Catheter.
4. Attach the Penumbra Aspiration Tubing to the Aspiration Pump and turn on the Aspiration Pump (Refer to the Aspiration Pump *Operation Manual*). Allow the Aspiration Pump to run for at least one minute prior to use, and confirm

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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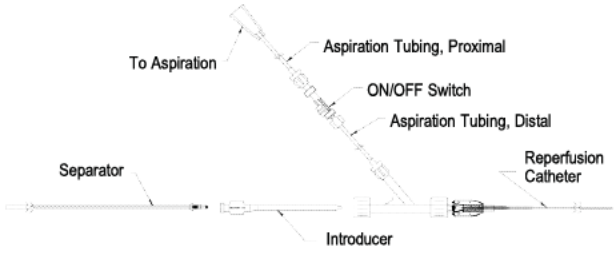
that the Aspiration gauge reads −20inHg. Ensure the valve on the Penumbra Aspiration Tubing is switched to the OFF position.

5. Connect the Aspiration Tubing to the side port of the rotating hemostasis valve as shown in **Figure 1**.

Figure 1 – Assembled Aspiration System with Penumbra Separator



6. Insert the Penumbra Reperfusion Catheter into a rotating hemostasis valve connected to the proximal hub of a guide catheter. If a guide catheter is not used, insert the Penumbra Reperfusion Catheter through the valve of the long femoral sheath using the peelable sheath. After inserting the Penumbra Reperfusion Catheter, remove the peelable sheath from the vascular sheath, and peel from the Penumbra Reperfusion Catheter shaft.
7. Using conventional catheterization techniques under fluoroscopic guidance, advance the Penumbra Reperfusion Catheter into the target vessel over an appropriate neurovascular guidewire. Position the Penumbra Reperfusion Catheter proximal to the thrombus. Remove the guidewire from the Penumbra Reperfusion Catheter.
8. To begin aspiration, open the valve on the Penumbra Aspiration Tubing to the ON position. To stop aspiration, switch the valve on the Penumbra Aspiration Tubing to the OFF position, and turn off the Aspiration Pump.
9. Using a 5cc or 10cc syringe, aspirate approximately 5cc of blood from the Penumbra Reperfusion Catheter to remove any thrombus that may remain in the catheter.
10. Obtain a post-treatment angiogram by injecting contrast media through the guide catheter.

Penumbra Separator Preparation and Use

1. If needed, select an appropriate size Penumbra Separator corresponding to the Reperfusion Catheter (see **Table 1**).

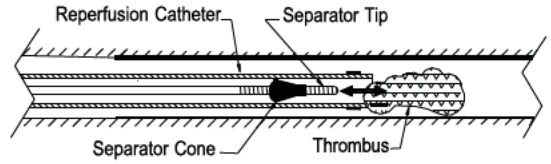
Table 1 – Separator/Reperfusion Catheter Device Size Selection

Vessel Size (mm)	Penumbra Reperfusion Catheter	Penumbra Separator
< 2.0	026	026
2.0 to 3.0	032 / 3MAX	032 / 3MAX
3.0 to 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX / ACE	054 / 5MAX

NOTE: Access to the site of occlusion may be aided by the triaxial use of a compatible inner microcatheter.

2. Using the introducer sheath provided, insert the Penumbra Separator through the rotating hemostasis valve and into the proximal hub of the Penumbra Reperfusion Catheter.
3. To begin aspiration, open the valve on the Penumbra Aspiration Tubing to the ON position, and advance/retract the Penumbra Separator to assist with aspiration and removal of the thrombus from the Reperfusion Catheter as shown in **Figure 2**.

Figure 2 – Thrombus Aspiration Using the Penumbra Separator



4. To stop aspiration, switch the valve on the Penumbra Aspiration Tubing to the OFF position, and turn off the Aspiration Pump.
5. Remove the Penumbra Separator, if used.
6. If necessary, additional Penumbra Separators and Reperfusion Catheters may be used to further remove thrombus at the discretion of the physician.

Clinical Data Summary

The Penumbra Pivotal trial was a prospective, single arm trial to assess the safety and effectiveness of the Penumbra System. A total of 125 patients were enrolled at 24 international centers. Main entry criteria were NIH Stroke Scale (NIHSS) score ≥ 8, presentation within 8 hours of symptom onset, and an occlusion (TIMI 0 or 1) of a treatable intracranial vessel. Patients who presented within 3 hours from symptom onset must have been ineligible for or refractory to rtPA therapy. Primary endpoints were revascularization of the target vessel (TIMI 2 or 3) and incidence of procedural serious adverse events (SAE). All patients were followed and assessed up to 90 days from the procedure.

Statistical Analysis

A sample size of 125 was selected for this study in order to generate at least 115 evaluable patients. A patient was considered evaluable if the patient met eligibility requirements for primary endpoint assessment and was treated with the Penumbra System. Since this was an uncontrolled study, a formal hypothesis test was not planned for the overall response rate for establishing a TIMI grade of 2 or 3. Standard descriptive statistics for categorical endpoints were the number and percent of patients with each level of the endpoint. For numeric endpoints, the standard descriptive statistics included the number of non-missing observations (n), the mean, the median, the standard deviation, the minimum value, and the maximum value.

Study Procedures

Arterial access to the target vessel was achieved using standard percutaneous technique and a four-vessel digital subtraction angiography was performed to define the angio-architecture of the occluded vascular segment. Each patient was required to have their cerebral large vessel occlusion confirmed by angiography and a site of primary occlusion designated a priori by the investigator. If the occlusion is in a treatable vessel, an appropriate guide catheter was positioned and the Penumbra Reperfusion Catheter advanced to the proximal end of the occluded target vessel. A patient was considered enrolled when the Reperfusion Catheter was deployed from the guide catheter.

Key Inclusion Criteria

- Clinical signs consistent with acute ischemic stroke, including:
  - Sudden numbness or weakness of face or extremities
  - Sudden confusion, trouble speaking or understanding speech
  - Sudden trouble walking, dizziness, or loss of balance
- From 18 to 79 years of age
- Neurological deficit resulting in a NIH Stroke Scale (NIHSS) score ≥ 8
- Complete occlusion (TIMI Grade 0) or contrast penetration with minimal perfusion but no distal branch filling (TIMI Grade I) in intracranial vessels accessible to the Penumbra Stroke System

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- Signed informed consent
- Present within 8 hours of stroke symptom onset
- Ineligible or refractory to intravenous rtPA therapy if presenting within 3 hours of symptom onset

Key Exclusion Criteria

- Evidence of rapidly improving neurological signs of stroke at time of enrollment
- NIHSS >30 or coma
- Females who are pregnant
- Vessel tortuosity too difficult to allow endovascular access
- Known hemorrhagic diathesis, coagulation deficiency, or on oral anticoagulant therapy with an INR >3.0
- PTT greater than 2 times the lab normal
- Admission platelets <30,000
- Pre-existing neurological or psychiatric disease that could confound the study results
- Known severe allergy to contrast media
- Uncontrolled hypertension (defined as systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg)
- CT evidence of the following conditions on presentation:
  - Significant mass effect with midline shift
  - Large hypodensity region >1/3 of the middle cerebral artery territory
  - Evidence of intracranial hemorrhage
- Angiographic evidence of an arterial stenosis proximal to the occlusion that could prevent thrombus removal
- Angiographic evidence of preexisting arterial injury
- Life expectancy less than 90 days
- Participation in another clinical investigation that could confound the evaluation of the study device

Summary of reasons for exclusion of enrolled subjects, especially those based on angiographic criteria

No enrolled patient was excluded for angiographic reasons.

Primary Effectiveness Endpoint

The Primary Effectiveness Endpoint was revascularization of the occluded target vessel. Revascularization was defined by a TIMI score of II or III following use of the Penumbra System only and prior to the use of any additional or adjunctive devices or therapies. Angiographic results were adjudicated by an independent Core Laboratory.

Effectiveness	% (n/N) [95% CI]†
Primary Effectiveness Endpoint (TIMI score of II or III) *TIMI scores before adjunctive therapies are used*	81.6% (102/125) [73.7%, 88.0%]
Post-Device Revascularization Success (TIMI ≥ 2) *Any Adjunctive Therapy Use Considered Treatment Failure*	81.6% (102/125) [73.7%, 88.0%]
Post-Device Revascularization Success (TIMI ≥ 2) *Any IA Lytic Use Considered Treatment Failure*	81.6% (102/125) [73.7%, 88.0%]

†Exact Clopper-Pearson confidence intervals

Primary Safety Endpoint

The Primary Safety Endpoint was incidence of device and/or procedure-related serious adverse events that occurred during the procedure as reported by the investigator. There were 18 procedural events reported in 16 patients (12.8%). Among these, 4 events in 3 patients were rated as serious by the CEC (2.4%).

Composite Adverse Events during the procedure	% (n/N) [95% CI]†
Composite SAE during the procedure	2.4% (3/125)
Primary Safety Endpoint: Composite Procedure/Device related SAE during the procedure	2.4% (3/125)

†Exact Clopper-Pearson confidence intervals

Each specific SAE through 90 days occurring in more than 2% of patients

SAE	% (n/N)
Composite SAEs	52.0% (65/125)
Cerebral Edema	11.2% (14/125)
ICH	8.0% (10/125)
Respiratory Dysfunction/Failure	8.0% (10/125)
Worsening Symptoms of Qualifying Stroke	7.2% (9/125)
Infection	5.6% (7/125)
Other Pulmonary Complications	5.6% (7/125)
Pneumonia	4.0% (5/125)
Cardiac Arrhythmia	3.2% (4/125)
Access Site Complication	2.4% (3/125)
Myocardial Infarction	2.4% (3/125)
Peripheral Vascular Complication	2.4% (3/125)
Renal Dysfunction/Failure	2.4% (3/125)
Stroke in New Territory	2.4% (3/125)

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Categorization of AEs through 90 days Under Anatomical System

Anatomical System	% (n/N)
Nervous System Disorders	62.4% (78/125)
Infections and Infestations	44.0% (55/125)
Cardiac Disorders	28.8% (36/125)
Metabolism and Nutrition Disorders	25.6% (32/125)
General Disorders and Administration Site Conditions	24.8% (31/125)
Respiratory, Thoracic and Mediastinal Disorders	24.8% (31/125)
Injury, Poisoning and Procedural Complications	18.4% (23/125)
Gastrointestinal Disorders	16.0% (20/125)
Blood and Lymphatic System Disorders	14.4% (18/125)
Vascular Disorder	11.2% (14/125)
Psychiatric Disorders	10.4% (13/125)
Renal and Urinary Disorders	8.0% (10/125)
Hepatobiliary Disorders	4.0% (5/125)
Investigations	3.2% (4/125)
Skin and Subcutaneous Tissue Disorders	3.2% (4/125)
Neoplasms Benign, Malignant and Unspecified (Incl Cysts And Polyps)	2.4% (3/125)
Musculoskeletal and Connective Tissue Disorders	0.8% (1/125)

Symbols Glossary

		Attention, see instructions for use	
Rx Only		Prescription only – US Federal Law restricts this device to use by or on the order of a physician	
		Nonpyrogenic	
STERILE EO		Sterilized using ethylene oxide	
	Manufacturer	EC REP	EU Representative
LOT	Lot number		Do not reuse
	Use by	REF	Catalogue number
STERILIZE	Do not resterilize	LATEX	Not made with natural rubber latex

Warranty

Penumbra, Inc. (Penumbra) warrants that reasonable care has been used in he design and manufacture of this device. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular use. Handling, storage, cleaning, and sterilization of this device as well as other factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond Penumbra's control directly affect the device and the results obtained from its use. Penumbra's obligation under this warranty is limited to the repair or replacement of this device and Penumbra shall not be liable for any incidental or consequential loss, damage, or expense directly or indirectly arising from the use of his device. Penumbra neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this device. Penumbra assumes no liability with respect to devices reused, reprocessed, or resterilized and makes no warranties, expressed or implied, including but not limited to merchantability or fitness for intended use, with respect to such device.

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Manufacturer:
Penumbra, Inc.
1351 Harbor Bay Pkwy
Alameda, CA 94502 USA

Tel: 1-888-BRA N06 (1-888-272-4606)
1-510-748-3200
Fax: 1-510-748-3232

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- Do not use the Penumbra System with a pump other than the Penumbra Aspiration Pump.

Precautions

- The device is intended for single use only. Do not resterilize or reuse. Resterilization and/or Reuse may result in ineffective catheter coating lubrication, which may result in high friction and the inability to access the target neuro vasculature location.
- Do not use kinked or damaged devices. Do not use open or damaged packages. Return all damaged devices and packaging to the manufacturer/ distributor.
- Use prior to the “Use By” date.
- Use the Penumbra System in conjunction with fluoroscopic visualization.
- Maintain a constant infusion of appropriate flush solution.
- When performing aspiration, ensure that the Penumbra Aspiration Tubing valve is open for only the minimum time needed to remove thrombus. Excessive aspiration or failure to close the Penumbra Aspiration Tubing valve when aspiration is complete is not recommended.
- The Penumbra Separator is not intended for use as a neurovascular guidewire. If repositioning of the Penumbra Reperfusion Catheter is necessary during the revascularization procedure, such reposition should be performed over an appropriate neurovascular guidewire using standard microcatheter and guidewire techniques.
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3. Prepare Penumbra System devices for use by flushing the packaging hoop and device with heparinized saline (includes Penumbra Reperfusion Catheter and Penumbra Separator only).
4. Prepare a guide catheter or long femoral sheath according to the manufacturer’s *Instructions for Use*.
5. Place the guide catheter or long femoral sheath into the appropriate cerebral artery that is proximal to the thrombus occlusion site.

Penumbra Reperfusion Catheter Preparation and Use

1. Confirm vessel diameter, and select an appropriate size Penumbra Reperfusion Catheter (See **Table 1**).
2. The Penumbra Reperfusion Catheter tip may be shaped using the steam shaping mandrel provided.
3. Attach the rotating hemostasis valve provided to the Penumbra Reperfusion Catheter.
4. Attach the Penumbra Aspiration Tubing to the Aspiration Pump and turn on the Aspiration Pump (Refer to the Aspiration Pump *Operation Manual*). Allow the Aspiration Pump to run for at least one minute prior to use, and confirm

[1] Adams, et al., Guidelines for the Early Management of Adults with Ischemic Stroke: A Guideline from the AHA/ASA Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists, *Stroke* May 2007; 38:1655-1711.

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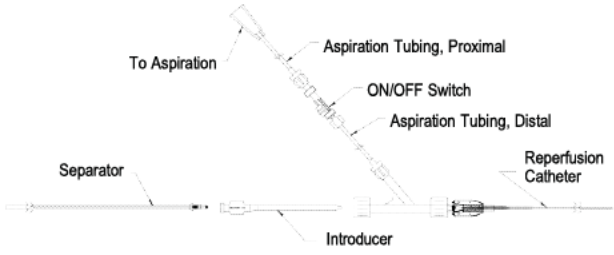
that the Aspiration gauge reads −20inHg. Ensure the valve on the Penumbra Aspiration Tubing is switched to the OFF position.

5. Connect the Aspiration Tubing to the side port of the rotating hemostasis valve as shown in **Figure 1**.

Figure 1 – Assembled Aspiration System with Penumbra Separator



6. Insert the Penumbra Reperfusion Catheter into a rotating hemostasis valve connected to the proximal hub of a guide catheter. If a guide catheter is not used, insert the Penumbra Reperfusion Catheter through the valve of the long femoral sheath using the peelable sheath. After inserting the Penumbra Reperfusion Catheter, remove the peelable sheath from the vascular sheath, and peel from the Penumbra Reperfusion Catheter shaft.
7. Using conventional catheterization techniques under fluoroscopic guidance, advance the Penumbra Reperfusion Catheter into the target vessel over an appropriate neurovascular guidewire. Position the Penumbra Reperfusion Catheter proximal to the thrombus. Remove the guidewire from the Penumbra Reperfusion Catheter.
8. To begin aspiration, open the valve on the Penumbra Aspiration Tubing to the ON position. To stop aspiration, switch the valve on the Penumbra Aspiration Tubing to the OFF position, and turn off the Aspiration Pump.
9. Using a 5cc or 10cc syringe, aspirate approximately 5cc of blood from the Penumbra Reperfusion Catheter to remove any thrombus that may remain in the catheter.
10. Obtain a post-treatment angiogram by injecting contrast media through the guide catheter.

Penumbra Separator Preparation and Use

1. If needed, select an appropriate size Penumbra Separator corresponding to the Reperfusion Catheter (see **Table 1**).

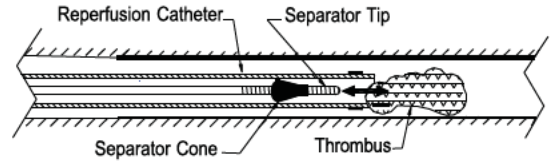
Table 1 – Separator/Reperfusion Catheter Device Size Selection

Vessel Size (mm)	Penumbra Reperfusion Catheter	Penumbra Separator
< 2.0	026	026
2.0 to 3.0	032 / 3MAX	032 / 3MAX
3.0 to 4.0	041 / 4MAX	041 / 4MAX
> 4.0	054 / 5MAX / ACE	054 / 5MAX

NOTE: Access to the site of occlusion may be aided by the triaxial use of a compatible inner microcatheter.

2. Using the introducer sheath provided, insert the Penumbra Separator through the rotating hemostasis valve and into the proximal hub of the Penumbra Reperfusion Catheter.
3. To begin aspiration, open the valve on the Penumbra Aspiration Tubing to the ON position, and advance/retract the Penumbra Separator to assist with aspiration and removal of the thrombus from the Reperfusion Catheter as shown in **Figure 2**.

Figure 2 – Thrombus Aspiration Using the Penumbra Separator



4. To stop aspiration, switch the valve on the Penumbra Aspiration Tubing to the OFF position, and turn off the Aspiration Pump.
5. Remove the Penumbra Separator, if used.
6. If necessary, additional Penumbra Separators and Reperfusion Catheters may be used to further remove thrombus at the discretion of the physician.

Clinical Data Summary

The Penumbra Pivotal trial was a prospective, single arm trial to assess the safety and effectiveness of the Penumbra System. A total of 125 patients were enrolled at 24 international centers. Main entry criteria were NIH Stroke Scale (NIHSS) score ≥ 8, presentation within 8 hours of symptom onset, and an occlusion (TIMI 0 or 1) of a treatable intracranial vessel. Patients who presented within 3 hours from symptom onset must have been ineligible for or refractory to rtPA therapy. Primary endpoints were revascularization of the target vessel (TIMI 2 or 3) and incidence of procedural serious adverse events (SAE). All patients were followed and assessed up to 90 days from the procedure.

Statistical Analysis

A sample size of 125 was selected for this study in order to generate at least 115 evaluable patients. A patient was considered evaluable if the patient met eligibility requirements for primary endpoint assessment and was treated with the Penumbra System. Since this was an uncontrolled study, a formal hypothesis test was not planned for the overall response rate for establishing a TIMI grade of 2 or 3. Standard descriptive statistics for categorical endpoints were the number and percent of patients with each level of the endpoint. For numeric endpoints, the standard descriptive statistics included the number of non-missing observations (n), the mean, the median, the standard deviation, the minimum value, and the maximum value.

Study Procedures

Arterial access to the target vessel was achieved using standard percutaneous technique and a four-vessel digital subtraction angiography was performed to define the angio-architecture of the occluded vascular segment. Each patient was required to have their cerebral large vessel occlusion confirmed by angiography and a site of primary occlusion designated a priori by the investigator. If the occlusion is in a treatable vessel, an appropriate guide catheter was positioned and the Penumbra Reperfusion Catheter advanced to the proximal end of the occluded target vessel. A patient was considered enrolled when the Reperfusion Catheter was deployed from the guide catheter.

Key Inclusion Criteria

- Clinical signs consistent with acute ischemic stroke, including:
  - Sudden numbness or weakness of face or extremities
  - Sudden confusion, trouble speaking or understanding speech
  - Sudden trouble walking, dizziness, or loss of balance
- From 18 to 79 years of age
- Neurological deficit resulting in a NIH Stroke Scale (NIHSS) score ≥ 8
- Complete occlusion (TIMI Grade 0) or contrast penetration with minimal perfusion but no distal branch filling (TIMI Grade I) in intracranial vessels accessible to the Penumbra Stroke System

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- Signed informed consent
- Present within 8 hours of stroke symptom onset
- Ineligible or refractory to intravenous rtPA therapy if presenting within 3 hours of symptom onset

Key Exclusion Criteria

- Evidence of rapidly improving neurological signs of stroke at time of enrollment
- NIHSS >30 or coma
- Females who are pregnant
- Vessel tortuosity too difficult to allow endovascular access
- Known hemorrhagic diathesis, coagulation deficiency, or on oral anticoagulant therapy with an INR >3.0
- PTT greater than 2 times the lab normal
- Admission platelets <30,000
- Pre-existing neurological or psychiatric disease that could confound the study results
- Known severe allergy to contrast media
- Uncontrolled hypertension (defined as systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg)
- CT evidence of the following conditions on presentation:
  - Significant mass effect with midline shift
  - Large hypodensity region >1/3 of the middle cerebral artery territory
  - Evidence of intracranial hemorrhage
- Angiographic evidence of an arterial stenosis proximal to the occlusion that could prevent thrombus removal
- Angiographic evidence of preexisting arterial injury
- Life expectancy less than 90 days
- Participation in another clinical investigation that could confound the evaluation of the study device

Summary of reasons for exclusion of enrolled subjects, especially those based on angiographic criteria

No enrolled patient was excluded for angiographic reasons.

Primary Effectiveness Endpoint

The Primary Effectiveness Endpoint was revascularization of the occluded target vessel. Revascularization was defined by a TIMI score of II or III following use of the Penumbra System only and prior to the use of any additional or adjunctive devices or therapies. Angiographic results were adjudicated by an independent Core Laboratory.

Effectiveness	% (n/N) [95% CI]†
Primary Effectiveness Endpoint (TIMI score of II or III) *TIMI scores before adjunctive therapies are used*	81.6% (102/125) [73.7%, 88.0%]
Post-Device Revascularization Success (TIMI ≥ 2) *Any Adjunctive Therapy Use Considered Treatment Failure*	81.6% (102/125) [73.7%, 88.0%]
Post-Device Revascularization Success (TIMI ≥ 2) *Any IA Lytic Use Considered Treatment Failure*	81.6% (102/125) [73.7%, 88.0%]

†Exact Clopper-Pearson confidence intervals

Primary Safety Endpoint

The Primary Safety Endpoint was incidence of device and/or procedure-related serious adverse events that occurred during the procedure as reported by the investigator. There were 18 procedural events reported in 16 patients (12.8%). Among these, 4 events in 3 patients were rated as serious by the CEC (2.4%).

Composite Adverse Events during the procedure	% (n/N) [95% CI]†
Composite SAE during the procedure	2.4% (3/125)
Primary Safety Endpoint: Composite Procedure/Device related SAE during the procedure	2.4% (3/125)

†Exact Clopper-Pearson confidence intervals

Each specific SAE through 90 days occurring in more than 2% of patients

SAE	% (n/N)
Composite SAEs	52.0% (65/125)
Cerebral Edema	11.2% (14/125)
ICH	8.0% (10/125)
Respiratory Dysfunction/Failure	8.0% (10/125)
Worsening Symptoms of Qualifying Stroke	7.2% (9/125)
Infection	5.6% (7/125)
Other Pulmonary Complications	5.6% (7/125)
Pneumonia	4.0% (5/125)
Cardiac Arrhythmia	3.2% (4/125)
Access Site Complication	2.4% (3/125)
Myocardial Infarction	2.4% (3/125)
Peripheral Vascular Complication	2.4% (3/125)
Renal Dysfunction/Failure	2.4% (3/125)
Stroke in New Territory	2.4% (3/125)

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Categorization of AEs through 90 days Under Anatomical System

Anatomical System	% (n/N)
Nervous System Disorders	62.4% (78/125)
Infections and Infestations	44.0% (55/125)
Cardiac Disorders	28.8% (36/125)
Metabolism and Nutrition Disorders	25.6% (32/125)
General Disorders and Administration Site Conditions	24.8% (31/125)
Respiratory, Thoracic and Mediastinal Disorders	24.8% (31/125)
Injury, Poisoning and Procedural Complications	18.4% (23/125)
Gastrointestinal Disorders	16.0% (20/125)
Blood and Lymphatic System Disorders	14.4% (18/125)
Vascular Disorder	11.2% (14/125)
Psychiatric Disorders	10.4% (13/125)
Renal and Urinary Disorders	8.0% (10/125)
Hepatobiliary Disorders	4.0% (5/125)
Investigations	3.2% (4/125)
Skin and Subcutaneous Tissue Disorders	3.2% (4/125)
Neoplasms Benign, Malignant and Unspecified (Incl Cysts And Polyps)	2.4% (3/125)
Musculoskeletal and Connective Tissue Disorders	0.8% (1/125)

Symbols Glossary

		Attention, see instructions for use	
Rx Only		Prescription only – US Federal Law restricts this device to use by or on the order of a physician	
		Nonpyrogenic	
STERILE EO		Sterilized using ethylene oxide	
	Manufacturer	EC REP	EU Representative
LOT	Lot number		Do not reuse
	Use by	REF	Catalogue number
STERILIZE	Do not resterilize	LATEX	Not made with natural rubber latex

Warranty

Penumbra, Inc. (Penumbra) warrants that reasonable care has been used in he design and manufacture of this device. This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether expressed or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular use. Handling, storage, cleaning, and sterilization of this device as well as other factors relating to the patient, diagnosis, treatment, surgical procedures, and other matters beyond Penumbra's control directly affect the device and the results obtained from its use. Penumbra's obligation under this warranty is limited to the repair or replacement of this device and Penumbra shall not be liable for any incidental or consequential loss, damage, or expense directly or indirectly arising from the use of his device. Penumbra neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this device. Penumbra assumes no liability with respect to devices reused, reprocessed, or resterilized and makes no warranties, expressed or implied, including but not limited to merchantability or fitness for intended use, with respect to such device.

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Alameda, CA 94502 USA

Tel: 1-888-BRA N06 (1-888-272-4606)
1-510-748-3200
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9126, Rev A

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

(b)(4) [redacted]

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(b	[redacted]	(b)(6) [redacted]	02/07/14	(b)(4) [redacted]
(b	[redacted] (	[redacted]	04/08/15	

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1. PURPOSE

(b)(6) [redacted]

2. SCOPE

(b)(6) [redacted]

3. RESPONSIBILITY

(b) [redacted]

4. REFERENCE DOCUMENTS

(b)(6) [redacted]

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(b	[redacted]	M. Vander Schaaf	02/20/15	

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(b)(4) Third Party Testing

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. REFERENCE DOCUMENTS

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1. PURPOSE

(b)(4) [redacted]

2. SCOPE

(b)(4) [redacted]

3. RESPONSIBILITY

(b)(4) [redacted]

4. REFERENCE DOCUMENTS

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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(b)(4)

[redacted]

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(b)(4)

[redacted]

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(b)(4)

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APPENDIX A

(b)(4)

[redacted]

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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APPENDIX B

(b)(4)

[redacted]

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Revision History

Rev	ECO #	Originator	Effective	Description of Change
([redacted]	[redacted]	(b)(6) [redacted]	07/21/14	(b)(4) [redacted]
([redacted]	[redacted]	(b)(6) [redacted]	08/07/14	

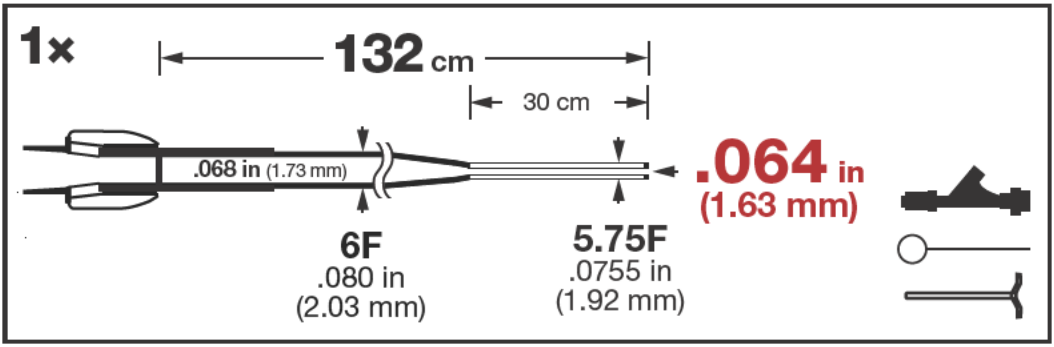
Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4313 Released by CDRH on 10-08-2015

Penumbra

Penumbra System® ACE™

64 Reperfusion Catheter



Use By
使用截止日期 YYYY-MM-DD

REF Catalog Number
型号 **5MAXACE064**

LOT Lot Number
批号 F12345

Rx Only

STERILE EO Sterile (ethylene oxide)
灭菌（环氧乙烷）

Nonpyrogenic
无热原

Do not resterilize
切勿重新灭菌

Single use only. Do not reuse.
仅供一次性使用。切勿重复使用。

LATEX Not made with natural rubber latex
不含天然乳胶

Attention, see Instructions for Use.
注意，请参阅使用说明。

(01)00814548013978(17)030531(10)F12345

ACE 64 Reperfusion Catheter 132 cm
REF 5MAXACE064
LOT F12345
(01)00814548013978
Penumbra System® ACE™

ACE 64 Reperfusion Catheter 132 cm
REF 5MAXACE064
LOT F12345
(01)00814548013978
Penumbra System® ACE™

ACE 64 Reperfusion Catheter 132 cm
REF 5MAXACE064
LOT F12345
(01)00814548013978
Penumbra System® ACE™

制造商

Manufacturer:
Penumbra, Inc.
One Penumbra Place
Alameda, CA 94502, USA
Tel: 1.888.BRAIN06
(1.888.272.4606)
1.510.748.3200
Fax: 1.510.748.3232

EC REP 欧盟授权代表

EU Representative:
MedPass International Ltd.
Windsor House, Bretforton
Evesham, Worcestershire WR11 7JJ, UK

Penumbra Neuro Australia Pty Ltd
Suite 3, Level 5, 1 Oxford Street
Darlinghurst NSW 2010, Australia
Tel: 1300 817 025
Fax: 1300 817 026
Email: order.anz@penumbrainc.com

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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

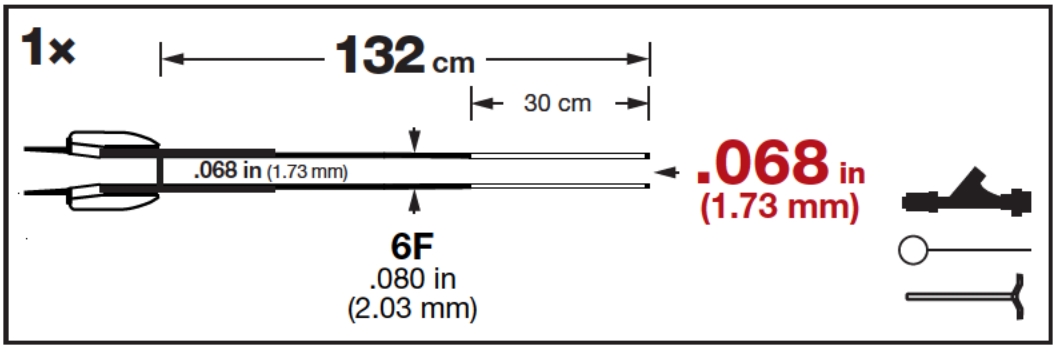
ACE 64 Reperfusion Catheter | REF 5MAXACE064 | 132 cm | Use By YYYY-MM-DD

Records processed under FOIA Request # 2015-5433 Released by CDRH on 10-08-2015

Penumbra

Penumbra System™ ACE™

68 Reperfusion Catheter



Use By
使用截止日期 2015-01

REF Catalog Number
型号 **5MAXACE068**

LOT Lot Number
批号 F12345

Rx Only

STERILE EO Sterile (ethylene oxide)
灭菌（环氧乙烷）

Nonpyrogenic
无热原

Do not resterilize
切勿重新灭菌

Single use only. Do not reuse.
仅供一次性使用。切勿重复使用。

LATEX Not made with natural rubber latex
不含天然乳膠

Attention, see Instructions for Use.
注意，请参阅使用说明。

(01)00814548013978(17)030531(10)F12345

ACE 68 Reperfusion Catheter 132 cm
REF 5MAXACE068
LOT F12345
(01)00814548013978
Penumbra System™ ACE

ACE 68 Reperfusion Catheter 132 cm
REF 5MAXACE068
LOT F12345
(01)00814548013978
Penumbra System™ ACE

ACE 68 Reperfusion Catheter 132 cm
REF 5MAXACE068
LOT F12345
(01)00814548013978
Penumbra System™ ACE

制造商

Manufacturer:
Penumbra, Inc.
1351 Harbor Bay Parkway
Alameda, CA 94502, USA
Tel: 1.888.BRAIN06
(1.888.272.4606)
1.510.748.3200
Fax: 1.510.748.3232

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EU Representative:
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Evesham, Worcestershire WR11 7JJ, UK

Penumbra Neuro Australia PTY LTD
Suite 3, Level 5, 1 Oxford Street
Darlinghurst NSW 2010, Australia
Tel: 1300 817 025
Fax: 1300 817 026
Email: order.anz@penumbrainc.com

8056.A

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

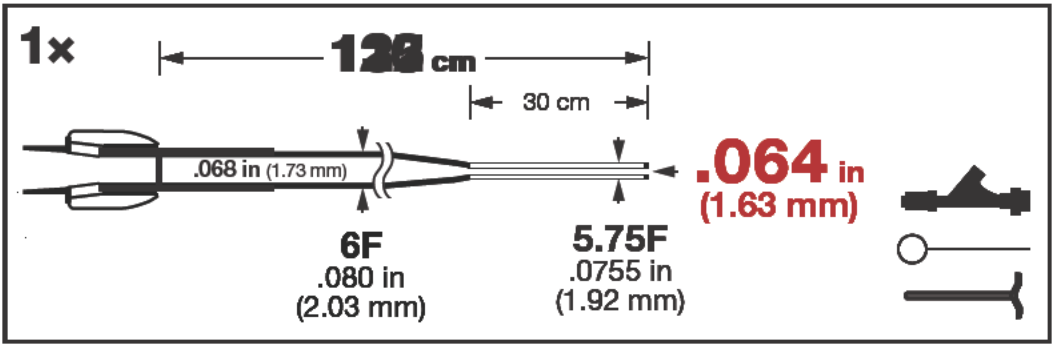
ACE 68 Reperfusion Catheter REF 5MAXACE068 132 cm Use By 2015-01

Records processed under FOIA Request # 2015-4313 Released by CDRH on 10-08-2015

Penumbra

Penumbra System® ACE™

64 Reperfusion Catheter



Use By 使用截止日期 YYYY-MM-DD

REF Catalog Number 型号 5MAXACE064L128

LOT Lot Number 批号 F12345

STERILE EO Sterile (ethylene oxide) 灭菌（环氧乙烷）

Nonpyrogenic 无热原

Do not resterilize 切勿重新灭菌

Single use only. Do not reuse. 仅供一次性使用。切勿重复使用。

LATEX Latex-free 不含胶乳 — Not made with natural rubber latex 不含天然乳胶

Attention, see Instructions for Use. 注意，请参阅使用说明。

(01)00814548013978(17)030531(10)F12345

Rx Only

ACE 64 Reperfusion Catheter 128 cm
REF 5MAXACE064L128
LOT F12345
(01)00814548013978
Penumbra System® ACE™

ACE 64 Reperfusion Catheter 128 cm
REF 5MAXACE064L128
LOT F12345
(01)00814548013978
Penumbra System® ACE™

ACE 64 Reperfusion Catheter 128 cm
REF 5MAXACE064L128
LOT F12345
(01)00814548013978
Penumbra System® ACE™

制造商
Manufacturer:
Penumbra, Inc.
One Penumbra Place
Alameda, CA 94502, USA
Tel: 1.888.BRAIN06
(1.888.272.4606)
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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

ACE 64 Reperfusion Catheter REF 5MAXACE064L128 128 cm Use By YYYY-MM-DD

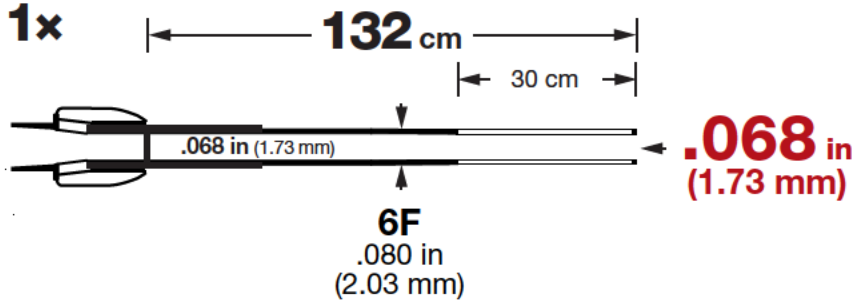
Records processed under FOIA Request # 2015-5433 Released by CDRH on 10-08-2015

Penumbra

Penumbra System™ ACE™

68 Reperfusion Catheter

1×



Use By 使用截止日期 2015-01

REF Catalog Number 型号 **5MAXACE068**

LOT Lot Number 批号 F12345

Rx Only

STERILE EO Sterile (ethylene oxide) 灭菌（环氧乙烷）

Nonpyrogenic 无热原

Do not resterilize 切勿重新灭菌

Single use only. Do not reuse. 仅供一次性使用。切勿重复使用。

LATEX Latex-free 不含胶乳 — Not made with natural rubber latex 不含天然乳膠

Attention, see Instructions for Use. 注意，请参阅使用说明。

(01)00814548013978(17)030531(10)F12345

ACE 68 Reperfusion Catheter 132 cm
REF 5MAXACE068
LOT F12345
(01)00814548013978
Penumbra System™ ACE

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(01)00814548013978
Penumbra System™ ACE

ACE 68 Reperfusion Catheter 132 cm
REF 5MAXACE068
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Penumbra System™ ACE

制造商

Manufacturer:
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Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

ACE 68 Reperfusion Catheter REF 5MAXACE068 132 cm Use By 2015-01

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8 510(k) Summary of Safety & Effectiveness

(as required by 21 CFR 807.92)

Pursuant to Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, Penumbra Inc. is providing the summary of Substantial Equivalence for the Penumbra System ACE.

8.1 Sponsor/Applicant Name and Address

Penumbra, Inc.
1351 Harbor Bay Parkway
Alameda, CA 94502 USA

8.2 Sponsor Contact Information

Michaela Mahl
Senior Manager, Regulatory Affairs
Phone: (510) 748-3288
FAX: (510) 217-6414
Email: michaela.mahl@penumbrainc.com

8.3 Date of Preparation of 510(k) Summary

April 09, 2015

8.4 Device Trade or Proprietary Name

Penumbra System ACE

8.5 Device Classification

Regulatory Class:	II
Classification Panel:	Neurology
Classification Name:	Catheter, Thrombus Removal
Regulation Number:	21 CFR §870.1250
Product Code:	NRY

8.6 Predicate Devices

510(k) Number / Clearance Date	Name of Predicate Device	Name of Manufacturer
K072718 [28Dec2007], K090752 [21Sep2009], K100769 [21May2010], K113163 [28NOV2011], K133317 [13MAY2014]	Penumbra System / Penumbra System MAX®	Penumbra, Inc. 1351 Harbor Bay Parkway Alameda, CA 94502 USA

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

8.7 Predicate Comparison

System Name	Penumbra System Reperfusion Catheter	Penumbra System ACE Reperfusion Catheter	
Device Name	**5MAX ACE**	**ACE 64**	**ACE 68**
510(k) No.	K090752	K142458	
Classification	Class II, NRY	SAME	
Indication	The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.	The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. The Reperfusion Catheters ACE 64 and ACE 68 are intended for use in revascularization within the Internal Carotid Artery (ICA) within 8 hours of symptom onset.	
Materials			
Proximal hub	Grilamid (TR55-LX)	SAME	
Strain Relief [Hub Sleeve]	Grilamid (TR55)	SAME	
Strain Relief	Stainless Steel, 304	SAME	
ID Band	Polyolefin, PET yellow [black ink]	SAME	
Catheter Shaft			
Distal Extrusions	Tecoflex 80A, Pellethane 80A, Pebas 35D, Pebax 35D/40D Blend, Pebax 40D, Pebax 55D, Pebax 63D	Pellethane 80A, Tecoflex 80A, Tecoflex 80A/Pebax 35D, Pebax 35D, Pebax 35D/40D Blend, Pebax 40D, Pebax 40D/55D Blend, Pebax 55D, Pebax 63D	
Proximal Extrusions	Pebax 55D, Pebax 72D, Vestamid	Pebax 55D, Pebax 72D, Vestamid	Pebax 55D/72D Blend, Pebax 72D, Vestamid
Proximal Coil Reinformcement	SS flat (0.002 in x 0.007 in)	SS flat (0.0015 in x 0.006 in) and SS round (0.0025 in)	SS flat (0.0015 in x 0.006 in) and NiTi round (0.0025 in)
Extrusion Colorants	Clear/ Natural or Purple	SAME	
Tip Shape	Straight	SAME	
Markerband	C-cut Pt/Ir band	SAME	
Coating	SRDX Harmony (proprietary)	SAME	
Dimensions			
Proximal OD	0.083 in Max	0.084 in Max	0.084 in Max
Proximal ID	0.068 in Min	0.068 in Min	0.068 in Min
Distal OD	0.074 in Max	0.080 in Max	0.084 in Max

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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System Name	Penumbra System Reperfusion Catheter	Penumbra System ACE Reperfusion Catheter	
Device Name	**5MAX ACE**	**ACE 64**	**ACE 68**
Distal ID	0.060 in Min	0.064 in Min	0.068 in Min
Effective Length	125, 127, 132 cm	115, 120, 125, 127, 132 cm	
Coating Length	30 cm	SAME	
Accessories			
Peelable Sheath	PTFE	SAME	
Rotating Hemostasis Valve	Polycarbonate, silicone o-ring	SAME	
Shaping Mandrel	0.038in OD	SAME	
Packaging Materials			
Pouch	Polyester/Polyethylene/ Tyvek®	SAME	
Packaging Hoop	Polyethylene	SAME	
Packaging Card	Polyethylene	SAME	
Display Carton	SBS Paperboard	SAME	
Packaging Configuration	Individual	SAME	
Sterilization	EO	SAME	
Shelf-Life	36 Months	SAME	

8.8 Device Description

The Penumbra System ACE components are additional components to the currently available Penumbra System / Penumbra System MAX. The Penumbra System ACE components provide a larger lumen to assist in the efficient removal of thrombus from the neurovasculature. The devices are provided sterile, non-pyrogenic, and intended for single use only.

8.9 Indications for Use

The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. The Reperfusion Catheters ACE 64 and ACE 68 are intended for use in revascularization within the Internal Carotid Artery (ICA) within 8 hours of symptom onset.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

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8.10 Summary of Non-Clinical Data

As required under Section 12, Part (a)(i)(3A) of the Safe Medical Devices Act of 1990, a summary of any information regarding safety and effectiveness of the device follows.

Included in this section are summary descriptions of the testing, which substantiates the safe and effective performance of the subject Penumbra System ACE as well as its substantial equivalence to the predicate devices:

- Biocompatibility
- Design Verification (Bench-Top Testing)
- Design Validation (GLP Animal Testing)

The subject Penumbra System ACE devices met all established requirements.

8.10.1 Biocompatibility Testing

Biocompatibility tests conducted on the materials of the Penumbra System ACE devices were selected in accordance with EN ISO 10993 -1 guidelines (Biological Evaluation of Medical Devices) for limited duration (<24 hours), external communicating devices, contacting circulating blood. All studies were conducted pursuant to 21 CFR, Part 58, Good Laboratory Practices. In summary, non-clinical testing found the Penumbra System ACE devices to be biocompatible according to the requirements of EN ISO 10993 requirements. The following tests were performed and all tests passed successfully:

Test	Acceptance Criteria	Results	Pass / Fail
In Vitro Cytotoxicity	Sample extracts must yield cell lysis grade 2 or lower	Grade 1: Slight	Pass
Sensitization	Test Group shall yield Grade < 1 score on Magnusson and Kligman scale (provided control Grade < 1)	Grade 0: No visible change	Pass
Acute Intracutaneous Reactivity (Irritation)	The difference in the mean test article and mean control score must be grade 1.0 or lower	Grade ≤ 1.0 difference between mean test article and mean control score	Pass
Systemic Toxicity			
Acute Systemic Toxicity	Sample extracts must not cause the following: • > 10% weight loss in 3 or more test animals • Mortality of 2 or more test animals • Abnormal behavior in 2 or more test animals	No evidence of systemic toxicity from sample extracts • No weight loss (all gained weight) • No death • All test animals appeared normal	Pass

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Test	Acceptance Criteria	Results	Pass / Fail
Rabbit Pyrogen Study	Sample Extracts must not cause a total rise in body temperature of ≥0.5°C	Non-pyrogenic: No evidence of material-mediated pyrogenicity; no single animal had a total body temperature rise of ≥0.5°C	Pass
Hemocompatibility			
In Vitro Hemolysis	Sample extracts must be non-hemolytic (≤ 2% hemolytic index)	Non-hemolytic: Hemolytic Index = 0.70% Corrected Hemolytic index = 0.00%	Pass
Complement Activation	The concentrations of C3a and SC5b-9 in the test samples are statistically similar to the predicate (Exposure Control & Ref Material) control and statistically lower than the positive control for all exposure times	The test sample concentrations of C3a and SC5b-9 were statistically similar or lower than the predicate control sample concentrations, and statistically lower than the positive control sample concentrations at all three exposure times	Pass
Dog Thrombogenicity	The device must be non-thrombogenic after 4 hours *in vivo* when compared to a control device (Boston Scientific Excelsior SL-10 microcatheter)	No significant thrombosis with a Grade of 0 was observed in 2 out 2 test site and 2 out of 2 control sites. Based on the evaluation criteria, the amount of thrombosis was not considered significant	Pass

In summary non-clinical testing substantiates that the Penumbra System ACE devices are non-cytotoxic, non-sensitizing, non-irritating, non-toxic, non-pyrogenic, non-hemolytic, and non-thrombogenic.

8.10.2 Bench-top Testing

The physical and mechanical properties of the Penumbra System ACE devices were assessed using standard test methods and pre-determined acceptance criteria. The following tests were performed and all tests passed successfully:

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Dimensional/ Visual Inspection	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Attribute	Sample Size	Specification	Acceptance Criteria	Results
Simulated Use [Intracranial Access & Vessel Access Entry Performance]	These evaluations confirm that the units used in this Design Verification testing meet all inspection criteria for release of finished goods (clinically acceptable) product.			Pass
Coating Integrity	(b) [redacted]	Coating has not delaminated, peeled, or flaked after simulated use	100% Must meet Specification	100% Pass
Particulate Testing (Reperfusion Catheter Hydrophilic Coating)	(b) [redacted]	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Particulate Testing (Reperfusion Catheter /Separator)	(b) [redacted]	The maximum number of particles: ≥ 10 µm will be ≤ 6000 particles ≥ 25 µm will be ≤ 600 particles.	100% Must meet Specification	10µm 100% Pass 25µm 100% Pass
Coating Integrity	(b) [redacted]	Coating is not grossly damaged after undergoing particulate testing	100% Must meet Specification	100% Pass
Hub/Catheter Air Aspiration	(b) [redacted]	When negative pressure is pulled, no air may leak into hub	100% Must meet Specification	100% Pass
Pressure Test	(b) [redacted]	45 psi for 30 sec MIN	100% Must meet Specification	100% Pass
Reperfusion Catheter/Sheath or 8F Guide & 0.014" Guidewire compatibility (Friction Force)	(b) [redacted]	Maximum value per specification	100% Must meet Specification	100% Pass
Markerband Section Bond Strength	(b) [redacted]	Minimum value per specification	100% Must meet Specification	100% Pass
Joint Sections Bond Strength	(b)(4) [redacted]	Minimum value per specification	100% Must meet Specification	100% Pass
Hub to Shaft & Hub to Hypotube Bond Strength	(b) [redacted]	Minimum value per specification	100% Must meet Specification	100% Pass
Elongation to Failure – Reperfusion Catheter	(b) [redacted]	% Elongation ≥ 5%	100% Must meet Specification	100% Pass
Corrosion	(b) [redacted]	No visible corrosion on Reperfusion Catheter immediately after Corrosion Testing procedure	100% Must meet Specification	100% Pass

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

The results of the tests appropriately address the physical and mechanical performance expectations of the device. This is further supported by the surgical handling and performance results reported in the *in vivo* study. Based on these overall results, the physical and mechanical properties of the subject Penumbra System ACE devices are acceptable for the intended use and substantially equivalent to the predicate device.

8.10.3 Animal Study

An animal study was conducted to evaluate the safe use of the Penumbra System ACE devices in a swine model. The study concluded that:

- No vessel injury was noted on the final angiograms following the vessel response procedure.
- No abnormal gross or histology findings were noted in test vessel segments.
- The use of the Penumbra System ACE devices resulted in no significant vascular response in these experimental conditions.

8.10.4 Summary of Substantial Equivalence

The subject Penumbra System ACE devices are substantially equivalent to the predicate device with regard to intended use, operating principle, design concept, materials, shelf-life, packaging and sterilization processes.

Questions? Contact FDA/CDRH/OCE/DID at CDRH-FOISTATUS@fda.hhs.gov or 301-796-8118

Records processed under FOIA Request # 2015-4313; Released by CDRH on 10-08-2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K142458

Device Name
Penumbra System ACE

Indications for Use *(Describe)*
The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (within the internal carotid, middle cerebral – M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset. The Reperfusion Catheters ACE 64 and ACE 68 are intended for use in revascularization within the Internal Carotid Artery (ICA) within 8 hours of symptom onset.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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ORIGINAL RESEARCH

The SPEED study: initial clinical evaluation of the Penumbra novel 054 Reperfusion Catheter

Don Frei,[1] Johannes Gerber,[2] Aquilla Turk,[3] Malia McPherson,[4] Don Heck,[5] Ferdinand Hui,[6] Gregory Joseph,[7] Reza Jahan,[8] Laszlo Miskolczi,[9] Jeffrey Carpenter,[10] Thomas Grobelny,[11] Jim Goddard,[12] Raymond D Turner,[3] Dan Huddle,[1] Richard Bellon,[1] Imran Chaudry[3]

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Don Frei, Johannes Gerber, Aquilla Turk, et al.

J NeuroIntervent Surg published online January 7, 2013
doi: 10.1136/neurintsurg-2012-010585

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STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

AAMI / ANSI ST72:2011, bacterial endotoxins - test methods, routine monitoring, and alternatives to batch testing. (Sterility)

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#14-360	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☒	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

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[6] The online search for CDRH Guidance Documents can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
AAMI / ANSI ST72:2011, bacterial endotoxins - test methods, routine monitoring, and alternatives to batch testing. (Sterility)

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
Annex B.4	Selection of BET methodology	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Turbidimetirc technique selected

DESCRIPTION
Test lab: Nelson Labs 6280 South Redwood Road, Salt Lake City, UT 84123

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ASTM D4169:2014 - Standard Practice for Performance Testing of Shipping Containers and Systems

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#14-300 [2009]	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☒	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: N/A

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
ASTM D4169:2014 - Standard Practice for Performance Testing of Shipping Containers and Systems

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
8.2	Procedure - Establish Assurance Level	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Assurance Level II selected

DESCRIPTION
Specifies level of test intensity
Test Center: Westpak Laboratory, 83 Great Oaks Boulevard, San Jose, CA, 95119

JUSTIFICATION
Assurance Level II is suggested unless conditions dictate otherwise

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

ASTM F2096:2011 - Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test)

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#14-359	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☒	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
ASTM F2096:2011 - Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test)

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
9	Procedure	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Test method B for porous packaging selected

DESCRIPTION
Test Center: Westpak Laboratory, 83 Great Oaks Boulevard, San Jose, CA, 95119

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

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TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

AAMI TIR42:2010 - Evaluation of particulates associated with vascular medical devices

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#3-99	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☒	☐
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☒	☐
Is there an FDA guidance [6] that is associated with this standard?	☒	☐
If yes, was the guidance document followed in preparation of this 510k?	☒	☐

Title of guidance: Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Deliv

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
AAMI TIR42:2010 - Evaluation of particulates associated with vascular medical devices

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
6	Establishment of product particle limits	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
All options were considered.

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
7.3.3	Light obscuration counter (LOC)	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
None

DESCRIPTION

JUSTIFICATION

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

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☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 10555-1:2013 Sterile, single-use intravascular catheters - Part 1: General requirements

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#6-301	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☐	☒
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Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☒
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☒	☐
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: Guidance on Pre-Market Notification [510(k)] Submission for Short-Term and Long-Term Intravascular C

[1] The formatting convention for the title is: [SDO] [numeric identifier] [title of standard] [date of publication]

[2] Authority [21 U.S.C. 360d], http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[4] The summary report should include: any adaptations used to adapt to the device under review (for example, alternative test methods); choices made when options or a selection of methods are described; deviations from the standard; requirements not applicable to the device; and the name and address of the test laboratory or certification body involved in conformance assessment to this standard. The summary report includes information on all standards utilized during the development of the device.

[5] The supplemental information sheet (SIS) is additional information which is necessary before FDA recognizes the standard. Found at http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[6] The online search for CDRH Guidance Documents can be found at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 10555-1:2013 Sterile, single-use intravascular catheters - Part 1: General requirements

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
4.6	Peak tensile force	☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Modified test speed and multiple joints tested at once

DESCRIPTION
Since multiple joints were tested at once, the gage length would necessitate speeds 1016 - 3556 mm/min which is not possible.

JUSTIFICATION
All joints were tested at 635 mm/min which provides a high level of assurance of bond strengths.

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
4.7	Freedom from leakage	☒ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆
Burst Pressure evaluated at 45psi/30s hold or 100 psi are acceptable by EN ISO 10555-1:2013 Annex C or Annex F respectively.

DESCRIPTION
Penumbra tests at 45psi/30s hold.

JUSTIFICATION
Penumbra is compliant with Annex C.

SECTION NUMBER	SECTION TITLE	CONFORMANCE?
		☐ Yes ☐ No ☐ N/A

TYPE OF DEVIATION OR OPTION SELECTED ◆

DESCRIPTION

JUSTIFICATION

* For completeness list all sections of the standard and indicate whether conformance is met. If a section is not applicable (N/A) an explanation is needed under "justification." Some standards include options, so similar to deviations, the option chosen needs to be described and adequately justified as appropriate for the subject device. Explanation of all deviations or description of options selected when following a standard is required under "type of deviation or option selected," "description" and "justification" on the report. More than one page may be necessary.

◆ Types of deviations can include an exclusion of a section in the standard, a deviation brought out by the FDA supplemental information sheet (SIS), a deviation to adapt the standard to the device, or any adaptation of a section.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Form Approved: OMB No. 0910-0120; Expiration Date: 1/31/2017

Department of Health and Human Services
Food and Drug Administration

STANDARDS DATA REPORT FOR 510(k)s

(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☒ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

EN ISO 11607-1:2009/R:2010 - Packaging for Terminally Sterilized Medical Devices – Part 1

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2]?	☒	☐
FDA Recognition number [3]	#14-193	
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☒
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)? If no, complete a summary report table.	☒	☐
Does the test data for this device demonstrate conformity to the requirements of this standard as it pertains to this device?	☒	☐
Does this standard include acceptance criteria? If no, include the results of testing in the 510(k).	☐	☒
Does this standard include more than one option or selection of tests? If yes, report options selected in the summary report table.	☐	☒
Were there any deviations or adaptations made in the use of the standard?	☐	☒
If yes, were deviations in accordance with the FDA supplemental information sheet (SIS) [5]?	☐	☐
Were deviations or adaptations made beyond what is specified in the FDA SIS? If yes, report these deviations or adaptations in the summary report table.	☐	☐
Were there any exclusions from the standard? If yes, report these exclusions in the summary report table.	☐	☒
Is there an FDA guidance [6] that is associated with this standard?	☐	☒
If yes, was the guidance document followed in preparation of this 510k?	☐	☐

Title of guidance: _____

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EXTENT OF STANDARD CONFORMANCE SUMMARY REPORT TABLE

STANDARD TITLE
EN ISO 11607-1:2009/R:2010 - Packaging for Terminally Sterilized Medical Devices – Part 1

CONFORMANCE WITH STANDARD SECTIONS*

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		

SECTION NUMBER	SECTION TITLE	CONFORMANCE? ☐ Yes ☐ No ☐ N/A
TYPE OF DEVIATION OR OPTION SELECTED ◆		
DESCRIPTION		
JUSTIFICATION		

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