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Image 2000

USER: MCINTOSH-LITTLE, KIMBERLY B (kml)

FOLDER: K063723 - 806 pages (FOI:08004401)

COMPANY: ABIOMED, INC. (ABIOMED)

PRODUCT: PUMP, BLOOD, CARDIOPULMONARY BYPASS, NON-ROLLER TYPE (KFM)

SUMMARY: Product: IMPELLA RECOVER LP 2.5 PERCUTANEOUS CARDIAC SUPPORT SYSTEM

DATE REQUESTED: Wed Dec 23 24:00:00 2009

DATE PRINTED: Wed Apr 28 10:48:07 2010

Note: Releasable Version

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

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-40
9200 Corporate Blvd.
Rockville, Maryland 20850

July 06, 2007

ABIOMED, INC.
22 CHERRY HILL DR.
DANVERS, MA 01923
ATTN: ROBERT T. KUNG

510(k) Number: K063723
Product: IMPELLA RECOVER LP 2.5 PERCUTANEOUS CARDIAC SUPPORT

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

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If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

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K063723/S1

ABIOMED

Recovering hearts. Saving lives.

William J. Bolt
Sr. Vice President of QA/RA
22 Cherry Hill Drive
Danvers, MA 01923
(p) 978-646-1451
(f) 978-739-0576

July 3, 2007

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Rockville, MD

Re: Response to AI letter for ~~K062723~~ K063723

Dear Sir:

Enclosed please find one original and 3 copies of a response to an Additional Information letter dated 2/12/2007 pertaining our 510(k) submission, K062723. An extension for our response until 8/10/2007 was granted on 3/5/07.

Thank you for your consideration in this matter. Please contact me with any comments or concerns.

Sincerely,

(b) (6) [redacted]

William J. Bolt

K21

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

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Response to the FDA February 12, 2007 Additional Information Letter

ABIOMED, Inc.

IMPELLA® RECOVER® LP 2.5 Percutaneous Cardiac Support System

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

RECEIVED FEB 20 2007

Abiomed, Inc.
c/o Mr. William J. Bolt
Senior Vice President
Cherry Hill Drive
Danvers, MA 01923

FEB 12 2007

Re: K063723
Trade Name: IMPELLA RECOVER LP 2.5 Percutaneous Cardiac Support System
Dated: December 14, 2006
Received: December 15, 2006

Dear Mr. Bolt:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a legally marketed predicate device based solely on the information you provided. To complete the review of your submission, please address the following deficiency:

> You have provided a comparison between your device and two (2) predicate devices. However, your device has different technological characteristics which could affect safety and effectiveness and raises a new type of question. We are not aware of a predicate device that has the following new type of question of safety and effectiveness: potential risk of damage to the aortic valve during placement and support, due to location of the pump within the heart. If you believe such a device exists, please provide a comparison between the predicate and your device.

The deficiency identified above represents the issue that we believe needs to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiency, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device.

We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least

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Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

You may not market this device until you have provided adequate information described above and required by 21 CFR 807.87(l), and you have received a letter from FDA allowing you to do so. If you market the device without conforming to these requirements, you will be in violation of the Federal Food, Drug, and Cosmetic Act (Act). You may, however, distribute this device for investigational purposes to obtain clinical data if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations.

If the information, or a request for an extension of time, is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days it will be considered and processed as a new 510(k)(21 CFR 807.87(l)); therefore, all information previously submitted must be resubmitted so that your new 510(k) is complete. Please note our guidance document entitled, "Guidance for Industry and FDA Staff FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the additional information request.

The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/cdrh/mdufma/guidance/1219.html.

The requested information, or a request for an extension of time, should reference your above 510(k) number and should be submitted in duplicate to:

Food and Drug Administration
Center for Devices and
Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

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

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If you have any questions concerning the contents of the letter, please contact Catherine Wentz at (240) 276-4266 or Kathryn O'Callaghan at (240) 276-4222. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or at (240) 276-3150, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

M. D. Hillebenne

for Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

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

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Appendix C: Langston Dual Lumen Catheter Labeling

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

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LANGSTON™

Dual Lumen Catheter

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EC REP

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

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International Symbols Glossary

	CONT		Latex			Manufactured by
International Symbols Glossary	Contents of package	No pressure Injection	Latex Free	Keep Dry	Keep away from Sunlight	Manufactured by Vascular Solutions, Inc.
Slovník mezinárodních symbolů	Obsah balení	Není určeno pro injekce pod tlakem	Neobsahuje latex	Udržujte v suchu	Chraňte před slunečním zářením	Vyrobeno společností Vascular Solutions, Inc.
Oversigt over internationale symboler	Pakkens indhold	Manglende tryk, injektion	Latexfri	Opbevares tørt	Tåler ikke direkte sollys	Fremstillet af Vascular Solutions, Inc.
Lijst van internationale symbolen	Inhoud van de verpakking	Geen drukinjectie	Latexvrij	Droog bewaren	Buiten het zonlicht bewaren	Vervaardigd door Vascular Solutions, Inc.
Kansainvälisten symbolien selitykset	Pakkauksen sisältö	Ei paineinjektiota	Lateksiton	Pidettävä kuivana	Pidä poissa auringonvalosta	Valmistaja Vascular Solutions, Inc.
Glossaire des symboles internationaux	Contenu de l'emballage	Aucune injection par pression	Sans latex	Maintenir au sec	Ne pas exposer au soleil	Fabriqué par Vascular Solutions, Inc.
Glossar der internationalen Symbole	Packungsinhalt	Keine Druckinjektion	Latexfrei	Vor Feuchtigkeit schützen	Vor Sonneneinstrahlung schützen	Hergestellt von Vascular Solutions, Inc.
Γλωσσάριο Διεθνών Συμβόλων	Περιεχόμενα συσκευασίας	Ένεση χωρίς πίεση	Δεν περιέχει ελαστικό κόμμι (Latex)	Διατηρείτε το στεγνό	Φυλάξτε μακριά από το φως του ήλιου.	Κατασκευάζεται από τη Vascular Solutions, Inc.
Glossario internazionale dei simboli	Contenuto della confezione	Iniezione senza pressione	Privo di lattice	Conservare in luogo asciutto	Non esporre alla luce diretta del sole	Prodotto da Vascular Solutions, Inc.
Objaśnienie symboli międzynarodowych	Zawartość opakowania	Urządzenie nie jest przeznaczone do iniekcji pod ciśnieniem	Nie zawiera lateksu	Chronić przed wilgocią	Chronić przed promieniami słonecznymi	Wyprodukowane przez firmę Vascular Solutions, Inc.
Glossário de símbolos internacionais	Conteúdo da embalagem	Não injectar pressão	Sem látex	Manter seco	Manter afastado da luz solar	Fabricado por Vascular Solutions, Inc.
Glosario de símbolos internacionales	Contenido del paquete	No apto para inyecciones a presión	No contiene látex	Mantener seco	No exponer a la luz solar	Fabricado por Vascular Solutions, Inc.
Förklaring av internationella symboler	Förpackningens innehåll	Ej för injicering med tryck	Latexfritt	Hållt torrt	Förvaras utom räckhåll för solljus	Tillverkad av Vascular Solutions, Inc.

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LANGSTON™ Dual Lumen Catheter Instructions For Use

USA CAUTION

Federal (USA) law restricts this device to sale by or on the order of a physician.

CAUTION

The LANGSTON dual lumen catheter should be used by physicians with adequate training in the use of the device.

DEVICE DESCRIPTION

The LANGSTON dual lumen catheter is intended for use as an angiographic pressure measurement catheter and for high pressure contrast injections. The LANGSTON catheter consists of an inner, braided high pressure lumen which extends the entire length of the catheter, which can be used for pressure measurement and rapid delivery of contrast medium and an outer lumen that ends approximately 3cm - 15cm proximal to the distal end of the catheter with sideholes for pressure measurement only. The inner and outer lumens are joined together using an adapter junction placed at the proximal end of the catheter. The adapter junction also incorporates a side port fitted with an extension tubing and a stopcock assembly for fluid flow and pressure measurement within the outer lumen. The distal end of the outer lumen is perforated with sideholes to allow simultaneous pressure measurement with the sideholes at the distal end of the inner lumen. The Langston dual lumen catheter is to be deployed through a standard introducer sheath of appropriate size and will accommodate standard ≤ 0.038" (0.965mm) diameter guidewire.

A single use pigtail straightener is supplied with all pigtail catheter models.

The Langston Straight Selective model has a single radiopaque marker located 1cm distal to the outer lumen pressure measurement sideholes.

INDICATIONS

Each LANGSTON dual lumen catheter is indicated for delivery of contrast medium in angiographic studies and for simultaneous pressure measurement from two sites. This type of pressure measurement is useful in determining transvalvular, intravascular and intraventricular pressure gradients.

CONTRAINDICATIONS

The LANGSTON catheter is contraindicated for use in:

- synthetic vascular grafts
- artificial heart valves

WARNINGS

The LANGSTON catheter is supplied sterile for single use only. Do not reuse, reshape or re-sterilize the device.

Do not exceed the maximum pressure rating when injecting contrast medium through the inner lumen. Maximum pressure ratings are listed in the table below for the specific model of Langston catheter.

Model	Catheter O.D.	Tip Configuration	Maximum psi Rating	Maximum kPa Rating
5500	8F	145° Pigtail	1200	8274
5540	6F	145° Pigtail	1000	6895
5550	6F	Multipurpose A2	1000	6895
5560	6F	Straight Selective	1000	6895

Do not use the outer lumen for the delivery or infusion of diagnostic, embolic, therapeutic materials or to perform pressure injections of contrast medium into the vascular system.

Check that all fittings and attachments are secure so that air is not introduced into the catheter during use.

COMPLICATIONS

As with all catheterization procedures, complications with the LANGSTON may occur. These may include:

- Myocardial Infarction
- local or systemic infection
- intimal disruption
- arterial dissection
- arrhythmias
- perforation and vessel rupture
- arterial thrombosis
- distal embolization of blood clots and plaque
- arterial spasm
- catheter fracture with tip separation and distal embolization

PRECAUTIONS

The LANGSTON catheter should be used by physicians thoroughly trained in percutaneous, intravascular techniques and procedures.

Do not use the LANGSTON catheter if the packaging has been damaged.

Inspect the catheter prior to use for any bends or kinks. Do not use a damaged catheter because vessel damage and/or inability to advance or withdraw the catheter may occur.

Do not crush or damage the outer lumen, as it may result in inaccurate pressure readings.

Ensure that the stopcock is in the closed position or connected to pressure tubing at all times. If the stopcock port is open, substantial bleed-back will result.

Both lumens must be flushed with heparinized saline to prevent clot formation and severe pressure damping. Aspiration of blood must be followed immediately with a flush.

Measures to prevent or reduce clotting should be taken when any catheter is used in the vascular system. At all times during use and immediately after removal from the vascular system, both lumens should always be flushed or filled with a flushing solution.

Use of systemic heparinization and heparinized sterile solution should be considered.

Exercise care in handling of the catheter during the procedure to reduce the possibility of accidental breakage, bending or kinking.

When the catheter is in the body, it should be manipulated only under fluoroscopy. Do not attempt to move the catheter without observing the resultant tip response.

Never advance or withdraw an intravascular device against resistance until the cause of the resistance is determined by fluoroscopy. Movement of the catheter or guidewire against resistance may result in separation of the catheter or guidewire tip, damage to the catheter, or vessel or ventricular perforation.

If extension tubing is used, select a type which is as short and rigid as possible. Use of an extension line with a large inner diameter or a soft material or over 4 feet (1.2m) in length may cause over damping of the pressure signal. This can manifest itself in severe smoothing of the recorded pressures and may lead to misinterpretation.

CLINICAL PROCEDURE

The following instructions provide technical direction but do not obviate the necessity of formal training in the use of angiographic catheters. The techniques and procedures described do not represent ALL medically acceptable protocols, nor are they intended as a substitute for the physician's experience and judgement in treating any specific patient. All available data, including the patient's signs and symptoms and other diagnostic test results, should be considered before determining a specific treatment plan.

Package contains:

- LANGSTON Dual Lumen Catheter model of choice

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

Note: Langston dual lumen pigtail catheters come with a tip straightener.

Other materials required but not provided:

- Sterile ≤ 0.038" (0.965mm) or smaller guidewire
- Sterile syringe
- Sterile heparinized saline

PREPARATIONS FOR USE

1. Carefully inspect the LANGSTON catheter packaging and components for damage prior to use.
2. Utilizing sterile technique, remove the LANGSTON catheter from its packaging and transfer to the sterile field.
3. Remove the catheter from the cardboard backing and inspect for any bends or kinks.

   Note: Remove the pigtail straightener from the cardboard holder when utilizing a pigtail model.
4. Utilizing sterile technique, thoroughly flush both ports. A sterile heparinized saline solution should be considered. Turn the outer lumen stopcock to the "off" position.

   Warning: Check that all fittings and attachments are secure so that air is not introduced into the catheter during the procedure.

   Precaution: During use ensure that the outer lumen stopcock is in the closed position or connected to pressure tubing at all times. If the stopcock port is not closed or connected to pressure-tubing, substantial bleed-back will result.
5. Load the inner lumen of a LANGSTON on a ≤ 0.038" (0.965mm) standard guidewire.

   The LANGSTON pigtail catheter is supplied with a tip straightener to use at your discretion, apply as follows: Advance the guidewire until the pigtail end is straight. Bypassing the handle (tab) load the lower (split end) of the straightener onto the guidewire, slide the straightener proximally until both tips align. At this point the handle (tab) should be pointed up and unattached to the catheter body. Pull the guidewire back to the tip of the pigtail.

DEPLOYMENT PROCEDURE

Deploy the LANGSTON according to the following steps:

1. Insert the catheter through the already positioned introducer sheath of appropriate size. If the tip straightener was used, remove as follows: Slide the straightener up the catheter until contact is made with the outer lumen. Apply gentle pressure pulling the handle (tab) away from the lumen until the slit opens and the straightener slides off the catheter.
2. Position the catheter in the proper location.

   Precaution: Never advance or withdraw an intravascular device against resistance until the cause of the resistance is determined by fluoroscopy. Movement of the catheter or guidewire against resistance may result in separation of the catheter or guidewire tip, damage to the catheter, or vessel or ventricular perforation.
3. Remove the guidewire. Aspirate and flush both lumens. A sterile heparinized solution should be considered. Lumens should be flushed at least once per minute to prevent clot formation. To minimize blood intrusion, keep both lumens of the catheter filled with sterile heparinized saline solution or contrast medium.

   Warning: Both lumens must be flushed with heparinized saline to prevent clot formation and severe pressure damping. Aspiration of blood must be followed immediately with a flush.
4. Connect both lumens to pressure tubing utilizing fluid to fluid connection. If extension tubing is used, select a type which is as short and rigid as possible. All lines should be free of all air. Even small air bubbles could cause patient injury or severe damping of transmitted pressure signals.

   Precaution: Use of an extension line with a large inner diameter or a soft material can cause over damping of the pressure signal. This can manifest itself in severe smoothing of the recorded pressures and may lead to misinterpretation.
5. Open outer lumen stopcock and obtain measurements and perform angiography as desired.

   Note: Langston catheters can record a continuous pressure measurement through the outer lumen while the inner lumen travels over the wire. For continuous pressure measurement, prepare the Langston as described above. Advance the Langston catheter over a ≤ 0.38" (0.965mm) wire so that the outer lumen sideholes are in a location distal to the lesion. Leaving the wire positioned through the inner lumen, connect only the clear extension arm of the outer lumen to the external transducer tubing. With the stopcock in the open position continuously record pressure while performing a pullback to a location proximal of the lesion.

   Warning: The outer lumen is designed for pressure measurements only and has not been tested for pressure injections. Do not use the outer lumen for the delivery or infusion of diagnostic, embolic, therapeutic materials or to perform pressure injections of contrast medium into the vascular system. Doing so could result in outer lumen rupture and arterial injury or damage.

   Warning: When injecting contrast medium through the inner lumen, do not exceed the maximum pressure rating as listed in the table below. Catheter rupture and arterial injury or damage could result.

Model	Catheter O.D.	Tip Configuration	Maximum psi Rating	Maximum kPa Rating
5500	8F	145° Pigtail	1200	8274
5540	6F	145° Pigtail	1000	6895
5550	6F	Multipurpose A2	1000	6895
5560	6F	Straight Selective	1000	6895

PACKAGING & STORAGE

Handle with care. Do not store in excessive heat. Prolonged exposure to ultraviolet light may cause discoloration and changes in the physical characteristics of the catheter material. Store in a cool, dry place. Keep away from sunlight.

Individually sterilized with ethylene oxide, packaged and supplied five (5) catheters to a carton.

LIMITED WARRANTY

Vascular Solutions, Inc. warrants that the LANGSTON catheter is free from defects in workmanship and materials prior to the stated expiration date. Liability under this warranty is limited to refund or replacement of any product, which has been found by Vascular Solutions, Inc. to be defective in workmanship or materials. Vascular Solutions, Inc. shall not be liable for any incidental, special, or consequential damages arising from the use of the LANGSTON catheter. Damage to the product through misuse, alteration, improper storage, or improper handling shall void this limited warranty.

No employee, agent, or distributor of Vascular Solutions, Inc. has any authority to alter or amend this limited warranty in any respect. Any purported alteration or amendment shall not be enforceable against Vascular Solutions, Inc.

THIS WARRANTY IS EXPRESSLY IN LIEU OF ALL OTHER WARRANTIES, EXPRESSED OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER OBLIGATION OF VASCULAR SOLUTIONS, INC.

PATENTS AND TRADEMARKS

International and U.S. patents pending.

LANGSTON™ is a trademark of Vascular Solutions, Inc.

See the International Symbols Glossary on page 3.

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Vascular SOLUTIONS

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Minneapolis, Minnesota 55369 USA
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Fax: +1 763-656-4250
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Tel: +49 (0) 721 5984 617
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42-0454-01 Rev B

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

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Appendix D: Video - Left Ventriculogram Procedure

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Left Ventriculogram Procedure

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

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Appendix E: Shiley Femoral 12 F Left Ventricular Venting Catheter

- 510(k) Clearance Information
- Buckberg et al. Cardiac Ischemia. Part II- Reperfusion and Treatment. West J Med 1987; 147 :54-61.
- United States Patent number 5,011,469

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

510(k) Premarket Notification Database

Device Classification Name	Catheter, Cannula And Tubing, Vascular, Cardiopulmonary Bypass
510(K) Number	K881734
Regulation Number	870.4210
Device Name	SHILEY FEMORAL LEFT VENTRICULAR VENT CATHETER
Applicant	SHILEY, INC. 17600 Gillette Ave. P.O. Box 19503 Irvine, CA 92714
Contact	Ganz Pobuda
Classification Product Code	DWF
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Specialty Conference

Cardiac Ischemia. Part II—Reperfusion and Treatment

Moderator
GLENN A. LANGER, MD

Discussants
GERALD D. BUCKBERG, MD, *and* JAN H. TILLISCH, MD

An edited summary of an Interdepartmental Conference arranged by the Department of Medicine of the UCLA School of Medicine, Los Angeles. The Director of Conferences is William M. Pardridge, MD, Professor of Medicine.

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GLENN A. LANGER, MD: In the previous issue we reviewed the physiologic and metabolic responses to cardiac ischemia. It was noted that there were immediate (within seconds to minutes) alterations in potassium flux and loss of contractile function after the onset of ischemia. These responses are implicated in the electrical dysfunction that results in sudden death and in the mechanical dysfunction that produces early pump failure. Following this acute phase there is a period of one to six hours during which metabolic dysfunction develops, which can be accurately monitored with the use of positron emission tomography (PET). These studies indicate the possibility of a major dissociation of blood supply and metabolic activity in the ischemic zone. The preservation of metabolic activity, as defined by PET, can be used as an objective indication in the determination of benefits to be expected by reperfusion.

In this issue the focus is on treatment with emphasis on surgical reperfusion (Dr Gerald Buckberg) and thrombolytic therapy and percutaneous transluminal angioplasty (PTCA) (Dr Jan Tillisch).

Myocardial Response to Reperfusion

GERALD D. BUCKBERG, MD:* The immediate recovery of regional contractility does not follow normal blood reperfusion after a duration of coronary occlusion as short as 15 minutes,[1] and segmental shortening may not return for as long as a month after two hours of temporary ischemia, if the working heart is reperfused with unmodified blood.[2,3] Coronary occlusion of six hours' duration is thought to produce such extensive transmural necrosis[4,5] that clinical muscle salvage cannot be expected even a year after reperfusion. Consequently, there is limited enthusiasm for either medical (streptokinase or angioplasty or both) or surgical—that is, coronary artery grafting—revascularization in patients who have had acute occlusion for six hours.

Our experimental studies have extended the period of regional ischemia to this six-hour interval. Our results, first, show the remarkable structural and functional integrity of transmural myocardial tissue after six hours of ischemia; second, document the extensive "reperfusion injury" produced by normal blood reperfusion with the heart in a beating working state after only four hours of ischemia, and third, show that modification of reperfusion damage, muscle salvage and immediate functional recovery is possible after six hours of ischemia by careful *control of the conditions and composition of reperfusion.*[6]

These experimental studies form the basis for our current clinical approach to treating acute myocardial infarction surgically. We shall present our preliminary surgical results and propose a new potential strategy whereby regional blood cardioplegic reperfusion on total bypass without thoracotomy—that is, in the catheterization laboratory—can be accomplished.

Experimental Studies in Animals

In experimental studies on anesthetized dogs whose chests have been opened, the proximal left anterior descending coronary artery was occluded with the heart in a working state to produce an area of risk of about 30%, and regional contractility was assessed by ultrasonic crystals.[6] All dogs underwent cannulation of the femoral artery and right atrium by way of the femoral vein; left ventricular venting was accomplished by the transaortic route (Figure 1) to allow reperfusion on total vented bypass in dogs undergoing controlled reperfusion. These cannulae were connected to a pump oxygenator circuit, and a catheter was placed into the distal left anterior descending coronary artery for regional cardioplegic reperfusion only in those dogs who received blood cardioplegic reperfusion.

Experimental groups differed in duration of ischemia and method of reperfusion:

- *Ischemia without reperfusion.* Seven dogs underwent six hours of acute coronary artery occlusion without reperfusion and transmural biopsy specimens were taken for ultra-

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ABBREVIATIONS USED IN TEXT

ATP = adenosine triphosphate
CoQ_{10} = coenzyme Q_{10}
IV = intravenously
PET = positron emission tomography
PTCA = percutaneous transluminal coronary angioplasty
TPA = tissue plasminogen activator
TTC = triphenyltetrazolium chloride

structural and mitochondrial functional analyses after prolonged ischemia.

• *Normal blood reperfusion in working hearts.* Nine dogs underwent two hours of acute coronary artery occlusion and seven dogs underwent four hours of acute occlusion followed by reperfusion with normal blood at systemic pressure (removal of occluding clamp) in working hearts to simulate angioplasty in a catheterization laboratory without the use of bypass.

• *Blood cardioplegic reperfusion during total vented bypass.* In 20 dogs, the left anterior descending coronary artery was occluded for two hours (5 dogs), four hours (8 dogs) and six hours (7 dogs), respectively. All hearts received regional blood cardioplegic reperfusion on total vented bypass. The conditions of reperfusion and composition of the reperfusion were controlled in the following manner: The conditions of reperfusion, which was modified, included (1) total heart decompression by vented bypass to prevent wall tension from developing in the damaged heart during reperfusion, thereby increasing its oxygen demands[7]; (2) gentle reperfusion pressure—that is, 50 mm of mercury—to limit postischemic edema produced by sudden reperfusion[8]; (3) regional cardioplegia to keep energy demands as low as possible during

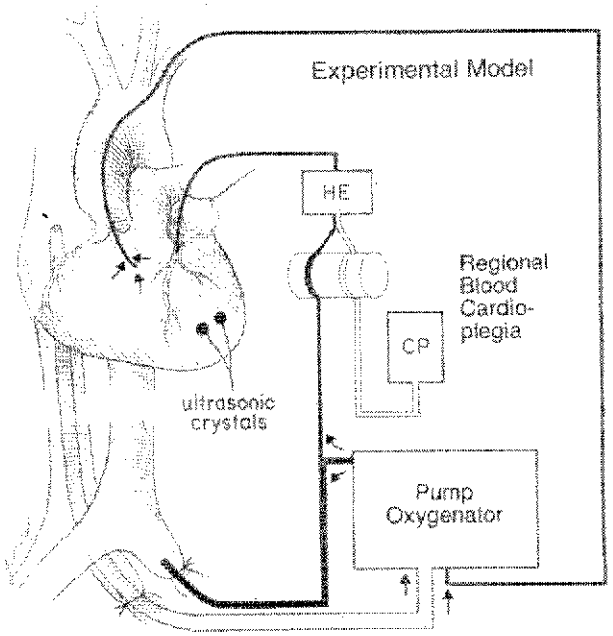

Figure 1.—Experimental model showing peripheral cannulation technique used to achieve total vented bypass without requiring direct right atrial, aortic or left ventricular penetration. Regional contractility was determined by ultrasonic crystals, and regional cardioplegic reperfusion delivered into the coronary artery directly (this can be achieved by a coronary balloon passed fluoroscopically; see text for description). CP = cardioplegic delivery system, HE = heat exchange

TABLE 1.—*Cardioplegic Solution*

Principle	*Constituent*	*Final Concentration*
Provide oxygen	Blood	Hematocrit 20% to 30%
Maintain arrest	Potassium chloride	12 to 16 mEq/liter
Buffer acidosis	Tromethamine	pH 7.5 to 7.6
Avoid edema	Glucose	>400 to 450 mosm
Restore substrate	Glucose	>400 mg per dl
	Aspartate	13 mmol/liter
	Glutamate	13 mmol/liter
Scavenger O_2 radical	Coenzyme Q_{10}	80 μg/ml
Limit calcium entry	Cardioplegic delivery	150 to 250 μmol Ca^{++}
	Diltiazem	300 μg/kg body weight

temporarily controlled reperfusion[8]; (4) normothermia to optimize the rate of cellular repair,[9] and (5) prolonged reperfusion duration—that is, 20 minutes—to maximize excess oxygen uptake relative to demands and avoid premature imposition of high-energy demands.[10] Total bypass was continued for 30 minutes after regional reperfusion and then stopped to allow observation for one additional hour with the heart in the working state.

The reperfusion composition was modified to permit (1) oxygenation with blood, providing substrate (O_2) to generate energy to repair cellular processes[11]; (2) cardioplegia (hyperkalemia) to keep the heart from resuming electromechanical activity and raising O_2 demand[9]; (3) replenishment of amino acid precursors or Krebs' cycle intermediates (that is, glutamate, aspartate) needed to ensure more effective oxidative metabolism to produce energy for cell repair and subsequent mechanical function[12]; (4) limiting calcium influx by reperfusate hypocalcemia (150 to 250 μmol) with citrate-phosphate-dextrose to reduce calcium load, and adding a calcium channel blocking drug (that is, diltiazem) (which could continue to retard calcium cell entry after normocalcemic reperfusion is started)[13]; (5) reversal of acidosis with a buffer to provide an optimal intracellular milieu for effective resumption of metabolic function[14]; (6) hyperosmolarity—that is, using glucose—to minimize postischemic edema and permit cell volume regulation to occur more gradually when normothermic blood flow is restored[15]; (7) membrane stabilization with the use of coenzyme Q_{10} (CoQ_{10}) to avoid damage to the phospholipid bilayer[16,17] and glucocorticoids to limit lysozymal disruption[18]; (8) counteracting oxygen free radicals with oxygen free-radical scavenger—that is, CoQ_{10}—to limit the cytotoxic effects of these compounds, and (9) hyperglycemia to enhance the osmotic effects and perhaps initiate compartmental anaerobic energy production at the onset of reperfusion.[19] These reperfusate principles were accomplished with the agents shown in Table 1—which defines the regional reperfusate used in these studies—but may also be accomplished by other, untested agents (that is, different buffers, oxygen radical scavengers, calcium channel blocking and cardioplegic drugs) that produce these desired effects.

Ischemia for six hours without reperfusion produced only mild structural alterations. Myofibrils were intact, mitochondria showed integrity of the inner and outer membranes and only mild clarification of the matrix. At least 200 mitochondria were examined in each muscle layer in each heart by the low protein denaturation technique,[20] and the average mitochondrial grades ranged from 1.2 in epicardial muscle to 1.9 in endocardial muscle (grade 6 is complete disruption) (Figure 2). This ultrastructural integrity was accompanied by

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substantial retention of mitochondrial respiratory function; the adenosine triphosphate (ATP) production rate (stage 3 respiration × adenosine diphosphate/0) was maintained at 64% of control levels (589 versus 925 nmol ATP per grams protein per minute) after six hours of regional ischemia.

Dyskinesia (systolic bulging) persisted throughout the ischemic interval in all experiments. Reperfusion with normal blood with the heart in the beating, working state failed to restore regional systolic shortening after two or four hours of ischemia ($-35\% \pm 6\%$ and $-13\% \pm 4\%$ systolic shortening) measured after the first hour of observation after revascularization. In contrast, immediate recovery of systolic shortening occurred in each of 13 hearts reperfused with substrate-enriched blood cardioplegia on total vented bypass after two and four hours of ischemia ($52 \pm 2\%$ and $40 \pm 7\%$) and in six of seven hearts ($21 \pm 6\%$ systolic shortening) undergoing control reperfusion after six hours of coronary artery occlusion (Figure 3).

Acute coronary artery occlusion produced profound transmural ischemia, reducing flow (radioactive microspheres) to less than 5% of control levels. Reperfusion with normal blood with the heart in the beating, working state after only two hours of ischemia restored transmural flow to only 47% of control levels. In contrast, all hearts reperfused after six hours of ischemia with blood cardioplegia on total vented bypass had pronounced transmural hyperemia (Figure 4).

Histochemical muscle damage (triphenyltetrazolium chloride [TTC] nonstaining) was least severe (12% area of nonstaining versus area at risk) after two hours of ischemia followed by controlled conditions and composition of reperfusate and most severe (73% area of nonstaining versus area at risk, $P < .05$) following normal blood reperfusion after four hours of regional ischemia. More extensive nonstaining followed controlled reperfusion in nonbypassed hearts after four hours of ischemia than after controlled reperfusion following six hours of regional ischemia (73% versus 55%, $P < .05$).

Uncontrolled reperfusion (normal blood in working hearts) after four hours of ischemia produced moderately severe transmural architectural disruption, with the most severe damage (grades 3.7 and 3.4) in endocardial and midmyocardial muscle; there was breakdown of mitochondrial cristae, with filling of the mitochondrial space with amorphous vesicles and intensely stained material. In contrast, the average grade for mitochondrial change after blood cardioplegia reperfusion on total vented bypass was comparable to that occurring with ischemia alone (1.2 and 1.9) where inner and outer mitochondrial membranes were intact and myofibrils were unaltered.

These experimental studies show that immediate partial recovery of regional contractile function is possible after as long as six hours of acute coronary artery occlusion, provided that the conditions of reperfusion and composition of reperfusate are controlled carefully. Such control results in higher postischemic flows and in superior ultrastructure when compared with normal blood reperfusion of working hearts after shorter ischemic intervals (two to four hours).

These data provide experimental confirmation of the inability of "successful" reperfusion with streptokinase or angioplasty, or both, to avoid infarction or restore early con-

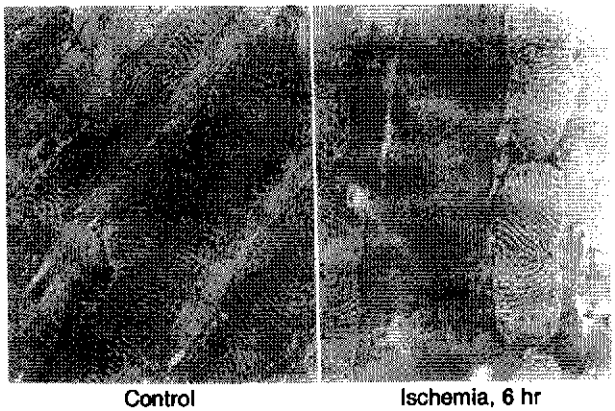

Figure 2.—The mitochondrial ultrastructure, prepared by the low denaturation embedding technique, shows a relatively normal appearance of mitochondria after 6 hours of ischemia (right panel) compared with control (left panel).

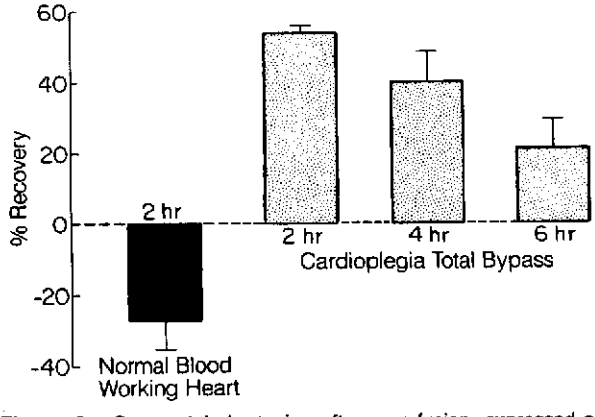

Figure 3.—Segmental shortening after reperfusion, expressed as percentage of recovery of systolic shortening, is compared with control after normal blood reperfusion in working heart (solid bar) and substrate-enriched blood cardioplegic reperfusion on total vented bypass (stippled bars). Note failure to recover systolic shortening after uncontrolled reperfusion at 2 hours (solid bar) and immediate recovery of systolic shortening after 2, 4 and 6 hours of ischemia after controlled reperfusion.

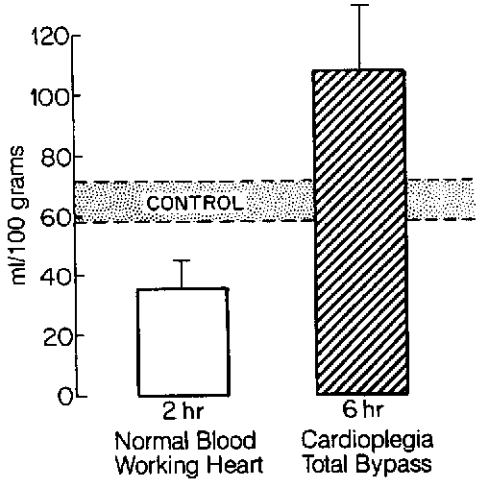

Figure 4.—Left ventricular transmural blood flow (microspheres) is shown after reperfusion with normal blood in working heart (open bar) and substrate-enriched blood cardioplegic solution on total bypass (hatched bar). Control values are shown in stippled bar. Note the low reflow with uncontrolled reperfusion after 2 hours of ischemia and hyperemic flows after 6 hours of ischemia and controlled reperfusion. Units given represent the mean ± standard error.

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TABLE 2.—*Global and Regional Contractility*

Cardiac Indices	*Medical Treatment*	*Surgical Treatment*
Global ejection fraction, %	41±2*	47±2*
Regional recovery		
Wall-motion score†	2.5±0.5*	1.3±0.2*‡
Points <2.0	2 of 21 (10%)	12 of 12 (100%)

*Values are mean ± standard error.
†Wall-motion grade: grade 0=normal, grade 1=mild to moderate hypokinesis, grade 2=severe hypokinesis, grade 3=akinesis, grade 4=dyskinesis.
‡$P<.05$.

TABLE 3.—*Control During Reperfusion*

Approach	*Surgical Treatment*	*Medical Treatment*
Arterial inflow	Aorta	Femoral artery
Venous return	Right atrium	Right atrium (via femoral vein)
Ventricular vent	Left ventricle (direct)	Left ventricle (transaortic)
Regional reperfusion	Coronary artery bypass grafting	Coronary catheter

tractile function to regional segments revascularized in the catheterization laboratory.[21-23]

Preliminary Clinical Studies

The principles of reperfusion control emerging from these experimental studies were applied by us in a preliminary series of patients with acute evolving myocardial infarction. We compared the results after surgical control of the conditions of reperfusion and composition of the reperfusate with those achieved by "successful" streptokinase or angioplasty or both, where no attempt was made to exert reperfusate control except to restore blood flow per se to the ischemic segment.

A total of 33 consecutive patients with acute coronary artery occlusion underwent either medical or surgical revascularization. Medical reperfusion was with normal blood in 21 patients in the catheterization laboratory (that is, streptokinase therapy, N = 11; angioplasty, N = 10) after 4.4 ± 0.5 hours of acute coronary artery occlusion. Surgical reperfusion was with substrate-enriched (glutamate plus aspartate) blood cardioplegia during coronary artery grafting after naturally occurring occlusion in 12 patients revascularized 8.8 ± 6 hours (range 7.4 to 13.5 hours) after occlusion.[21]

Medical revascularization produced cardiogenic shock (stroke work index <20 grams • m per m^2, pulmonary artery wedge pressure >20 mm of mercury) in 7 of 21 previously hemodynamically stable patients—5 with single-vessel disease—whereas surgical revascularization reversed cardiogenic shock in 6 of 12 patients with preoperative hemodynamic instability due to coronary occlusion. Surgical results were superior in incidence of infarction as recorded by electrocardiogram (57% versus 100%, $P<.05$), severe ventricular tachyarrhythmias (0% versus 43%, $P<.05$), recovery of global ejection fraction (47% versus 41%), recovery of significant regional contractility (100% versus 9%, $P<.05$) and duration of hospital stay (8.8 versus 11 days, $P<.05$), despite a delay of surgical treatment for as long as 12 hours. No patient died (Table 2).

These preliminary clinical results are directly comparable with those achieved experimentally and may lead to the conclusion that selected patients with acute coronary artery occlusion should be treated surgically. Control of the conditions and composition of reperfusion may, however, be achieved medically without thoracotomy (Table 3). The right atrium can be decompressed by way of the femoral vein, arterial influx can be delivered through the femoral artery and left ventricular decompression can be achieved by using a catheter passed transaortically from a peripheral artery, while the regional cardioplegic reperfusate can be administered through a reperfusion catheter advanced through the clot and stenosis as occurs with angioplasty done emergently.

This proposed future approach to patients with acute coronary artery occlusion is shown in Figures 5 and 6. The process of infarction can be arrested by placing a patient on total

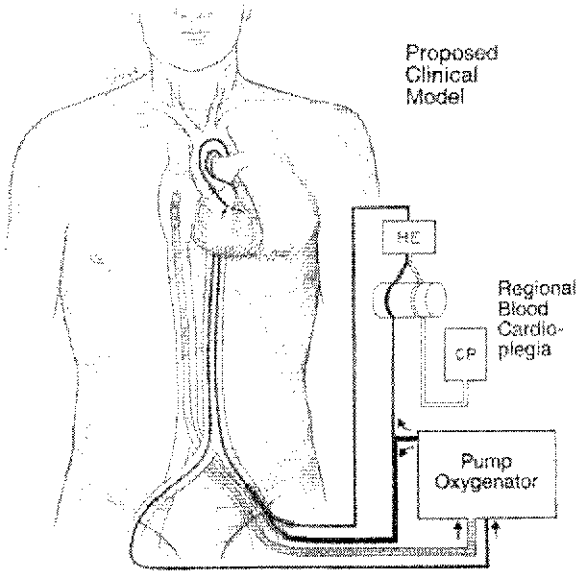

Figure 5.—Proposed experimental model of total vented bypass and regional cardioplegic reperfusion without thoracotomy. Note that the venous return catheter is advanced from the femoral vein to the right atrium, that arterial inflow is through the femoral artery, that left ventricular decompression is achieved by means of a transaortic catheter from the femoral artery and that the reperfusate catheter is passed into the coronary artery by way of the coronary ostia from the femoral artery. CP = cardioplegic delivery system, HE = heat exchanger

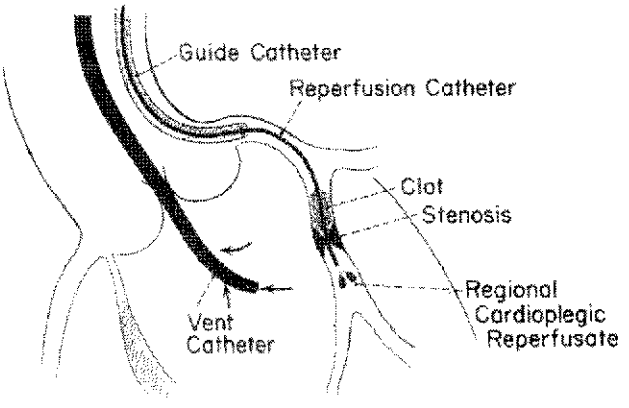

Figure 6.—A close-up version is shown of a proposed technique to decompress the left ventricle via a ventricular vent catheter passed across the aortic valve and a regional cardioplegic catheter passed through a coronary guide catheter, through clot and across the stenotic region into a distal coronary vascular bed (see text for description).

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vented bypass in the catheterization laboratory so that an angiogram can be safely carried out and the decision made whether to do controlled regional reperfusion followed by angioplasty (single-vessel disease) or to transport the patient to the operating room on total vented bypass for surgical revascularization (multivessel disease or occluded arteries, or both, that cannot be penetrated by a guidewire).

We interpret the findings of these experimental and clinical studies to indicate that muscle salvage and restoration of early contractile function is possible in myocardium that is ischemic for six or more hours, if there is rigid control of the reperfusate conditions and composition.

Current Approaches in the Treatment of Ischemia

JAN H. TILLISCH, MD:* After many decades of therapeutic focus on the consequences of ischemic injury—arrhythmias, pump failure or mechanical lesions, such as mitral regurgitation, aneurysm or septal defects—in the past decade there has been a shift in the focus toward ameliorating the ischemic injury itself, first by attempting to reduce myocardial oxygen demands and, more recently, by pharmacologically or mechanically restoring perfusion during the evolution of an ischemic injury.

The development of clinical techniques of reperfusion during acute myocardial infarction has made necessary the careful examination of the complex interplay of factors that result in ischemic injury. The duration of ischemia is not the sole determinant of the degree of myocardial injury. The severity of the ischemia (as determined by the presence or absence of collateral flow or by spontaneous early partial reperfusion), the myocardial oxygen demands during the ischemic period and, more important, at the time of reperfusion, the preocclusive metabolic state of the myocardium, the nature of the reperfusate and the hydrodynamics of the actual reperfusion process all may have a significant determinative effect on the degree of myocardial salvage achieved by reperfusion.

We have witnessed during the past five years a flood of clinical and experimental studies showing the technical ability to achieve reperfusion in patients with acute infarction with safety and with a success rate varying between 30% and 100%, depending on the techniques chosen and the patient population studied. The metabolic and functional state of the reperfused myocardial region and the functional and survival characteristics of the patient population are now being addressed in various investigative studies.

Ischemic Injury

A brief review of the consequences of ischemia has been presented in the previous sections (see Part I in the June 1987 issue of THE WESTERN JOURNAL OF MEDICINE, volume 146, pp 713-723).

The temporal sequence of these processes depends on the severity of the ischemia and the metabolic state of the myocardium, as determined largely by the relation between oxygen supply and demand before and during the ischemic interval and at the time of reperfusion.

The optimal current and future therapy for acute ischemic injury must be considered in light of these events. Three general approaches to acute ischemic injury may be considered: first, the more "traditional" approach of attempted pharmacologic reduction in myocardial oxygen demands and enhancement of supply, coupled with aggressive treatment of secondary complications of myocardial infarction (arrhythmia, pump failure) but without attempts at reperfusion; second, attempted reperfusion using thrombolytic agents, particularly streptokinase or tissue plasminogen activator, and third, "mechanical" reperfusion using percutaneous transluminal angioplasty or coronary artery bypass grafting.

Therapy Without Reperfusion

The first mode of therapy is clearly not a static one. Recent studies have suggested that the aggressive use of nitroglycerin given intravenously (IV) in the early stages of acute myocardial infarction reduces postinfarction morbidity.[24] Controversy remains about the initial use of β-blockade in patients with evolving myocardial infarction.[25] Metabolic enhancement with glucose-insulin-potassium infusions seems to be beneficial.[26] The impact, however, of newer pharmacologic means of manipulating myocardial metabolic demands has been difficult to discern, hampered to some extent by the lack of sensitivity of the diagnostic methods used to judge that impact.

Thrombolytic Therapy

Thrombolytic reperfusion has been achieved by the intracoronary administration of streptokinase in about 60% to 80%[22,27] of patients with occluded infarct-related arteries. In these two large randomized studies, the mortality results were discrepant; in the study reported by Rentrop and associates,[22] no significant difference in mortality rates was observed, while in the western Washington trial, a slightly improved survival was noted in the treatment group at one year, but only after statistical adjustment for nonmatching variables in the two groups.[27] As with previous uncontrolled trials, those patients in whom reperfusion was achieved had improved mortality rates, not surprisingly showing that thrombolysis had apparent benefit but that the overall success in a large patient group was limited by the actual success in achieving reperfusion. Because of the need for cardiac catheterization to use this form of therapy, with the attendant delay in application and the logistic difficulties of having catheterization facilities on demand, intracoronary thrombolysis seems to have only a limited application, given the marginal effects observed on mortality results and the lack of effect on ventricular function.[23,27]

Intravenous administration of thrombolytic agents has the obvious appeal of greater speed and ease of administration, with the concomitant drawback, particularly in the case of streptokinase, of an increased systemic thrombolytic state with consequent increased risk of bleeding complications. The reports of nonrandomized trials have suggested again that successful thrombolysis was associated with an improvement in survival both of myocardium at risk and of patients. Documented successful reperfusion, however, was achieved in only 35%[28] in one randomized trial, although higher rates of successful thrombolysis have been reported.[29]

Despite the rather low success rate of the use of IV streptokinase, several studies have shown a lower mortality rate with its use as compared with conventional therapy.[30,31] Factors that may influence those results will be discussed subsequently. Nonetheless, a more consistently effective thrombolytic agent has been sought, and initial trials with tissue plasminogen activator (TPA), derived from recombinant

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DNA technology, are promising. TPA does not induce a systemic thrombolytic state, a theoretic advantage in terms of hemorrhagic complication. The risk of hemorrhage, however, appears to be due to subsequent heparin therapy in most instances, rather than the dose or type of thrombolytic agent. A study comparing IV streptokinase with IV TPA found that 60% achieved reperfusion with TPA as against 35% with streptokinase. Despite this large difference in successful thrombolysis, the hospital mortality rate was not significantly different. The previously shown benefits of successful thrombolysis (as against the benefits accruing to the applied therapy as a whole) suggest that an improved incidence of successful reperfusion is associated with improved myocardial salvage and therefore mortality in the treatment group. The correlation, however, of improved myocardial salvage and improved patient mortality figures has not as yet been conclusively shown with intravenous thrombolytic agents.

Several factors influence the success of thrombolytic reperfusion in myocardial salvage; other factors may influence the effect on patient mortality rates.

The time to reperfusion is obviously a critical factor. Attempted reperfusion after more than 1½ to 2 hours of chest pain in patients with evolving "transmural" infarctions has been associated with little or no effect on regional myocardial function judged by wall-motion studies within one to two weeks of therapy.[32,33] This was found despite comparable success in reperfusion in "early" and "late" treatment groups. Indeed, no study has suggested that reperfusion success itself is influenced by the time of treatment relative to the onset of symptoms. It is the degree of myocardial salvage that seems influenced. Nonetheless, one cannot definitively state from present data that beneficial effects of thrombolytic reperfusion accrue only to those treated early. Subgroup analysis of the reported studies has not been done in such a way as to determine whether enhancing global myocardial blood flow by reperfusion may affect long-term morbidity without necessarily affecting myocardial salvage in the region of the infarction. Findings of the western Washington intracoronary streptokinase trial, where mortality was marginally improved in the treated group without a discernible effect on ventricular function, may be interpreted as supporting the hypothesis of improved survival without "salvage" of infarcting tissue.[23,27] Moreover, analysis of ventricular function in this trial was done at a mean of eight weeks after acute infarction, a sufficient time period to permit return of function of "stunned" but viable myocardium. Determination of regional or global ventricular function at shorter intervals (3 to 14 days in most published thrombolytic trials) may fail to show recovery of function of reperfused myocardium, which at a later date will show improvement in contractile performance, particularly in those patients treated beyond one to two hours of ischemia.

The intensity of ischemia may be an even more important influence on ventricular function and ultimate patient survival than the duration. Three components of this factor may be operative. First, the degree of residual flow through a partially occluded artery, or the degree of spontaneous early reperfusion—that is, before treatment—has been seen only in studies where coronary angiography was done before administration of the thrombolytic agent. The presence of an incompletely occluded artery before therapy (or in control groups) is associated with greater short-term improvement in ventricular function.[22,34] The second component affecting the intensity of ischemia is the presence of collateral flow at the time of pretreatment angiography. Several studies have shown that the improvement in ventricular function after successful reperfusion occurs largely in patients who had angiographically demonstrable collateral flow to the infarct vessel distribution.[35,36] The presence of collateral, residual or early spontaneous reperfused flow seems to have a major effect on the degree of ventricular salvage achieved by thrombolysis, despite being insufficient to avoid infarction altogether. A third component of the ischemic state is the degree of residual coronary luminal narrowing after thrombolysis. Several studies indicate more successful return of contractility in the region of infarct when the residual stenosis was modest[37] or when percutaneous transluminal coronary angioplasty (PTCA) was done early after successful thrombolysis.[38] In addition to the possible beneficial effects of increased blood flow through a minimally obstructed artery on myocardial recovery, the incidence of postthrombolytic reocclusion was lower in those patients with less residual stenosis.[37]

Another factor that may influence the extent of myocardial salvage consequent to reperfusion is the mechanical loading condition of the ventricle at the time of reperfusion. Although often difficult to assess clinically, experimental studies by Buckberg (see previous section) and by Laschinger and associates[39] show the importance of reduced myocardial oxygen requirements through reduction of mechanical work during reperfusion. Whether pharmacologic manipulation of hemodynamics using aggressive coronary and systemic vasodilatation, calcium channel blocking agents or β-blockade have particularly beneficial effects at the time of reperfusion is as yet unexplored but theoretically attractive.

Percutaneous Transluminal Angioplasty

Percutaneous transluminal coronary angioplasty as a mode of primary reperfusion during the evolution of acute infarction has advantages over thrombolytic therapy but clearly counterweighing disadvantages, principally related to the delay in initiating therapy.

The published success rate for reperfusion with PTCA is comparable to the intracoronary administration of thrombolytic agents.[40] The concern noted earlier about the deleterious effects of the residual stenosis is of course obviated by PTCA. Evidence from several studies suggests enhanced recovery of ventricular function with PTCA compared with that with thrombolysis alone.[41,42] The delay inherent in angioplasty, however, although of only modest statistical significance in a large study, may be of major individual significance in a patient with a large but partially collateralized anterior infarction. Again, one must weigh the risk of delay with PTCA as against the risk of failure to reperfuse with IV streptokinase or TPA.

The combination of PTCA with the intracoronary administration of streptokinase or TPA does not seem to enhance successful reperfusion, nor does it diminish the delay in therapy associated with the use of an angiographic technique. The initial use of IV thrombolytic agents (after placing an intraarterial sheath) and then the subsequent use of PTCA seem to offer several advantages: therapy is begun early, ineffective reperfusion may be addressed at cardiac catherization with either additional intracoronary thrombolysis or with PTCA and residual stenosis can be directly dealt with at the time. The disadvantages are that the safety of urgent coronary artery bypass grafting should PTCA result in vascular trauma or reocclusion is compromised by the thrombolytic state; the

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logistic concerns regarding the necessity for 24-hour availability of catheterization laboratory remain, and a post-thrombolytic, late-catheterization procedure to determine the degree of vessel patency means a patient would require two coronary angiograms, with the additional expense and risk. If these objections are met with evidence of improved long-term survival, morbidity and ventricular function, then this form of therapy may be an appropriate choice.

Coronary Artery Bypass Grafting

DeWood and colleagues have repeatedly shown that there is a low mortality rate when coronary artery bypass grafting is done within the first six hours of infarction.[43] Although uncontrolled, these studies are compelling if not totally convincing. The delay in reperfusion with immediate coronary artery bypass grafting is substantially greater than with other forms of reperfusion. Logistic and as-yet-undetermined cost considerations aside, the ability to achieve adequate and complete revascularization must be weighed against the loss of possibly salvageable myocardium with this delay. Data discussed previously by Dr Buckberg, however, show that the experimental treatment of ischemic injury is best done when "the conditions and composition" of the reperfusate can be controlled. The period of time during which substantial myocardial salvage can be expected is prolonged substantially by confining initial metabolic efforts after reperfusion to the cellular tasks of membrane maintenance, calcium sequestration, volume regulation and replenishment of metabolic intermediates, high-energy phosphate precursors and stores before requiring contractile work to be done.

The clinical dilemma is determining when the time is past for unmodified and uncontrolled reperfusion. When, in an ischemic injury, does the benefit of a rapidly administered but only partially successful reperfusion technique become less than that provided by modified controlled reperfusion with the attendant delay in application? Moreover, will the logistic concerns and associated co-morbidity of immediate coronary artery bypass grafting be small enough to permit the widespread application of this technique? These critical questions remain to be answered.

Combining PTCA with modification of reperfusion as previously presented has exciting potential for shortening the delay and lessening the morbidity of surgical intervention implicit in selecting immediate coronary artery bypass grafting as therapy, but retains some of the advantages of more effective myocardial salvage, as shown experimentally with coronary artery bypass grafting and controlled reperfusion. This form of therapy awaits further development and validation of its effectiveness.

Current Clinical Choices

At this time, hard clinical data sufficient to determine a clinical course in a patient with acute myocardial infarction are not yet available. Clinical experience, however, coupled with current understanding of the pathophysiology of ischemic injury, permits some guidelines to be developed, with the usual caveats that individual patients require individual approaches and that continued reevaluation of results is required in areas where proof does not yet exist.

Patients who present with acute myocardial infarction and symptoms of a duration of one to two hours or less are best treated with intravenous thrombolytic therapy. Exceptions would of course be those with major hemorrhagic risk or advanced age. The presence of prior myocardial infarction, severe hemodynamic compromise or extension of an acute infarction into other vascular distributions would be situations wherein myocardial salvage may not entirely depend on thrombolysis of a single vessel but rather on the cascade of increased demand on adjacent myocardium with a compromised blood supply. In such cases, the best approach seems to be immediate coronary artery bypass grafting with modified reperfusion of the infarcted vessel and revascularization of other arteries.

In patients who present with an apparent duration of ischemia of between two and four hours, the ability to preserve substantial myocardium seems to be limited largely to those with incomplete occlusion or a collateralized infarct region. The delay associated with demonstration of that state by angiography and proceeding to use either PTCA or thrombolysis with PTCA to follow may therefore have relatively little consequence in terms of myocardial salvage. The greater reperfusion success rate with PTCA, or the intracoronary use of thrombolytic agents, and the opportunity at catheterization to discover a need for multiple lesion revascularization by coronary artery bypass grafting or PTCA might lead one to select coronary angiography as the first step in managing a patient with ischemic injury of two to four hours' duration. If IV tissue plasminogen activator proves to be as successful as PTCA or intracoronary thrombolysis (about 70%), then this would seem to be the preferred initial choice, until such time that nonsurgical controlled reperfusion might become a reality.

It is in this group of patients with ischemia of sufficient duration to militate against myocardial salvage with any but modified reperfusion that there is the greatest confusion as to appropriate therapy. Clearly, diagnostic methods are needed to attempt to differentiate patients in whom sufficient residual flow in the infarct region persists to mandate an early attempt at noninvasive thrombolysis. A short delay in therapy attendant to applying some diagnostic method of differentiating the potentially salvageable from irreversibly injured myocardium would be a reasonable price to pay, if it permits more appropriate application of therapy.

Patients who present with evidence of ischemia for longer than four to six hours will, in general, derive no benefit from immediate thrombolytic techniques. The maximum interval with modified direct reperfusion is as yet unknown. Clearly some patients with chest pain of more than four to six hours will still have substantial myocardium at risk but salvageable. The absence of electrocardiographic Q waves, the continued presence of substantial ST-segment elevation and the presence of hypokinesis or dyskinesis as against akinesis on echocardiography may be "soft" indicators of continued viability. Again, diagnostic methods of determining tissue viability need to be validated.

With any of these techniques, concurrent therapy with IV nitroglycerin, aggressive treatment of congestive heart failure, rigorous control of hypertension and treatment of tachycardia are supplemental and important. Continued investigation into the benefits of pharmacologic agents that may enhance anaerobic metabolism, diminish transmembrane calcium flux, prevent generation of oxygen-free radicals and diminish myocardial membrane injury must be particularly tested in the reperfusion model and subsequently in that clinical setting.

What was once conceived of as an irreversible insult—the

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cessation of flow to contracting myocardium—has been shown after short intervals to be partially and potentially reversible. The temporal limits of reversibility in cases of acute ischemic injury have not as yet been clearly defined.

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United States Patent [19]

Buckberg et al.

[11] **Patent Number: 5,011,469**

[45] **Date of Patent: Apr. 30, 1991**

[54] **PERIPHERAL CARDIOPULMONARY BYPASS AND CORONARY REPERFUSION SYSTEM**

[75] Inventors: **Gerald D. Buckberg; James V. Maloney, Jr.**, both of Los Angeles; **Kenneth A. Jones**, Lake Elsinore; **Weldon D. West**, Mission Viejo, all of Calif.

[73] Assignee: **Shiley, Inc.**, Irvine, Calif.

[21] Appl. No.: **237,969**

[22] Filed: **Aug. 29, 1988**

[51] **Int. Cl.**[5] **A61M 37/00**

[52] **U.S. Cl.** **604/4**; 604/8; 604/53

[58] **Field of Search** 604/4–8, 604/50–54

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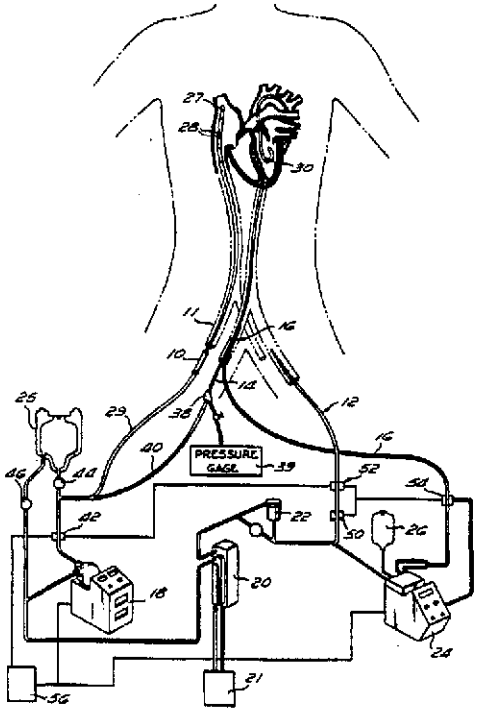
Primary Examiner—Randall L. Green
Assistant Examiner—Randy Shay
Attorney, Agent, or Firm—Knobbe, Martens, Olson & Bear

[57] **ABSTRACT**

A method and apparatus to arrest or reverse heart damage from myocardial infarction by using a peripheral, femoral-femoral full bypass along with the venting of the left ventricle wherein the rate at which blood is drawn from the femoral vein and the rate at which the left ventricle is vented are related in a predetermined manner. The damaged area is treated with a cardioplegic solution; the blockage causing the heart attack is then removed by a thrombolytic solution or by angioplasty, while blood is prevented from entering the ventricle and from reactivating the heart from its at-rest condition. Normal blood flow is then restored, and the various catheters and bypass mechanisms removed. The system is also useful for peripheral cardiopulmonary bypass systems not involving the application of a cardioplegic solution. The catheters are specially designed for their function.

35 Claims, 7 Drawing Sheets



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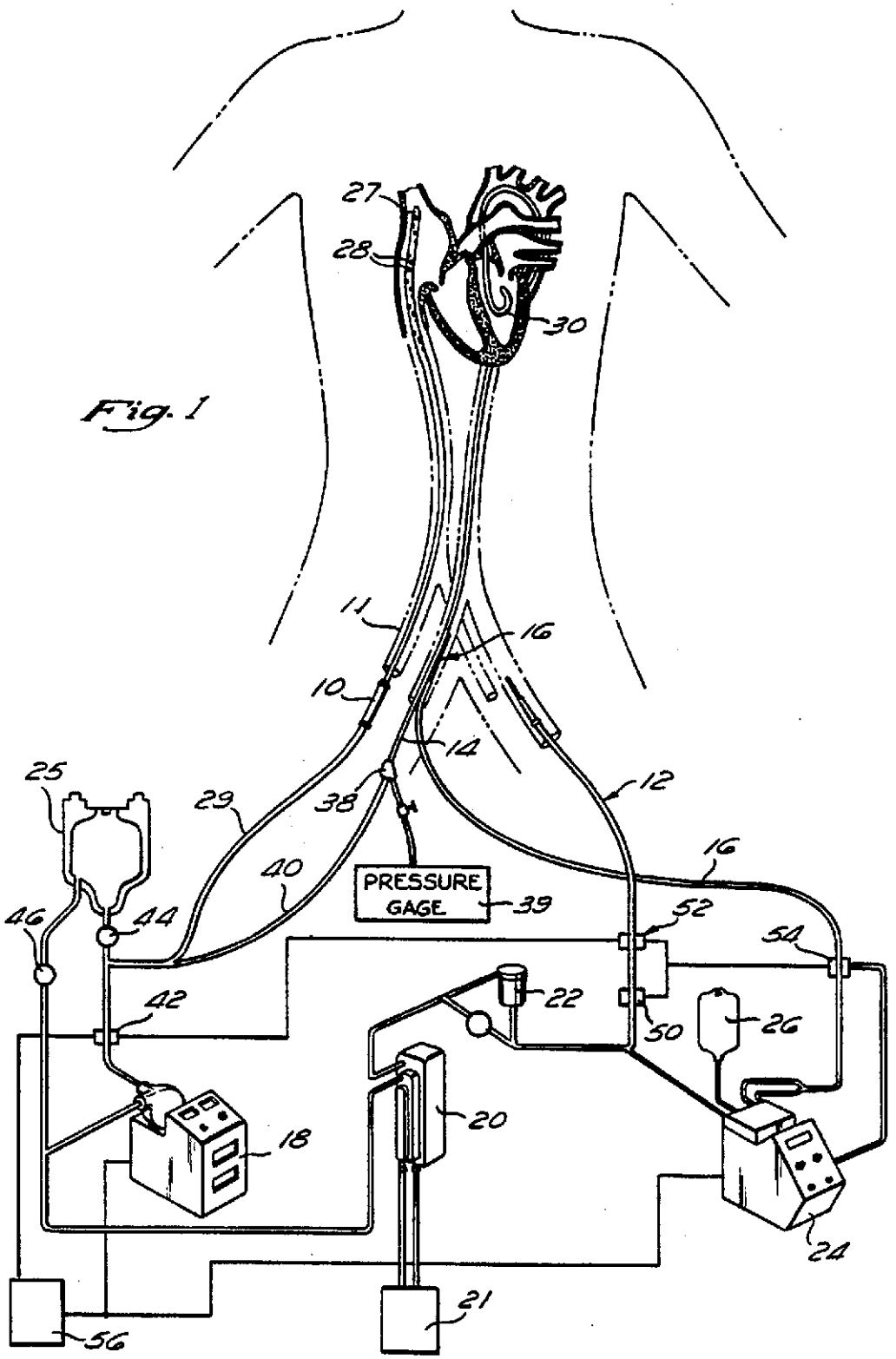

Fig. 1

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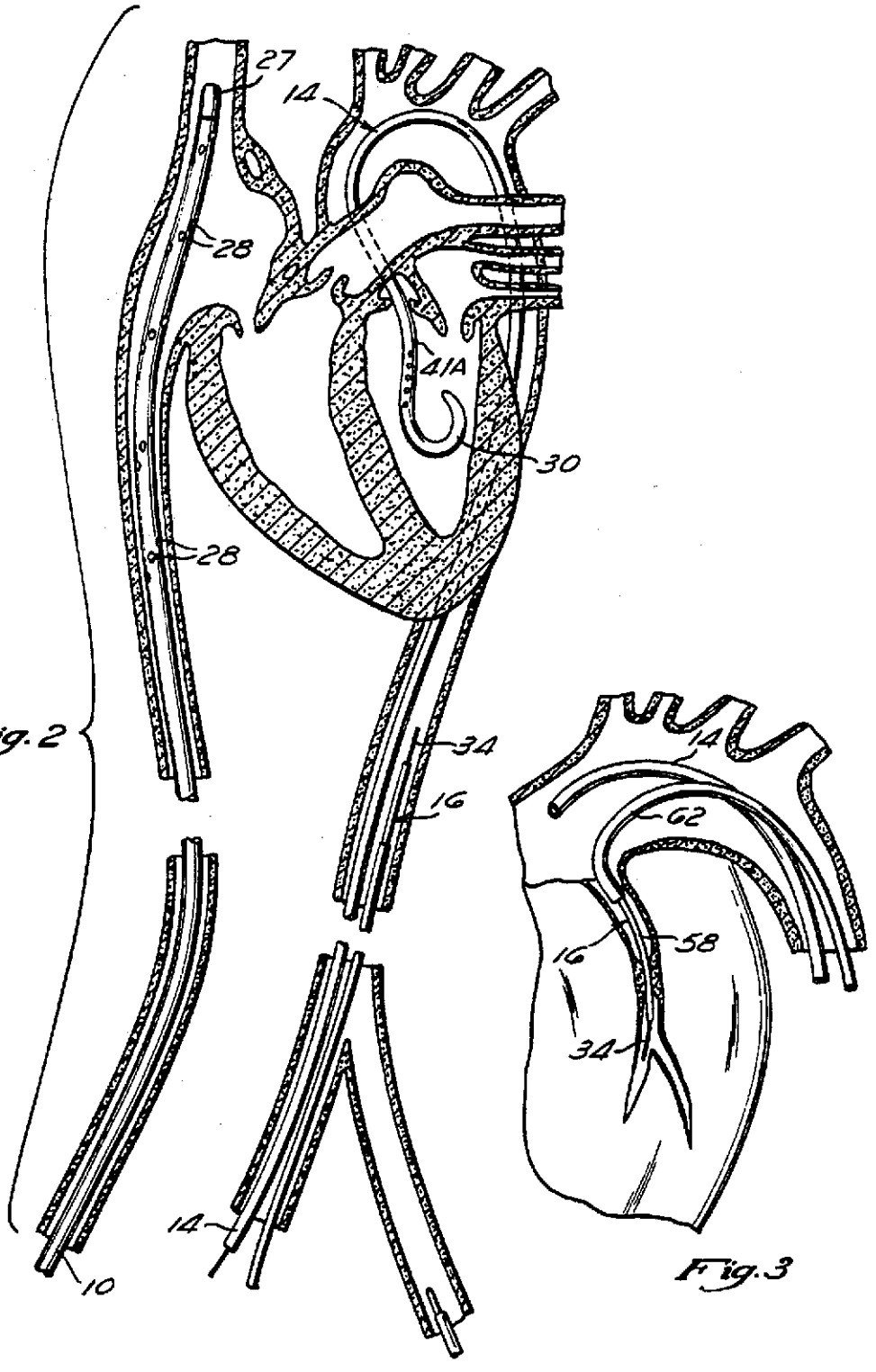

Fig. 2

Fig. 3

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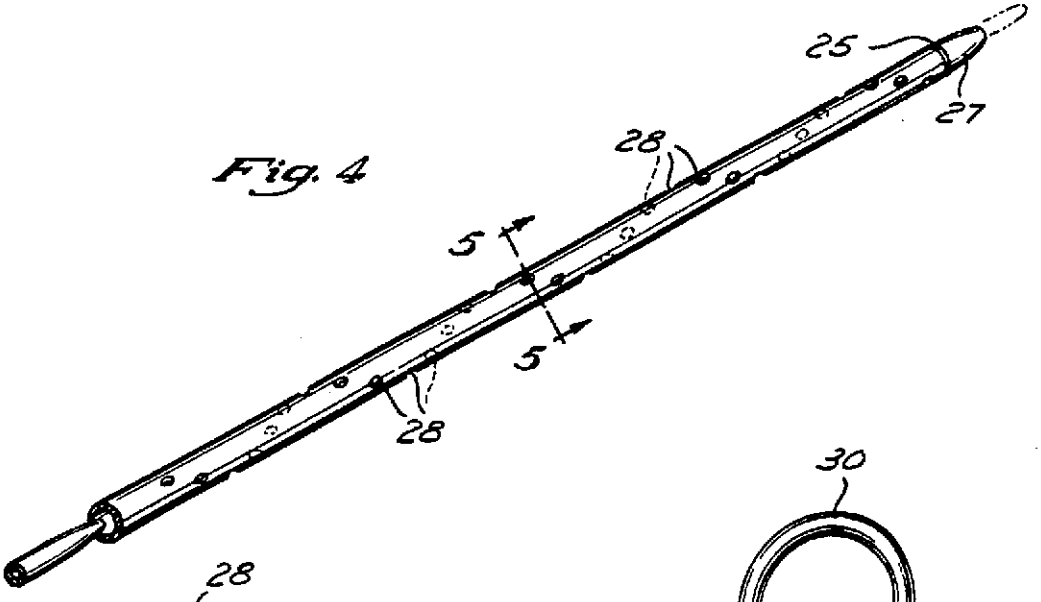
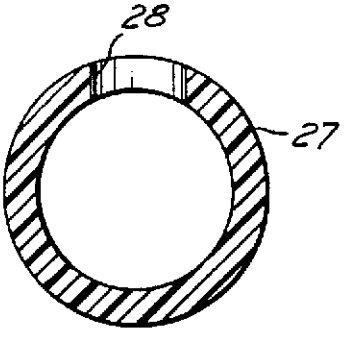


Fig. 4



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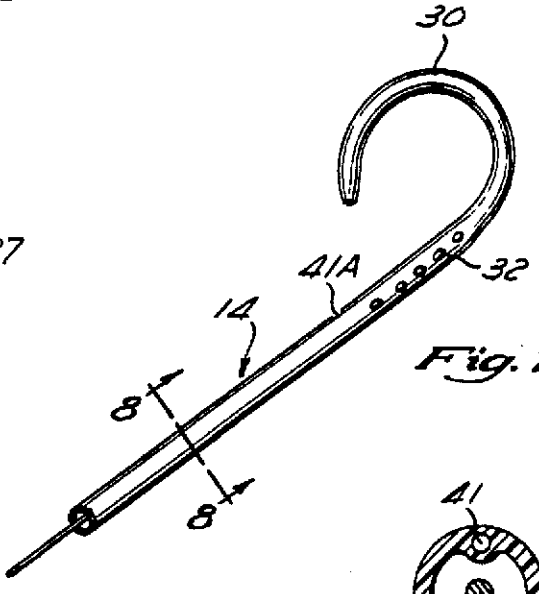

Fig. 7

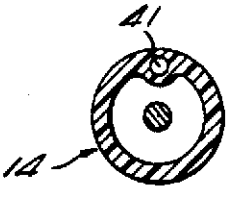

Fig. 8

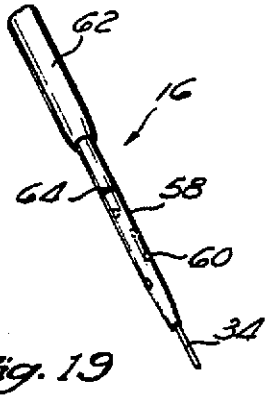

Fig. 19

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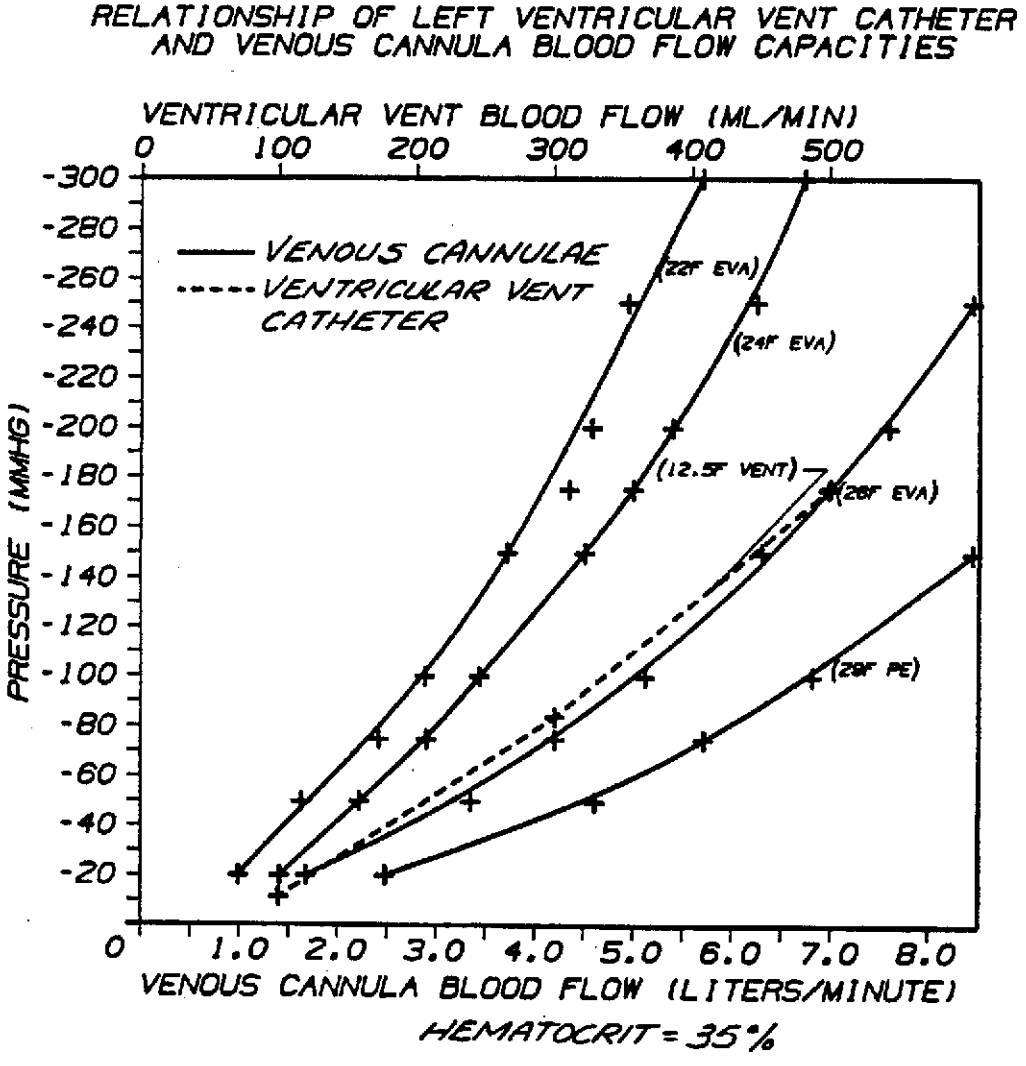

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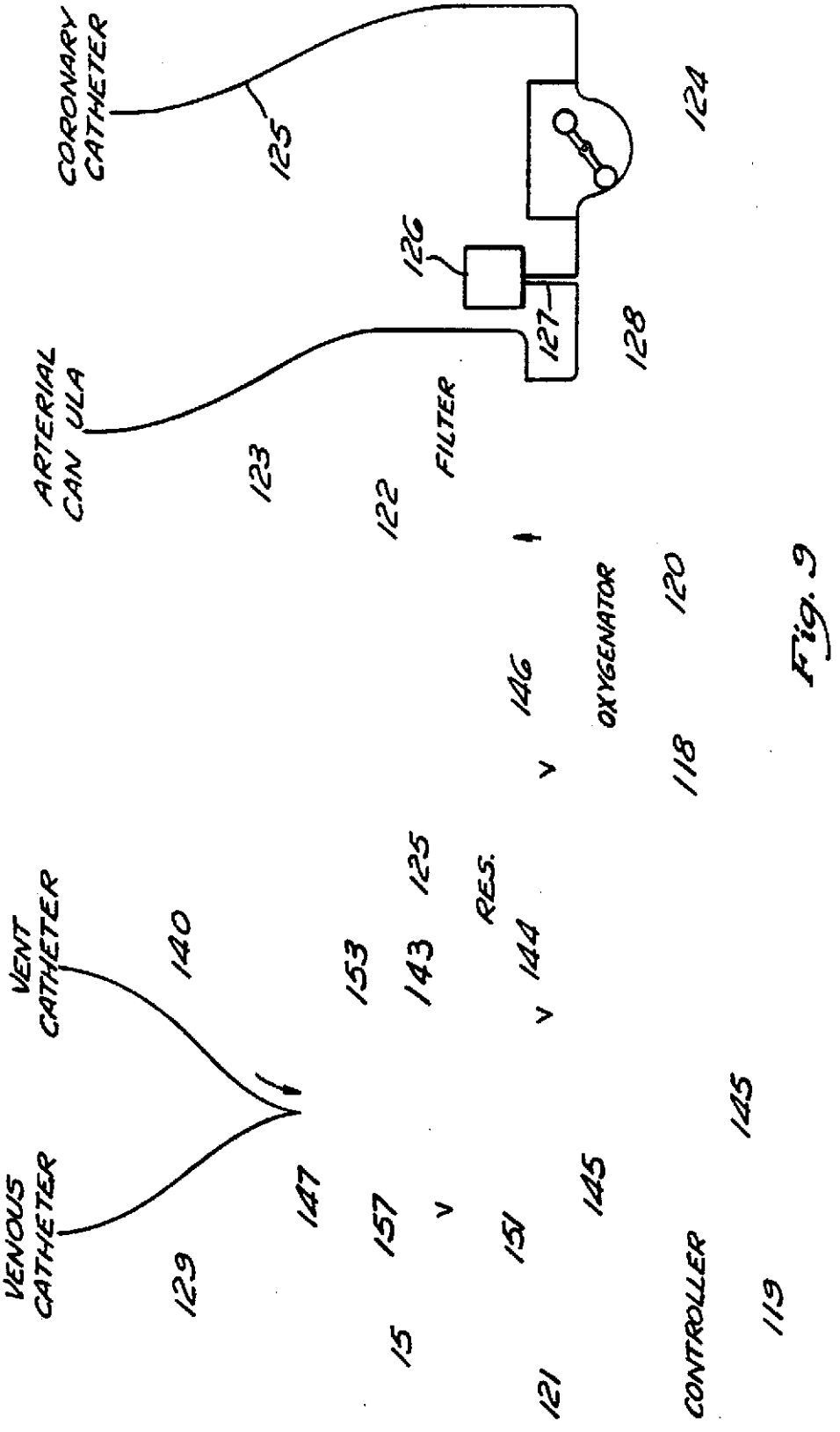

Fig. 9

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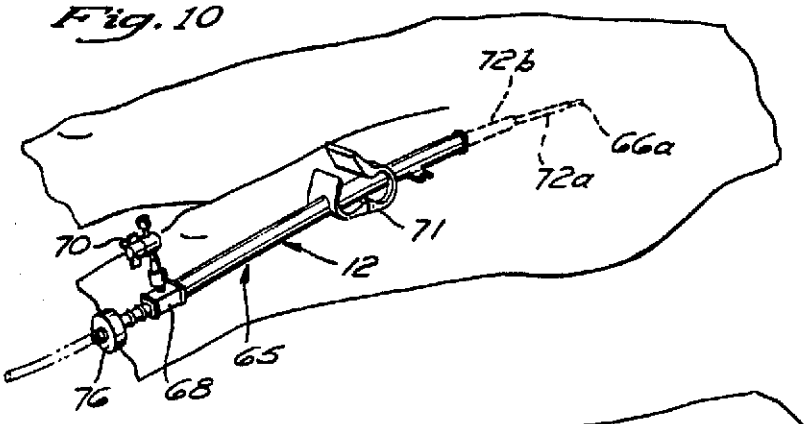
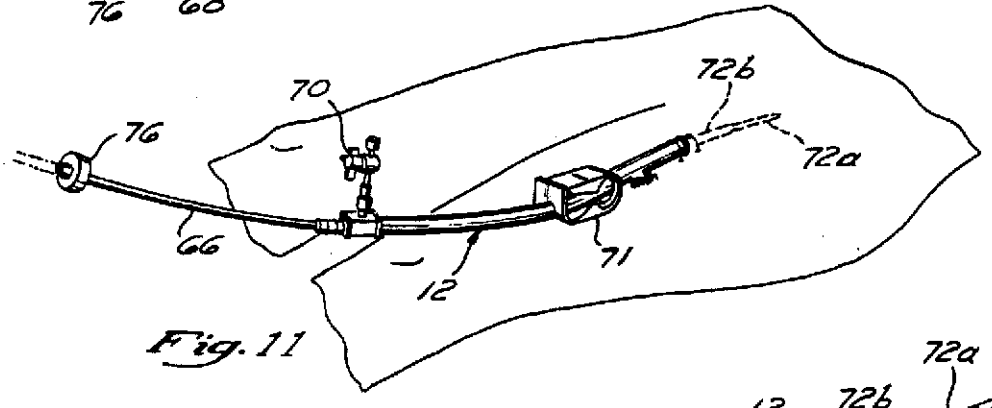
Fig. 10





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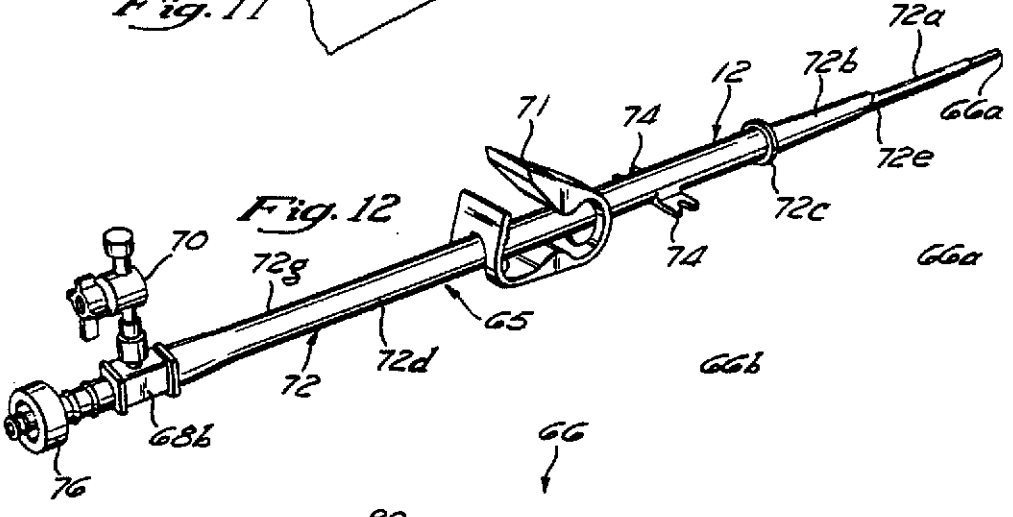

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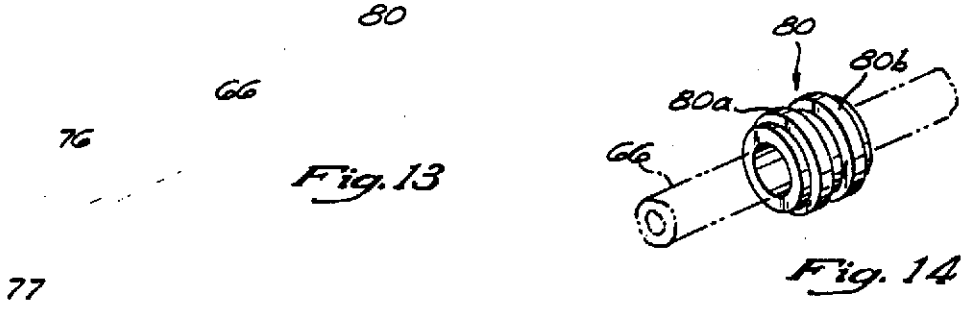

Fig. 13

Fig. 14

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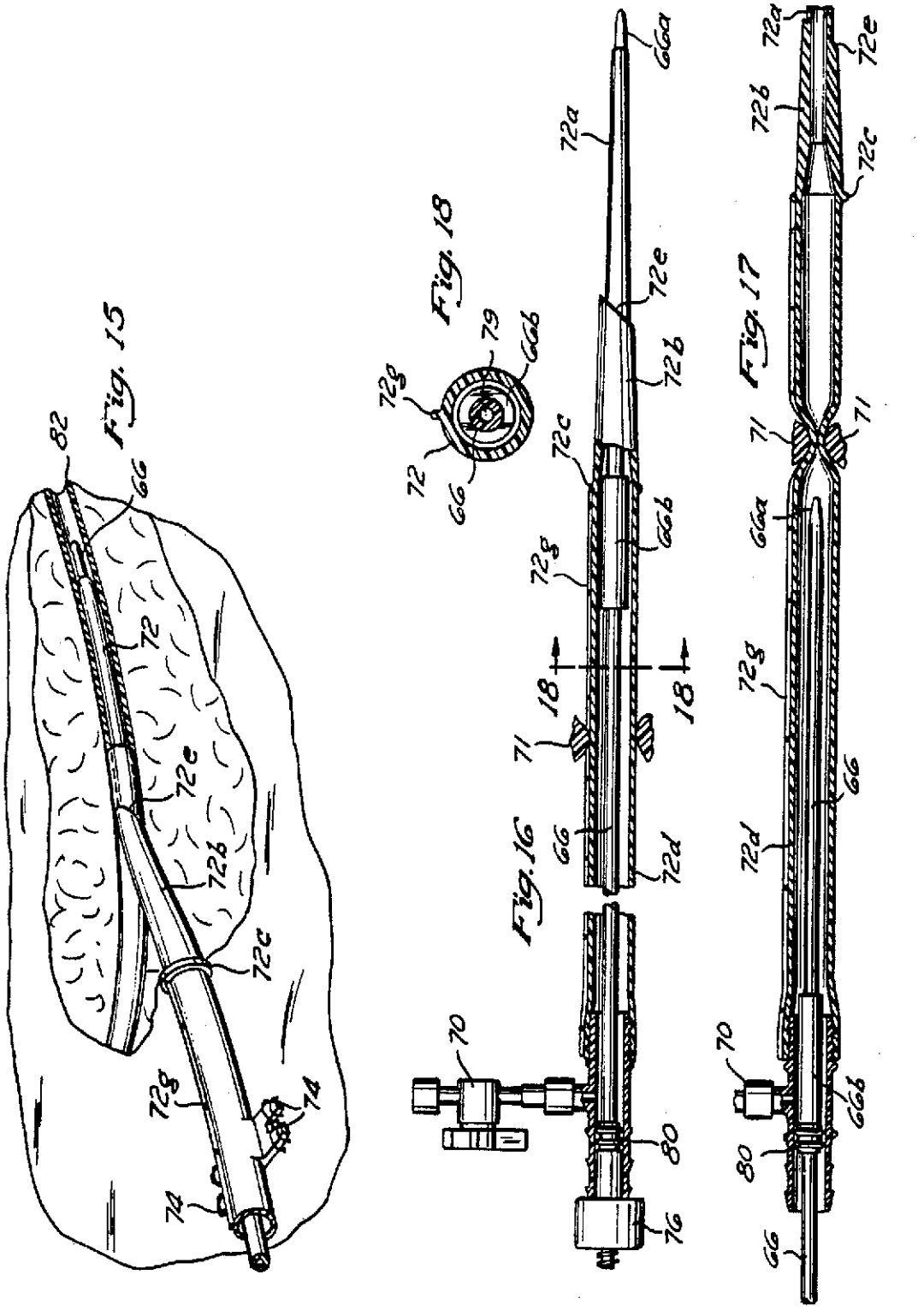

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PERIPHERAL CARDIOPULMONARY BYPASS AND CORONARY REPERFUSION SYSTEM

FIELD OF THE INVENTION

The subject invention relates to the treatment of heart attacks by placing the patient on a heart/lung machine without the necessity of a conventional open-chest operation, and to the treatment of the heart attack by the infusion of a special solution directly into the coronary arteries supplying the heart muscle.

BACKGROUND OF THE INVENTION

Each year numerous people suffer a heart attack (acute myocardial infarction) due to the obstruction of a coronary artery which supplies blood to the heart muscle. Of this number, a significant percentage die before reaching medical attention. Another group succumbs after reaching the hospital. Of those which survive, more than half suffer permanent loss of a portion of the heart muscle owing to the damage done during the period of a heart attack by the lack of blood supply (ischemia). This damage impairs the quality of life, shortens life expectancy, and increases the probability of death with subsequent heart attacks.

Currently the methods of treatment of heart attack victims include:

(1) observation and medication in a coronary care unit;

(2) thrombolysis - dissolving by drugs the clot which blocks the coronary artery;

(3) percutaneous coronary angioplasty (PTCA) reopening the obstructed artery with a balloon dilator threaded through the arterial system;

(4) emergency operations for coronary artery bypass-detouring blood around the blockage with a blood vessel graft;

(5) balloon counterpulsation - relieving about 10–15 percent of the work of the heart with a pulsating balloon placed in the body's main artery, usually used as a temporizing measure prior to or during the foregoing methods of treatment; and

(6) assist devices - tubes temporarily left in the heart following a bypass operation where the heart is too weakened to support the circulation, even with the balloon treatment of (5) above.

Despite the best available therapy, a significant percent of the patient's die, and those who are not treated fairly promptly suffer permanent loss of heart muscle supplied by the blocked artery. The primary damage to the heart muscle during a heart attack occurs because of the blood supply to a portion of the heart being interrupted; and therefore, the primary goal of the treatments referred to above has been to restore the blood supply as quickly as possible. However, while some of the methods outlined above have decreased the time required to restore blood flow to the portion of the heart subjected to ischemia, they have not resulted in that heart muscle being able to restore its function to the degree previously hoped. Recent studies show that limitations of previous techniques of reperfusion to restore heart muscle function are due to their inability to control the conditions of reperfusion (for example, the blood pressure, the work of the heart) or the composition of the reperfusate blood. The solution used for this purpose keeps the region of the heart muscle from beating (cardioplegia) to minimize its need for oxygen. The cardioplegic solution contains oxygen because it is mixed with oxygenated blood from the heart/lung machine (blood cardioplegia).

Recent experimental studies have demonstrated that controlled reperfusion, which can be achieved via surgical intervention, may facilitate recovery of the left ventricular function after myocardial infarction to a greater degree than can be achieved using conventional pharmacologic or mechanical strategies. The September 1986 issue of the *Journal of Thoracic and Cardiovascular Surgery*, entitled "Studies of Controlled Reperfusion After Ischemia," discloses results of laboratory experience supporting the conclusion that controlled reperfusion is necessary. More specifically, it has been determined that damage can be avoided by administering a special blood cardioplegia reperfusate to the damaged area before normal blood flow is resumed. Tests on dogs and other animals indicate that the blood cardioplegia negates the adverse effects of toxins which build up in the myocardium during the ischemia caused by the obstruction of blood to that portion of the heart. The re-introduction of normal blood flow, without the cardioplegia, does not revive the oxygendeprived tissue and results in loss of all or a portion of the affected myocardium. It appears that the cardioplegia solution flushes the damaged capillary bed of toxins that have accumulated during the infarct episode. This cleansing apparently facilitates the recovery of the heart tissue when normal blood flow is resumed. Included in this issue is a preliminary series of patients treated by surgically controlled reperfusion who experienced the same excellent recovery of heart muscle function that occurred under experimental conditions. These results have been confirmed in a recent series of patients who were treated in a multi-center trial of thrombolytic treatment (TAMI) and who did not qualify for or failed the more conventional pharmacologic approach of thrombolysis. The surgical treatment was that of controlled reperfusion following the protocol described in the September 1986 Journal referenced above.

In addition, the studies referred to in the above-mentioned Journal have shown that the foregoing treatment produces good recovery only when the heart is decompressed (left ventricle vented) by extracorporeal circulation. Without such venting during the extracorporeal circulation, there can be sufficient blood returned into the ventricle to cause it to eject, and thereby raise the metabolic demands of the damaged muscle by stretching it.

The studies reported in the above-referenced Journal utilized open-chest techniques for the extracorporeal circulation, with a secondary pump for the venting of the ventricle to obtain the desired decompression condition. However, it is suggested that instead of an open-chest operation, a peripheral bypass technique be employed wherein catheters are connected to the vascular system. With a peripheral technique, catheters may be introduced percutaneously or by using a cutdown procedure along with vessel dilation.

The aforementioned Journal article (page 560) proposes an experimental model of a peripheral (in this case) femoral-to-femoral vented bypass system in humans, together with regional cardioplegia reperfusion, without thoracotomy. This, however, is a desired goal, and the specific manner and apparatus of accomplishing this is not disclosed in detail because it had not been done.

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There have been some femoral-to-femoral bypass systems, such as in U.S. Pat. No. 4,540,399, but it is not clear that total bypass is obtained, and there is no provision for ventricular venting.

Summarizing some of the foregoing background, it can be simply stated that: heart attacks are caused by closed coronary arteries; opening an artery does not cure the heart attack; and controlling the conditions and composition of the initial reperfusion of a blocked coronary artery does permit salvage of the damaged myocardium beyond the obstruction. The only accepted way to control the conditions and composition of coronary reperfusion of individuals undergoing a heart attack is by open-chest surgical operation with direct decompression of the heart, decompression of the left ventricle and direct infusion of the coronary arteries through surgically connected saphenous vein grafts. Although the results of this approach have been proven superior to results obtained by any of the current methods of treating acute myocardial infarction, the performance of a major operation has risks of mortality and morbidity, and a high level of expense.

There is thus a clear need for an improved system which will minimize the damage to the myocardium following heart attacks. Such a system should be able to be applied quickly after the onset of symptoms. It should provide for the opening of the blocked artery without permitting normal blood flow to enter the ischemic area. It should permit infusion of a fluid of a specific composition under controlled conditions of temperature, pressure and flow. Further, the system should relieve the workload of the heart by supporting the body on an extracorporeal circulation to eliminate the flow work of the heart and relieve the left ventricle of all blood to eliminate pressure work of the heart. Further, it is highly desirable that the foregoing be accomplished without the risk of a major chest operation in critically ill patients.

It is also desirable that an improved extracorporeal circulation system be available for applications other than in connection with cardioplegia reperfusion.

SUMMARY OF THE INVENTION

The invention comprises a unique cardiopulmonary bypass system, method and apparatus, including a venous catheter for insertion into a femoral vein and an arterial cannula for insertion into a femoral artery. An arterial pump and oxygenator are connected between the venous catheter and the arterial cannula to circulate all of the patient's blood. A vent catheter is inserted preferably through a femoral artery and passed backwards through the arterial system to the left ventricle of the heart where it removes bronchial blood and permits complete rest to the ventricle. Preferably, the vent catheter is connected in parallel with the venous catheter and is connected in the same line to the pump. With this arrangement, negative pressure developed by the pump is simultaneously applied to the venous catheter and the vent catheter in a manner such that all of the patient's blood which would normally return to the heart is bypassed through the venous catheter, and the blood reaching the left ventricle of the heart is withdrawn through the vent catheter so that the ventricle is decompressed. This is in contrast to previous techniques of ventricular decompression which have required a separate pump to aspirate blood from the left ventricle.

The venous catheter is of special design which, for the first time, permits the induction of percutaneous total extracorporeal circulation, without producing dangerous increases in negative pressure. The hydrodynamics of the venous catheter system are selected so that they permit full normal cardiac output of 5 to 7 liters per minute without exceeding a maximum negative pressure, or suction, in the range of 140 to 200 mm Hg. This constraint minimizes blood damage and avoids creating bubbles in the blood.

Likewise, the vent catheter is carefully sized to handle the volume needed to ensure that the ventricle remains decompressed while operating within the same upper negative pressure limitation. This volume ranges from 50 to 500 ml per minute. The cardioplegia treatment is effective only if the heart is decompressed completely (total vented bypass). Left ventricular decompression is not possible by arterial and venous cannulation alone, as the venous cannula may fail to collect all of the venous return, and some blood from the lungs may enter the left ventricle via the bronchial veins. Connecting the venous return catheter and the vent catheter conduits in parallel to a single pump facilitates monitoring and maintaining the negative pressure below the maximum permitted.

Preferably, the vent catheter includes a separate lumen for continuous monitoring of ventricular pressure to ascertain that the heart is at rest. The vent catheter is specially designed to be inserted through the aortic valve without injury to the valve or producing insufficiencies by distorting the valve. Also, the pressure lumen inlet is located spaced from the catheter tip so that when the lumen inlet is in the ventricle, the attendant knows the vent catheter holes are in the ventricle.

To accommodate possible fluctuations in the volume of the flow required, and to regulate the blood volume of the patient, a reservoir, preferably compliant, is provided bridging the pump, with an inlet to the reservoir being connected to the pump outlet, and an outlet from the reservoir being connected between the venous catheter connection and the pump. Inflow and outflow valves in the connections permit circulating blood volume and therefore blood flow rates to be controlled.

The arterial catheter employs an angled shoulder which limits insertion of the cannula and provides a seal with the artery. Also, it includes a removable seal which prevents hemorrhage from the femoral artery as the stylet within the cannula is withdrawn.

For use of this system in a heart attack situation, there is provided a blood cardioplegia delivery system having an inlet connected to the output of the arterial pump. The coronary reperfusion catheter connected to the output of the pump is inserted through an artery to reach the area of the heart that has been deprived of blood. The reperfusion catheter traverses a clot in a coronary artery narrowing (stenosis) to allow precise control of the reperfusate blood composition and conditions (i.e., flow and pressure). Cardioplegia solution is then supplied to that area while the bypass system is in operation, including maintaining decompression of the ventricle. Following the cardioplegia application, the normal blood flow may be resumed, and an angioplasty can be performed to relieve the narrowing in the coronary artery.

The femoral-femoral bypass system is particularly versatile in that it can be employed in a cardiac catheterization laboratory, since it does not require an open-chest operation. This is very advantageous in connection with patients who would not likely survive the initiation of anesthesia or the opening of the chest for

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conventional heart surgery under emergency circumstances. With the system apparatus on a cart, the patient and the system may be transported from the catheterization lab into the operating room for use during open-heart surgery. Previous, less than total bypass, percutaneous systems needed to be discarded when patients were brought to the operating room.

The system is also useful in connection with patients in cardiac shock (providing up to 100% support of the circulation, rather than 15% support as in balloon counterpulsation). The system is also useful for routine extracorporeal circulation situations. The system further advantageously lends itself to electronic and mechanical control systems uniquely designed for performance of total extracorporeal circulation and controlled coronary reperfusion.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is an overall schematic view of the system of this invention;

FIG. 2 is a schematic, partial sectional view of the heart and venous and arterial passages to the heart.

FIG. 3 is a partial sectional view of a portion of a human heart with a vent catheter and a reperfusion catheter inserted into the heart;

FIG. 4 is a perspective view of a portion of a femoral venous catheter;

FIG. 5 is a cross sectional view on line 5—5 of FIG. 4;

FIG. 6 is a graph illustrating the fluid flow dynamics of the venous catheter and the vent catheter;

FIG. 7 is a perspective view of a portion of a vent catheter used in this invention;

FIG. 8 is a cross section of the vent catheter on line 8—8 of FIG. 7;

FIG. 9 is a schematic illustration of the use of an alternate pumping arrangement;

FIG. 10 is a schematic perspective view of an arterial cannula assembly inserted in the femoral artery;

FIG. 11 is a view similar to FIG. 10, but with a stylet of the cannula assembly partially withdrawn;

FIG. 12 is a perspective view of the cannula assembly of FIGS. 10 and 11;

FIG. 13 is a perspective view of the stylet of the assembly of FIG. 12;

FIG. 14 is a perspective view of an anti-backflow ring of the cannula assembly;

FIG. 15 is an enlarged, perspective, schematic view of the cannula assembly inserted in a femoral artery;

FIG. 16 is a side elevational, partially sectionalized view of the assembly of FIG. 12;

FIG. 17 is a cross-sectional view of the cannula assembly with the stylet partially withdrawn and with the cannula clamped to prevent flow therethrough;

FIG. 18 is a cross-sectional view on line 18—18 of FIG. 16; and

FIG. 19 is a perspective view of the detail end of the reperfusion catheter assembly.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

By way of a brief overview the system will be described in connection with FIGS. 1, 2 and 3, as applied to a recent heart attack victim. A femoral-femoral bypass is performed wherein a femoral venous catheter 10 allows right heart access via the femoral vein 11. A femoral arterial cannula 12 allows the return of oxygenated blood to the femoral artery, and is used in connection with the venous catheter 10 to achieve femoral-femoral total extracorporeal circulation.

A left ventricular vent catheter 14 is used to vent the left heart during extracorporeal circulation with the introduction of the catheter 14 made at the femoral artery and passing transaortically into the left ventricle. A coronary reperfusion catheter 16 is inserted into, and transverses a stenosed vessel in order to reperfuse the heart region beyond the stenosis.

The venous catheter 10 and the vent catheter 14 are in fluid communication with an arterial pump 18 which provides a negative pressure in order to draw venous blood into the arterial pump and to draw blood out of the left ventricle, and maintain that portion of the heart in an at rest condition. The arterial pump 18 forces the blood through an oxygenator/heat exchange 20 and an arterial filter 22. A heater/circulator 21 provides fluid flowing into the heat exchanger contained within the oxygenator 20.

A bridging venous reservoir 25 is connected in fluid communication with both the arterial pump 18 and the membrane oxygenator 20 in order to prime the system and to maintain sufficient fluid for proper operation. A cardioplegia delivery pump 24 is in fluid communication with the oxygenated blood after it leaves the arterial filter 22, and is also in fluid communication with a cardioplegia source 26 so as to mix the oxygenated blood and cardioplegia before delivering it at a predetermined flow rate to the coronary reperfusion catheter 16.

The vent catheter 14 removes all residual blood from the left ventricle and enables the heart to maintain an at-rest condition while the reperfusion catheter 16 enables reperfusion of the heart region beyond the stenosis which precipitated the heart attack.

VENOUS CATHETER

In more detail, the femoral venous catheter 10 is preferably made from ethylene-vinyl-acetate (EVA) tubing, preferably having about 18% acetate. The tubing has a constant inner diameter from the insertion tip up to the proximal end. The proximal end of the catheter 10 connects to a ⅜-inch connector which is in fluid communication with the arterial pump. The catheter 10 should be long enough to reach the right atrium from the femoral triangle. An intravascular length about 70 cm, and an overall length of about 85 cm, has been found to be suitable. The thin wall and flexibility of the catheter allow for its introduction percutaneously into the femoral vein of a wide range of patients, and resist the kinking that might otherwise occur with other thin wall catheters as they are advanced through the iliac veins and across the curve of the pelvis.

The distal end 27 of the venous catheter lo, as seen in FIGS. 4 and 5, has a plurality of drainage holes 28 which in a prototype product have a diameter of 0.165 with ¼-inch center to center spacing. These holes have smooth edges and are formed by a tubular cutter, with the catheter internally supported on a mandrel. The holes are arranged in a spiral pattern so that if some holes are blocked by vessel walls, others will be open. This arrangement also minimizes weakening of the catheter while providing the necessary hole area. The holes extend sufficiently far from the distal end of the catheter to span the area from which blood is to be withdrawn. The preferred technique for introducing this cannula into the body is to use the Seldinger technique (percutaneous) or a cutdown procedure along

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with vessel dilation. A radiopaque tip marker **25** near the distal end enables the drainage holes to be oriented in the superior vena cavae. An elongated removable stylet **31** which receives a 0.045 inch guidewire (not shown) is used to introduce and guide the catheter into position.

The cross-sectional size and the material of the catheter **10** is particularly critical. Since a total bypass system is needed to accomplish the goals of the invention, it is necessary that the venous catheter fit within various constraints. Bypassing the patient's total blood flow requires a capacity in the range of up to 5–7 liters per minute. An overall flow rate of 5 liters per minute is expected in most patients. A thin-walled construction is advantageously used to provide a larger blood flow within the size limitations that may be accommodated by human veins. The EVA material, in connection with the thin-walled construction, provides the needed flexibility to be properly positioned, yet sufficient strength to prevent kinking during normal handling. Moreover, the characteristics of the material are such that if the tubing is kinked and then released, it is self-restoring without significant weakening.

It has been determined that a negative pressure of 200 mm of mercury is an appropriate safe maximum. Higher levels of negative pressure, which could create greater blood flow, run the increasing risk of creating bubbles in the blood. Although a minimum wall thickness is desired, the tubing must not collapse when subjected to such negative pressure. It has been determined that a catheter size of 26 French (O.D. - 0.341 inch, 8.66 mm) is suitable. Preferably, the catheter has an inner diameter of 0.277 inch (7.03 mm), thus making a wall thickness of 0.032 inch (0.825 mm). An alternative approach is to use two smaller venous catheters that will carry the flow at the same negative pressure.

FIG. **6** illustrates the constraints of the venous catheter construction graphically from test data. It can be seen that the fluid flow dynamics are such that significant negative pressure is needed to approach the required flow rates, but yet the increased flow from increased suction diminishes quickly at higher levels, particularly for the smaller lumens. Within the acceptable pressure limit, it can be seen that inadequate flow is obtained from a 22F or 24F (French) thin-walled lumen. A 29 French thin-walled size provides adequate flow, but is too large for the vein of some patients, and produces insufficient negative pressure to assist vent drainage optimally (as discussed below). Incidentally, the 29 French lumen was made of polyethylene rather than EVA. It is believed that the flow curve would be similar for EVA. The 26 French size provides adequate flow within an acceptable pressure range of about 100–200 mm Hg, and it can be accommodated by the femoral vein of most adults.

VENT CATHETER

Referring to FIGS. **7** and **8**, the vent catheter **14** is preferably a size 12.5 French (0.164 inch, 4.166 mm O.D.) (0.120 inch, 3.04 mm I.D.). The catheter is preferably made from a flexible polyvinyl chloride (PVC) tubing. The distal end **30** is formed in a loop providing a so-called "pigtail." This loop, when unstressed, has an outside diameter of about ⅛-inch, and has a plurality of spaced apertures **32** which are preferably about 0.050 inch in diameter and extend over a vent length of about 4 cm. A series of apertures **32** are located on opposite sides of the catheter.

The catheter **14** must be long enough to reach the left ventricle from the femoral triangle when passed retrograde through the arterial system. A catheter with an intravascular length of 100 cm, and an overall length of about 112 cm is preferred.

As seen from FIG. **8**, the catheter **14** includes a pressure monitoring lumen **41** which is integral with and formed in a wall of the vent catheter **14**. Preferably, this lumen **41** has a diameter of about 0.030 inch. The lumen **41** extends from the proximal end of the catheter **14** to a pressure inlet **41*a*** which is spaced from the catheter tip a distance further from the tip than the apertures **32**. The inlet **41*a*** is positioned about 4 inches from the distal end of the catheter. The inlet **41*a*** is located on the same side of the catheter **14** as the pigtail to prevent obstruction of the inlet **41*a*** when the catheter contacts the ventricular wall.

Preferably, the catheter **14** is extruded with the lumen **41** extending throughout the length of the tubing. After the apertures **32** are formed, the distal end of the tubing is heated and stretched to reduce its diameter and increase flexibility, and to form the pigtail into its curled shape. In the stretching and heating operation, the lumen **41** is closed on the distal end of the catheter. The opening **41*a*** is formed by cutting the tubing at the desired location spaced further from the tip than the apertures **32**.

In the stretching of the distal end, the exterior diameter of the catheter is decreased from 0.164 inch to about 0.100 inch, and the interior diameter is decreased from 0.120 inch to 0.062 inch. The very tip of the catheter is reduced a slight amount further. That is, the tip 0.030 inch is tapered on its exterior and is reduced on its interior diameter to about 0.040 inch.

The preferred method of introducing the vent catheter **14** into the femoral artery is by using a sheath introducer procedure. After a tubular sheath (not shown) is positioned in the entrance to the artery, a guidewire **47** is introduced into a stiffening stylet (now shown) that is in the flow lumen of the catheter. The guidewire extends beyond the pigtail distal end **30** sufficiently to straighten it and to permit insertion. The assembly is then inserted through the sheath into the artery. The guidewire and stylet are stopped when the wire approaches the aortic valve. The guide wire and the stylet are then withdrawn approximately 10 cm. As the guide wire and stylet are withdrawn past the distal tip, the pigtail recurls, due to its memory, into the position shown in FIG. **7**. Thus, the curled distal end resiliently engages the aortic valve and passes through the valve without trauma when the valve opens. The distal end then assumes the position illustrated in FIG. **2** wherein the pressure lumen hole **41*a*** in the distal end is shielded from the ventricle walls so as to prevent blockage when pressure is monitored through the catheter. The flexibility of the catheter permits its presence in the ventricle, across the aortic valve, without causing distortion of the cusps of that valve and therefore avoids aortic insufficiency.

A tube **40** is in fluid communication with the proximal end of the vent catheter via one aperture in a Wye connector **38** with the tube also communicating with the arterial pump **18**. The catheter **14** is sized to allow transmission of approximately up to 500 ml per minute of blood flow at the same negative pressure at which the catheter **11** is operated by the arterial pump **18**. A pressure transducer is connected to a second aperture in the Wye connector **38** which in turn is connected to the

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second lumen **41**. Thus, the lumen **41** monitors the pressure in the left ventricle directly. If the ventricle is being properly decompressed, the sensed pressure should be about zero. Thus, there is a significant difference in pressure on the opposite sides of the aortic valve. This can be observed on a pressure monitoring instrument by moving the catheter so that the pressure lumen inlet **41***a* is exposed to either ventricular pressure or arterial pressure. The location of the inlet **41***a* is important in that, if the pressure is at the ventricular levels, ejecting or decompressed, it is known that the vent apertures **32** are in the ventricle.

The vent catheter is, as noted, necessary to ensure the left ventricle is completely decompressed, and does not fill with fluid and cause the heart to eject (pump), even though the heart is being bypassed. The venous drain cannula **10** does not ensure continual left ventricle decompression. Some coronary sinus return and/or bronchial flow will enter the left ventricle, distend it, allow wall tension to develop and result in occasional ejection despite apparent right heart decompression from the venous catheter **10**. Thus, it is important that the catheter and its connecting tube **40** are sized to transmit the maximum anticipated flow from the left ventricle. This can range from 50 to 500 ml. Further, it is necessary to restrict negative pressure to the 200 mm Hg limitation mentioned above in connection with the venous catheter.

With reference to FIG. **6**, the relationship between applied negative pressure (ordinate) and venous cannula flow (lower abscissa) and vent catheter flow (upper abscissa) is presented. Note: (a) The venous flows of 5 to 7LPM are achieved at negative pressures of less than 200 mm Hg only with EVA catheters #26 and #29 French. (b) The 12.5 French vent catheter always drains 7 percent of venous flow, the maximum expected flow from the left ventricle at venous flows of 5 to 7LPM.

FIG. **6** also illustrates the constraints of tubing size and pressure for the vent catheter identified as 12.5F vent on the graph. The curve for the vent catheter shows a vent flow capacity of about 100 ml/minute at a very flow negative pressure, and up to 500 ml/minute at about 175 negative pressure. This is a very satisfactory pressure limit for providing the desired vent flow capacity. As shown in FIG. **1**, the suction provided by the venous catheter **10** and the ventricular vent catheter **14** are both advantageously provided by the same arterial pump. The diameter and flow resistance of the tubes **29**, **40** and the catheters **10**, **14** are selected with a diameter and length to provide a predetermined ratio of flow from each of the catheters for a given suction by the pump. Thus, the amount of suction provided to the left ventricle by the vent catheter **14** will vary in a predetermined relationship with respect to the blood withdrawn from the femoral vein by the venous catheter. While a separate pump can be employed for the vent catheter, as in the prior art, it is highly desirable that the single pump approach be employed. To accomplish this, it is necessary to balance and coordinate those two catheters. That is, it is necessary to utilize a vent catheter that provides the needed flow within the pressure constraints required in connection with the venous flow. Thus, the amount of suction provided to the left ventricle by the vent catheter will vary in a predetermined relationship with respect to the blood withdrawn from the femoral vein by the venous catheter. As seen, the curve for the vent catheter is very similar to that for the 26 French venous catheter in the flow range desired. Thus, if there is a need for change of flow in either catheter, the flow through the other catheter will be satisfactory. With the above specified flow rates, the flow rate of the venous catheter **10** will be, in a preferred construction, about 14 times greater than the flow capacity in the vent catheter **14** for the same negative pressure, but may range from 10 to 50 times greater for tubes of different sizes.

If, in monitoring the pressure in the ventricle, it is observed that the pressure is becoming too high, indicating an accumulation of blood, pump speed can be increased to increase the flow through the vent catheter and the venous catheter, so long as the maximum negative pressure of 200 mm Hg is not exceeded. Thus, for example, if the ventricle pressure should start to climb with vent flow at 360 ml and venous flow at **51**, pump speed can be increased to provide 500 ml of vent flow capacity, venous flow only increasing to 7 liter a minute, and the negative pressure is at a safe 180. A venous pressure transducer **42** monitors the pressure in the tubes **29** and **40** generated by the arterial pump **18**.

A ventricular vent catheter of the type described above is also useful for reducing volume of the ventricle in partial bypass situations, i.e., when not using a venous catheter and an oxygenator. In such situations a larger catheter is desired, such as 18 French. The inlet holes **32** may also be enlarged to accommodate increased blood flow. Possibly with a larger catheter yet, a 100% assist can be attained.

BRIDGING RESERVOIR

The bridging reservoir **25** is connected in parallel with the arterial pump **18**, with flow clamp **44** between the reservoir and the pump inlet, and a flow clamp **46** between the pump outlet and the reservoir. With this arrangement wherein the flow is not through the reservoir, the volume in the circuit can be controlled by temporarily opening one or the other of the clamps. If more volume is needed, the clamp **44** is briefly opened and then closed when the volume is at the desired level. Similarly, if less volume in the circuit is desired, the clamp **46** is briefly opened until the desired volume is attained.

The system and method of this invention is a closed system; the chest is not opened to access the heart and there is no blood-to-air interface (other than in the oxygenator **20**). Thus, whatever blood is taken out of the body must be returned to the body via catheter **12**. The bridging reservoir **25** facilitates circulatory stability during the initiation and conduct of the bypass by providing volume control. Maintaining a stable fluid flow in the body is especially important during the time immediately following the initiation of extracorporeal circulation, as such instability can cause severe hypotension, possibly exacerbate the infarction, and cause secondary arrhythmias or cerebral symptoms. The reservoir provides sufficient fluid to maintain circulatory stability and has the capacity to allow fluid removal if the patient's blood volume is excessive due to heart failure. Further, the fluid in the reservoir can be used to prime the system.

ARTERIAL PUMP, OXYGENATOR, FILER, BUBBLE DETECTOR

The arterial pump **18** withdraws blood from the body under a negative pressure (suction), along with the appropriate amount of fluid from the reservoir **25**, if any

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is needed, and pumps the blood and fluid mixture out of the pump under a positive pressure. The arterial pump **18** is schematically illustrated in FIG. **1** as a centrifugal pump. Such a pump is known in the art and hence is not described in detail herein. One suitable centrifugal pump is that provided by Biomedicus of Minneapolis, Minn. A primary advantage of a centrifugal pump is that it has "hydrodynamic slippage" such that if the patient's blood volume falls, the blood flow diminishes without producing high negative pressures and creating nucleation ("boiling") of gases as might occur with a displacement pump. The pump is connected to an electronic controller to prevent negative pressure from going above 200 mm Hg.

From the pump **18**, the blood is forced under pressure to the oxygenator **20** where the blood is oxygenated and the temperature of the blood is controlled. The oxygenator **20** and heater circulator are known in the art and are not described in detail herein.

From the blood oxygenator, the blood is preferably forced through an arterial filter **22**, although a bypass is provided. After leaving the arterial filter **22**, the main portion of the oxygenated and filtered blood is directed to the arterial cannula **12** where it is returned to the femoral artery of the body.

A bubble detector **50** and an arterial pressure transducer **52** may be located on the tube carrying the blood to the arterial cannula **12**.

In lieu of aspirating blood through the venous catheter with a centrifugal pump, a positive displacement pump may be attached to the venous line with an interposed compliance chamber (to dampen phasic pressure variations) such that a servo based on negative pressure in the venous line achieves the desired flow. Such a system is schematically illustrated in FIG. **9**. A venous drainage line **129**, and a vent catheter line **140**, comparable to the lines **29** and **40** in FIG. **1**, are joined at a Y-connection to a common line **141** leading to a compliance chamber **143**. This chamber is in turn connected by tubing **145** to a positive displacement pump **118** schematically illustrated as a peristaltic pump. A suitable example of a peristaltic pump is made by Stockert/Shiley, in Munich, Germany. The pump **118** is controlled by an electronic controller **119** which receives pressure feedback from the compliance chamber through a suitable pressure transducer connection **121**.

The balance of the system of FIG. **9** is comparable to that shown in FIG. **1**. A reservoir **25** with inlet and outlet controls **144** and **146** bridges the pump **118** to provide for volume adjustment. The output of the pump is directed through an oxygenator **120**, and optionally a filter **122** to a line **123** leading to an arterial cannula. A portion of the oxygenator output is directed through a line **129** to a cardioplegia pump **124** and conducted through a line **125** to a coronary artery by a suitable perfusion catheter. A cardioplegia supply **126** is connected by a line **127** to the pump **124**.

The compliance chamber **143** includes a flexible bladder or reservoir **151**, having an inlet connected on one end to the venous drainage line **147** and an outlet connected on its other end to pump inlet tube **145**. A rigid outer housing **153** encloses the bladder **151**. This housing is sealed around the bladder **151** so that the negative pressure applied to the bladder **151** by the pump **118** is also applied to the space within the housing **153** surrounding the bladder **151**. This negative pressure within the housing **153** is, as indicated above, sensed by a transducer **155** and fed back to the controller **119**. A valved outlet **157** from the housing **153** is opened to atmosphere during priming to allow the bladder to initially expand due to the head pressure of the fluid in the system. The valve is then closed so that any changes in the size of the bladder are then reflected in pressure changes in housing.

The peristaltic pump **118** is desirable in that the pumping mechanism does not actually contact the blood, thus eliminating a source of contamination and allowing reuse of the pump. Its shortcoming, however, is that if the blood supply falls, the pump can quickly increase the negative pressure applied on the venous drainage line to unsafe levels, even with a pressure sensor in the line to send a signal to a controller, the negative pressure can rise undesirably before the pump speed reacts to reduce pressure. The compliance chamber **143** in combination with a sensor and the pump controller solves this problem. The pressure within the rigid housing **153**, being the same as that within the flexible bladder **151**, is continually sensed and fed back to the pump controller. Thus, if there is a sudden loss of blood which would result in an increase in negative pressure, the bladder will contract to reduce the rate of the negative pressure rise, giving the controller **119** and the pump time to reduce the speed of the pump **118**.

As another variation, the housing **153** can be configured to replace the bridging reservoir **125**, including being provided with the necessary inlet and outlet valves or clamps. Similarly, venous return can be augmented by negative pressure applied to the space between the housing **153** and the reservoir **151**.

CARDIOPLEGIA PUMP

A portion of the oxygenated blood through the arterial filter **22** is directed to the cardioplegia delivery pump **24**. A cardioplegia solution from a cardioplegia source **26** is mixed with the blood and provided under a controlled temperature and pressure to the coronary reperfusion catheter **16**. A normal body temperature of 37° Celsius is believed suitable for the reperfused solution. A suitable cardioplegia solution is believed to be an aspartateglutamate-enriched, hypocalcemia, buffered, hypersomolar blood solution, as discussed more particularly in the above-mentioned Journal, Thoracic Cardiovascular Surgery, September 1986.

CONTROLS

A reperfusion pressure transducer **54** and monitor/-pump feedback helps regulate the pressure with which the cardioplegia solution is provided to the catheter **16**. A flow rate of 50 ml/min or that rate obtained with 50 mm Hg over the pressure drop in the system, whichever is greater, is believed suitable for the reperfusion. Thus, flow is reduced if the pressure exceeds 50 mm Hg, but the rate is best at 50 ml/min if the pressure drops below 50 mm Hg. Further information regarding reperfusion flow rate may be found in Article XVI in the above-mentioned journal. The various pressure transducers **42**, **52**, **54** and the bubble detector **50** all electronically communicate with a system controller **56**, which in turn monitors the vital signs of the heart attack victim and regulates the amount of fluid withdrawn from, and reintroduced to, the victim.

ARTERIAL CANNULA

The femoral arterial cannula **12** is, as shown in FIG. **12**, a component of a cannula assembly **65**. The assembly further includes a stylet **66**, which is slidably re-

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ceived within the cannula, a fitting 68 secured to the proximal end of the cannula, a stopcock 70 on the fitting, and a clamp 71. The cannula 12 which is disclosed in detail in FIGS. 10–18 and below is separately claimed in a copending application since it is useful in systems other than that illustrated in FIG. 1.

The cannula 12 comprises an elongated tubular body 72 preferably made from a medical-grade silicone rubber or a polyvinyl chloride material. The body 72 has three primary sections including a distal tip section 72*a* for insertion into the femoral artery, an intermediate section 72*b* adapted to extend from the artery to a raised suture stabilizing ring 72*c* to be located near the exterior skin of the leg, and an exterior section 72*d* extending from the suture ring 72*c* to the fitting 68.

The tip of section 72*a* is tapered to facilitate insertion into an artery. In a preproduction version of the cannula, the exterior diameter of the tip section 72*a* is 6.68 mm or 20 French, and the interior diameter is 5.08 mm. The intravascular length of the tip section 72*a* in a preproduction version is 5.88 cm, which is a desirable length to ensure adequate seating within the artery.

The intermediate section 72*b* has a length of about 5 cm, with an interior diameter that tapers to about 9.27 mm, and with an exterior diameter which tapers from the tip end of about 8.4 mm and increases to about 12–13 cm. Thus, it can be seen that there is a significant exterior diameter change from the tip section 72*a* to the tip end of the intermediate section 72*b*. This diameter change forms an annular shoulder 72*e* adapted to engage the exterior of an artery. That shoulder is formed at an angle of approximately 45° with respect to a diametrical plane through the cannula. It has been found that this angle is particularly desirable for sealing with the exterior of the femoral artery when the cannula is inserted in the direction towards the heart.

Due to the angled shoulder and the angle at which the cannula tip is inserted in the femoral artery, it is important the cannula be rotationally oriented properly. Thus, for orientation purposes, there is formed an elongated orientation rib 72*g* on the exterior of sections 72*b* and 72*d* extending from the suture ring 72*c* to the proximal end of the body which mates with the fitting 68. The section 72*d* is about 19 cm in length, making the overall length of the cannula about 33 cm. The interior and exterior diameters are constant with the end of section 72*b*.

A pair of suture wings or flaps 74 are formed integral with and extend outwardly from the cannula exterior section 72*d*. The wings have a lower surface which is approximately tangent with the exterior of the section 72*d*. The suture wings in a prototype are positioned about 5 cm from the suture ring 72*c*.

Referring to FIGS. 12 and 13, the stylet 66 is an elongated flexible tubular element preferably made of polyvinyl chloride. The stylet 66 is slightly longer than the cannula 12 having a tapered tip 66*a* on one end which extends beyond the tip of the cannula when the stylet is fully inserted therein. The overall length is about 42 cm. A knob 76 on the other end of the stylet extends beyond the fitting 68 and is useful for installing and removing the stylet from the cannula. The diameter of the stylet is slightly smaller than the inner diameter of the tip of the cannula. A small diameter lumen 77 is formed throughout the length of the stylet and is adapted to receive a small diameter guidewire. Included on the stylet 66 is a cylindrical stop 66*b* having an exterior diameter which is sized to slide relatively easily within the cannula, but nevertheless there is resistance to movement caused by the stop 76*b* engaging the interior of the cannula. The stop 76*b* is spaced from the tip end of the stylet about 15 cm and has a length of about 4 cm. This means that the end of the stop 76*b* closest to the tip 66*a* of the stylet is located at the suture ring of the cannula when the stylet is fully inserted in the cannula, as seen in FIG. 16.

Also included in the cannula assembly is an antibackflow ring 80 preferably made of medical-grade silicone rubber. The ring has a short barrel-like tubular shape with two axially spaced outwardly extending annular ribs 80*a* and 80*b*. The ribs are dimensioned such that they snugly engage the interior wall of the fitting 68 or cannula 12 and the exterior of the stylet to form a liquid inner and outer seal.

Mounted on the exterior of the cannula between the suture wings and the fitting 68 is the adjustable medical clamp 71. The clamp is of standard construction, adapted to be manually set to pinch the cannula closed when the stylet is removed.

In use, the guidewire is inserted into the femoral artery followed by the cannula and stylet with the stylet fully inserted, as shown in FIGS. 10, 11 and 15. The cannula is preferably introduced by use of the Seldinger technique, or a cutdown procedure along with vessel dilation. The assembly, guided by the guidewire, is inserted to the point where the cannula angled shoulder 72*e* engages the exterior of an artery 82 with the cannula tip section 72*a* extending into the artery, together with the tip of the stylet, as illustrated in FIG. 15. It can be seen from that figure that the angled shoulder 72*e* engages the artery in a manner such that the artery substantially conforms to the shoulder with the exterior of the artery to form a seal, and limits insertion. With the cannula so positioned, it is sutured to the leg by means of the wings, as shown in FIG. 15.

With the cannula so positioned, there is little blood leakage through the hole in the artery as a result of the seal with the shoulder 72*e*. Also, the backflow ring 80 prevents leakage through the annular passage between the stylet and the cannula, as seen in FIG. 10. With the forward portion of the cannula relatively firmly positioned on the patient's leg, the other end of the cannula is free to be raised or manipulated, as may be appreciated from FIGS. 10 and 11.

When it is desirable to connect the cannula to an extracorporeal circuit, the stylet 66 is partially withdrawn by pulling on the knob 76 to the position shown in FIG. 17, wherein the stop 66*b* on the stylet engages anti-backflow ring 80 in the fitting. There is firm resistance to withdrawing the ring 80 out of the cannula so that an operator recognizes that is the point to stop. The tip 66*a* of the stylet is spaced considerably from the suture ring since the length of the stylet from the stop 66*b* to its tip 66*a* is somewhat less than the length of the cannula from its fitting end to the suture ring 72*c*. As the stylet 66 is withdrawn, a small quantity of blood enters the cannula, limited by the volume displaced by the stylet. With the stylet stop engaging the ring 80, the clamp 71 is squeezed onto the cannula section 72*d* at a location between the tip 66*a* of the stylet and the suture ring 72*c*, as seen in FIG. 17. By locating the clamp close to the tip 66*a* of the stylet, there is only a small quantity of blood between the clamp and the stylet stop. Once the clamp has been positioned, and closed, the stylet can be withdrawn completely with a pulling force greater than that to previously move the stylet, such that the

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ring 80 in the end of the fitting is also withdrawn. The ring 80 remains captured on the stylet 66. At this stage, there is only a small quantity of blood in the open end of the cannula, and it is not under pressure. Because of this and the suture wings, the end of the cannula can be easily handled for making connections to the pump and priming this cannula without loss of blood.

REPERFUSION CATHETER

The reperfusion catheter 16 is preferably made from flexible polyvinylchloride (PVC) tubing, preferably in the range of 3.5 to 5 French. The catheter 16 include a female luer lock fitting (not shown) at the proximal end. Preferably, the PVC tubing is barium impregnated or incorporates two radiopaque bands for locating purposes, one of such bands being located at 61 in FIG. 19. The reperfusion catheter 16 has a distal end 58 which contains a plurality of apertures 60 oriented in a spiral along the longitudinal axis of the catheter 16. The holes are about 0.030 inch (0.762 mm) and extend for a tip length of about 2 cm. The tip of the catheter 16 tapers to a reduced size of about 3 French (0.039 inch, 0.91 mm).

In installing the coronary reperfusion catheter 16, there is first inserted a flexible guidewire 34, such as 0.018 inch diameter, which is capable of being inserted through the occlusion in the heart. A guiding catheter 62 is inserted onto the guidewire 34 to a point just short of the coronary ostium. The catheter 16 is inserted onto the guidewire 34 and into the guide catheter 62. Once the smaller reperfusion catheter 16 is positioned with its distal end 58 beyond the occlusion, the guidewire 34 is withdrawn, and the reperfusion solution can be passed through the catheter 16 to exit through the apertures 60. The tapered tip of the catheter facilitates penetration of the blockage and forms a seal with the blockage to prevent blood flow through the occlusion.

SYSTEM OPERATION

The application of the above system and method will now be described with respect to FIG. 1. A heart attack victim has a heart/lung bypass initiated by cannulating the femoral artery by arterial cannula 12 for arterial inflow, and by cannulating the femoral vein by the venous catheter 10 and advancing it under fluoroscopic control into the right atrium for venous return. The femoral-femoral bypass is sustained by the above-identified apparatus.

The left ventricular vent catheter 14 is inserted through the femoral artery through the aortic valve, and into the left ventricle to provide left ventricular decompression. The vent catheter 14 maintains the heart in an at-rest condition by removing all blood flowing into the left ventricle. The process of the heart attack has been slowed markedly by placing the heart in such at-rest condition.

The reperfusion catheter 16 is inserted as outlined above to administer a regional blood cardioplegia distal to the site of the occlusion which precipitated the heart attack. After reperfusion therapy, the occlusion which caused the heart attack is then dissolved by thrombolytic agents or by balloon angioplasty. The reperfusion catheter 16 or the guide catheter 62 may advantageously be used for these methods of removing the occlusion. Once the reperfusion is completed, a guidewire is reinserted through it and the reperfusion catheter 16 is removed. An angioplasty catheter is then advanced in the guide catheter and conventional angioplasty is performed to relieve the stenosis in the coronary artery which caused a clot to form. The guidewire, angioplasty catheter are removed and, after an additional 30 minutes on total bypass the catheter 14 is withdrawn. The catheters 14, 16 are withdrawn and blood is allowed to enter the left ventricle. The patient can then be taken off the heart bypass system. If the closed artery cannot be penetrated, the patient can be transported to the operating room for coronary bypass grafting around the blockage.

The above procedure, whereby normal blood is excluded from the area of the injured myocardium until after a period of reperfusion, has been shown in animal tests to lead to the consistent recovery of 40–100% of the muscle function when the treatment is given within four to six hours of the occlusion.

The apparatus and procedure thus offer the possibility of allowing greatly improved, if not complete, recovery by heart attack victims who would otherwise suffer from reduced heart function and shortened life span because a portion of the myocardium necrosed from the prolonged absence of blood.

Another advantage is provided by the use of one pump for both the venous catheter 10 and the vent catheter 14. The single pump greatly simplifies the system operation, and requires less personnel, with less training, to maintain the appropriate blood pressure in the heart attack victim, while adequately venting the heart.

The system further advantageously lends itself to electronic and mechanical control systems uniquely designed for performance of total extracorporeal circulation and controlled coronary reperfusion.

While the above description is of the preferred embodiment, the disclosure will suggest or render apparent various modifications and variations to those skilled in the art which are within the spirit and scope of the subject invention.

I claim:

1. An extracorporeal bypass apparatus, comprising:

a venous catheter for insertion into a femoral vein, such catheter being sufficiently long and flexible to reach the atrium area of a patent's heart;

an arterial cannula;

a single pump connected between the venous catheter and the arterial cannula for withdrawing blood from a patient through said venous catheter and pumping it into a patient through the arterial cannula; and

a vent catheter for insertion into an artery sufficiently long and flexible to reach the left ventricle of the heart, said vent catheter being connected in parallel with the venous catheter connected to the pump in a manner such that the negative pressure developed by said pump is applied to the venous catheter and the vent catheter,

said venous catheter and said pump being constructed such that substantially all of the patient's blood which would normally be returned to the heart is bypassed through the venous catheter, and the blood reaching the left ventricle of the heart is withdrawn through the vent catheter so that the ventricle is decompressed;

said vent catheter being a thin-walled flexible tube which has a coiled distal end, which is adapted to conform to a guide wire used in inserting the vent catheter.

2. An extracorporeal bypass apparatus, comprising:

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a venous catheter for insertion into a femoral vein, such catheter being sufficiently long and flexible to reach the atrium area of a patent's heart;

an arterial cannula;

a single pump connected between the venous catheter and the arterial cannula for withdrawing blood from a patient through said venous catheter and pumping it into a patient through the arterial cannula; and

a vent catheter for insertion into an artery sufficiently long and flexible to reach the left ventricle of the heart, said vent catheter being connected in parallel with the venous catheter connected to the pump in a manner such that the negative pressure developed by said pump is applied to the venous catheter and the vent catheter;

said venous catheter and said pump being constructed such that substantially all of the patient's blood which would normally be returned to the heart is bypassed through the venous catheter, and the blood reaching the left ventricle of the heart is withdrawn through the vent catheter so that the ventricle is decompressed;

said vent catheter including a plurality of apertures in the side wall of its distal end, and said vent catheter including a pressure lumen extending from the proximal end of the vent catheter to an inlet adjacent said apertures, the apertures being between the tip of the vent catheter and the inlet to the pressure lumen.

3. An extracorporeal bypass apparatus, comprising:

a venous catheter for insertion into a femoral vein, such catheter being sufficiently long and flexible to reach the atrium area of a patent's heart;

an arterial cannula;

a single pump connected between the venous catheter and the arterial cannula for withdrawing blood from a patient through said venous catheter and pumping it into a patient through the arterial cannula; and

a vent catheter for insertion into an artery sufficiently long and flexible to reach the left ventricle of the heart, said vent catheter being connected in parallel with the venous catheter connected to the pump in a manner such that the negative pressure developed by said pump is applied to the venous catheter and the vent catheter,

said venous catheter and said pump being constructed such that substantially all of the patient's blood which would normally be returned to the heart is bypassed through the venous catheter, and the blood reaching the left ventricle of the heart is withdrawn through the vent catheter so that the ventricle is decompressed;

said vent catheter having a flexible coiled distal end which presents an exterior curved surface to the aortic valve when the tip of the vent catheter is to be inserted into the ventricle, and said coiled end being adapted to fit totally within the ventricle.

4. An extracorporeal bypass apparatus, comprising:

a venous catheter for insertion into a femoral vein, such catheter being sufficiently long and flexible to reach the atrium area of a patent's heart;

an arterial cannula;

a single pump connected between the venous catheter and the arterial cannula for withdrawing blood from a patient through said venous catheter and pumping it into a patient through the arterial cannula;

a vent catheter for insertion into an artery sufficiently long and flexible to reach the left ventricle of the heart, said vent catheter being connected in parallel with the venous catheter connected to the pump in a manner such that the negative pressure developed by said pump is applied to the venous catheter and the vent catheter,

said venous catheter and said pump being constructed such that substantially all of the patient's blood which would normally be returned to the heart is bypassed through the venous catheter, and the blood reaching the left ventricle of the heart is withdrawn through the vent catheter so that the ventricle is decompressed; and

a reservoir having an inlet in communication with the output of said pump and having an outlet in communication with the connection between said venous cannula and said pump, and including means for adjusting the flow of liquid into and out of said reservoir.

5. An extracorporeal bypass apparatus, comprising:

a venous catheter for insertion into a femoral vein, such catheter being sufficiently long and flexible to reach the atrium area of a patent's heart;

an arterial cannula;

a single pump connected between the venous catheter and the arterial cannula for withdrawing blood from a patient through said venous catheter and pumping it into a patient through the arterial cannula;

a vent catheter for insertion into an artery sufficiently long and flexible to reach the left ventricle of the heart, said vent catheter being connected in parallel with the venous catheter connected to the pump in a manner such that the negative pressure developed by said pump is applied to the venous catheter and the vent catheter,

said venous catheter and said pump being constructed such that substantially all of the patient's blood which would normally be returned to the heart is bypassed through the venous catheter, and the blood reaching the left ventricle of the heart is withdrawn through the vent catheter so that the ventricle is decompressed; and

a blood cardioplegia delivery system, comprising:

a cardioplegia delivery pump having an inlet connected to the output of said arterial pump;

a source of cardioplegic liquid connected as an input to said cardioplegia pump; and

a coronary reperfusion catheter assembly including a catheter connected to the output of said cardioplegia pump, the coronary reperfusion catheter being sufficiently long and flexible to be adapted to be inserted through a patient's artery to reach an area of the heart that has been deprived of blood so that a cardioplegia solution can be applied to that area before resuming normal blood flow.

6. The apparatus of claim 5, wherein said reperfusion catheter assembly includes a guidewire adapted to guide the reperfusion catheter through said area, and a guide catheter through which said reperfusion catheter is inserted in reaching a point just short of said area.

7. The apparatus of claim 5, wherein said venous catheter is made of ethylene-vinyl-acetate material with a thin-walled construction that resists kinking.

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8. An extracorporeal bypass apparatus, comprising:

a venous catheter for insertion into a femoral vein, such catheter being sufficiently long and flexible to reach the atrium area of a patent's heart;

an arterial cannula;

a single pump connected between the venous catheter and the arterial cannula for withdrawing blood from a patient through said venous catheter and pumping it into a patient through the arterial cannula;

a vent catheter for insertion into an artery sufficiently long and flexible to reach the left ventricle of the heart, said vent catheter being connected in parallel with the venous catheter connected to the pump in a manner such that the negative pressure developed by said pump is applied to the venous catheter and the vent catheter,

said venous catheter and said pump being constructed such that substantially all of the patient's blood which would normally be returned to the heart is bypassed through the venous catheter, and the blood reaching the left ventricle of the heart is withdrawn through the vent catheter so that the ventricle is decompressed; and

said arterial cannula comprising an elongated tube having a tip section adapted to be inserted into the femoral artery, said tube having a shoulder adjacent to said tip section adapted to engage the exterior of the artery to limit insertion of the tip section into the artery and to form a seal at the exterior of the artery.

9. The apparatus of claim 8, wherein the surface of said shoulder which engages the artery is formed at an angle of approximately 45° with respect to the diameter of the cannula.

10. The apparatus of claim 9, including a pair of suture wings extending outwardly from the exterior of the cannula and adapted to be sutured to a patient's skin so as to maintain the cannula tip section properly in the artery while leaving the proximal end of the cannula outwardly from the wings to be easily manipulated.

11. The apparatus of claim 8, including a stylet adapted to fit within the cannula, said stylet including a stop on its exterior which slides within the cannula.

12. The apparatus of claim 11, including an antibackflow ring positioned in the proximal end of the cannula or a fitting connected to the cannula and slidably receiving the stylet, the ring sealing the cannula and being engaged by the stylet stop as the stylet is being withdrawn, but the ring being removable from the cannula by an increased pulling force on the stylet.

13. An extracorporeal bypass apparatus, comprising:

a venous catheter for insertion into a femoral vein, such catheter being sufficiently long and flexible to reach the atrium area of a patent's heart;

an arterial cannula;

a single pump connected between the venous catheter and the arterial cannula for withdrawing blood from a patient through said venous catheter and pumping it into a patient through the arterial cannula;

a vent catheter for insertion into an artery sufficiently long and flexible to reach the left ventricle of the heart, said vent catheter being connected in parallel with the venous catheter connected to the pump in a manner such that the negative pressure developed by said pump is applied to the venous catheter and the vent catheter,

said venous catheter and said pump being constructed such that substantially all of the patient's blood which would normally be returned to the heart is bypassed through the venous catheter, and the blood reaching the left ventricle of the heart is withdrawn through the vent catheter so that the ventricle is decompressed; and

a stylet slidably positioned in the cannula and a removable seal extending between the interior of the cannula and the stylet so that, if the tip of the cannula is in the artery, the seal prevents liquid flow out of the cannula.

14. An extracorporeal bypass system, comprising:

a venous catheter for insertion into a femoral vein, such catheter being sufficiently long and flexible to reach the right atrium area of a patent's heart;

an arterial cannula;

a pump connected between the venous catheter and the arterial cannula for withdrawing blood from a patient through said venous catheter and pumping it into a patient through the arterial cannula; and

a bridging, non-dynamic reservoir having an inlet connected to the output of said pump in an outlet connected to the inlet of said pump;

whereby said reservoir is connected in parallel with said pump so that blood may be pumped directly from the pump to said arterial cannula without passing through said reservoir and so that said reservoir inlet and outlet can be opened or closed to permit flow into or out of said reservoir.

15. The system of claim 14, including means for controlling the liquid flow through said system to about 5 liters per minute, maintaining the negative pressure on the venous catheter at an amount no greater than about 200 mm Hg.

16. The system of claim 14, including control means for periodically permitting flow into or out of said reservoir.

17. A percutaneous cardiopulmonary bypass apparatus, comprising:

a venous catheter for insertion into a femoral vein;

an arterial cannula for insertion into an artery;

an oxygenator;

a pump connected between the venous catheter and the oxygenator for withdrawing blood from a patient through said venous catheter and pumping it through the oxygenator and the arterial cannula into a patient, said catheter being sufficiently long and flexible to reach the atrium area of a patient's heart, said catheter having an interior diameter large enough to permit blood flow of 7 liters per minute with a negative pressure provided by said pump being no greater than 200 mm Hg, and said catheter being thin-walled, but nonkinkable with normal handling,

said catheter having a plurality of holes in its side wall extending from the distal end of the tip far enough to not only draw blood from the atrium area of the heart, but to also draw blood from the portion of the vein draining in the lower portion of the body.

18. The apparatus of claim 17, wherein said catheter is made of ethylene-vinyl-acetate and has a wall thickness of about 0.825 mm.

19. The apparatus of claim 17, wherein said catheter is made of ethylene-vinyl-acetate having about 18% acetate.

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20. The apparatus of claim 17, wherein said catheter is constructed such that it will not collapse when positioned within a patient and subjected to 200 mm of negative pressure.

21. A percutaneous cardiopulmonary bypass apparatus, comprising:

a venous catheter for insertion into a femoral vein;

an arterial cannula for insertion into an artery;

an oxygenator;

a pump connected between the venous catheter and the oxygenator for withdrawing blood from a patient through said venous catheter and pumping it through the oxygenator and the arterial cannula into a patient, said catheter being sufficiently long and flexible to reach the atrium area of a patient's heart, said catheter having an interior diameter large enough to permit blood flow of 7 liters per minute with a negative pressure provided by said pump being no greater than 200 mm Hg, and said catheter being thin-walled, but nonkinkable with normal handling; and

said catheter being in the form of two venous catheters one for insertion in a femoral vein and the other for insertion in a second femoral vein, and said two catheters combined permit blood flow up to approximately 7 liters per minute with a negative pressure of no greater than approximately 200 mm Hg.

22. A method for providing a peripheral cardiopulmonary bypass system, comprising:

inserting a venous catheter into a femoral vein with the tip of the catheter extending to the right atrium area of a patient's heart;

inserting an arterial cannula into a femoral artery;

inserting a vent catheter into a femoral artery with the tip of the vent catheter extending to the left ventricle of the heart;

connecting the two catheters to the input side of a single heart bypass pump and connecting the output of the pump to the arterial cannula;

pumping substantially all of the patient's venous return blood out of the patient and back into the patient through the femoral artery while withdrawing blood through the vent catheter so as to maintain the ventricle in a decompressed condition; and

monitoring the negative pressure developed by said pumps so as to maintain the negative pressure with no greater than 200 ml of mercury.

23. The method of claim 22, including monitoring the pressure in the patient's ventricle and adjusting the system as necessary to maintain the ventricle in a decompressed condition and keeping the negative pressure applied to the vent catheter at a safe level.

24. The method of claim 22, including connecting a reservoir to the output of said pump and to the input to said pump, and adjusting controls to and from the reservoir so as to periodically add liquid to the system or remove liquid from the system as needed to maintain the desired flow through the system within the desired pressure range.

25. A method for providing a peripheral cardiopulmonary bypass system, comprising:

inserting a venous catheter into a femoral vein with the tip of the catheter extending to the right atrium area of a patient's heart;

inserting an arterial cannula into a femoral artery;

inserting a vent catheter into a femoral artery with the tip of the vent catheter extending to the left ventricle of the heart;

connecting the two catheters to the input side of a single heart bypass pump and connecting the output of the pump to the arterial cannula;

pumping substantially all of the patient's venous return blood out of the patient and back into the patient through the femoral artery while withdrawing blood through the vent catheter so as to maintain the ventricle in a decompressed condition; and

monitoring the speed of said pump so as to provide a flow in the system of up to 7 liters per minute.

26. A method for providing a cardiopulmonary bypass system, comprising:

inserting a venous catheter into a femoral vein with the tip of the catheter extending to the right atrium area of a patient's heart;

inserting an arterial cannula into a femoral artery;

pumping blood from the venous catheter through a blood oxygenator to the arterial cannula;

connecting a bridging reservoir in parallel to the pumping means with an inlet to the reservoir being connected to the outlet of the pumping means and with an outlet of the reservoir connected to the inlet of the pump; and

selectively opening and closing the reservoir inlet and outlet to add or withdraw liquid from the system as needed.

27. The method of claim 26, including inserting a vent catheter into a femoral artery with the tip of the vent catheter extending to the left ventricle of the heart; and applying negative pressure to said vent catheter to decompress the left ventricle.

28. A method for providing a cardiopulmonary bypass system, comprising:

inserting an arterial cannula into a femoral artery;

inserting a vent catheter into a femoral artery with the tip of the vent catheter extending to the left ventricle of the heart;

pumping blood from the vent catheter to the arterial cannula; and

connecting a reservoir in parallel to the pumping means with an inlet to the reservoir being connected to the outlet of the pumping means and with an outlet of the reservoir connected to the inlet of the pump.

29. The method of claim 28, including selectively opening and closing the reservoir inlet and outlet to add or withdraw liquid from the system as needed.

30. An extracorporeal heart bypass apparatus comprising:

a venous catheter;

a positive displacement pump connected to apply negative pressure to said catheter to withdraw blood from a patient;

a compliance chamber connected between said pump and said catheter to reduce the rate of change of negative pressure applied by said pump on said catheter, said chamber comprising the space between an expandable reservoir connected between said pump and said catheter, and a closed housing surrounding said reservoir whereby the pressure in the chamber is related to the pressure in the reservoir; and

a controller to control the speed of said pump, said controller being responsive to the pressure in said

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space so as to decrease pump speed with an increase in negative pressure in the compliance chamber.

31. The apparatus of claim 30, including a pressure transducer sensing the pressure in said space, with the transducer connected to provide its pressure information to said controller.

32. The apparatus of claim 30, wherein said positive displacement pump is a peristaltic pump.

33. The apparatus of claim 30, including a vent catheter connected in parallel to said venous catheter such that the negative pressure provided by said pump is also applied to the vent catheter.

34. The apparatus of claim 30, including a reservoir bridging said pump with said bridging reservoir having controls for increasing or decreasing the volume of fluid in the system; and an arterial cannula for conducting the output of said pump to a patient's artery.

35. A method of controlling negative pressure changes to a patient's venous blood supply in withdrawing blood from a patient in connection with a cardiopulmonary bypass system, comprising:

inserting a venous catheter into a patient's vein;

operating a positive displacement pump to apply a negative pressure to said catheter;

reducing the rate at which negative pressure on said catheter can be changed by said pump so as to keep the negative pressure at a safe level and prevent the nucleation of gas in the blood;

sensing said negative pressure;

changing pump speed in response to sensed pressure changes;

said reducing step including applying the negative pressure of said pump to an expandable reservoir positioned in a conduit between said catheter and said pump, with a housing surrounding the reservoir creating a chamber responsive to changes of said pressures, the volume of blood in said reservoir being reduced upon increases in negative pressure, thereby reducing the rate at which negative pressure can be increased; and

said sensing step including sensing the pressure in the chamber between said reservoir and said housing and utilizing the sensed pressure to a said controller to decrease the speed of said pump in response to increases in the negative pressure in said chamber.

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Appendix F: Various Vent Catheters

- K834352- DLP, Inc., Adult Vent Catheter 510(k) Labeling
- K012143- Medtronic 24 Fr Left Heart Vent w/ Pressure Monitoring Line 510(k) Summary
- K981601- California Medical Laboratories- Malleable Vent Catheter 510(k) Summary
- From Chapter 21 titled "Anesthesia for Cardiovascular Surgery" Section B. Left Ventricular Vent. (Page 437). in Clinical Anesthesia, Third Addition. Morgan CE, Jr., Makhail MS, Murray MJ, eds.New York: McGraw Hill, 2002.
- From Chapter 11 titled "Extracorporeal Circulation: Perfusion Systems" Eugene A. Hessel, L. Henry Edmunds, Jr. in Cardiac Surgery in the Adult. Cohn LH, Edmunds LH, Jr, eds.New York: McGraw Hill, 2003.
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- Zwart et al. First clinical application of transarterial closed-chest left ventricular (TaCLV) bypass. Trans Am Soc Artif Intern Organs 1970;16:386-391.
- Golding L. A simplified blood access method for a temporary left ventricular assist system in humans. Artif Organs. 1978 2:317-8. and Golding L et al. Initial clinical experience with a new temporary ventricular assist device. Ann Thor Surg 1980;29:66-69.
- Duncan et al. Myocardial-Sparing Cannulation Technique for Left Ventricular Assist Device Support. Ann Thor Surg. 1991;52:565-6.

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

343 52

EXHIBIT II

MATERIALS

The numbers referenced below refer to the ballon numbers on the associated drawing on the next page:

12002 Catheter

Number(s)	Description	Material
1.	Tip	Medical Grade Silicone [redacted]
2.	Tubing	Medical Grade Clear Silicone USP Class VI [redacted]
3.	1/4" Tube Connector Fitting	Acrylic - Clear USP Class VI
4.	Introducer	[redacted] Stainless Steel [redacted]
5.	Introducer Handle	Acrylic - Clear USP [redacted]

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892

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K834352

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
8757 Georgia Avenue
Silver Spring MD 20910

Mr. James H. De Vries
President
DLP Inc.
620 Watson, S.W.
Grand Rapids, Michigan 49504-6383

Ref: K834352 - Adult Vent Catheter

Dated: October 27, 1983
Received: December 13, 1983
Regulatory class: II

Dear Mr. De Vries:

We have reviewed your premarket notification submission and have found the device to be substantially equivalent to devices introduced into interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendment . You may, therefore, market your device subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act). This product has been placed into the regulatory class shown above by a final regulation published in the Federal Register. Class I devices are regulated by the general control provisions of the Act applicable to all medical devices including annual registration, listing of devices, good manufacturing practice, labeling, and the misbranding and adulteration provisions of the Act; class II devices are those for which future performance standards will be developed; class III devices are those which will be required to undergo premarket approval at some time in the future.

Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Section 800. In addition, the Food and Drug Administration (FDA) may publish further announcements concerning your device in the Federal Register. We suggest you subscribe to this publication so that you can convey your views to FDA if you desire. Also, the Federal Register will notify you of any additional requirements subsequently imposed on your device. Subscriptions may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402. Such information also may be reviewed in the Dockets Management Branch (HFA-305), Food and Drug Administration, Room 4-62, 5600 Fishers Lane, Rockville, Maryland 20857.

This letter does not in any way denote official FDA approval of your device. Any representation that creates an impression of official approval of this device because of compliance with the premarket notification regulations is misleading and constitutes misbranding. If you need further assistance on the labeling for your device, please contact the Office of Medical Devices, Division of Compliance Operations (HFK-110), 8757 Georgia Avenue, Silver Spring, Maryland 20910.

Sincerely yours,

Robert G. Britain

Robert G. Britain
Associate Director for
Device Evaluation
Office of Medical Devices
National Center for Devices
and Radiological Health

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Memorandum

Date

From — REVIEWER(S) - NAME(S) Shang W Hwang 1-17-83

Subject — 510(k) NOTIFICATION K834352

To — THE [redacted]

It is my recommendation that the subject 510(k) Notification:

✓ (A) Is substantially equivalent to marketed devices.

____ (B) Requires premarket approval. NOT substantially equivalent to marketed devices.

____ (C) Requires more data.

____ (D) Is an incomplete submission. (See Submission Sheet).

Additional Comments:

I called Mr. De Vries and asked him how the sterilization was done. He said that the device was packaged in Tyvek and ETO-Sterilized by WalPACK. Inc of Ill. S. W Hwang

The [redacted] requests:

✓ No Confidentiality

____ Confidentiality for 90 days

____ Continued Confidentiality exceeding 90 days

Class Code w/Panel: 74 DRA II

REVIEW: [signature] (BRANCH CHIEF) 1/18/84 (DATE)

FINAL REVIEW: [signature] (~~DIVISION~~ DIRECTOR) 1/19/84 (DATE)

895

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

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K834352

DLP INC. 620 WATSON, S.W. / GRAND RAPIDS, MI 49504 6393 (616) 242 5200 1 800-253-1540 TLX 234130

Food and Drug Administration
Bureau of Medical Devices
Document Control Center (HFK-20)
8757 Georgia Ave.
Silver Spring, MD 20910

Re: 510 (K) Submission

Adult Vent Catheter

October 27, 1983

Gentlemen;

As required by Section 510 (K) of the Medical Device Amendments of 1976 and in accordance with 21 CFR, Par 807, we are providing you with 90 days prior notice that we intend to market this device. This device is used during Cardiopulmonary Bypass surgery to perform the following function:

1. Vent excess fluids or air from the left heart.

This device has been classified by the Cardiovascular Classification Panel in Class II under the Classification Name: Cardiopulmonary Bypass; Catheter; Cannula and Tubing; Vascular.

The specific Catalog Code under consideration is:

1. #12002 Adult Vent Catheter with side vent 20 French.

The device is intended for use in venting the left heart during Cardiopulmonary Bypass with entrance made in the Left Atrium and passing through the Mitral Valve.

We feel that the device is substantially equivallent to the adult disposable curved Left Heart Vent Catheter (#12345) manufactured by Sarns, Inc., Ann Arbor, MI.

The device under consideration offers these advantages over using other Left Vent Catheters:

1. A silicone tube that will give greater flexibility and reduce rigidity during Cardioplegia Administration.

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896

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

DLP INC. 620 WATSON, S.W. / GRAND RAPIDS, MI 49504 6393 (616) 242-5200 1-800-253-1540 TLX 234130

2. An annealed introducer of stainless steel will allow surgeons to obtain desired radius and angle for insertion.

Specific materials used in the construction of this device are included in the supporting documentation.

The equivalency of this device to the existing product is supported by the following attachments.

1. Photographs of the new catheter.
2. List of materials used.
3. Advertising literature on the 12345 Sarns Catheter.
4. Comparison of features between products.
5. Draft labeling Catalog Code; 12002.
6. Copies of labeling on existing products.

To the extent applicable at this time, we submit that we are in compliance with the requirements of Section 514 and 515 as to this device. The device will be produced in our facility located at 4221 Richmond N.W., Grand Rapids, MI 49504.

If you have any questions or desire additional information, please contact me at (616) 242-5200.

Sincerely yours,

James H. De Vries
President

JHD/ldv

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

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Letter

898

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

DLP INC. 620 WATSON, S.W. / GRAND RAPIDS, MI 49504-6393 / (616) 242-5200 / 1-800-253-1540 / TLX 234130

Food and Drug Administration
Bureau of Medical Devices
Document Control Center (HFK-20)
8757 Georgia Ave.
Silver Spring, MD 20910

Re: 510 (K) Submission

Adult Vent Catheter

October 27, 1983

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

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DLP INC. 620 WATSON, S.W. / GRAND RAPIDS, MI 49504-6393 / (616) 242-5200 / 1-800-253-1540 / TLX 234130

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4. Comparison of features between products.
5. Draft labeling Catalog Code; 12002.
6. Copies of labeling on existing products.

To the extent applicable at this time, we submit that we are in compliance with the requirements of Section 514 and 515 as to this device. The device will be produced in our facility located at 4221 Richmond N.W., Grand Rapids, MI 49504.

If you have any questions or desire additional information, please contact me at (616) 242-5200.

Sincerely yours,

James H. De Vries
President

JHD/ldv

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

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Photographs

901

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

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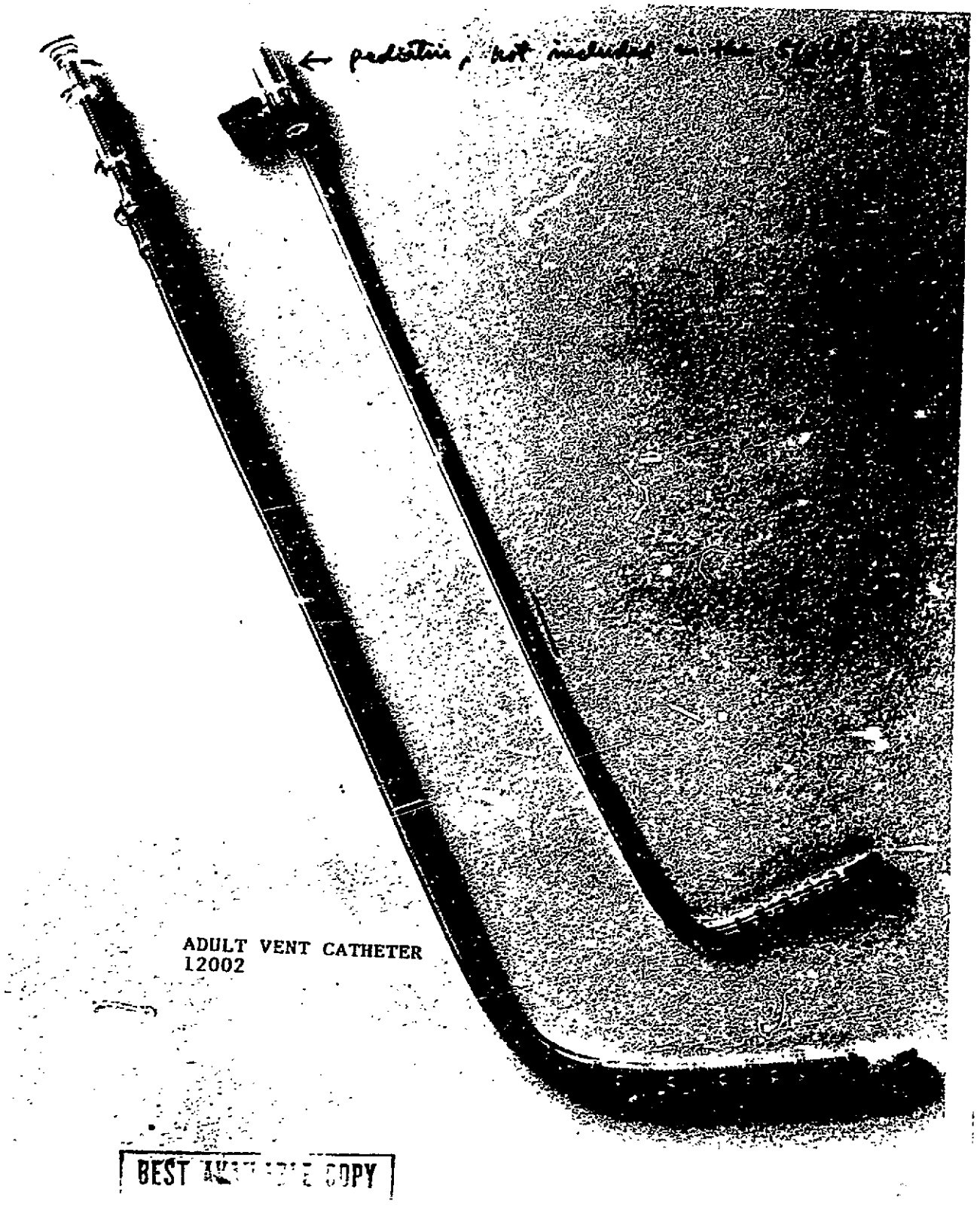

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902

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

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Materials

903

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

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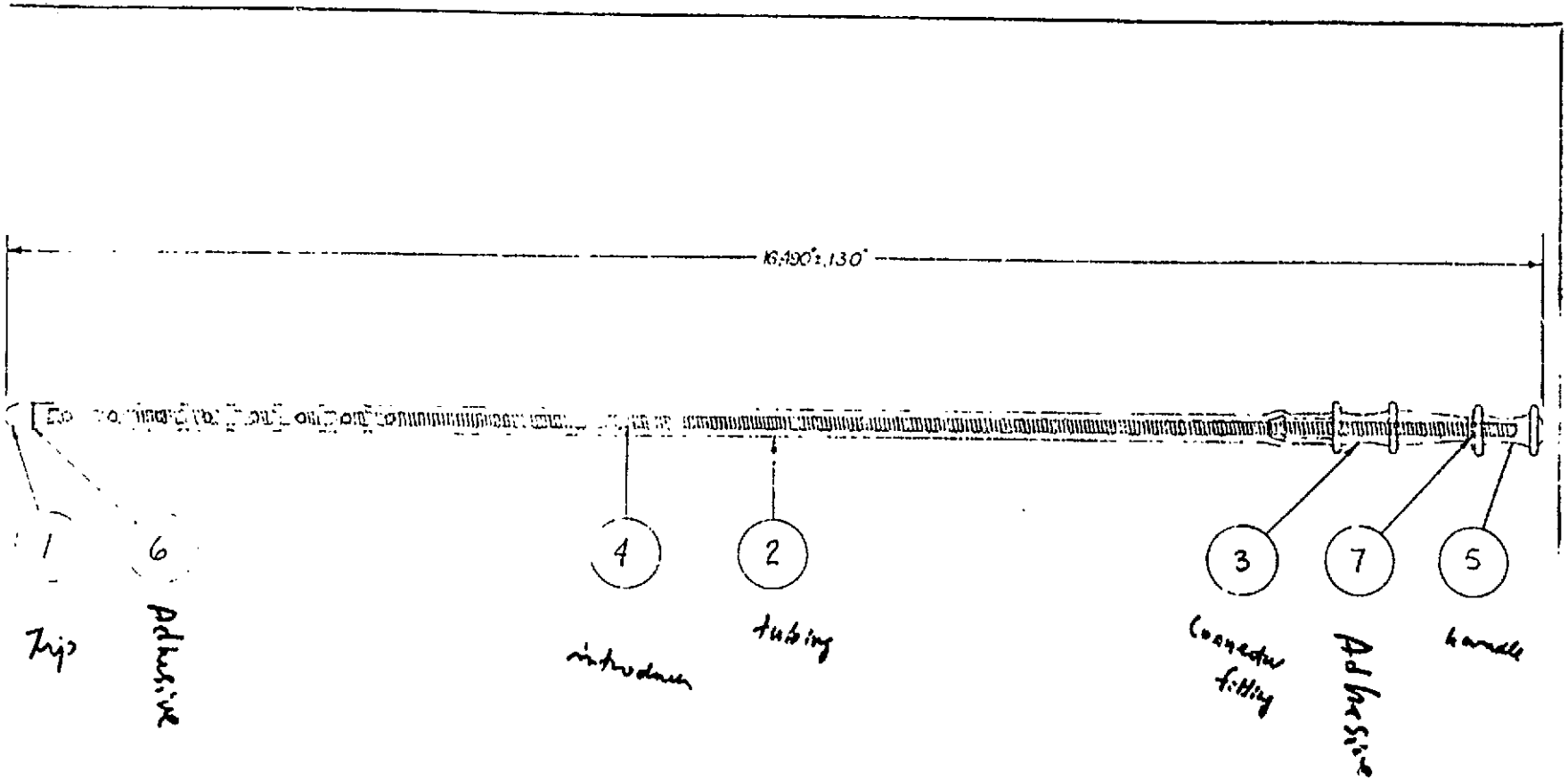

ADULT VENT CATHETER

SCALE 1:1 | APPROVED BY: | DRAWN BY: TJ

DATE 11-22-93 | DIVISION

ULP INC.

DRAWING NUMBER

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

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Literature

906

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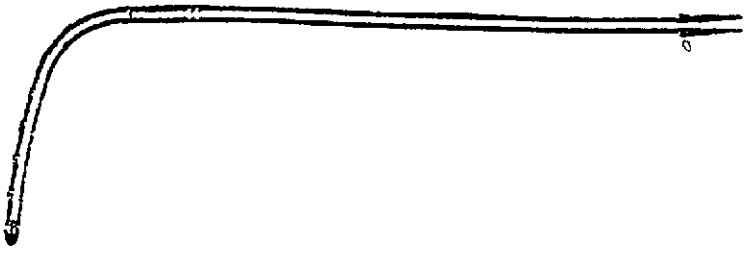
sarns

Disposable Curved Left Heart Vent Catheter

DESCRIPTION A sterile, disposable vent catheter consisting of a 35.5 cm (14") long, preformed, flexible, plastic tube (20 French), with a 11.4 cm (4.5") perforated section. A small tapered tip of rigid plastic is attached to the perforated section to aid in the insertion of the catheter. A rigid plastic tube connector for 6.1 mm (1/4") I.D. tubing is permanently attached to the other end of the catheter tube. Marking rings on the tube serve as an indication of insertion depth.

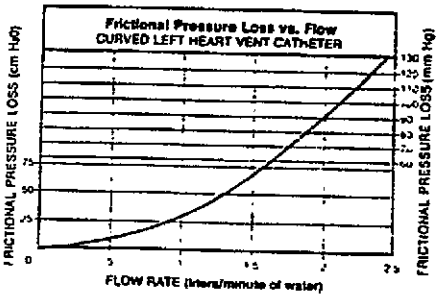
INDICATIONS The Curved Left Heart Vent Catheter is indicated for use in venting the left heart during cardiopulmonary bypass with entrance made at the juncture of the right superior pulmonary vein with the left atrium and passing through the mitral valve.



CONTRAINDICATIONS This device is not designed, sold, or intended for use except as indicated. Specifically, it should not be used if surgery on the mitral valve is anticipated.

PART NO. 12345
Curved Left Heart Vent Catheter

Carton of ten presterilized vents
Venting length 11.4 cm (4½")
Overall Length 35.5 cm (14")
Tube connector for 6.1 mm (1/4") I.D. tubing



NOTE: The above flow data represent in vitro, laboratory testing with water as the test solution. The data represent isolated, frictional pressure losses. The data are furnished for information purposes only and do not necessarily represent the flows to be achieved under clinical conditions.

sarns [redacted]

907

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

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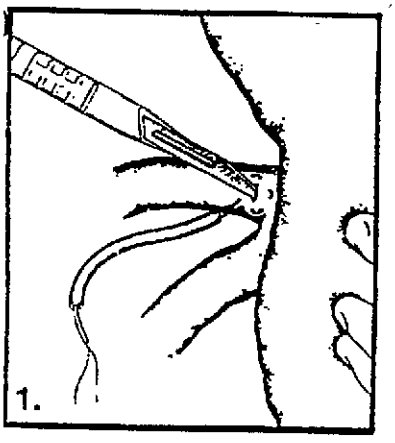
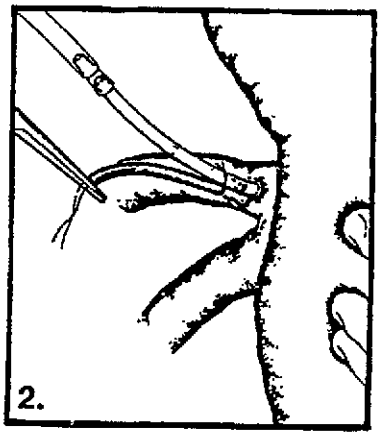
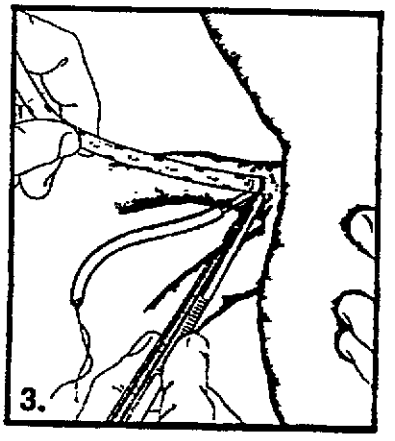
Surgical Procedures
Sarns Disposable Curved Left Heart Vent Catheter



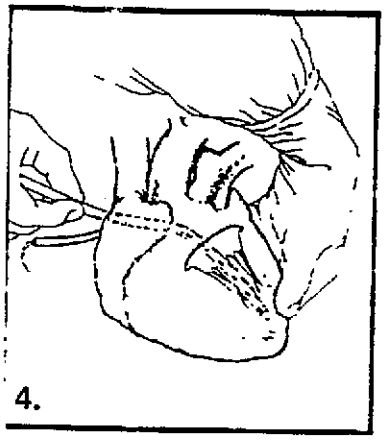
After instituting cardiopulmonary bypass, retract the right atrium and place a purse string suture at the juncture of the right superior pulmonary vein and the left atrium. Draw the sutures through a rubber ligature tube. Make an incision within the purse string suture.



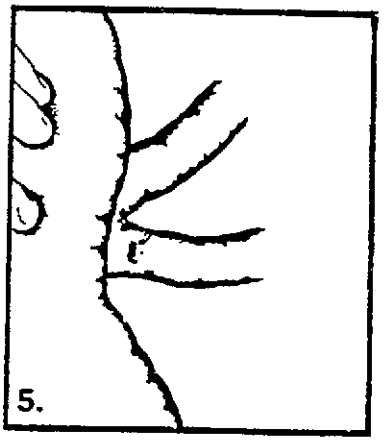
Insert the rigid tip just through the wall of the atrium.



Insert the catheter at least to the first line on the catheter through the atrium and mitral valve into the left ventricle. Palpate the heart during insertion to insure proper positioning of the catheter.



Tighten the suture and clamp the ligature tube. Connect the catheter to the pump tubing.



After the procedure, remove the vent and tie the suture.

WARNINGS:

Gravity drainage is recommended in procedures where the left heart will remain closed. This will help reduce the possibility of air embolism and hemolysis due to excessive pump suction.

Gravity drainage is not recommended where excessive vent flow is anticipated due to aortic valvular incompetence.

PRECAUTION:

Palpation of the heart during the insertion of the catheter is recommended to insure proper positioning of the catheter within the heart.

Proper surgical procedures and techniques are necessarily the responsibility of the medical profession. The described procedure is furnished for information purposes only. Each surgeon must, of course, evaluate the appropriateness of the surgical procedure based upon his own medical training and experience.

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SARNS
6200 JACKSON ROAD, ANN ARBOR, MICHIGAN 48103 313-663-4145
TELEX: 23-0508 SARNS INC ARB, CABLE, SARNSEQUIP

SARNS INC 7-77 Printed in U.S.A. UL 3M
Form No. 12447001

908

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

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features

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COMPARISON OF FEATURES

	Proposed Device : 12002 Catheter	Existing Device : #12345 Catheter
USE:	Venting of the left heart during Cardiopulminary Bypass	SAME
Materials of Construction	Silicone	Plastic with PVC Tubing
Catherter Size	20 French	SAME
Packaging	Sterile, Disposable	SAME

910

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

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Labeling

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Warnings:

Gravity drainage is suggested in procedures where the Left Heart is kept closed. This will reduce the possibility of air embolism .

Gravity drainage is not suggested where relatively high flows may be encountered.

Precautions:

The catheter is made of silicone which will not stiffen as much as PVC at Cardioplegia temperatures. Neccessary care must still be taken when manipulating the heart.

CAUTION: Restricted Device: Federal law (USA) restricts the sale, distribution, or use of thi, device to, by, or on the lawful crder of a physician.

Note: Proper surgical procedures and techniques are necessarily the responsibility of the medical profession. The described procedure is furnished for information purposes only. Each surgeon must, of course, evaluate the appropriateness of the procedure based on his own medical training and experience, the type of surgical procedure, and the type of suction systems utilized.

When removing the catheter, withdraw it completely before tightening the purse string suture to prevent catching the suture in the perforated section of the catheter.

The catheter is designed and intended for single use only: **DO NOT REUSE**

Adverse Effects:

None Known.

Information For Use:

1. Inspect the package for damage. If undamaged, open the package and transfer the catheter into the sterile field utilizing aseptic technique.

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

DRAFT

Directions For Use

'roduct Name: Adult Vent Catheter

lodel: Code #12002 20 French

'escription:

Adult Vent Catheter
Sterile, nonpyrogenic, disposable, 16.50 inches long, flexible silicone tube (20 French) with a 3.50 inch perforated section. A small ~~tapered~~ tip is attached to perforated section to aid in the insertion of the catheter. A Rigid Plastic Tube Connector, for 1/4 inch I.D. tubing, is permanently attached to the other end of the catheter, ~~stainless steel~~ introducer with annealed core wire and permanently attached handle is inserted into the catheter.

Photo

:ndications and Usage:

This catheter is intended for use in venting the left heart during Cardiopulmonary Bypass.

:nformation For Use:

See reverse side for detailed information.

:ontraindications:

This device is not intended for use except as indicated above.

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2. If the catheter is to be placed in a difficult location it can be bent to the desired shape by simply forming the catheter with the annealed introducer in place. Take care to avoid abrupt angles.

3. Retract the Right Atrium and place a purse string suture at the cannulation site. Draw the suture through a rubber ligature tube. Make an incision within the purse string sucture.

4. Insert the tip of the catheter just through the wall of the Atrium.

5. Insert the catheter at least past the last holes of the perforated section on the catheter. During insertion palpate the heart to insure proper postioning of the catheter.

6. Tighten the suture and tie or clamp the ligature tube at a convenient site. Remove the introducer. Connect the catheter to the suction tubing.

7. After the procedure remove the vent and tie the suture.

DLP Inc.
Grand Rapids, MI 49501-0409
616-253-1540
800-253-1540
Rev. / /
(Printed in the U.S.A.)

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

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LABEL PRINTING SPECIFICATION - 12002:

POUCH:

CONTENTS: 01 EA. CODE 12002
ADULT
VENT CATHETER
20 FRENCH

15.5" (39.5 cm) SILICONE
TUBING WITH MALE SLIP ON
CONNECTION FOR 1/4" TUBING
AND A STAINLESS STEEL
INTRODUCER WITH HANDLE.

CARTON:

DLP INC. • 820 WATSON S.W. • GRAND RAPIDS, MI 49504-6393 • (800) 253-1640

CATALOG CODE:12002 CONTENTS: 20 EACH
ADULT VENT CATHETER
20 FRENCH

Store Below 40° (104°F) In A Clean Dry Area
CAUTION
RESTRICTED DEVICE: Federal Law (U.S.A.) Restricts The Sale, Distribution, Or Use Of This Device To, By, Or On The Lawful Order Of A Physician.

Lot Number: Sterilization Date: Expires:

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

PEEL HERE TO OPEN

CONTENTS: 01 EA. CODE 12002
ADULT
VENT CATHETER
20 FRENCH

15.5" (39.3 cm) SILICONE TUBING WITH MALE SLIP ON CONNECTION FOR 1/4" TUBING AND A STAINLESS STEEL INTRODUCER WITH HANDLE.

Caution: Federal (U.S.A.) law restricts this device to sale and use by or on order of a physician.

Contents are sterile, nonpyrogenic if pouch is not open or damaged.

DISPOSABLE: DO NOT REUSE

(X30-013-01/21X2)

dip inc

4221 RICHMOND N.W.
WALKER, MICH. 49504
Made in the U.S.A.

LOT NUMBER

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

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Existing

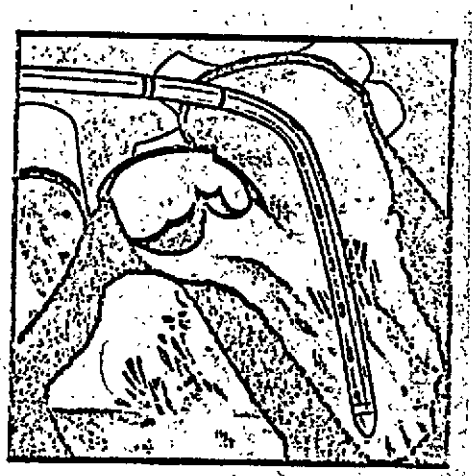
917

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

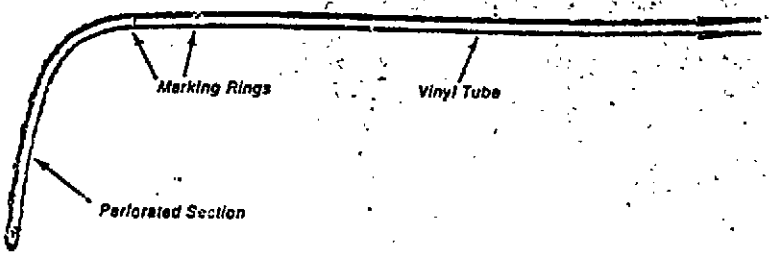
Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

Curved Left Heart Vent Catheters

INDICATIONS The Curved Left Heart Vent Catheter is indicated for use in venting the left heart during cardiopulmonary bypass with entrance made at the juncture of the right superior pulmonary vein with the left atrium and passing through the mitral valve.



DESCRIPTION This vent catheter consists of a preformed, flexible plastic tube, (20 French), with a perforated section. A small tapered tip of rigid plastic is attached to the perforated section to aid in the insertion of the catheter. A rigid plastic tube connector for 6.4 mm (¼") I.D. tubing is permanently attached to the other end of the catheter tube. Marking rings on the tube serve as an indication of insertion depth.



CONTRAINDICATIONS This device is not designed, sold, or intended for use except as indicated. Specifically, it should not be used if surgery on the mitral valve is anticipated.

Carton of 10 presterilized disposable vents
PART NO. 12345
Curved Left Heart Vent Catheter
Venting length 11.4 cm (4½")
20 French (6.7 mm)
Overall length 35.5 cm (14")
Tube connector for 6.4 mm (¼") I.D. tubing

PART NO. 14622
Curved Left Heart Vent Catheter
Venting length 9.5 cm (3¾")
20 French (6.7 mm)
Overall length 33.5 cm (13")
Tube connector for 6.4 mm (¼") I.D. tubing

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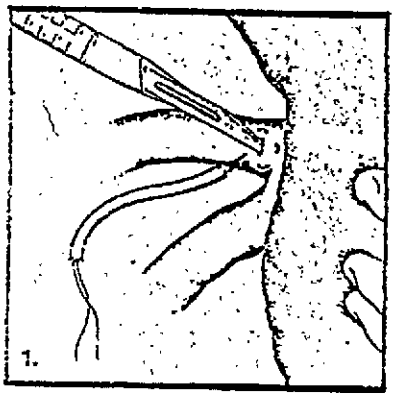
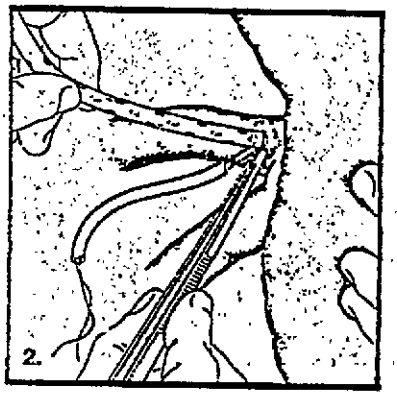
Surgical Procedures

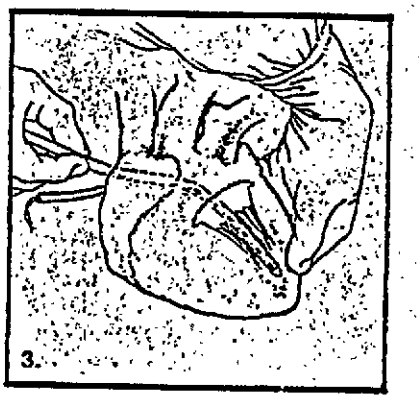
Curved Left Heart Vent Catheters



After instituting cardiopulmonary bypass, retract the right atrium and place a purse string suture at the juncture of the right superior pulmonary vein and the left atrium. Draw the sutures through a rubber ligature tube. Make an incision within the purse string suture.



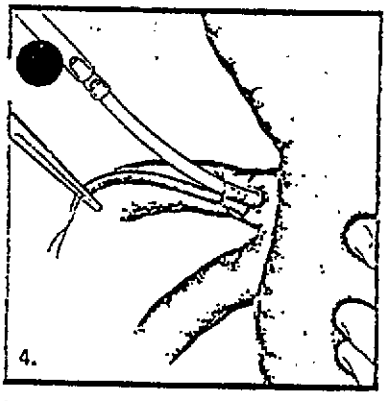
Insert the rigid tip just through the wall of the atrium.



Insert the catheter at least to the first line on the catheter through the atrium and mitral valve into the left ventricle. Palpate the heart during insertion to insure proper positioning of the catheter.

WARNING:

Avoid impingement of the vent catheter tip against the ventricular wall.



Tighten the suture and clamp the ligature tube. Connect the catheter to the pump tubing.

After the procedure, remove the vent and tie the suture.

WARNINGS:

A vent catheter inserted through the right superior pulmonary vein or left atrium can perforate the left ventricular apex if undue pressure is exerted by the tip. Care must be taken to avoid overinsertion of the catheter and possible impingement of the vent catheter tip against the ventricular wall.

Use of cold solutions and cardioplegic agents, externally, or via the coronary circulation, renders the myocardium flaccid and increases the stiffness of polyvinylchloride plastic, and may contribute to ventricular perforation under conditions of catheter tip pressure during manipulation of the heart.

Direct infusion of cold solutions into the left ventricle is not recommended when a polyvinylchloride plastic vent catheter is present.

WARNINGS:

Gravity drainage is recommended in procedures where the left heart will remain closed. This will help reduce the possibility of air embolism and hemolysis due to excessive pump suction.

Gravity drainage is not recommended where excessive vent flow is anticipated due to aortic valvular incompetence.

PRECAUTION:

Palpation of the heart during the insertion of the catheter is recommended to insure proper positioning of the catheter within the heart.

Proper surgical procedures and techniques are necessarily the responsibility of the medical profession. The described procedure is furnished for information purposes only. Each surgeon must, of course, evaluate the appropriateness of the surgical procedure based upon his own medical training and experience.

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OCT 2 4 2001

K012143

APPENDIX III

SUMMARY OF SAFETY AND EFFECTIVENESS
TRUTHFUL AND ACCURATE STATEMENT
DECLARATION OF CONFORMITY

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SUMMARY OF SAFETY AND EFFECTIVENESS

COMPANY

Medtronic, Inc.
Medtronic Cardiac Surgical Products
620 Watson Street S.W.
Grand Rapids, MI 49504

CONTACT PERSON

Melissa Harriger
Associate Product Regulations Manager
Medtronic Cardiac Surgical Products
620 Watson Street SW
Tel: 616-643-5519
FAX: 616-643-1017

DEVICE NAME

24 Fr. Left Heart Vent Catheter w/ Pressure Monitoring Line (12524)

NAME OF PREDICATED OR LEGALLY MARKETED DEVICE

Adult Vent Catheter (K834352)
Aortic Root Cannula with Pressure Monitoring Line (K831591)

DESCRIPTION OF DEVICE

The 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line is designed for use in venting the left heart during cardiopulmonary bypass surgery.

The 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line is equipped with a pressure monitoring line, which allows measurement of left ventricular pressure.

STATEMENT OF INTENDED USE

The 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line is intended for use in venting the left heart during cardiopulmonary bypass surgery.

STATEMENT OF INTENDED USE OF PREDICATED/MARKETED DEVICE

The Adult Vent Catheter is intended for use in venting the left heart during cardiopulmonary bypass surgery.

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STATEMENT OF TECHNOLOGICAL CHARACTERISTICS COMPARISON

Information regarding technological characteristics comparison is provided in the following section, "Determination of Substantial Equivalence".

DETERMINATION OF SUBSTANTIAL EQUIVALENCE

This **"SPECIAL 510(k)"** is being submitted for a modification to the Adult Vent Catheter. The modification to the current Adult Vent Catheter is to include a pressure monitoring line and material change.

The 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line is being compared to the following Marketed Devices:

- Adult Vent Catheter (K834352)
- Infant Vent Catheter (K834039)
- Aortic Root cannula(s) with Integral Pressure Monitoring Line (K831591)

The 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line has the same indications statement and intended uses as the:

- Adult Vent Catheter (K834352)
- Infant Vent Catheter (K834039)

The 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line has no new technological characteristics (e.g. materials and manufacturing processes). The technological characteristic of the pressure monitoring line is common to other products in commercial distribution as follows. Additionally, using Polyvinyl Chloride (PVC) is common to other catheter products in distribution, as indicated below in the Infant Vent Catheter.

- Aortic Root Cannula with Integral Pressure Monitoring Line (K831591)
- Infant Vent Catheter (K834039)

This technological characteristic "could affect the safety and effectiveness of the device". However, this technological characteristic does not raise new types of safety or effectiveness questions. In addition, "there are acceptable scientific methods which exist for assessing effects of this technological characteristic".

"Performance data to assess the effects of this technological characteristic" has been performed. These "performance data demonstrate" that the 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line is substantially equivalent to other Medtronic marketed cannula.

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The biocompatibility rationale and *in vitro* bench testing demonstrated that when compared to the predicate devices, the 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line does not significantly affect safety and effectiveness and are substantially equivalent to other commercially distributed devices. The *in vitro* bench testing included analysis of: kink testing, clamp testing, flexibility testing, burst, leak testing, pull testing and pressure monitoring capability.

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

OCT 24 2001

Ms. Melissa Harriger
Associate Product Regulation Manager
Medronic Cardiac Surgery
620 Watson SW
Grand Rapids, MI 49504

Re: K012143
Trade Name: 24 Fr. Left Heart Vent Catheter w/ Pressure Monitoring Line
Regulation Number: 21 CFR 870.4210
Regulation Name: Catheter, Steerable
Regulatory Class: Class II (two)
Product Code: DRA
Dated: September 24, 2001
Received: September 25, 2001

Dear Ms. Harriger:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

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

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Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 21 CFR Part 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4646. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,

James E. Dillard III
Director
Division of Cardiovascular
and Respiratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

Indications for Use

510(k) Number if known: K012143

Device Name: 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line

Indications for Use:

The 24 Fr. Left Heart Vent Catheter with Pressure Monitoring Line is intended for venting the left heart during cardiopulmonary bypass surgery.

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter use

(Per 21 CFR 801.109)

Division of Cardiovascular & Respiratory Devices
510(k) Number K012143

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Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

K981601

JUL 28 1998

Summary of Safety and Effectiveness

DETERMINATION OF SUBSTANTIAL EQUIVALENCE

The California Medical Laboratories, Inc. devices are substantially equivalent to the DLP and Research Medical predicate device. The California Medical Laboratories, Inc. devices have substantially equivalent intended uses as the predicate device. The California Medical Laboratories, Inc. devices have technologic characteristics which are substantially equivalent to the DLP and Research Medical predicate device.

COMPANY AND CONTACT PERSON

California Medical Laboratories Inc.
2681 Kelvin Avenue
Irvine, California 92614

Mehmet Bicakci
President

DEVICE NAME

California Medical Laboratories Inc. Malleable Vent Catheter

NAME OF PREDICATE OR LEGALLY MARKETED DEVICE

The claim of substantial equivalence is based upon the following devices:

- Research Medical, Inc. Left Ventricular Vent Catheter
- DLP, Inc. Left Ventricular Malleable Vent Catheter

DESCRIPTION OF DEVICE

The Malleable Vent Catheter is designed to vent/drain the left ventricular during coronary artery bypass surgery.

It consists of soft polyvinyl chloride (PVC) tubing with a radius tip and vent holes 3.5 cm along the distal tip. The soft PVC tubing consists of two lumens; one large lumen for venting/drainage and one smaller lumen which encapsulates the stainless steel wire. The encapuslated stainless steel wire enables preshaping of the catheter prior to insertion and support during catheter placement. The proximal end of the catheter contains a rigid PVC connector and depth markings along the large lumen.

STATEMENT OF INTENDED USE

The Malleable Vent Catheter is intended for use during cardiopulmonary bypass Surgery to vent/drain the left ventricle.

STATEMENT OF INTENDED USE OF PREDICATE/MARKETED DEVICES

The predicate devices have the same intended use as stated above.

STATEMENT OF COMPARISON OF TECHNOLOGIC CHARACTERISTICS BETWEEN DEVICE AND PREDICATE DEVICE

The California Medical Laboratories, Inc devices have technologic characteristics which are substantially equivalent to the predicate device.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUL 28 1998

Mr. Mehmet Bicakci
President
California Medical Laboratories, Inc.
2681 Kelvin Avenue
Irvine, CA 92614

Re: K981601
Malleable Vent Catheter
Regulatory Class: II (Two)
Product Code: DWF
Dated: May 1, 1998
Received: May 4, 1998

Dear Mr. Bicakci:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4648. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Thomas J. Callahan

Thomas J. Callahan, Ph.D.
Director
Division of Cardiovascular, Respiratory,
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

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510(k) Number (if known): K981601

Device Name: California Medical Laboratories Inc. Malleable Vent Catheter.

Indications For Use: The Malleable Vent Catheter is indicated for use during cardiopulmonary bypass surgery to vent/drain the left ventricle.

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Cardiovascular, Respiratory, and Neurological Devices
510(k) Number K981601

Prescription Use X OR Over-The-Counter Use _____
Per 21 CFR 801.109

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Clinical Anesthesiology

Third edition

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OrthoSource Medical Clinics, Inc
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Clinical Anesthesiology, Third Edition

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ISBN: 0-8385-1453-3

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Text below taken from Chapter 21-

Anesthesia for Cardiovascular Surgery

21

ally via a cannula in the ascending aorta. A normally functioning aortic valve prevents blood from entering the left ventricle.

The filter is always connected with a (normally clamped) bypass limb in case it becomes clogged or develops high resistance. For the same reason, arterial inflow pressure is measured before the filter. The filter is also designed to trap air, which can be bled out through a built-in stopcock.

Accessory Pumps & Devices

A. Cardiotomy Suction:

The cardiotomy suction pump aspirates blood from the surgical field during CPB and returns it to the main pump reservoir. A cell-saver suction device may also be used, but that blood is returned to a separate reservoir. At the end of the procedure, the cell-saver blood is centrifuged, washed, and given back to the patient. Excessive suction pressure contributes to red cell trauma. Moreover, excessive use of cell-saver suction (instead of cardiotomy suction) during bypass depletes CPB circuit volume. The high negative pressure of ordinary wall suction produces excessive red cell trauma and precludes blood salvage from that source.

B. Left Ventricular Vent:

With time, even after institution of total bypass, blood accumulates in the left ventricle as a result of residual pulmonary flow from the bronchial arteries (which arise directly from the aorta or the intercostal arteries) or thebesian vessels (see Chapter 19) or as a result of aortic regurgitation. Aortic regurgitation can occur as a result of either structural valvular abnormalities or surgical manipulation of the heart (transiently). Distention of the left ventricle compromises myocardial preservation (see below) and requires decompression (venting). In most centers, this is accomplished by a catheter inserted into the left ventricle via the right superior pulmonary vein and left atrium. Venting is less commonly accomplished through a catheter in the left ventricular apex or through the aortic valve. The blood aspirated by the vent pump normally passes through a filter and is returned to the venous reservoir.

D. Ultrafilter:

Ultrafiltration can be used during CPB to increase the patient's hematocrit without transfusion. Hemofilters consist of hollow capillary fibers that can function as membranes, allowing separation of the aqueous phase of blood from its cellular and proteinaceous elements. Blood can be directed to pass through the fibers either from the arterial side of the main pump or from the venous reservoir using an accessory pump. Hydrostatic pressure forces water and electrolytes across the fiber membrane. Effluents of up to 40 mL/min may be removed.

SYSTEMIC HYPOTHERMIA

Intentional hypothermia is routinely used following the initiation of CPB. Core body temperature is usually reduced to 28–32 °C. Metabolic oxygen requirements are generally halved with each reduction of 10 °C in body temperature. At the end of the surgical procedure, rewarming via the heat exchanger restores normal body temperature.

Profound hypothermia to temperatures of 15–18 °C allows total circulatory arrest for complex repairs for up to 60 minutes. During that time, both the heart and the CPB machine are stopped.

The adverse effects of hypothermia are platelet dysfunction; potentiation of citrate toxicity, which leads to reductions in serum ionized calcium; reversible coagulopathy; and depression of myocardial contractility.

MYOCARDIAL PRESERVATION

Optimal results in cardiac surgery not only require perfect surgical repair of cardiac pathology but also prevention of myocardium damage and maintenance of normal cellular integrity and function during CPB. Nearly all patients sustain some myocardial damage during cardiac surgery. With proper preservation techniques, however, most of the damage is usually reversible. Although myocardial injury can be related to the anesthetic or surgical technique, it most commonly appears to be related to suboptimal myocardial preservation during CPB. The common denominator in most in-

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Second Edition
CARDIAC SURGERY IN THE ADULT
Lawrence H. Cohn & L. Henry Edmunds, Jr

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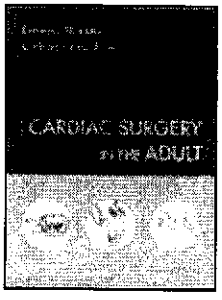

- Part I: Fundamentals
- Part II: Perioperative/Intraoperative Care
- Part III: Ischemic Heart Disease
- Part IVa: Valvular Heart Disease: Aortic Valve Disease
- Part IVb: Valvular Heart Disease: Mitral Valve Disease
- Part IVc: Valvular Heart Disease: Other Valve Lesions
- Part V: Diseases of the Great Vessels
- Part VI: Surgery for Cardiac Arrhythmias
- Part VII: Other Cardiac Operations
- Part VIII: Cardiothoracic Transplantation and Chronic Circulatory Support

---

Part I: Fundamentals:

Larry W. Stephenson
History of Cardiac Surgery
Pages 3-29. [Full Text]

Michael R. Mill, Benson R. Wilcox, and Robert H. Anderson
Surgical Anatomy of the Heart
Pages 31-52. [Full Text]

Jakob Vinten-Johansen, Zhi-Qing Zhao, and Robert A. Guyton
Cardiac Surgical Physiology
Pages 53-84. [Full Text]

James M. Bailey, Kenichi A. Tanaka, and Jerrold H. Levy
Cardiac Surgical Pharmacology
Pages 85-118. [Full Text]

Frederick J. Schoen and Robert F. Padera, Jr.

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Hessel EA II, Edmunds LH Jr. Extracorporeal Circulation: Perfusion Systems.
In: Cohn LH, Edmunds LH Jr, eds. Cardiac Surgery in the Adult. New York: McGraw-Hill, 2003:317338.

Chapter 11A

Extracorporeal Circulation

Perfusion Systems

Eugene A. Hessel, II/
L. Henry Edmunds, Jr.

COMPONENTS
- Venous Cannulation and Drainage
  - PRINCIPLES OF VENOUS DRAINAGE
  - VENOUS CANNULAS AND CANNULATION
  - PERSISTENT LEFT SUPERIOR VENA CAVA
  - AUGMENTED OR ASSISTED VENOUS RETURN
  - COMPLICATIONS ASSOCIATED WITH VENOUS CANNULATION AND DRAINAGE
  - CAUSES OF LOW VENOUS RETURN
- Arterial Cannulation
  - ARTERIAL CANNULAS
  - CONNECTION TO THE PATIENT
  - ATHEROSCLEROSIS OF THE ASCENDING AORTA
  - ASCENDING AORTIC CANNULATION
  - CANNULATION OF THE FEMORAL OR ILIAC ARTERY
  - OTHER SITES FOR ARTERIAL CANNULATION
- Venous Reservoir
- Oxygenators
- Heat Exchangers
- Pumps
- Filters and Bubble Traps
  - MICROEMBOLI
  - LEUKOCYTE-DEPLETING FILTERS
- Tubing and Connectors
- Heparin-Coated Circuits
- Cardiotomy Reservoir and Field Suction
- Venting the Heart
- Cardioplegia Delivery Systems
- Hemoconcentrators (Hemofiltration/Ultrafiltration)
- Perfusion Monitors and Safety Devices

CONDUCT OF CARDIOPULMONARY BYPASS
- The Perfusion Team
- Assembly of Heart-Lung Machine

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or by vacuum applied to the rigid outer shell of the reservoir. The degree of negative pressure and blood level must be monitored to avoid excessive suction or introducing air into the perfusate.

The cardiotomy suction and reservoir are major sources of hemolysis, particulate and gaseous microemboli, fat globules, cellular aggregates, platelet injury and loss, thrombin generation, and fibrinolysis.[82,118,126,181,182] Air aspirated with wound blood contributes to blood activation and destruction and is difficult to remove because of the high proportion of nitrogen, which is poorly soluble in blood. High suction volumes and admixture of air are particularly destructive of platelets and red cells.[181,183] Commercial reservoirs are designed to minimize air entrainment and excessive injury to blood elements. Air and microemboli removal are also facilitated by allowing aspirated blood to settle within the reservoir before it is added to the perfusate.

An alternative method for recovering field-aspirated blood is to dilute the blood with saline and then remove the saline to return only packed red cells to the perfusate. Centrifugal cell washers (e.g., Haemonetics Cell Saver, Meomonetics Corp., Braintree, MA) automate this process, which has the advantage of removing air, thrombin, and nearly all biologic and nonbiologic microemboli from the aspirate at the cost of discarding plasma. A third alternative is to discard all field-aspirated blood.[184] Increasingly, field-aspirated blood is recognized as a major contributor to the thrombotic, bleeding, and inflammatory complications of CPB (see sections 11B and 11C).

Venting the Heart

If the heart is unable to contract, distention of either ventricle is detrimental to subsequent contractility.[185] Right ventricular distention during cardiac arrest or ventricular fibrillation is rarely a problem, but left ventricular distention can be insidious in that blood can enter the flaccid, thick-walled chamber from multiple sources during this period. During CPB blood escaping atrial or venous cannulas and from the coronary sinus and thebesian veins may pass through the unopened right heart into the pulmonary circulation. This blood plus bronchial venous blood, blood regurgitating through the aortic valve, and blood from undiagnosed abnormal sources (patent foramen ovale, patent ductus, etc.) may distend the left ventricle unless a vent catheter is used (Fig. 11-6). During CPB bronchial venous blood and noncoronary collateral flow average approximately 140 ± 182 and 48 ± 74 mL/min, respectively.[186]

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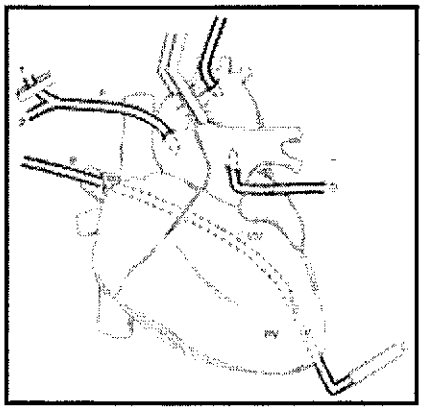

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FIGURE 11-6 Diagram shows locations used to vent (decompress the heart). (A) Aortic root vent, which can also be used to administer cardioplegic solution after the ascending aorta is clamped. (B) A catheter placed in the right superior pulmonary vein/left atrial junction can be passed through the mitral valve into the left ventricle. (C) Direct venting of the left ventricle at the apex. (D) Venting the main pulmonary artery, which decompresses the left atrium because pulmonary veins lack valves.

There are several methods for venting the left heart during cardiac arrest. Few surgeons vent the left ventricular apex directly because of inconvenience and myocardial injury. Most often a multihole, soft-tip catheter (8–10F) is inserted into the junction of the right superior pulmonary vein and left atrium (see Fig. 11-6) or left atrial appendage and may or may not be passed into the left ventricle. Others prefer to place a small suction catheter into the pulmonary artery.[187] The ventricle can also be vented by passing a catheter retrograde across the aortic valve when working on the mitral valve. Vent catheters are drained to the cardiotomy reservoir by a roller pump, vacuum source, or gravity drainage,[188,189] but must be carefully monitored for malfunction. Although inspection and palpation may detect ventricular distention, TEE monitoring or direct measurements of left atrial or pulmonary arterial pressures are more reliable. The heart is no longer vented for most myocardial revascularization operations, but the ventricle must be protected from distention.[190–192] If the heart cannot remain decompressed during distal anastomoses, a vent should be inserted. Often the cardioplegia line inserted into the aortic root is used for venting when not used for cardioplegia.[193]

The most common and serious complication of left heart venting is residual air when the heart is filled and begins to contract. De-airing maneuvers and TEE are important methods for ensuring removal of all residual air. In addition, many surgeons aspirate the ascending aorta via a small metal or plastic cannula to detect and remove any escaping air as the heart begins to eject.[194,195] Bleeding problems or direct injury to the myocardium are other complications associated

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with left ventricular vents.

Cardioplegia Delivery Systems

Cardioplegic solutions contain 8 to 20 mEq/L potassium, magnesium, and often other components and are infused into the aortic root proximal to the aortic cross clamp or retrograde into the coronary sinus to arrest the heart in diastole. The carrier may be crystalloid or preferably blood and is infused at temperatures around 4°C or 37°C, depending upon surgeon's preference. Normothermic cardioplegia must be delivered almost continuously to keep the heart arrested; cold cardioplegia is infused intermittently. Cardioplegic solutions are delivered through a separate perfusion system that includes a reservoir, heat exchanger, roller pump, bubble trap, and perhaps microfilter (see Fig. 11-2). Temperature and infusion pressure are monitored. The system may be completely independent of the main perfusion circuit or branch from the arterial line. The system also may be configured to vent the aortic root when between infusions.

Antegrade cardioplegia is delivered through a small cannula in the aortic root or via handheld cannulas directly into the coronary ostia when the aortic valve is exposed. Retrograde cardioplegia is delivered through a cuffed catheter inserted blindly into the coronary sinus.[196] Proper placement of the retrograde catheter is critical, but not difficult, and is verified by palpation, TEE, color of the aspirated blood, or pressure waveform of a catheter pressure sensor.[197] Complications of retrograde cardioplegia include rupture or perforation of the sinus, hematoma, and rupture of the catheter cuff.[198,199]

Hemoconcentrators (Hemofiltration/Ultrafiltration)

Hemoconcentrators, like oxygenators, contain one of several available semipermeable membranes (typically hollow fibers) that transfer water, electrolytes (e.g., potassium), and molecules up to 20 kD out of the blood compartment.[200] Hemoconcentrators may be connected to either venous or arterial lines or a reservoir in the main perfusion circuit, but require high pressure in the blood compartment to effect fluid removal. Thus a roller pump is needed unless connected to the arterial line. Suction may or may not be applied to the air side of the membrane to facilitate filtration. Up to 180mL/min of fluid can be removed at flows of 500 mL min.[201] Hemoconcentrators conserve platelets and most plasma proteins as compared to centrifugal cell washers and may allow greater control of potassium concentrations than diuretics.[202] Aside from cost,

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BRIEF REPORT

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Ventricular unloading with a miniature axial flow pump in combination with extracorporeal membrane oxygenation

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Abstract *Objective:* ECMO for acute cardiorespiratory failure is an established therapeutic option. Persistent insufficient unloading of the left ventricle (LV) can compromise recovery of ventricular function. We decided to insert a miniature rotary blood pump (Impella) for decompression of the LV. In contrast to previous experience with this new device, where it was generally used for postcardiotomy heart failure or cardiogenic shock and inserted in the operating room or the catheter laboratory, this is the first report describing the potential of this technology in the intensive care unit, in a patient on ECMO and the value of echocardiography guidance. *Patient:* A 13-year-old boy with a history of congenital heart disease was admitted to the ICU with acute cardio-respiratory failure. *Interventions:* On day 2 venoarterial ECMO was instituted because of worsening cardiorespiratory insufficiency refractory to conventional treatment. On day 5 a percutaneous rotary blood pump was inserted to decompress the LV. *Conclusions:* A percutaneous miniature rotary blood pump can be an alternative to decompress a failing LV in the setting of VA-ECMO. Echocardiography can avoid the use of fluoroscopy and the transport to a catheter laboratory to insert the rotary pump.

Keywords Extracorporeal membrane oxygenation · Ventricular assist device · Rotary blood pump · Echocardiography

Abbreviations *AV:* aortic valve · *ECMO:* extracorporeal membrane oxygenation · *LA:* left atrium · *LV:* left ventricle · *LVOT:* left ventricular outflow tract · *MODS:* multiple organ dysfunction syndrome · *RV:* right ventricle · *TEE:* transesophageal echocardiography · *TTE:* transthoracic echocardiography · *VAD:* ventricular assist device · *VA-ECMO:* veno-arterial ECMO

Introduction

The rotary VAD Impella (Impella CardioSystems AG, Aachen, Germany) is a potent miniaturized pump for unloading the left ventricle (LV). The pump incorporates a rotor driven by an electrical motor and has an inflow cannula. The pump is placed across the aortic valve (AV) into the LV, aspirates blood from the LV-cavity and expels it in the ascending aorta. The first developed pump (Impella Recover) has a diameter of 6.4 mm and provides a continuous blood flow of 4.2–4.6 l/min. The driving console allows the management of the pump speed (9 gradations) and displays the pressure difference between inflow and outflow. The Recover-pump has been used successfully in settings of postcardiotomy heart failure [1, 2] and for patients in cardiogenic shock [3] with or without combination of ECMO. Meanwhile, for introduction via a femoral percutaneous approach a 4 mm Impella LP 2.5 has been developed, allowing 2.4 l/min continuous blood flow (Fig. 1). To our knowledge, this

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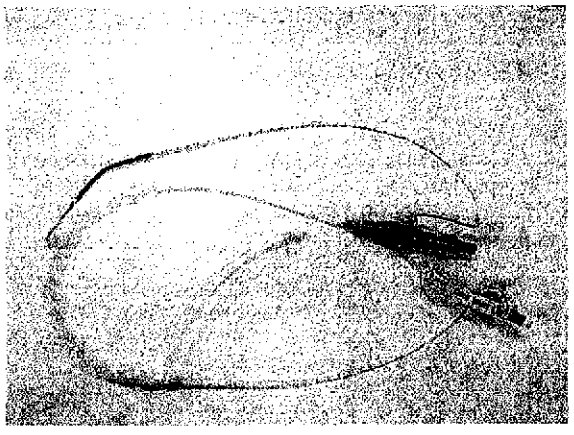

Fig. 1 The Impella LP 2.5 pump

is the first report describing the insertion under transesophageal echocardiography (TEE) guidance of this percutaneous pump at the bedside for unloading the LV in a patient on VA-ECMO.

Case Report

A 13-year-old boy (42 kg, 152 cm) was referred to our institution from a local hospital because of acute respiratory failure. His medical history comprises CATCH 22 syndrome (Di George phenotype, with lymphopenia, T-cell dysfunction, hypocalcemia, limited mental retardation), a truncus arteriosus repair as a neonate followed by aortic root replacement combined with replacement of the right ventricular outflow tract homograft at the age of 5 years, highly reactive airways and recurrent pulmonary infections. Frequent cardiac follow-up at the cardiology clinic showed persistent good myocardial and valvular function.

On admission the child was sedated, intubated and mechanically ventilated. He was poorly perfused and hypoxic on 70% O_2. Chest radiography revealed cardiomegaly and an infiltrate in the right middle and lower lobe. Echocardiography showed a postoperative status after truncus arteriosus repair with minimal aortic regurgitation and a dilated and hypocontractile LV. Arterial blood gas examination upon admission revealed a combined respiratory and metabolic acidosis and hypoxia (pH 7.137, pCO_2 50.1 mmHg, pO_2 86.5 mmHg, SaO_2 91.4%, base deficit of −11.2 mmol/L, lactate 6.1 mmol/L). Blood count revealed a hemoglobin of 12.6 g/dL, platelet count of 113/mm^3, and a leukocyte count of 16.8/mm^3. Further biochemistry results showed an elevated C − reactive protein, renal insufficiency (creatinine 1.7 mg/dL), and elevated liver enzymes and cardiac troponin I. Table 1 gives an overview of laboratory results.

The diagnosis of an acute infection, causing pneumonia and possible myocarditis in an immunodeficient patient was put forward. An extensive microbiological screening, however, remained negative. Therapy consisted of inotropic and vaso-active agents (dobutamine, epinephrine, norepinephrine, and milrinone) under guidance of invasive hemodynamic monitoring with an arterial, central venous and Swan–Ganz catheter; antibiotics, intravenous corticosteroids and immunoglobulines, a lung protective ventilatory management and tight glycemic control (ranges 80–110 mg/dl) with intensive insulin treatment. Despite aggressive support his cardio-respiratory status deteriorated with progressive secondary multiple organ system dysfunction. Repeated echocardiography failed to show any improvement in the cardiac function despite extensive pharmacological support, and it was decided to incorporate mechanical cardiac support.

A femoral VA ECMO was instituted on day 2. VA ECMO was chosen because of the combination of acute respiratory and circulatory failure with the expectancy of recovery. A 21-F venous cannula was placed in the right femoral vein and advanced with the tip in the right atrium. A 19-F arterial cannula was inserted in the right femoral artery through a Dacron graft. Heparin infusion was started after a bolus to maintain activated partial thromboplastin time of 50–80 s. ECMO was initiated at a rate of 120–150 ml/kg per minute. Continuous venovenous hemofiltration was incorporated into the ECMO-circuit to compensate for the renal insufficiency. His overall status gradually improved and over the following hours the inotropic support, and ventilator settings could be firmly diminished.

On day 5 his condition worsened again. He had increased production of foamy and slightly bloody pulmonary secretions, and chest radiography showed worsened cardiomegaly and bilateral infiltrates suggestive of pulmonary edema. TEE revealed a serious dilated and hypocontractile LV with severe mitral valve insufficiency. To unload the LV the decision was made to insert an Impella LP 2.5 system. Surgical insertion at the bedside of a classical LV venting catheter in the left atrium was considered to be very complicated in view of the previous cardiac surgical procedures and anticoagulation. The medical condition of the boy did not allow safe transportation to the catheter laboratory, the Impella device was therefor placed bedside using a percutaneous femoral artery approach, under TEE guidance (procedure is described below). After this intervention the overall hemodynamics, oxygenation, and chest radiography improved, and cardiac troponin levels subsequent declined. Variables monitoring hemolysis are shown in Table 1.

On day 10 the patient developed an acute inflammatory syndrome with new bilateral infiltrates on chest radiography. Combination antibiotic treatment for a multiresis-

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Table 1 Laboratory results (*CRP* C-reactive protein, *bili* total bilirubin, *free Hb* free hemoglobin, *cTnI* cardiac troponin I)

	Day 1	Day 2[a]	Day3	Day 4	Day 5[b]	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Normal values
CRP	19.9	28.9	44.3	35.4	27.1	21.8	102.8	165.4	186	225.7	228	< 5-mg/dl
AST	231	7,769	6,094	3,556	1,039	439	243	–	153	215	320	< 38 U/l
ALT	140	3,728	3,883	3,160	2,265	1,690	864	–	423	286	231	< 41 U/l
LDH	1,189	16,920	11,098	7,161	2,721	2,063	2,218	–	2,940	4,636	6,123	240–480 U/l
Bili	1.37	1.32	1.78	2.68	2.61	2.92	4.47	7.77	14.61	25.8	36.21	< 1-mg/dl
Free Hb	< 5	5	8	17	21	< 5	5	7	27	193	136	< 10-mg/dl
Platelet	113	117	156	51	53	62	49	37	45	30	23	150–450
Hb	12.6	10.3	10.5	9.8	8.6	8.8	8.8	9.3	8.2	7.3	9.3	13–16 g/dl
cTnI	6.19	8.90	14.36	48.74	17.98	15.45	12.60	–	–	11.19	–	< 0.13-µg/l

[a] Start ECMO
[b] Start Impella

tant *Pseudomonas aeruginosa* obtained from culture of an endotracheal aspirate was started. Despite VA ECMO and pharmacological support severe metabolic acidosis and hypotension further developed. Respiratory function was further compromised by recurrent serious pulmonary hemorrhages. Despite maximal pharmacological and mechanical support, the child died on day 11 of refractory septic shock.

Autopsy showed an acute bilateral pneumonia with bilateral hemorrhagic syndrome and associated capillaritis. On myocardial microscopic examination the diagnosis of myocarditis could not be confirmed, although presumed at macroscopic inspection. The AV homograft showed calcifications but no endocarditis or traumatic injury caused by the rotary pump. Further cardiac examination confirmed normal findings posttruncus repair.

Impella LP 2.5 device: characteristics and placement

The Impella LP 2.5 support system is a miniaturized rotary blood pump, with a cannula 4.0 mm in diameter. The inflow cannula is prolonged with a pigtail for easier introduction and positioning in the LV (Fig. 1). The pump is placed across the AV, aspirates blood from the LV cavity and expels it into the ascending aorta. The performance depends on the rotary speed of the pump and the physiological afterload. The position of the device is important for optimal function: the pressure signal indicates correct positioning of the pump and is confirmed with echocardiography [4]. Placement is by percutaneous femoral arterial approach using a 13-F sheath. Secondly, through a pigtail-wire, advanced retrograde across the AV into the LV, a 0.014-in. wire is placed in the LV and the pigtail-wire withdrawn. After a test run outside the patient, the pump is advanced over the wire into the LV chamber under fluoroscopic guidance. After withdrawal of the wire, pump rotation is started and gradually increased.

Since this child's condition did not allow safe transportation to the catheter laboratory, the Impella LP 2.5 device was placed bedside under TEE guidance. During and after implantation of the device useful information was provided for correct positioning of the guide wire and the device and for evaluation of ventricular function, as previously reported [2, 4]. After percutaneous placement of a 14-F "peal-away" sheath in the femoral artery, a Judkins right (JR-4) diagnostic coronary catheter was advanced, over a 0.034-in. guide wire until the AV was reached (Fig. 2). By guide wire manipulation the AV was crossed and the diagnostic JR-4 catheter advanced in the LV. A 0.014-in. Trooper support wire (Boston Scientific, Boston, Mass., USA) was advanced through this catheter into the LV. The pump was advanced over this wire, crossed the AV and correct intracardiac position was demonstrated on TEE (Fig. 3). The wire was removed and the pump started. Several follow-up echocardiography examinations showed correct position of the device and good unloading of the LV (Fig. 4).

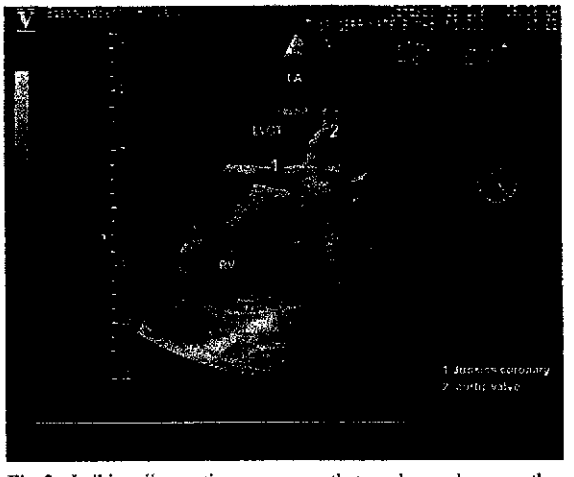

Fig. 2 Judkins diagnostic coronary catheter advanced across the aortic valve into LV

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Fig. 3 Impella LP 2.5 intracardiac position mid esophageal long axis view of aortic valve

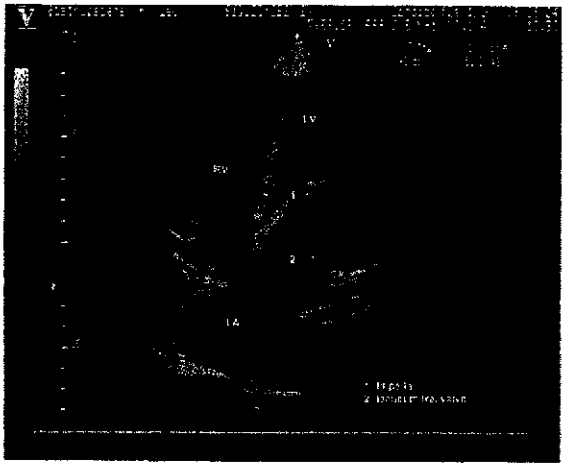

Fig. 4 Transthoracic follow-up echo: position Impella and unloaded LV

Discussion

VA ECMO in the face of severe LV dysfunction often mandates LV decompression (often referred to as venting) because prolonged increased LV wall stress reduces the chances of recovery of ventricular function. This venting can be achieved in several ways: surgically with a catheter placed in the left atrium or percutaneously with a catheter that crosses the atrial septum. This invasive percutaneous technique can be performed in the catheter laboratory or under echocardiography guidance [5]. This transseptal approach requires puncture of the atrial septum and is not without risk. Because of our experience over several years with axial flow pumps in different clinical settings of acute cardiac failure, with or without association of VA ECMO [1, 3], and the possibility in this case of an unsuccessful septostomy after previous closure during truncus arteriosus repair of a patent foramen ovale , we decided to decompress the LV with the Impella LP 2.5. As shown, this miniaturized rotary blood pump can be safely inserted percutaneously at the bedside under TEE guidance, avoiding the risk of transportation of unstable patients. Furthermore, using a percutaneous approach, a (redo) thoracotomy to surgically insert a catheter to unload the LV can be avoided. This case report shows that the Impella LP 2.5 can be a valuable alternative for unloading the LV in patients on VA ECMO.

Close monitoring for hemolysis is advocated during the follow-up of patients treated with the Impella device, as is the case with other VAD. Free hemoglobin, lactate dehydrogenase and total bilirubin were routinely measured for monitoring hemolysis (Table 1). ECMO and VAD can cause hemolysis since red blood cells can be traumatized when passing through the artificial device. The progressive rise in hemolytic parameters in this patient can be explained in multiple ways: prolonged use of the ECMO circuit, association of the axial flow pump, transfusion-related hemolysis, and micro-angiopathic hemolysis as suggested by the autopsy finding of capillaritis, and sepsis and multiple organ system dysfunction.

Conclusion

We report here a valuable alternative for more classical decompression techniques of the LV during VA ECMO, although our patient finally died of sepsis. This technique is less invasive than surgery and can be performed at the bedside under echocardiography guidance. Clinical studies with this new device are ongoing to verify the safety and efficacy in various clinical settings of acute cardiac failure.

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Case Report / Critical Care Medicine

Percutaneous bridge to heart transplantation by venoarterial ECMO and transaortic left ventricular venting

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ABSTRACT: We report a case in which life support for cardiogenic shock was achieved by a nonpulsatile venoarterial bypass, and left ventricular decompression was obtained by a catheter placed percutaneously through the aortic valve into the left ventricle. The blood drained from the left ventricle was pumped into the femoral artery. The normalization of left heart filling pressures allowed the resolution of pulmonary edema, and the patient underwent a successful heart transplantation following 7 days of mechanical cardiocirculatory support. (Int J Artif Organs 2004; 27: 410-3)

KEY WORDS: Extra corporeal membrane oxygenator (ECMO), Cardiogenic shock, Ventricular venting

INTRODUCTION

The management of low cardiac output syndrome or cardiogenic shock is still a major problem in clinical practice. The mortality associated with cardiogenic shock ranges from 20 to 50% (1, 2). Many causes of acute heart failure are however potentially reversible or amenable to transplantation, while the injured heart function is temporarily supported. Although venoarterial bypass can be easily and quickly accomplished with peripheral cannulation, it does not adequately decompress the left ventricle resulting in a wall stress increase in the postischemic failing heart (3, 4).

We report here a case in which life support was achieved by a nonpulsatile venoarterial bypass, and left ventricular decompression was obtained by a catheter placed percutaneously through the aortic valve into the left ventricle. The blood drained from the left ventricle was pumped into the femoral artery. The normalization of left heart filling pressures resolved the pulmonary edema, and the patient underwent a successful heart transplantation following seven days of mechanical cardiocirculatory support.

CASE REPORT

One morning, a 34-year-old man was referred to the emergency room of our hospital because of severe dyspnea. During the preceding night the patient complained of severe thoracic pain. After clinical evaluation a diagnosis of acute pulmonary edema was made. An EKG was compatible with an anterior septal and right acute myocardial infarction.

Blood gases revealed hypoxemia (PaO_2 37 mmHg) and hypocapnia ($PaCO_2$ 32 mmHg). Arterial blood pressure was 100/70 mmHg and heart rate was 110 bpm. He was also oliguric and with a normal WBC count.

The patient was admitted to the coronary care unit. Then the patient was intubated and ventilated with a continuous positive pressure ventilation (CPPV). FiO_2 was 0.9, PEEP 5 cmH_2O, tidal volume 0.7 l, with a respiratory rate of 15 breaths/minute. A pulmonary artery catheter thermodilution was also positioned. Dopamine was administered at 5 µg/kg/min. At the moment of the first hemodynamic measurements heart rate was 122 bpm, arterial pressure 80/60, pulmonary artery pressure 29/20

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mmHg, wedge pressure (WP) 17 mmHg, central venous pressure (CVP) 10 mmHg. Cardiac output was 3.58 l/min with a cardiac index of ~ 2 l/min/m². It was decided to increase the dopamine infusion to 10 µg/kg/min. Due to persisting hypotension and low cardiac output dobutamine 10µg/kg/min was added. A fluid challenge was performed, without significant hemodynamic improvement.

At this point dobutamine was being infused at a rate 15 µg/kg/min, dopamine 15 µg/kg/min and epinephrine 4 µg/min. Oliguria and hypotension persisted (BP 74/52 mmHg). Dobutamine was increased up to 20 µg/kg/min, without any significant improvement in hemodynamics.

The following morning a myocardial biopsy was done, and the suspicion of myocarditis was rejected. A history of familiar hypercholesterolemia came out.

The patient was transferred to the general ICU. At admission heart rate was 160 bpm, blood pressure 72/56 mmHg, cardiac output 2.55 l/min cardiac index 1.5 L/min/m². The need for mechanical circulatory support emerged because of metabolic lactic acidosis.

The patient received an initial 5000 UI heparin bolus. A 25 F heparin coated (Biomedicus Medtronic) venous drainage catheter was placed percutaneously in the inferior vena cava (IVC) through the femoral left vein. The left femoral artery was cannulated by a 19 F percutaneous arterial cannula. Blood was drained from IVC to a heparin coated centrifugal pump (Biomedicus Carmeda Medtronic), pumped through a 4.5 m² Scimed Kolobow membrane lung, warmed by an integral heat exchanger, and returned in nonpulsatile mode to the aorta through the femoral artery cannula. The extracorporeal blood lines were made of 3/8' ID PVC tubings and connectors also heparinized by the carmed process. The right to left bypass flow was set at 2.5 l/min/m². Nitrates dobutamine and dopamine were infused. Peripheral perfusion substantially improved, and diuresis stimulated with furosemide.

To oxygenate any blood delivered to the pulmonary vascular bed by residual myocardial activity and to avoid atelectasis, low frequency mechanical ventilation with a high positive end-expiratory pressure (10-15 cm H_2O) and the lowest fraction of inspired oxygen possible was used. Oxygen saturation was monitored by arterial blood gas determination or pulse oxymetry on the right arm. When upper body hypoxemia secondary to poorly oxygenated blood ejected by the heart was detected, the fraction of inspired oxygen was adjusted accordingly.

Heart rate was 139 bpm, blood pressure was 93/70 mmHg, cardiac output was 3.65 l/min, CVP 11 mmHg, PAP 39/22, WP 24 mmHg.

During the following 24 hrs however, in spite of good peripheral perfusion, WP continued to increase, reaching the value of 40 mmHg, with a mixed venous saturation of 65.

Lung function and chest X-ray continued to worsen, in spite of increased extracorporeal blood flow and pharmacological support.

We decided that left ventricular venting was necessary.

A J tip guide was positioned in the left ventricle through punction of the left axillary artery. A 17 F pediatric venous drainage catheter was then advanced from the axillary artery to the left ventricle under X-ray guidance over the guidewire. The cannula was connected to extracorporeal circuit by a second, independent centrifugal pump. A left bypass completed the right to left one.

The patient blood temperature was reduced to decrease both the oxygen consumption and hemodynamic needs. The right to left flow was set at 2.0 - 2.5 l/min/m², while the left to left was set at 0.300 l/min.

To detect insufficient left ventricular unloading during mechanical circulatory support with the pulmonary capillary wedge pressure, we regularly monitored left ventricular filling pressures with the help of pulmonary capillary occlusion pressure or left ventricular end-diastolic volume with echocardiography.

The procedure went uneventfully, with dramatic radiological clearing of the lungs. In the 7th day a donor heart became available in the cardiac surgery department of Bergamo, approximately 30 miles from our institution. At that time wedge pressure was 7 mmHg, PAP 14 mmHg, SAP 95/85, HR 107 bpm, CVP 3 mmHg)

The patient was transferred there by ambulance, while still under mechanical circulatory support.

The patient was then successfully transplanted.

DISCUSSION

The state of the art sequence treatment of cardiogenic shock was substantially different with respect to now in the early 90s, when the patient was treated, and the treatment provided describes what at that time was available in an institution without expertise in angioplasty; the aim of the report is to focus attention on mechanical support.

The use of mechanical means to assist circulation in a selected number of patients is now generally accepted

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(5-9). The goal of mechanical assistance is twofold: in many cases recovery of heart function may be aimed at, while in other instances a transplant is viewed as the only solution.

Different approaches may be used in these two different situations: if recovery of function is the goal, then the anatomy and physiology of the heart has to be preserved as much as possible, while if transplant is envisaged, then it is even possible to resort to techniques contemplating the removal of the diseased heart for the temporary implantation of a mechanical device. We reported here a method that may be applied in principle to both situations, being minimally invasive and preserving the anatomy of the natural circulation.

The earliest and simplest method of cardiac support is based on various modifications of the extracorporeal cardiopulmonary bypass. This system is used routinely in the operating room, and has proved very safe for up to several hours. There have been attempts to use long term CPB perioperatively (10-13). Such approaches are associated with substantial morbidity related in part to the need for thoracotomy, the difficulty to decompress the left heart, or the evolution of combined right and left failure.

It has been shown that right to left bypass actually overloads the left ventricle in failing hearts (3, 14-16).

This is exactly what initially happened in our patient following the institution of a life saving right to left bypass, which, though ameliorating effectively peripheral perfusion, caused a substantial increase in left filling pressures and worsening of pulmonary edema. We were faced by the additional problem of being a general ICU, in a hospital where cardiac surgery was not available. We needed therefore a support system that could be performed expeditiously while waiting for either functional improvement or transfer to a cardiac surgery center with an active transplant program for this kind of patient.

Expanded left ventricular assistance application indeed requires a method that does not require thoracotomy or the experience of a skilled cardiac surgeon.

The dramatic physiological benefit of left ventricular assistance compels an effort to broaden its clinical use.

Zwart and associates first reported in 1970 a transarterial closed-chest left ventricular (TaCLV) bypass (17). In 1990 the Nimbus Hemopump was introduced (18). This pump aspirates blood from an intraventricular location and expels it into the aorta. However many mechanical and technical problems limit its application, not least the need to introduce a 7mm diameter pump through a peripheral artery up to the left ventricle.

Rossi et al (19) demonstrated that long term cardiopulmonary bypass could maintain effective circulation and eventual recovery, by decompressing the left heart through a percutaneous helical spring positioned within the lumen of the tricuspid and pulmonary artery valves. In so doing they were able to decompress the left heart through retrograde flow from the left atrium and incompetence of the right heart valves. The concept of this experimental work guided the clinical application in this clinical case, though left heart decompression was achieved by direct venting of the left ventricle.

Downing et al (20) proposed left ventricular assistance without thoracotomy by transeptal positioning of a left venting cannula. However, we have no experience with this technique, and to our knowledge, it has not been used in humans. Moreover it requires the production of an interatrial defect, which may not close easily following the long term placement of a rather big catheter (17 to 21 F) through it.

The successful performance of cardiocirculatory support by venous arterial bypass rests on two principles: an adeguate venous drainage, an adeguately low central venous pressure, and an effective means to maintain an adequately low left arterial pressure.

Promising therapeutic options to prevent left ventricular distension such as retrograde left ventricular unloading through a modified Swan-Ganz catheter or antegrade unloading through a transaortic venting catheter have only been evaluated in experimental animal models (15, 16).

CONCLUSIONS

In accordance with our previous results, these observations suggest that the idea of closed-chest cardiopulmonary bypass for emergency mechanical circulatory support can be of use in a few selected patients with prolonged cardiogenic shock or cardiopulmonary arrest. Long-term survival rates are encouraging in patients with an underlying cardiocirculatory pathology amenable to immediate corrective intervention (angioplasty, surgery, transplantation), whereas prolonged extracorporeal support with PCBP because of the lack of an immediate therapeutic intervention is associated with mortality rates that, in general, do not justify the use of this technique.

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FIRST CLINICAL APPLICATION OF TRANSARTERIAL CLOSED-CHEST LEFT VENTRICULAR (TaCLV) BYPASS

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A technique for substitution of left ventricular function without thoracotomy has been developed[1]. Blood is removed from the left ventricle with a flexible cannula which is inserted via the right carotid (animals) or axillary (man) artery (Figure 1). The blood is returned into the arterial vascular bed through a femoral artery. The method is called Transarterial Closed-Chest Left Ventricular (TaCLV) Bypass.

EQUIPMENT+ AND OPERATION

The equipment used initially has been described in detail previously[1]. The cannula (1 in Figure 2) to remove blood from the left ventricle is specially fabricated from polyurethane (Estane, 5701 F 1, Goodrich) and reinforced with glass-fiber (Owens-Corning). It is flexible, the wall-thickness is only 0.2-0.4 mm., it is stiff enough to be inserted without a stylet, and once in the body it softens and adapts to the geometry of the arterial system.

The blood circuit (Figure 2) consists of a 6' long 1/2" I.D. 3/4" O.D. silastic tube with 2 1/2-3/8" connectors (Bentley Sales, Inc., Norwalk, Conn.) at each end. The tube is mounted in a roller pump (Travenol 5 M 6002). At the inflow part (2 in Figure 2), the tube is connected to the left ventricular cannula with a 1/2" O.D. 3/8" I.D., 3 cm. long silastic tube. This short piece of thin-walled tubing (3 in Figure 2) is attached to the cannula during insertion and indicates when the cannula tip enters the left ventricle; the barely visible pulsations of the tubing become vigorous. Once it is a part of the circuit the same tube indicates the amount of suction applied to the cannula base by the roller pump. The pump should be slowed down as soon as the tubing starts to collapse. At the outflow part (4 in Figure 2), the tube is connected to a blood return cannula (5 in Figure 2). In between pump and blood return cannulae, the silastic tube of the circuit is interrupted by a silastic thin-walled reservoir (6 in Figure 2). The reservoir serves to trap air and to depulsate the roller pump so that a non-pulsatile flow is produced through the blood return cannula. Three silastic side lines are attached to the reservoir, one for removal of air, the other for perfusion of the right arm or leg, in case collateral circulation beyond the cannulation sides is insufficient.

Recently equipment has been fabricated with which blood return can be pulsed. The pulsations can be counterphased to those of the natural heart. Pulsatile blood return is produced with a rigid cylinder, covered on the inside with a natural latex sleeve (7 in Figure 2 and Figure 1a). The cylinder is to be shoved over the reservoir. If compressed air is forced in between cylinder and latex sleeve, it causes the latter to collapse and the reservoir to be squeezed. The resulting pulsations can be programmed in between natural heart beats by applying the pressure to the cylinder synchronously with the EKG using an R-wave detector with proper delay and duration settings (Figure 3).

The blood circuit has a priming volume of 300 ml. The blood is in contact with silastic (tubing, reservoir), polyurethane (cannula), and polycarbonate (connectors). These materials can be treated[2] so that systemic heparinization is not necessary. Preliminary experiments on sheep, where TaCLV-Bypass, using a heparin treated circuit, was applied without administration of heparin to the animal, were promising; the sheep survived, but there were some small clots around the connectors. In addition, the inner surface of the circuit is coated with albumin because there is evidence[3] that this will decrease platelet adhesion to the surface and probably decrease hemolysis as well. It is sufficient to add some 25 mg. of albumin to the priming volume.

COMPILED DATA FROM ANIMAL EXPERIMENTS (18 DOGS, 42 SHEEP)

1. With TaCLV-Bypass the left ventricle can be effectively emptied without thoracotomy, the circulation being maintained by a pump outside the body (Figure 3).
2. The maximum flow (blood, hematocrit 23%, temp. 22°C.) through the system is 6.2 L./min. In vitro, the highest flow obtained in a sheep was 5.3 L./min.
3. The circulation can be maintained during ventricular fibrillation for periods up to 14 hr.[4,5]. Under these circumstances the pressure in the left ventricle is kept around atmospheric.

*By invitation.

+Equipment can be obtained through our Laboratory.

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4. With a little practice, cannulation of the left ventricle with the wide bore cannula can be mastered without the aid of electronic or X-ray equipment. If a pressure catheter is present in the left ventricle, the outflow cannula can be easily inserted using the catheter as a guide.
5. The aortic valve is competent during and after the bypass.
6. Coronary flow is not impaired by left ventricular cannulation[1,6].
7. Deep shock, produced in 5 closed-chest dogs by embolizing the left coronary artery with plastic microspheres, could be restored, and in 4 cases the heart recovered - 2 long-term survivals were obtained[7].
8. Six sheep survived 4 hr. and 2 sheep, 24 hr. of bypass uneventfully. The maximum plasma hemoglobin value obtained was 23 mg.%[8].
9. Four sheep survived a one hour period of ventricular fibrillation; one of these animals gave birth to 2 healthy lambs 2 months later. In the latter sheep, a specially treated blood circuit was used. Heparin was not supplied to the animal.
10. Damage inflicted by the cannula consists of subendocardial hemorrhages, but they are small and usually absent.

CLINICAL EXPERIENCE (TWO CASES BY MARCH, 1970)

Patient 1. We were called to apply TaCLV-Bypass on a 62-year old man with a myocardial infarction. During the preceding 10 hr. his blood pressure was around 80/50 mm.Hg. There was mild venous congestion, slight cyanosis, and the patient complained of angina and shortness of breath. The EKG revealed sinus tachycardia with occasional premature ventricular contractions and slight nonspecific ST-T changes. Physical examination suggested enlargement of the heart and slight pulmonary edema. Urine production had been 150 ml. during the last 6 hr., during which time he had been given diuretics. The EKG later showed a complete atrioventricular block and 2 hr. before mechanical assistance was applied, ventricular fibrillation occurred. After successful defibrillation the systolic pressure was not obtainable or at times was between 50 and 80 mm.Hg. The patient was unconscious, the skin was cold and clammy, there was pulmonary edema on physical examination, and cyanosis notwithstanding assisted intratracheal respiration. Medical treatment did not improve the condition.

We accepted the patient for TaCLV-Bypass, it took 30 min. to perform the necessary cannulations; a cannula inserted into the left ventricle via the right axillary artery and one inserted into the right femoral artery. The patient was heparinized with 2 mg. /Kg. body weight and additional doses were given as necessary to keep the clotting time around 25 min. Medical treatment was continued as necessary. The mean bypass flow (Figure 4) gradually decreased from 3.9 L. /min. during the first hour to values around 3.3 L. /min. after 4-9 hr. of bypass (range 2.2 - 5.8). The flow could be increased by supplying intravenous fluids. The blood pressure (Figure 4), measured with an intra-arterial catheter, increased during the first 4 hr. of bypass to values around 80/60 mm.Hg, then it decreased, whereafter it increased again, and after 8 hr. it was around 90/65 mm. Hg. Occasionally, especially during the first 4 hr. of bypass, there were no pulsations visible on the arterial pressure tracing (Figure 5) indicating that the bypass was complete. The right atrial pressure, measured with a catheter which was inserted after 6 hr., was around 10 cm. H_2O initially but tended to decrease despite the administration of fluids.

The urine production (Figure 6) was 190 m. during the first hr. of bypass, thereafter it decreased gradually to around 50 ml. /hr. Large amounts of fluids were supplied, especially after 4 hr. of bypass. The bypass flow and arterial pressure increased after fluid administration but only for a short time. The hematocrit, 63% initially, decreased to 43% after 4 hr. of bypass and to a minimum of 21% after 10 hr. A total amount of 8000 ml. of blood was given to the patient. The pH (Figure 7) was usually within normal range; 528 mEq. of $NaHCO_3$ were supplied. The pCO_2 was most often between 45-50 mm. Hg. The arterial oxygen saturation was too low initially (74-85%) but after 6 hr. of bypass it increased to normal values (over 90%). The plasma was clear throughout the procedure and the electrolytes were within the normal range towards the end of the pumping period. The temperature, measured in the rectum, increased to 101° F.

The patient regained consciousness after 2 hr. of bypass. The rales disappeared gradually from the lungs and the skin became warm and pink. Respiration was assisted with pure oxygen or a mixture of oxygen and air throughout the procedure. Blood loss and pooling were suspected because of the large amounts of fluids that had to be supplied in order to keep up bypass flow and arterial and right atrial pressure. It is estimated that 1000 ml. of blood were lost from the wounds during the entire period of bypass. During the 7th hr. of bypass, a small amount of blood was lost with the urine; however, no other bleeding site could be detected and there was normal peristalsis over the abdomen. The EKG was not much different from that obtained at admission. The circulation in the right arm was like that in the rest of the body. In the right leg circulation became inadequate after 6 hr. but it could be restored by additional perfusion with a side line from the arterial reservoir.

After 9 hr. of bypass the pump was switched off for one hour in an attempt to wean the patient from the assist. The blood pressure fell during the second half of this hour, while right atrial pressure, the EKG, arterial oxygen saturation, and urine production did not change significantly. The bypass was applied for 2 more hours, during which period urine production increased. During the last hour of bypass the blood pressure fell again.

It was decided to discontinue the bypass because blood loss was suspected. The cannulas were removed and the heparin was neutralized with protamine sulfate. The patient remained in the same condition during the next 3 hr., producing some 100 ml. of urine each hour. Thereafter urine production decreased and finally ceased after 3 more hours. Eight hours after the bypass had been discontinued, large amounts of blood were lost per rectum, ventricular fibrillation occurred, defibrillation was unsuccessful, and the patient died.

At autopsy there was generalized arteriosclerosis, the right coronary and the anterior descending branch of the left coronary artery were found to be occluded, and there was massive infarction of the anterior wall and the interventricular septum. No damage was observed that could have been caused by the cannula. The occlusion in the right coronary artery was fresh and could have been removed surgically. Sclerotic plaques were present in the aorta but there was no damage to the aortic wall. Large amounts of blood had accumulated in the gastrointestinal tract. The mucosa of the stomach and the bowel showed congestion but no bleeding site could be detected.

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Patient 2. A 52 year old man was admitted in deep shock. There was no history of heart disease; poisoning was suspected. The ECG showed no remarkable abnormalities. The arterial pressure could not be measured but after insertion of a catheter, a reading of 20 mm. Hg was found. The right atrial pressure, measured with a catheter was 45 mm. Hg. Medical treatment did not improve the condition. The patient was given 150 mg. of heparin, and additional doses of 50 mg. were supplied every hour. Medical treatment was continued as necessary. TaCLV-Bypass was instituted within 20 min. and applied for the next 5 1/2 hr. The left ventricular cannula was inserted via the right subclavian artery. Within 3 min., the right atrial pressure had decreased to 5-8 mm. Hg. and the arterial pressure increased to 90-100/80-90 mm. Hg.

Before bypass the skin was cyanotic and had a mottled appearance. Within 10 min. after start of the bypass, the skin turned pink. The circulation in the right arm and leg did not appear different from that in the rest of the body. The hematocrit was 42% before and at the end of the bypass period. After 5 hr. of bypass the pH was 7.20 and the pCO_2 was 40 mm. Hg, the electrolytes were within normal range except for a high K of 5.2 mEq./L., the platelet count was 165,000/mm.^{2}, the clotting time was over 50 min., and the PTT and fibrinogen were normal. No urine was produced.

After 5 1/2 hr. of bypass, massive uncontrollable bleeding occurred from the gastrointestinal tract, treatment was discontinued, and the patient died. At autopsy no abnormalities were observed in the heart, and there was no damage that could be related to the bypass. Throughout the upper part of the gastrointestinal tract multiple ulcers were found from which bleeding had apparently occurred. No poison has as yet been identified.

DISCUSSION

During advanced stages of cardiogenic shock, the cardiac output is decreased and tissue perfusion is inadequate. The left side of the heart is dilated with elevation of end diastolic left ventricular and left atrial pressure, the pulmonary veins are congested, and the arterial blood pressure is low[9]. If medical treatment fails, the mortality is 100%[10]. In these cases application of mechanical assist devices is justified. Decompression of the left ventricle and infusion of oxygenated blood into the arterial vascular bed is likely to improve the condition. During counterpulsation it is hoped that such is effected by the heart itself; if left ventricular function improves, cardiac output increases, and left ventricular end diastolic pressure decreases[11]. Techniques are available for non-invasive[12,13] and minimally invasive counterpulsation[11,14]. Clinical experience[11,15,16] seems to indicate that shock is reversed and that the heart can recover if counterpulsation is applied early. Long-term survival may then range from 0-55%. Counterpulsation is not effective during cardiac standstill or ventricular fibrillation. In contrast, the circulation can still be maintained under these circumstances with bypass procedures. A bypass, however, requires dissection of blood vessels and, up until now, systemic heparinization is necessary. Complications such as embolism (air, clots, other particles), infection, blood damage, blood loss, and damage to blood vessels can occur.

Clinical experience with successful closed-chest partial cardiopulmonary bypass as a treatment for cardiogenic shock dates back as far as 1957[17]. More recently[18] a 50% recovery rate was reported. The procedure was time-limited because of the blood damage caused by extracorporeal oxygenation. Since membrane oxygenation became feasible[19] the bypass is being applied again as a circulatory assist[20]. Although a substantial amount of blood is diverted from the heart and infused into the arterial vascular bed there is experimental evidence that there is no effective decompression of the left ventricle[21]. The failing left ventricle is not able to pump out the blood flowing to the left atrium from the bronchial arteries and that which escapes the venous cannulas.

There is only limited clinical experience with closed-chest left heart bypass using a transvenous cannulation technique[22]. Although the shock could be reversed, no patients survived. Since the cannula removes blood from the left atrium, maximum decompression of the left ventricle cannot be obtained if the mitral valve is competent. With TaCLV-Bypass, the left ventricle is maximally decompressed and the blood removed from the left heart is returned to the arterial vascular bed. Artificial oxygenation is not necessary if pulmonary function is adequate.

In our first clinical experience with 2 patients the bypass could be instituted within 20-30 min. The outflow cannula did not cause damage to the heart or adjacent structures. The circulation did improve as evidenced from the skin color and temperature, as did the arterial and right atrial pressures, and, in the first patient, the pH, the urine production, and the return of consciousness. The anuria and acidosis in the second patient might be due to poison.

Usually the bypass was incomplete, the left ventricle ejected blood, and since the arterial pressure had increased, it is likely that myocardial work did increase rather than decrease. For this reason, equipment was designed to counterpulsate blood return (Figures 1-3); if applied during incomplete bypass it is expected to minimize myocardial work. In the first patient, the bypass was occasionally complete and a straight arterial pressure tracing was obtained (Figure 5) while the circulation was maintained with the roller pump. During such circumstances it might be advantageous to produce a pulsatile blood return. Initially there was cyanosis in both patients

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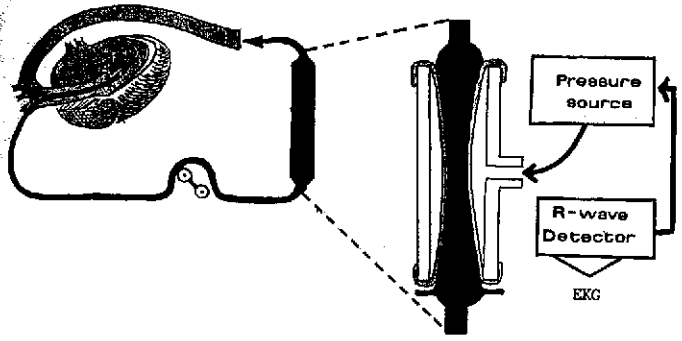

Figure 1. Schematic drawing of TaCLV-Bypass. Blood is removed from left ventricle with transarterial cannula and returned to aorta. (Figure 1a). Enlargement of arterial reservoir. A rigid cylinder, covered on the inside with a natural latex sleeve is fitted around reservoir for counterpulsation.

Figure 2. The blood circuit for TaCLV-Bypass. 1. Cannula to be inserted into left ventricle. 2. Inflow part of blood circuit. 3. Short piece of thin-walled silastic tubing, indicates position of outflow cannula and amount of suction produced by roller pump. 4. Outflow part of blood circuit. 5. Blood return cannula. 6. Arterial reservoir. Note the 3 side-lines. 7. Counterpulsation equipment.

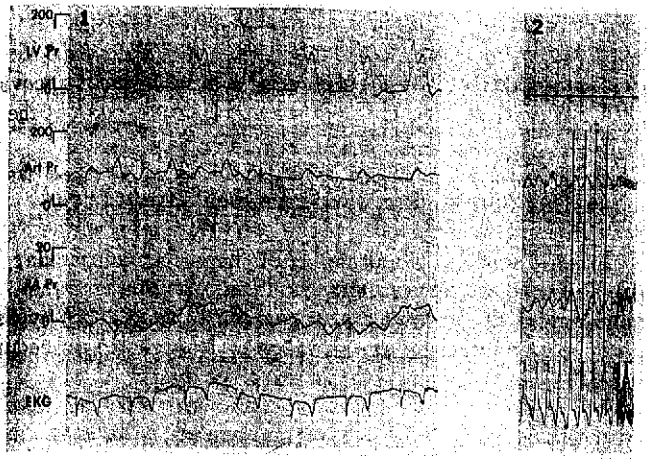

Figure 3. Tracings obtained from TaCLV-Bypass in a sheep. During the first half of period 1, blood return was counterpulsated. During period 2, the bypass is complete, the pressure in the left ventricle is atmospheric. Note that artificially produced pulsations in aorta are still synchronous with EKG. LV Pr. - pressure, left ventricle; Art. Pr. - pressure, thoracic aorta; RA. Pr. - pressure, right atrium. Pressures in mm. Hg.

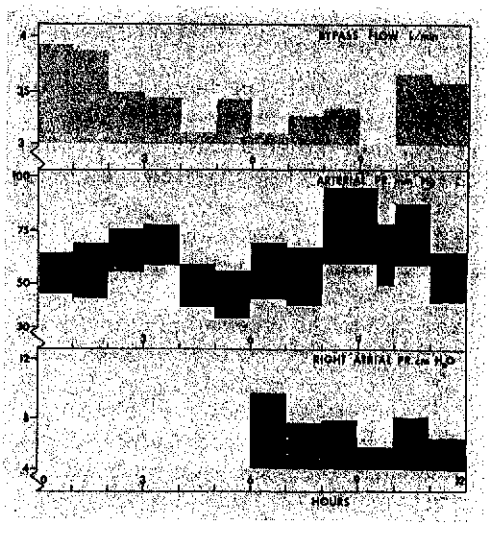

Figure 4. Bypass flow, arterial pressure and right atrial pressure during TaCLV-Bypass in patient 1.

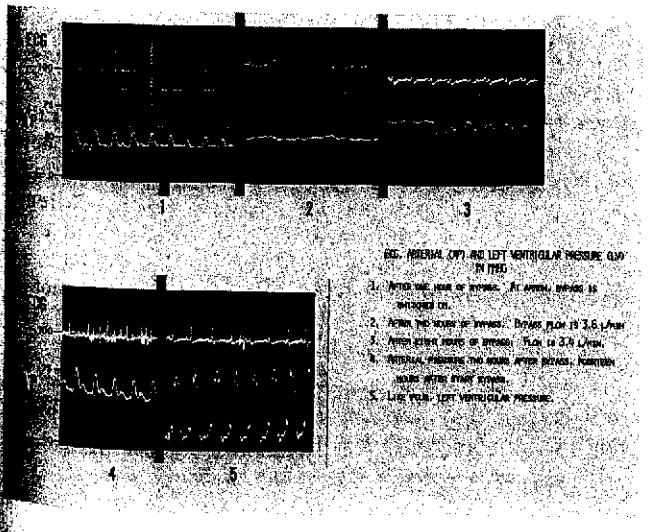

Figure 5. Tracings obtained during TaCLV-Bypass in patient 1. During period 2, left ventricle is bypassed completely. Art. Pr. - pressure in thoracic aorta. The left ventricular pressure, displayed at the lower right corner of the picture was measured through the outflow cannula while the bypass was switched off. Pressures in mm. Hg.

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and in the first patient signs of pulmonary edema. The arterial oxygen saturation improved almost immediately during the bypass in the second patient. In the first patient this took 6 hr. The improvement of blood oxygen content could be the result of effective decompression of the left side of the heart. Physical signs of pulmonary edema disappeared during bypass in the first patient. If oxygenation does not improve within a short time, a membrane oxygenator might be included in the blood circuit. The temperature in neither of the patients decreased so that a heat exchanger does not seem to be necessary. In the first patient an extra perfusion line had to be inserted into the right femoral artery, distal from the cannulation site. Therefore, it seems wise that side lines connected to the arterial reservoir are provided. The bypass flow did not change abruptly, and the roller pump had to be slightly adjusted about every 30 min. if undue suction or low flow became apparent from the thin-walled piece of silastic tubing (indicator tube, 3 in Figure 2). One person could easily operate the bypass.

In both patients death was ultimately caused by massive bleeding from the gastrointestinal tract. Such bleeding is a known complication of massive myocardial infarction, especially during the advanced stages of shock. In the second patient, the bleeding was related to multiple ulcers - no clotting abnormalities other than those caused by heparinization could be detected. The heparin made the bleeding worse and these experiences initiated attempts to modify the blood circuit so that systemic heparinization is not necessary.

In the first patient it is likely that the sudden impairment of cardiac function was caused by a clot which occluded the right coronary artery. At autopsy, the clot could easily be removed. This finding suggests that diagnostic procedures, such as coronary angiography, be performed during the bypass if the heart does not recover within a reasonable time. Probably such studies could lead to surgical correction, eg., removal or bypass of the clot in this case.

The management of cardiogenic shock will change in the near future; if medical treatment fails, a non-invasive mechanical assist device, such as external counterpulsation, is applied. If the condition does not improve a bypass procedure is instituted. If during partial closed-chest cardiopulmonary bypass left ventricular end diastolic pressure is too high, the ventricle is decompressed with a transarterial cannula. If, during transarterial closed-chest left ventricular bypass, arterial oxygen content is too low, an oxygenator is used. If a bypass is incomplete blood return is counterpulsated, and if it is complete, pulsations are produced. Diagnostic procedures and surgical correction are carried out as necessary.

SUMMARY

Clinical experience with the application of Transarterial Closed-Chest Left Ventricular (TaCLV) Bypass in 2 patients has been described. During the bypass blood is removed from the left ventricle with a flexible, wide bore, thin-walled cannula which is inserted via the right axillary or subclavian artery. The blood is pumped back to the arterial vascular bed via a femoral artery. The method has been studied during experiments on 18 dogs and 42 sheep.

The blood circuit consists of a silastic tube, interrupted by a silastic reservoir. The tube is mounted in a roller pump. The reservoir serves to catch air bubbles and to depulsate the pump. Silastic side-lines are attached to the reservoir for additional perfusion of the right arm and the leg if necessary. With some additional equipment blood return can be pulsated and the pulses can be phased in between heart systoles (counterpulsation).

TaCLV-Bypass was applied in 2 patients with intractable shock. It took 20-30 min. to institute the bypass. A complete bypass was occasionally obtained, usually left ventricular pressure pulses were observed on the pressure tracing. The circulatory condition improved and cyanosis disappeared. One person could easily operate the bypass. The first patient was pumped for 11 hr. until bypass was discontinued because blood loss was suspected. Eight hours later the patient died from massive gastrointestinal bleeding. The same complications occurred after 5 1/2 hr. of bypass in the second patient. At autopsy, massive myocardial infarction was found in the first patient, while in the second, the heart appeared normal but multiple ulcers were found in the gastrointestinal tract and a poison was suspected of having caused the circulatory collapse. The prolonged shock-state and, in the second patient, the poison might have caused the profuse bleeding. Damage that could be related to the cannulas was not detected in the heart or adjacent structures.

Clinical results with other mechanical assist devices are described. It is suggested that diagnostic procedures such as coronary angiography be performed during the bypass if the heart does not recover. This could possibly lead to surgical correction. The management of patients with intractable shock is discussed.

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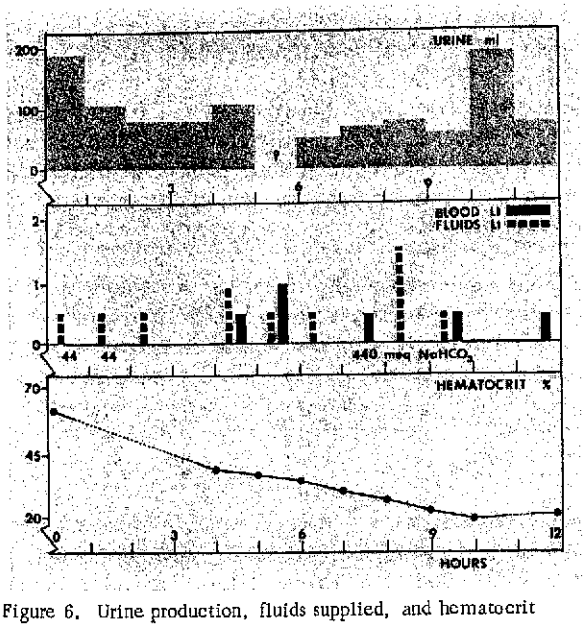

Figure 6. Urine production, fluids supplied, and hematocrit during TaCLV-Bypass in patient 1.

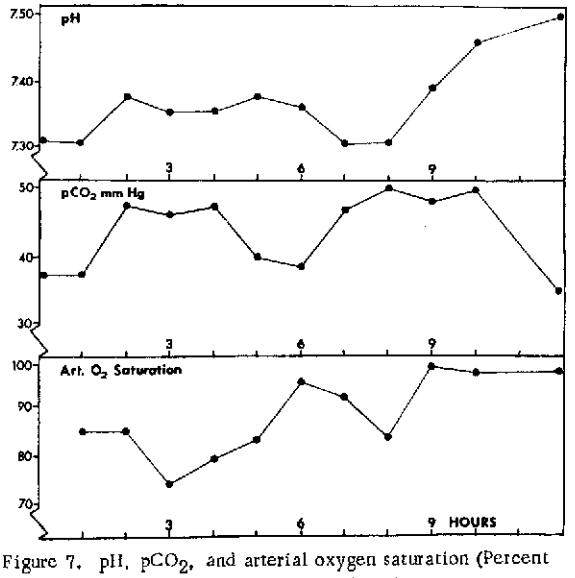

Figure 7. pH, pCO_2, and arterial oxygen saturation (Percent of normal) during TaCLV-Bypass in patient 1.

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A Simplified Blood Access Method for a Temporary Left Ventricular Assist System in Humans

Leonard Golding, from the Department of Cardiovascular and Thoracic Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio, 44106.

Zwart[1,2] and Geddes[3,4] independently described the use of a cannula passed retrograde across the aortic valve into the left ventricle to gain access to blood in the ventricle for partial support of the failing left heart. More recently, Bernstein[5] has used the same approach in many calves for short periods without producing aortic regurgitation or valve damage.

Figure 1 shows a modified version of this approach which has allowed easy and rapid access to th the left ventricle and aorta in calf experiments. bifurcated, tightly-woven 18 mm Cooley Dacron

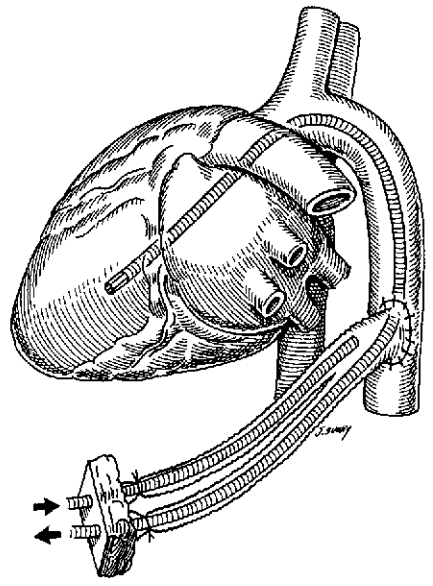

FIG. 1. Technique of insertion in calves using the descending thoracic aorta.

graft is anastomosed end-to-side to the descending thoracic aorta. One 9 mm limb is used for retrograde insertion of an armored 7.2 mm O.D. cannula into the left ventricle for drainage and the second limb of the graft is used for the arterial return cannula from the pump, terminating in the unbifurcated segment of the graft. Both limbs are of sufficient length to terminate in the animal's subcutaneous tissues where they are ligated to the cannulas. This allows simple removal of the cannulas under local anesthesia at the termination of pumping.

The method was evaluated in four animals. With continuous pumping for five to twenty days (mean: thirteen days), mean flows of 3.5 to 4.0 L/min and peak flows of 7 L/min could be generated. No aortic regurgitation was seen, hemolysis was minimal (mean plasma hemoglobin and serum bilirubin normal), and the cannulas could be easily removed at the termination of pumping. Autopsy studies in all animals showed no myocardial damage and firmly adherent thrombus in the retained graft. In one animal pumped for twenty days, there was a minor thickening in one aortic valve leaflet which, microscopically, was observed to be the result of bacterial endocarditis, all other leaflets being entirely normal.

Figures 2 and 3 show the proposed use in humans. This method has the following potential advantages for clinical temporary ventricular assist: 1) simple and rapid to insert, 2) produces no further myocardial damage (in comparison with apical cannulation), 3) removable under local anesthesia at termination of pumping, and 4) allows insertion of a

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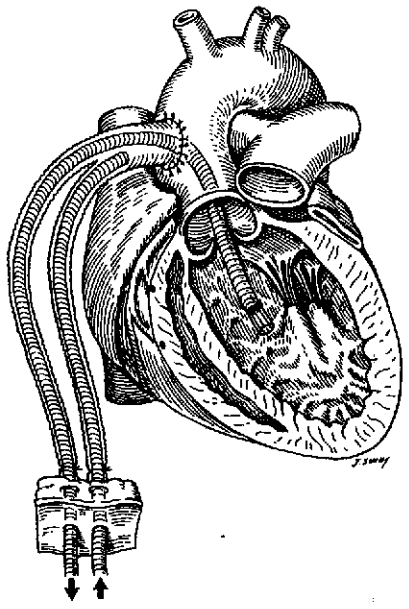

FIG. 2. Proposed insertion technique in humans via the ascending aorta.

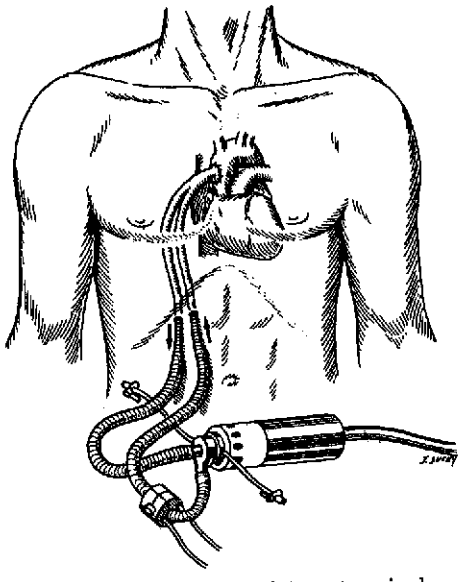

FIG. 3. Schematic of temporary assist system in humans.

permanent pump system via the apex when such devices are perfected.

A contraindication to the use of this system is the presence of an artificial or abnormal aortic valve, and the use of such a method is probably limited to ten days.

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Standard Recommended Practice for the Assessment of the Hemolytic Properties of Materials*

Draft 4.20.06.60/4.40.02.06

Seventh Draft (5-22-78)

The following Proposed Standard Recommended Practice has been written by the Hemolysis Task Force F 4.20.06.60/4.40.02.06 under the auspices of Resources/Biocompatibility and Cardiovascular Devices/Hematological Compatibility Subcommittees. The proposed recommended practice is a screening procedure intended for materials designed for use in medical devices which may come in contact with blood or vascularized tissues. The proposed Standard Method is based on techniques commonly in use by university, independent and manufacturer affiliated testing laboratories throughout the United States and Canada. The resulting document is a consensus practice to be used for evaluating materials as opposed to devices.

The following Proposed Standard represents the consensus of the Hemolysis Task Force but does not necessarily reflect the opinions of other members of Committee F-4 or the ASTM. Comments are welcome and should be addressed to the Task Force Chairman, Dr. Richard J. Schlesinger, c/o Bio-Technics Laboratories, Inc., 1127 Crenshaw Boulevard, Los Angeles, California, 90019.

1. Scope

1.1 This recommended practice provides a protocol for the assessment of hemolytic properties of materials used in the fabrication of medical devices that will contact blood.

1.2 This protocol is intended to evaluate the acute *in vitro* hemolytic properties of materials intended for use in contact with blood.

*This specification is under the jurisdiction of ASTM Committee F-4 on Surgical Implants and is the direct responsibility of Subcommittee FO.4.20 on Resources.

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Myocardium-Sparing Cannulation Technique for Left Ventricular Assist Device Support

J. Michael Duncan, MD, Robert T. Baldwin, MD, Stephen R. Igo, and O. H. Frazier, MD

Cullen Cardiovascular Research Laboratories, Texas Heart Institute, Houston, Texas

The left atrium and the left ventricular apex are the most commonly used sites of inflow cannulation for postcardiotomy left ventricular support. A new cannulation technique that requires only an ascending aortotomy is introduced. This procedure can be undertaken with equipment present in any cardiac operating room and may prove to cause fewer complications than conventional cannulation techniques.

(Ann Thorac Surg 1991;52:565–6)

Postcardiotomy shock that is too advanced for inotropic and intraaortic balloon pump therapy is frequently treated by left ventricular bypass. Several different pumps have been used for successful support of the failed ventricle, and most investigators have used either the left atrium or the left ventricular apex as sites for inflow cannulation. Complications have occurred at both of these sites. Thus, we developed a new cannulation technique for left ventricular support in which only the ascending aorta is cannulated.

Material and Methods

We used a new cannulation technique to institute left ventricular assist device support in 3 patients who could not be weaned from cardiopulmonary bypass after aortocoronary bypass grafting. None of the patients had evidence of aortic valve disease.

In each case, a Bio-Medicus centrifugal pump (Bio-Medicus, Minneapolis, MN) and standard Tygon tubing were used. A longitudinal aortotomy was performed on the right lateral aspect of the ascending aorta, proximal to the aortic cross-clamp, while cardiopulmonary bypass was continued. A 22 × 11-mm woven Dacron bifurcation graft was fashioned so that only 5 cm of the body and two limbs remained. The body was beveled so that it could be directed inferiorly. No preclotting of the graft or other preparation was necessary. A 3-0 polypropylene running suture was used to anastomose the 22-mm limb of the graft to the ascending aorta (Fig 1). A 24F wire-reinforced cannula (USCI, Billerica, MA) was then inserted through the superior limb of the graft and across the aortic valve, so that it sat in the left ventricular chamber near the apex. Umbilical tape was used to secure the graft around the cannula. The cannula and ventricle were aspirated and connected to the inflow tubing of the pump. The return cannula was placed through the remaining limb of the graft, directed distally past the anastomosis and into the aorta, and secured to the graft with umbilical tape. After the circuit was aspirated (Fig 2), left ventricular support was instituted.

The patients were successfully weaned from cardiopulmonary bypass, and the heparin was allowed to wear off. Standard chest tube drainage was performed. Both cannulas were brought out the inferior aspect of the sternotomy incision and secured to the skin. The patients were then transported to the intensive care unit for postcardiotomy care.

Results

The technique of ascending aorta cannulation to institute left ventricular assist device support was performed rapidly in all 3 patients, thereby minimizing bypass times. Excessive bleeding at the anastomosis, around the umbilical tape, or through the graft did not occur. Chest tube

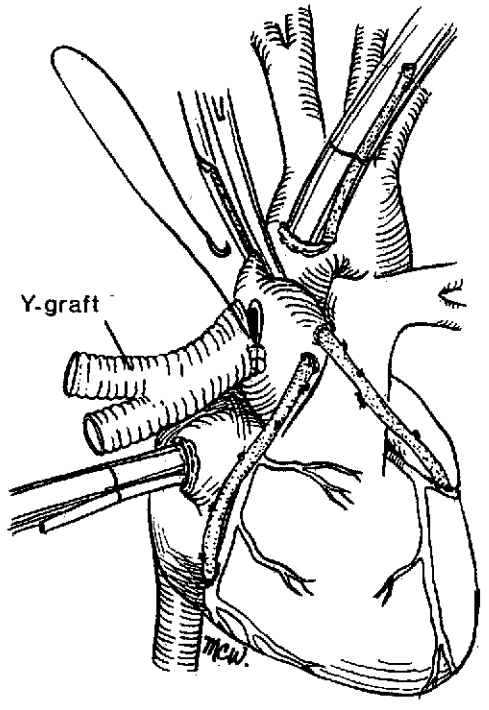

Fig 1. A woven, bifurcated Dacron graft is sewn to the ascending aorta to introduce the cannulas.

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Address reprint requests to Dr Duncan, Texas Heart Institute, PO Box 20345, Houston, TX 77225-0345.

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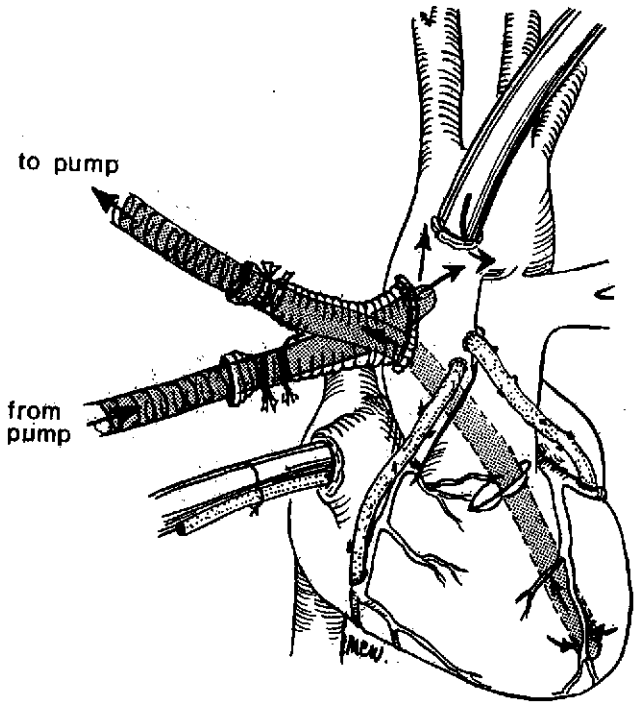

Fig 2. The reinforced cannula is placed across the aortic valve to decompress the left ventricle. Blood is returned from the centrifugal pump through a cannula inserted into the ascending aorta.

output ranged from 50 to 300 mL/h and was believed to be the result of coagulopathy, which commonly occurs in this patient population. The average pump flow was 4 to 6 L/min in all patients and was highly dependent on the patient's intravascular volume status. The ventricle appeared to be decompressed, and the pulmonary capillary wedge pressure remained low postoperatively. The cannulas did not kink or impede inflow, even when directed inferiorly below the skin at the time of closure.

The duration of support ranged from 6 hours to 3 days, and pump function was excellent. No focal neurological insults occurred. All 3 patients died of irreversible cardiac failure.

Comment

Left atrial cannulation to institute left ventricular assist device support is easy to perform, but this procedure may cause complications such as mitral valve damage, incomplete ventricular decompression, inflow cannula obstruction by the pliable walls of the atrium, and increased right-to-left shunting of blood in the presence of an unrecognized patent foramen ovale [1]. Inflow cannulation of the ventricular apex is time-consuming, and it may cause bleeding—either during the period of support or after repair following successful weaning—and regional hypokinesis in the surrounding myocardium, thereby limiting ultimate recovery [2, 3].

The technique of ascending aorta cannulation described in this report, which was inspired by Golding's work in calves using the descending thoracic aorta cannulation site [4], seems to have several advantages. It is simple and fast, and it requires only a Bio-Medicus pump, standard cannulas, and a bifurcated woven Dacron graft. In addition, the technique allows direct ventricular decompression but avoids the complications of bleeding and hypokinesis associated with direct ventriculotomy. Although more experience with this procedure is necessary before any solid conclusions can be drawn, we believe that this technique may prove satisfactory for cannulating patients requiring postcardiotomy left ventricular support.

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Appendix G: Boston Scientific StereoCath-Dx Electrophysiology (EP) Catheter

- K940168- EP Technologies/Boston Scientific Diagnostic II Catheter 510(k) Clearance Information
- Boston Scientific StereoCath-Dx Electrophysiology (EP) Catheter Product Labeling

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U.S. Food and Drug Administration

Department of Health and Human Services

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

510(k) Premarket Notification Database

Device Classification Name	Catheter, Electrode Recording, Or Probe, Electrode Recording
510(K) Number	K940168
Device Name	DIAGNOSTIC II CATHETER
Applicant	EP TECHNOLOGIES, INC. 350 Potrero Ave. Sunnyvale, CA 94086
Contact	Alan Marquardt
Regulation Number	870.1220
Classification Product Code	DRF
Date Received	01/07/1994
Decision Date	07/27/1994
Decision	Substantially Equivalent (SE)
Classification Advisory Committee	Cardiovascular
Review Advisory Committee	Cardiovascular
Statement/Summary/Purged Status	Summary/Purged 510(K)
Type	Traditional
Reviewed By Third Party	No
Expedited Review	

Database Updated 6/07/2007

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Steerocath-Dx ™ Spec. Procedure Octa Catheters

Prescriptive Information

Refer to the operator's manual for complete instructions for use.

Indications

The catheter is intended for temporary use in electrophysiology studies for intracardiac stimulation (pacing) and/or recording of electrical potentials.

Contraindications

Caution should be exercised, in the use of this or any other catheter, in patients with prosthetic valves. Patients with recurrent sepsis or with hypercoaguable state should not be considered candidates for transvascular catheters, since the catheter could serve as a focal point for septic or blood thrombus formation.

Warnings

Contents supplied **STERILE** using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found call your Boston Scientific representative. For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which in turn may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient. The device(s) should be used by physicians thoroughly trained in the techniques of invasive cardiology and in the specific approach to be used. Care must be taken to ensure that any equipment used in connection with the EP Catheters meets IEC 601-1 and IEC 601-1-2 Safety Standards.

- The use of catheters or cables with unprotected male pin connectors presents a risk of electrical hazard. Inadvertent attachment of pin connectors to power supply sockets of connectors could result in electrocution of the patient or operator. Diagnostic electrophysiology involves x-ray exposure that present the potential risk for somatic and genetic effects, to both patients and laboratory staff due to the x-ray beam and intensity and duration of the fluoroscopic imaging. Steps should be taken to minimize this exposure as much as possible. Careful catheter manipulation must be performed to avoid cardiac damage, perforation, or tamponade. Catheter advancement should be performed under fluoroscopic guidance. Do not use excessive force to advance or withdraw the catheter when resistance is encountered. This catheter is not indicated for use in Cardiac Ablation or Coronary Artery Mapping.

[redacted] general guidance

DEVICE DETAILS

Device Overview
Prescriptive Information

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Potential Adverse Effects
The following potential risks or discomforts may be associated with diagnostic EP procedures. The frequency and severity of these adverse events can vary, and may necessitate additional medical intervention, including surgery: Allergic reaction, Arrhythmias, Cardiac or respiratory arrest, Cardiac valve damage, Catheter entrapment/entanglement, Chest pain, Damage to vessel intima or cardiac structures, Death, Embolus, air embolus, Hematoma/ecchymosis, Hemorrhage, Hypotension, Infection, Myocardial infarction, Perforation, Pericardial effusion, Pericarditis/ pleuritis, Pneumothorax, Pseudoaneurysm, Pulmonary edema, Sinus or AV node injury, Stroke, Stroke or cerebral vascular accident, Tamponade, Thrombosis, Vasovagal reaction, X-ray exposure.

Cautions
Excessive bending or kinking of the catheter shaft may damage internal wires. Manual prebending of the distal curve can damage the steering mechanism and/or electrical wires, and may cause patient injury.

Trademark
Steerocath-Dx is a trademark of Boston Scientific Corporation or its affiliates.

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U.S. Health Information Privacy (HIPAA)

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Special Procedure SteeroCath-Dx™ Catheters

Steerable catheter that is ideal for mapping unusual anatomy.

- Bidirectional steering facilitates the ability to counter-steer, allowing for uncomplicated cannulation of the Coronary Sinus os.
- Extended soft distal tip enables the catheter to track the entire Coronary Sinus.
- Braided proximal shaft allows for enhanced torque control and greater pushability upon insertion.

Product Information

Catheter Model No.	Shaft Size	Distal Shaft Length	Tip	Curve Style	Electrode Configuration	Electrode Spacing	Cable Model No
M004 2027BL 0	7F	Extended	7F/2mm	Standard	Octapolar	2.5mm	M004 626S 0
M004 2028BL 0	7F	Extended	7F/2mm	Standard	Octapolar	2.5/5/2.5mm	M004 626S 0

- All Special Procedure Octapolar SteeroCath-DX catheters are 110cm in length.

Indications: Diagnostic catheters are intended for temporary use in electrophysiology studies for intracardiac stimulation and/or recording of electrical potentials. **Contraindications:** Caution should be exercised, in the use of this or any other catheter, in patients with prosthetic valves. Patients with recurrent sepsis or with hypercoaguable state should not be considered candidates for transvascular catheters, since the catheter could serve as a focal point for septic or blood thrombus formation. **Warnings:** This catheter is not indicated for use in cardiac ablation or coronary artery mapping procedures. **Precautions:** Federal (USA) law restricts these devices to sale by or on the order of a physician. Carefully read all instructions prior to use.

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EP TECHNOLOGIES™

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Appendix H: Boston Scientific Sonicath Ultra Imaging Catheter (9F/12 MHz)

- K902245- Boston Scientific Sonicath Ultra Imaging Catheter 510(k) Clearance Information
- Boston Scientific Sonicath Ultra Imaging Catheter Product Labeling

- Foster et al. Determination of Aortic Valve Area in Valvular Stenosis by Direct Measurement Using Intracardiac Echocardiology: A Comparison with the Gorlin and Continuity Equations." J Am Coll Cardiol 1996;27:392-398.

- Fuji et al. Contribution of Stent Underexpansion to Recurrence after Sirolimus-Eluting Stent Implantation for In-stent Restenosis. Circulation. 2005;109-1085-88.
- Page from Information for Manufacturers Seeking Marketing Clearance of Diagnostic Ultrasound Systems and Transducers. Issued by the Computed Imaging Devices Branch, Division of Reproductive, Abdominal, Ear, Nose, Throat and Radiological Devices (ODE), September 30, 1997.

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U.S. Food and Drug Administration

Department of Health and Human Services

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

510(k) Premarket Notification Database

Device Classification Name	Transducer, Ultrasonic, Diagnostic
510(K) Number	K902245
Device Name	SONICATH(TM) 9F, 12 MHZ
Applicant	BOSTON SCIENTIFIC CORP. 480 Pleasant St. P.O. Box 7407 Watertown, MA 02272
Contact	Jeanne M Lesniak
Regulation Number	892.1570
Classification Product Code	ITX
Date Received	05/18/1990
Decision Date	10/09/1990
Decision	Substantially Equivalent (SE)
Classification Advisory Committee	Radiology
Review Advisory Committee	Obstetrics/Gynecology
Statement/Summary/Purged Status	Purged, No Summary Or Statement
Type	Traditional
Reviewed By Third Party	No
Expedited Review	

Database Updated 6/07/2007

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iLab™ System with Ultra ICE™ Catheter Ultrasound Imaging System & Catheter

Performing a transseptal procedure doesn't have to seem like a leap of faith.

Product Information - Ultra ICE Catheter Indications for Use

INDICATIONS

The Ultra ICE Catheter is indicated for enhanced ultrasonic visualization of intracardiac structures.

CONTRAINDICATIONS

The device is not to be used in the presence of conditions which create unacceptable risk during catheterization.This device is not to be used in the coronary arteries.

WARNINGS/REACTIONS

- Contents supplied STERILE using a gamma radiation (Cobalt 60) process. Do not use if sterile barrier is damaged. If damage is found call your Boston Scientific representative.
- For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which in turn may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.
- The device(s) should be used by physicians thoroughly trained in the techniques of invasive cardiology and in the specific approach to be used.
- Care must be taken to ensure that any equipment used in connection with the EP Catheters meets IEC 601-1 and IEC 601-1-2 Safety Standards.
- During the procedure, inspect the catheter carefully for any damage which may have occurred during use.
- The catheter has no user serviceable parts. Do not attempt to repair or to alter any component of the catheter assembly as provided. Do not attempt to connect the catheter to electronic equipment other than the designated System.
- Never attempt to attach or detach the catheter while the motor is running. To do so may damage the connector.
- Peri-procedural anticoagulation therapy is recommended for patients undergoing left-sided and transeptal cardiac procedures and should be considered for selected patients undergoing right sided procedures.
- DO NOT advance the catheter if resistance is encountered. The catheter should never be forcibly inserted into lumens narrower than the catheter body or forced through a tight stenosis.
- Avoid any sharp bends, pinching, crushing or pulling of the catheter.
- Care should be taken when a guidewire is exposed in a stented vessel. Catheters that do not encapsulate the guidewire may engage the stent between the junction of the catheter and guidewire.
- Care should be taken when readvancing a guidewire after stent deployment. A guidewire may exit between stent struts when recrossing a stent that is not fully opposed to the vessel wall. Subsequent advancement of the catheter could cause entanglement between the catheter and the stent. Care should be taken to slowly remove the catheter from a stented vessel.
- Do not kink or sharply bend the catheter at any time. This can cause drive cable failure. An insertion angle greater than 45° is considered excessive.
- Turn the MDU "OFF" before withdrawing the imaging catheter into the introducer sheath.
- In order to achieve the lowest possible acoustic output, the frame rate and maximum burst settings should be set to the lowest possible values as reasonably achievable to obtain images.
- If resistance is met upon withdrawal of the catheter, verify resistance using fluoroscopy, then remove the entire system simultaneously.

POTENTIAL ADVERSE EFFECTS

1. The risks and discomforts involved in imaging cardiac structures include those associated with similar types of diagnostic procedures in the heart. However, any of these risks or discomforts may occur with greater frequency or severity than previously reported. Unknown future risks not identified below may also occur. Additionally, these complications may necessitate additional medical treatment including surgical intervention.

- Myocardial infarction
- Abnormal heart rhythms
- Thrombosis
- Hematoma
- Cardiac wall injury including perforation
- Vascular wall injury including perforation
- Infection/discomfort
- Damage to cardiac valvular structures
- Hypotension/Hypertension
- Endocarditis
- Stroke/embolism
- Death
- Allergic reaction
- Phrenic or intercostal nerve damage
- Cardiac or respiratory arrest
- Catheter entrapment/entanglement
- Chest pain
- Embolus/air embolus
- Pneumothorax
- Bradycardia
- Palpitations and rhythmical disturbances
- Vascular thrombosis
- Arterial perforation
- Ventricular fibrillation
- Distal emboli

2. As with all procedures that utilize the Seldinger Technique for introducing a catheter into an artery, the following complications have been reported:
- Infection and pain in the region of the insertion site
- Hemorrhage
- Arteriovenous Fistula

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iLab™ System with Ultra ICE™ Catheter
Ultrasound Imaging System & Catheter

Performing a transseptal procedure doesn't have to seem like a leap of faith.

- The radiopaque tip of the Ultra ICE Catheter allows easy placement and serves as a fluoroscopic marker during the procedure. Detailed near-field resolution; with a unique 360° panoramic view of the anatomy.
- The iLab System is available in two configurations to meet your facilities particular needs - a portable cart-based system, or an installed system that can be fully integrated into your EP Lab. Compatible with all Boston Scientific ultrasound platforms: Intracardiac (ICE), Intravascular (IVUS), and Peripheral.

Product Information

System Information	Model No.	Description
	M004 **EPiL120CART** 0	iLab Ultrasound Imaging System (on cart)
	M004 **EPiL120INS** 0	iLab Ultrasound Imaging System (installed*)

Catheter Information	Model No.	Description
	M004 **9900** 0	Ultra ICE™ Catheter Size: 9F Frequency: 9 MHz Usable Length: 110cm
	M004 **9915** 1	Fluid Dock® Filling Device Box of 10 individual sterile units *(Filling device enables filling of the Ultra ICE Catheter tip without damage to the ultrasound sensor during catheter preparation.)*

Convoy® Sheaths are recommended to deploy the Ultra ICE Catheter. For septal imaging, use Convoy Sheath Model M004 **56625T** 0.

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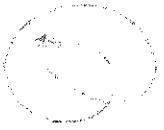
Ultra ICE ™ 9F/9 MHz Catheters

iLab™ Ultrasound Imaging System with the Ultra ICE Catheter

Total lab integration

DEVICE PHOTOS CLINICAL PHOTOS MULTIMEDIA



Ultra ICE™ Catheter
The Ultra ICE Catheter contains a 9F/9 MHz ultrasound transducer for intracardiac imaging

1 of 4

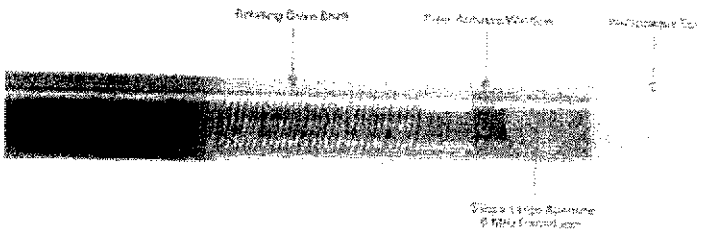
Click image to enlarge

- The radiopaque tip of the Ultra ICE Catheter allows easy placement and serves as a fluoroscopic marker during the procedure. The area of interest is then the central point in the ultrasound image, providing a clear panorama of what you want to visualize and all the surrounding structures.

- The Ultra ICE Catheter generates a panoramic 360° image perpendicular to the catheter, with the tip as a central reference point. Compatible with all Boston Scientific Ultrasound Imaging Systems: ClearView® Ultra™ System, Galaxy® System, Galaxy²™System and the iLab System.

- The Boston Scientific iLab System is available in two configurations to meet your particular facilities needs - a portable cart-based system, or an installed system that can be fully integrated into your EP Lab. Compatible with all Boston Scientific Ultrasound platforms: Intracardiac (ICE), Intravascular (IVUS), and Peripheral.

Device Illustration



1. Rotating Drive Shaft
2. Clear Acoustic Window
3. Radiopaque Tip
4. Single Large Aperture 9 MHz Transducer

Additional Information
Click here to view a video presentation of the benefits of ICE for transseptal catheterization.

DEVICE DETAIL
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presentations in
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Procedures
Devices
Reimbursement
Resource Library

Site Search

Ultra ICE ™ 9F/9 MHz Catheters

Prescriptive Information

Refer to the operator's manual for complete instructions for use.

Indications

The Ultra ICE Catheter is indicated for enhanced ultrasonic visualization of intracardiac structures.

Intended Use and Indication(s) for iLab™ System Use:

The iLab Ultrasound Imaging System is intended for ultrasound examinations of intravascular pathology. Intravascular ultrasound is indicated in patients who are candidates for transluminal interventional procedures such as angioplasty and atherectomy. Refer to the Catheter DFU provided with all BSC Ultrasound Imaging Catheters to determine compatibility with the iLab System. The Imaging Catheters generate ultrasound images and are intended for patient examination of vascular and cardiac anatomies. BSC manufactures a wide variety of imaging catheters for different applications. The recommended use of each of these catheters may vary depending on the size and type of catheter.

Contraindications

The Ultra ICE Catheter is contraindicated in the presence of conditions which create unacceptable risk during catheterization.
This device is not to be used in the coronary arteries.
This device is not intended for fetal use.

Warnings

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if barrier is damaged. If damage is found, call your Boston Scientific representative.

For single patient use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

DEVICE DETAILS

Device Overview
Prescriptive Information

RESERVED RESOURCES

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Care must be taken to ensure that any equipment used in connection with the BSC catheters, be type CF, be defibrillation proof, meet IEC 60601-1 and IEC 60601-1-2 electrical safety requirements, and comply with all local regulatory requirements for the specified intended use.

• Before using, inspect for physical damage including electrical insulation on the cables and the catheter shaft. Replace damaged equipment.

• DO NOT advance the catheter if resistance is encountered. The catheter should never be forcibly inserted into lumens narrower than the catheter body or forced through a tight stenosis

• If resistance is met upon withdrawal of the catheter, verify resistance using fluoroscopy, then remove the entire system simultaneously.

Potential Adverse Effects

1. The risks and discomforts involved in imaging cardiac structures include those associated with similar types of diagnostic procedures in the heart. However, any of these risks or discomforts may occur with greater frequency or severity than previously reported. Additionally, these complications may necessitate additional medical treatment including surgical intervention.

o Myocardial infarction
o Abnormal heart rhythms
o Thrombosis
o Hematoma
o Cardiac wall injury including perforation
o Vascular wall injury including perforation
o Infection/discomfort
o Damage to cardiac valvular structures
o Hypotension/Hypertension
o Endocarditis
o Stroke/embolism
o Death

2. As with all procedures that utilize the Seldinger Technique for introducing a catheter into an artery, the following complications have been reported:

o Infection and pain in the region of the insertion site
o Hemorrhage
o Arteriovenous Fistula

Cautions

Federal (USA) law and governing law outside the USA restricts these devices to sale by or on the order of a physician.

PRECAUTIONS:

• This device should be used by physicians thoroughly trained in the

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techniques of invasive cardiology and in the specific approach to be used.

• After the procedure, inspect the catheter carefully for any damage which may have occurred during use.

• The catheter has no user serviceable parts. Do not attempt to repair or to alter any component of the catheter assembly as provided. Do not attempt to connect the catheter to electronic equipment other than the designated systems.

• Never attempt to attach or detach the catheter while the motor is running. To do so may damage the connector.

• Throughout the procedure anticoagulant therapy is recommended for patients undergoing left-sided and transseptal cardiac procedures and should be considered for selected patients undergoing right-sided procedures.

• Avoid any sharp bends, pinching or crushing of the catheter.

• **Do not kink or sharply bend the catheter at any time.** This can cause drive cable failure. An insertion angle greater than 45° is considered excessive.

• Turn the MDU "OFF" before withdrawing the imaging catheter, or when advancing the catheter in the body.

Trademark

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Determination of Aortic Valve Area in Valvular Aortic Stenosis by Direct Measurement Using Intracardiac Echocardiography: A Comparison With the Gorlin and Continuity Equations

GARY P. FOSTER, MD,*† NEIL J. WEISSMAN, MD,† MICHAEL H. PICARD, MD, FACC,† PHILLIP J. FITZPATRICK, MD, FACC,* SAMUEL J. SHUBROOKS, JR., MD, FACC,* STUART W. ZARICH, MD, FACC*

Boston, Massachusetts

Objectives. **This study sought to 1) show that intracardiac echocardiography can allow direct measurement of the aortic valve area, and 2) compare the directly measured aortic valve area from intracardiac echocardiography with the calculated aortic valve area from the Gorlin and continuity equations.**

Background. **Intracardiac echocardiography has been used in the descriptive evaluation of the aortic valve; however, direct measurement of the aortic valve area using this technique in a clinical setting has not been documented. Despite their theoretical and practical limitations, the Gorlin and continuity equations remain the current standard methods for determining the aortic valve orifice area.**

Methods. **Seventeen patients underwent intracardiac echocardiography for direct measurement of the aortic valve area, including four patients studied both before and after valvuloplasty, for a total of 21 studies. Immediately after intracardiac echocardiography, hemodynamic data were obtained from transthoracic echocardiography and cardiac catheterization.**

Results. **Adequate intracardiac echocardiographic images were obtained in 17 (81%) of 21 studies. The average aortic valve area (mean ± SD) determined by intracardiac echocardiogra the 13 studies in the Gorlin analysis group was 0.59 ± 0. (range 0.37 to 1.01), and the average aortic valve area dete by the Gorlin equation was 0.62 ± 0.18 cm² (range 0.31 to The average aortic valve area determined by intracardiac cardiography for the 17 studies in the continuity analysis was 0.66 ± 0.23 cm² (range 0.37 to 1.01), and that f continuity equation was 0.62 ± 0.22 cm² (range 0.34 to There was a significant correlation between the aortic valv determined by intracardiac echocardiography and the aorti area calculated by the Gorlin (r = 0.78, p = 0.002) and con equations (r = 0.82, p < 0.0001).**

Conclusions. **In the clinical setting, intracardiac echoca raphy can directly measure the aortic valve area with an ac similar to the invasive and noninvasive methods currently This study demonstrates a new, quantitative use for intrac echocardiographic imaging with many potential clinical ap tions.**

(J Am Coll Cardiol 1996;27:

In 1951, Gorlin and Gorlin introduced a formula for deriving the orifice area of a stenotic valve utilizing hemodynamic variables (1). Although this formula has undergone several revisions, the original formula continues to be widely used and is considered the "gold standard" for the determination of the aortic valve area. There are many theoretical and practical shortcomings in the use of the Gorlin equation (2–4). These shortcomings include the variability of the Gorlin constant at extremes of flow, as well as practical difficulties in obtaining an accurate cardiac output and mean transvalvular gradient.

Transthoracic echocardiography with Doppler is the standard noninvasive method for determining the aortic valv by use of the continuity equation. Although there are theoretical assumptions with the continuity equation remain practical limitations in the acquisition of accurat Validation of the continuity equation has been bas correlation with the Gorlin equation and in vitro model In spite of their theoretical and practical shortcomin Gorlin and continuity equations remain the current sta methods for determining the aortic valve orifice area.

Intracardiac echocardiography is a new technology th been used in the quantitation of left ventricular functi the morphologic evaluation of the aortic valve (9,10). In diac echocardiography may be preferable to other m that directly measure the aortic valve area, because ima obtained from within the valve. In addition, the ab perform intracardiac echocardiography in the cathete laboratory allows the acquisition of nearly simultaneo which makes a controlled comparison with the Gor continuity equations possible.

From the *Cardiovascular Division, Deaconess Hospital, and †Cardiac Ultrasound Laboratory, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts.

Manuscript received May 25, 1995; revised manuscript received August 25, 1995, accepted August 31, 1995.

Address for correspondence: Dr. Gary P. Foster, Cardiac Ultrasound Laboratory (VBK508), Massachusetts General Hospital, 32 Fruit Street, Boston, Massachusetts 02114.

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The purpose of this study was 1) to show that intracardiac echocardiography can allow direct measurement of the aortic valve area in a clinical setting in patients with moderate to severe valvular aortic stenosis, and 2) to compare the directly measured aortic valve area with the calculated aortic valve area using the Gorlin and continuity equations.

Methods

Study patients. Consecutive patients undergoing elective cardiac catheterization for the evaluation of valvular aortic stenosis were evaluated for entry into the study. Patients were not considered eligible for the study if they had mechanical prosthetic valves, hemodynamic instability or a mean gradient of <20 mm Hg, as determined by cardiac catheterization. For patients undergoing percutaneous aortic valvuloplasty the pre- and postvalvuloplasty images were analyzed separately.

Intracardiac echocardiography. Under fluoroscopic imaging, an 8F multipurpose guiding catheter was placed in the left ventricle, through which a 4.8F, 20-MHz intravascular ultrasound catheter (Sonicath, Boston Scientific) was advanced over a 0.014-in. diameter guide wire. The imaging catheter was advanced to a position 1 cm distal to the end of the guiding catheter inside of the left ventricular cavity. The guiding catheter, imaging catheter, and guidewire were then manipulated as a unit slowly back and forth across the aortic valve until the minimal cross-sectional area was optimally imaged (Hewlett-Packard Sonos 100 Intravascular Imaging System). Images were recorded using simultaneous single-lead electrocardiography on super-VHS videotapes. Immediately after intracardiac echocardiographic study was performed, data of transthoracic echocardiography and cardiac catheterization were sequentially obtained.

Cardiac catheterization. Right and left heart catheterization was performed in all patients. Cardiac output was determined by the Fick or thermodilution (valvuloplasty patients) methods. In studies using the Fick method, a metabolic rate meter (MRM-2 Oxygen Consumption Monitor, Waters Instruments) was placed and 10 readings were averaged to determine oxygen consumption. Supplemental oxygen was discontinued at least 10 min before measurement of oxygen consumption. In studies using the thermodilution method, five measurements were obtained and averaged. Left ventricular and central aortic pressures were simultaneously recorded halfway through the metabolic rate meter recordings (or halfway through the thermodilution recordings) using a dual sensor, micromanometer catheter (Millar Mikro-tip, model SPC-784A, Millar Instruments). When the micromanometer catheter was not used (cases), simultaneous left ventricular and femoral artery pressures were recorded using a fluid-filled catheter system. Blood samples were subsequently taken from the pulmonary artery and the left ventricular cavity for the determination of oxygen content.

Transthoracic echocardiography. Immediately after the determination of cardiac output and mean transvalvular pressure gradient, transthoracic echocardiography was performed (Hewlett-Packard Sonos 1500 Ultrasound Imaging System). The left ventricular outflow tract diameter was obtained from the parasternal long-axis view. Pulsed wave Doppler samples were obtained in the apical five-chamber view (12). Spectral flow velocities were recorded from the left ventricular outflow tract with care taken to avoid prevalvular flow acceleration. Continuous wave Doppler flow signals across the aortic valve were then obtained from the apical, right parasternal, and suprasternal windows with an imaging transducer and dedicated Doppler transducer. When necessary, the patient was positioned in the left lateral decubitus position to obtain optimal echocardiographic data.

Data analysis: intracardiac echocardiography. All video images were analyzed off-line. Intracardiac echocardiographic images were prospectively graded for quality: grade I = >90% of the aortic valve border seen; grade II = 75% to 90% of the aortic valve border seen; grade III = <75% of the aortic valve border seen. Grade III images were excluded from further analysis. The aortic valve area was planimetered at its maximal systolic excursion during five separate systolic intervals and averaged. Each aortic valve area was measured by two independent observers (G.P.F., N.J.W.) for the determination of interobserver variability.

Cardiac catheterization. The mean gradient was determined by direct manual planimetry of the recorded pressure tracings using a mechanical polar planimeter (Los Angeles Scientific Instrument Co.). The pressure tracings from the fluid-filled catheter group were shifted so that the downslope of the left ventricular systolic tracing was superimposed on the dicrotic notch of the aortic tracing (11). Five consecutive systolic gradients were planimetered and averaged. All patients were in sinus rhythm. The aortic valve area was calculated by the Gorlin equation (1). Patients with 2+ or greater aortic insufficiency, as determined by transthoracic echocardiography and aortography, were excluded from this part of the analysis.

Transthoracic echocardiography. The continuous and pulsed wave Doppler data and left ventricular outflow tract diameter were measured off-line. The aortic valve area was calculated using the continuity equation (5). The measurements for intracardiac echocardiography, cardiac catheterization, and transthoracic echocardiography were made independently.

Statistical methods. The aortic valve area determined by intracardiac echocardiography was compared with the aortic valve area determined by the Gorlin and continuity equations using linear regression analysis and the Bland-Altman method (13). Error was expressed as the mean difference and as the standard deviation of the difference between the aortic valve area determined by intracardiac echocardiography and the Gorlin and continuity equations. The differences between the aortic valve areas determined by intracardiac echocardiography and the Gorlin and continuity equations were also determined and analyzed as a function of cardiac output, aortic valve area, image quality, and postvalvuloplasty status using the Student t test. The Wilks-Shapiro test to determine normality was also performed for these differences. Values for

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Table 1. Mean Gradients by Catheterization and Doppler Ultrasound and Aortic Valve Areas by Gorlin Equation, Continuity Equation and Intracardiac Echocardiography

	Mean Gradient		AVA			
Pt No.	Catheterization (mm Hg)	Doppler (mm Hg)	Gorlin (cm^2)	Continuity (cm^2)	ICE (cm^2)	Clinical Characteristic
1	47	50	NA	0.42	0.54	2+ AI, fluid catheter
2	31	35	NA	0.75	1.02	3+ AI, fluid catheter, BA
3	68	28	0.81	1.06	1.01	Native AS
4	67	67	0.75	0.54	0.72	Native AS
5	63	47	0.64	0.57	0.58	Prevalvuloplasty, TD
6	37	34	0.83	0.73	0.64	Postvalvuloplasty, TD
7	49	68	0.69	0.52	0.80	Native AS
8	38	35	0.66	0.50	0.63	Prevalvuloplasty
9	24	24	0.88	0.70	0.68	Postvalvuloplasty
10	63	53	NA	0.86	1.04	2+ AI, native AS
11	57	52	0.36	0.57	0.42	Native AS
12	34	31	0.31	0.34	0.38	Prevalvuloplasty, TD
13	23	23	0.45	0.38	0.41	Postvalvuloplasty, TD
14	22	35	0.70	0.49	0.52	Native AS
15	64	64	0.54	0.44	0.43	Native AS
16	46	45	0.45	0.67	0.49	Native AS, fluid catheter
17	36	20	NA	1.06	1.00	2+ AI, native AS
Mean ± SD*	45 ± 16	42 ± 15	0.62 ± 0.18†	0.62 ± 0.22	0.66 ± 0.23 0.59 ± 0.18†	

*Excluding grade III data. †For 13 patients in the Gorlin analysis group. AI = aortic insufficiency; AS = aortic stenosis; BAV = bioprosthetic aortic va NA = not applicable; Pt = patient; TD = cardiac output by thermodilution.

aortic valve area are expressed as the mean value ± SD (range). A p value <0.05 was considered significant.

Interobserver variability for the measurements of intracardiac echocardiographic images was determined by two independent observers. Linear regression analysis and the standard deviation of the difference were used to compare each observer's measurements.

Results

Seventeen patients with varying degrees of aortic stenosis met inclusion criteria and comprised the study group (mean age 71 years, range 40 to 86; 10 men, 7 women). Four patients underwent intracardiac echocardiographic imaging before and after aortic valvuloplasty. Of the 21 studies performed, intracardiac echocardiographic images of sufficient quality for analysis (grades I and II) were obtained in 17 (81%) (Table 1). Poor quality images (grade III) were obtained in four studies (19%). No easily identifiable features, such as aortic valve area by Gorlin or continuity, cardiac output, mean transvalvular gradient or postvalvuloplasty status, were predictive of poor image quality. Significant aortic insufficiency was present in four patients who were removed from analysis in the Gorlin group. Of the patients with adequate intracardiac echocardiographic images, four had cardiac outputs determined by the thermodilution technique and three had mean transvalvular gradients determined by fluid-filled catheters.

The average aortic valve area determined by intracard echocardiography for the 13 patients in the Gorlin analy group was 0.59 ± 0.18 cm^2 (range 0.37 to 1.01 cm^2), a by the Gorlin equation, 0.62 ± 0.18 cm^2 (range 0.31 0.88 cm^2). The average aortic valve area determined intracardiac echocardiography for the 17 studies in continuity analysis group was 0.66 ± 0.23 cm^2 (range 0.37 1.04 cm^2), and by the continuity equation, 0.62 ± 0.19 c (range 0.34 to 1.06 cm^2). The aortic valve area determin by intracardiac echocardiography underestimated the ao valve area determined by the Gorlin equation by an aver of 5.1%. The aortic valve area determined by intracard echocardiography overestimated the aortic valve area de mined by the continuity equation by an average of 6. Intracardiac echocardiographic images of two stenotic a tic valves with planimetry of the aortic valve areas are sho in Figure 1.

There were significant correlations between the ao valve area determined by intracardiac echocardiography the Gorlin and continuity equations (Table 2, Fig. 2 and

The mean difference between aortic valve area measu ments obtained from intracardiac echocardiography and Gorlin equation was analyzed as a function of cardiac out aortic valve area (by intracardiac echocardiography), im quality and postvalvuloplasty status, and no statistically sig icant trends were found.

Interobserver variability, determined by two independ observers, of aortic valve area measurements obtained fr

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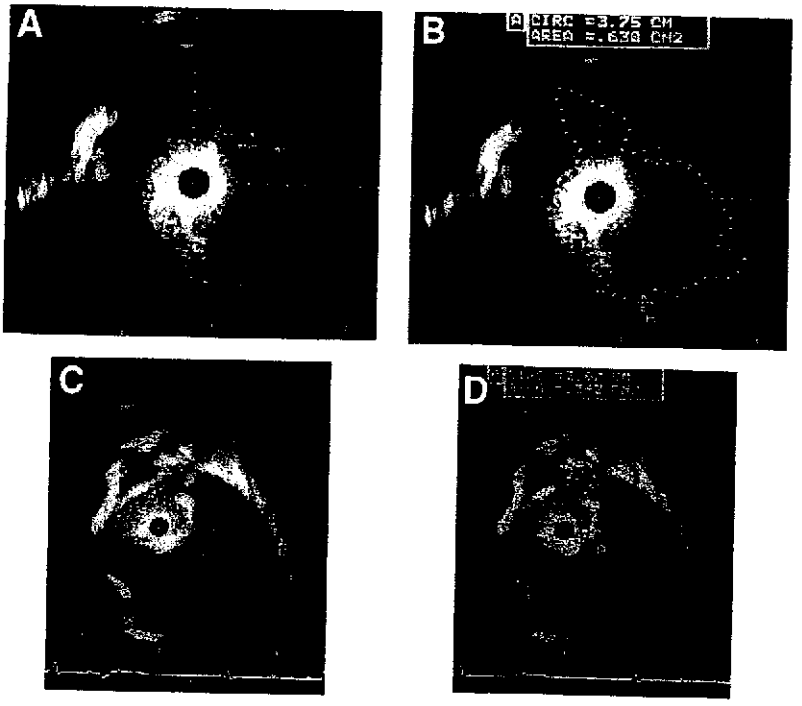

1. Intracardiac echocardiographic images of (A, C) tative stenotic aortic valves and (B, D) the same aortic valves with the planimetered areas demon-

diac echocardiography revealed a close correlation 97, $p < 0.001$, standard deviation of the difference =).

Discussion

ians largely rely on the combination of symptoms and a in the management of patients with valvular aortic To this end, an accurate method of determining the ive area would be clinically useful.

tations of current standards. The currently used inva- ndard—the Gorlin equation—has been extensively r the past four decades and has proved to be prog- ly valuable. However, the Gorlin equation has many scribed theoretical and practical limitations (2,3). The uses a constant that is inaccurate in low flow states assumes a single coefficient of discharge and contrac- a range of valve morphologies. In addition, the uation requires data that are difficult to acquire y, such as oxygen content, oxygen consumption and nsvalvular gradient. In spite of the equation's wide- ceptance and use, it has been inadequately validated inical setting (2).

urrently used noninvasive standard—the continuity —has been extensively compared with the Gorlin n and has been validated in several in vitro hemo- models (5–8). Although the continuity equation theoretical considerations, it has many practical ns in data acquisition. The major theoretical con- n is that the continuity equation (like the Gorlin equation) determines the cross-sectional area at the vena contracta. This is the cross-sectional area to which flow is confined by the stenotic orifice, which, by definition, is smaller than the actual orifice area. A major technical limitation with accurate data acquisition is in the measurement of the left ventricular outflow tract diameter. Inaccuracies in the measurement of the left ventricular outflow tract diameter are magnified when the value is squared to calculate the left ventricular outflow tract area. In addition, accurate Doppler samples are often difficult to obtain, especially in older patients with ectatic aortas and poststenotic dilation. If the Doppler samples are not obtained in the same direction of flow, an underestimation of the velocities will be made (12). Prevalvular flow acceleration and nonuniform left ventricular outflow tract flow velocities are additional sources of error that may be introduced into the continuity calculation (14). Like all indirect methods, the continuity equation has been incompletely validated in the clinical setting owing to difficulty in obtaining direct measurements for comparison.

Direct imaging and measurement of aortic valve area. An ideal method of determining the aortic valve area is by direct measurement. Direct measurement overcomes many of the practical and theoretical shortcomings associated with indirect methods. From a practical standpoint, direct measurements have a single parameter rather than the many necessary for the indirect methods; thus, there is less introduction of variability. Direct measurements of the mitral valve area by transthoracic echocardiography are well established and have been validated in vitro (15,16). Direct measurement of the aortic valve area by transthoracic echocardiography is difficult owing to the degradation of image quality caused by heavy calcification as well as

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Table 2. Intracardiac Echocardiographic Correlations

Equation	Correlation Coefficient (r)	p Value	Mean Difference (cm^2)	SD of Differences (cm^2)
Gorlin	0.78	0.002	0.03	0.12
Continuity	0.82	<0.0001	0.04	0.13

the limitations of resolution in the range of the area being measured.

Other methods of directly measuring the aortic valve area have been successful compared with the Gorlin and continuity equations. Computed tomography, magnetic resonance imaging, and transesophageal echocardiography have demonstrated good correlations with either the Gorlin or continuity equations; however, these comparisons were generally nonsimultaneous, with small patient numbers (17–22).

Compared with other methods, intracardiac echocardiography has many advantages in directly measuring the aortic valve area. Intracardiac echocardiography has proved to be accurate in the quantitative determination of left ventricular volumes and the qualitative evaluation of the aortic valve (9,10). Other studies utilizing catheter-based ultrasound imaging techniques have also demonstrated a high degree of accuracy in the measurement of cardiac dimensions (9,23–28). In the current study, we had no difficulty in measuring aortic valve areas <0.4 cm^2. This ability to measure a small orifice is probably the result of high near-field resolution as well as positioning the transducer within the valvular orifice. Imaging from within the valve causes less shadowing of the orifice from calcified leaflets, resulting in improved definition of the orifice edges.

Computed tomography and magnetic resonance imaging ca not be performed simultaneously with cardiac catheterizati making an accurate comparison with indirect methods diffic Additionally, computed tomography and magnetic resonan imaging probably lack the temporal resolution needed accurately distinguish the rapid changes in aortic valve ar which occur throughout the cardiac cycle. Transesophage echocardiography could potentially be used as an alternati method of determining the aortic valve area; however, a la number of these patients also require coronary angiograp As such, this strategy would likely necessitate an additional t with the associated risks and patient discomfort. Becau intracardiac echocardiography is catheter based, it can easily performed in conjunction with cardiac catheterizati with no additional patient discomfort.

Results of current study. This study demonstrated t feasibility of directly measuring the aortic valve area usi intracardiac echocardiography, with successful imaging in 8 of the studies. There were no complications and the additio time required in each case for intracardiac echocardiograp imaging was minimal.

Sources for the discrepancies seen between the aortic va area determined by intracardiac echocardiography and t Gorlin and continuity equations are probably the result inaccuracies in each of the three methods. The directly m sured aortic valve area underestimated the aortic valve a derived by the Gorlin equation by an average of 5.1%. Fac in the Gorlin equation that may account for a portion of discrepancy between the two groups include inaccuracies in acquisition of oxygen content, oxygen consumption and m pressure gradient. As the Gorlin equation calculates the a

Figure 2. Correlation plot of the aortic valve area derived from the Gorlin equation compared with the aortic valve area determined by intracardiac echocardiography (ICE). **Dashed line** = regression line; **solid line** = line of identity.

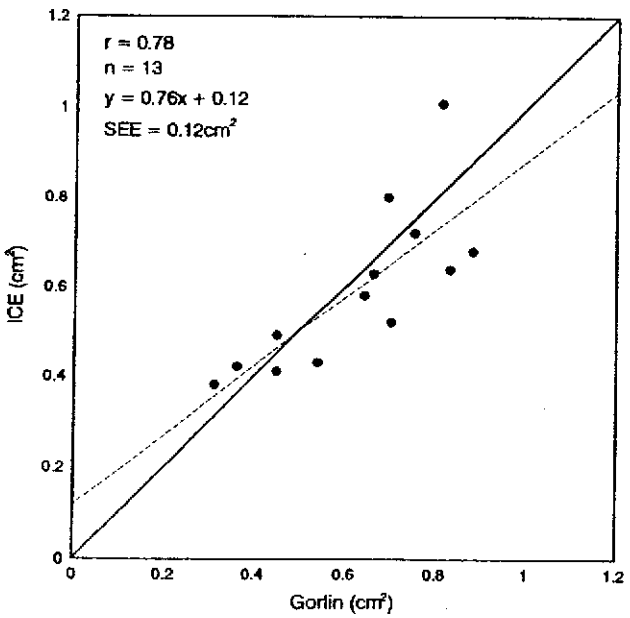
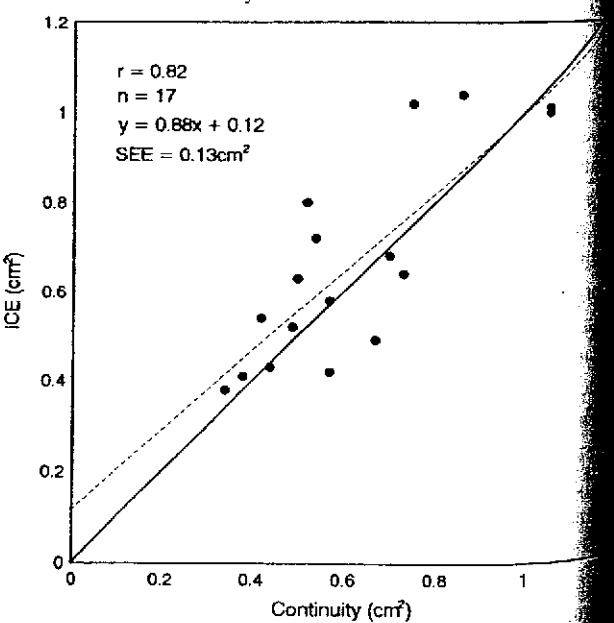


Figure 3. Correlation plot of the aortic valve area derived from continuity equation compared with the aortic valve area determine intracardiac echocardiography (ICE). **Dashed line** = regression **solid line** = line of identity.



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the vena contracta, an underestimation of the directly measured area would theoretically be expected. Because there was no statistical difference between the two sets of data, a larger study will probably be necessary to test this theoretical concern. No relationship was found when the mean difference between the aortic valve area determined by intracardiac echocardiography and the Gorlin equation was analyzed as a function of cardiac output or valve area.

The directly measured aortic valve area overestimated the continuity-derived aortic valve area by 6.2%. Like the Gorlin equation, the continuity equation calculates the effective aortic valve area, which, by definition, is smaller than the actual orifice area. This may theoretically explain the systematic underestimation seen in the present study. Another possible explanation for the overestimation seen by direct measurement is that the values obtained for the continuity equation used the velocity integrals, which calculate the mean aortic valve area throughout the systolic period, as opposed to direct measurement in which the maximal aortic valve area during systolic period was used. However, when the mean difference between the aortic valve area determined by intracardiac echocardiography and the aortic valve area calculated by the continuity equation was analyzed as a function of cardiac output or valve area, no relationship was found.

Another possible source of discrepancy is due to inaccurate imaging of the true aortic valve area by intracardiac echocardiography. Off-axis imaging of the orifice may have contributed to error by overestimating the true aortic valve area. Image foreshortion due to nonuniform transducer rotation may have caused an overestimation of aortic valve area measurements. The exact maximal excursion of the aortic leaflets may have been missed owing to the temporal resolution of the video system (one updated image every 33 ms). In addition, the complex three-dimensional shape of certain orifices made accurate planimetry in a single two-dimensional plane difficult. Rapid movement of the imaging transducer within the aortic orifice during systole made optimal imaging of the leaflet tips challenging in certain cases. In spite of these possible sources of error, good correlation and agreement between the aortic valve area determined by intracardiac echocardiography and the aortic valve area calculated by the Gorlin and continuity equations were found.

Clinical implications and conclusions. In this study, the feasibility of using intracardiac echocardiography to measure aortic valve area directly in a clinical setting was established. The correlation and agreement between intracardiac echocardiography and the standard methods for determining aortic valve area demonstrate the relative accuracy of this technique. Given the limitations and indirect nature of the Gorlin and continuity equations, this study was unable to define the "true" accuracy of intracardiac echocardiographic measurements. Additionally, intracardiac echocardiography provided the first nearly simultaneous comparison of the Gorlin and continuity equations with a directly measured aortic valve area in a clinical setting. Further study with direct measurements of the aortic valve area in a larger population of patients with valvular aortic stenosis is necessary to evaluate the entire range of clinical situations, for example, in the patient with a low cardiac output and a low mean gradient in the presence of apparently severe aortic stenosis. One such patient was included in the current study and intracardiac echocardiography proved useful in defining the severity of valvular stenosis. Intracardiac echocardiography performed in conjunction with provocative maneuvers, such as inotropic stimulation, would presumably reveal changes in the orifice size and be useful in determining the etiology of clinical symptoms in this setting (29). Intracardiac echocardiography may also prove useful in the evaluation and guidance of percutaneous aortic valvuloplasty procedures. Thus, this study demonstrates a new, quantitative use for intracardiac echocardiographic imaging with many potential clinical applications.

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Kenichi Fujii, Gary S. Mintz, Yoshio Kobayashi, Stéphane G. Carlier, Hideo Takebayashi, Takenori Yasuda, Issam Moussa, George Dangas, Roxana Mehran, Alexandra J. Lansky, Arlene Reyes, Edward Kreps, Michael Collins, Antonio Colombo, Gregg W. Stone, Paul S. Teirstein, Martin B. Leon and Jeffrey W. Moses

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Contribution of Stent Underexpansion to Recurrence After Sirolimus-Eluting Stent Implantation for In-Stent Restenosis

Kenichi Fujii, MD; Gary S. Mintz, MD; Yoshio Kobayashi, MD; Stéphane G. Carlier, MD, PhD; Hideo Takebayashi, MD; Takenori Yasuda, MD; Issam Moussa, MD; George Dangas, MD, PhD; Roxana Mehran, MD; Alexandra J. Lansky, MD; Arlene Reyes, MD; Edward Kreps, MD; Michael Collins, MD; Antonio Colombo, MD; Gregg W. Stone, MD; Paul S. Teirstein, MD; Martin B. Leon, MD; Jeffrey W. Moses, MD

Background—We used intravascular ultrasound (IVUS) to evaluate recurrence after sirolimus-eluting stent (SES) implantation treatment of in-stent restenosis (ISR).

Methods and Results—Forty-eight ISR lesions (41 patients with objective evidence of ischemia) were treated with SES. Recurrent ISR was identified in 11 lesions (all focal); repeat revascularization was performed in 10. These were compared with 16 patients (19 lesions) without recurrence as documented by angiography. Nine of 11 recurrent lesions had a minimum stent area (MSA) <5.0 mm^2 versus 5 of 19 nonrecurrent lesions ($P=0.003$); 7 of 11 recurrent lesions had an MSA <4.0 mm^2 versus 4 of 19 nonrecurrent lesions ($P=0.02$); and 4 of 11 recurrent lesions had an MSA <3.0 mm^2 versus 1 of 19 nonrecurrent lesions ($P=0.03$). A gap between SESs was identified in 3 of 11 recurrences versus 1 of 19 nonrecurrent lesions.

Conclusions—Stent underexpansion is a significant cause of failure after SES implantation treatment of ISR. (***Circulation.* 2004;109:1085-1088.**)

Key Words: ultrasonics ■ restenosis ■ stents

Although coronary stenting has reduced restenosis compared with conventional balloon angioplasty, in-stent restenosis (ISR) remains an important problem.[1,2] Sirolimus is a macrocyclic lactone that inhibits cytokine-mediated and growth factor–mediated proliferation of lymphocytes and smooth muscle cells, reducing neointimal hyperplasia.[3] Previous randomized trials have shown that sirolimus-eluting stents (SESs) strongly suppress neointimal hyperplasia and prevent target-lesion revascularization in de novo lesions.[4,5] However, efficacy of SES treatment of ISR is less certain.[6,7] The present report summarizes clinical and intravascular ultrasound (IVUS) findings of patients with ISR treated with SES.

Methods

The present IVUS analysis was a single-center (Lenox Hill Hospital) substudy of SECURE (Sirolimus-Eluting BX Velocity Balloon-Expandable Stent in a Compassionate Use REgistry), a multicenter, open-label, prospective study of high-risk lesions. Forty-eight consecutive ISR lesions (41 patients) treated with SES (Cypher, Cordis) in whom IVUS was performed after restenting and/or at follow-up were enrolled in this substudy. This study was approved by the Institutional Review Board; written informed consent was obtained from all patients.

ISR was defined as $>50\%$ diameter stenosis by quantitative coronary angiography within a previously stented vessel and classified as suggested by Mehran et al.[8] All SESs were implanted according to standard clinical practice (with or without predilation) with maximum balloon pressures of ≥ 14 atm. Fifty-five SESs (1.8/lesion) were implanted; mean stent length was 30.1 ± 21.9 mm. Eighteen lesions were treated with 1 stent, 6 with 2 stents, 1 with 3 stents, and 5 with ≥ 4 stents.

Procedural success was residual stenosis $<30\%$ by quantitative coronary angiography with Thrombolysis In Myocardial Infarction (TIMI) flow grade 3. Quantitative coronary angiography was performed with computer-assisted automated edge-detection (CMS, MEDIS) by an independent observer who was unaware of the clinical and IVUS findings.

A dedicated Data Coordinating Center performed all data management and analysis. Prespecified clinical and laboratory demographic information was obtained from hospital charts.

IVUS Imaging and Analysis

IVUS imaging was performed with a commercially available mechanical sector scanner (Boston Scientific) that incorporated a 40-MHz single-element beveled transducer that rotated at 1800 rpm. All IVUS studies were performed after 100 to 200 μg of intracoronary nitroglycerine was administered. The ultrasound catheter was advanced >10 mm beyond the lesion, and an imaging run was performed to a point 10 mm proximal to the lesion with motorized transducer pullback at 0.5 mm/s. Data were recorded onto 0.5-inch high-resolution super-VHS videotape for offline analysis.

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Quantitative volumetric IVUS analysis was performed by computerized planimetry (TapeMeasure, Indec Systems) by an independent experienced observer who was unaware of the clinical data. Postinterventional and/or follow-up stent and intimal hyperplasia (stent minus lumen) cross-sectional areas were measured every 1 mm. In proximal and distal reference segments, external elastic membrane, lumen, and plaque and media (external elastic membrane minus lumen) cross-sectional area and plaque burden (plaque and media divided by external elastic membrane) were measured. The proximal and distal reference segments were the least-diseased image slices (largest lumen with least plaque) proximal and distal to the lesion but within the same segment and before any major side branch. Residual edge stenosis was defined as stent edge plaque burden >50%.[9] A gap between stents was the absence of stent struts in at least 1 IVUS cross section in the region between multiple stents.[9]

Continuous variables were expressed as mean±1 SD and compared by unpaired Student's t test. Categorical variables are presented as number (%) and compared with χ^2 statistics. $P<0.05$ was considered significant.

Results

Coronary angiography was performed >30 days after SES implantation in 27 patients (30 lesions), which was motivated by angina or positive stress test in 14 patients and scheduled follow-up in 13 asymptomatic patients. Baseline clinical and angiographic findings and postprocedural IVUS findings are presented in Table 1. Procedural success was obtained in 29 (97%) of 30 lesions.

Recurrent ISR was identified in 11 lesions (11/30, 37%), with a mean time to recurrence of 200±74 days. Individual patient and lesion information is listed in Table 2. There was no significant difference in patient characteristics or baseline Mehran classification between recurrent and nonrecurrent lesions. The recurrent ISR pattern was focal in 7 and multifocal in 4; 5 of these were focal and 6 were diffuse at the time of SES implantation. Seven recurrences were intrastent; 2 were at the proximal edge, and 2 were at the distal edge. Recurrence lesion length was significantly shorter than at pre-SES implantation (5.8±1.8 versus 14.6±8.0 mm, $P<0.001$).

Stent underexpansion was more common in recurrent lesions than in nonrecurrent lesions despite the use of high inflation pressures at the time of implantation (18±4 atm). Nine (82%) of 11 recurrent lesions had a minimum stent area (MSA) <5.0 mm^2 versus 5 (26%) of 19 nonrecurrent lesions ($P=0.003$). Seven (64%) of 11 recurrent lesions had an MSA <4.0 mm^2 versus 4 (21%) of 19 nonrecurrent lesions ($P=0.02$). Four (36%) of 11 recurrent lesions had an MSA <3.0 mm^2 versus 1 (5%) of 19 nonrecurrent lesions ($P=0.03$).

A gap between SESs was detected in 3 recurrent lesions, 1 by retrospective analysis of the IVUS performed at SES implantation and 2 by analysis of the follow-up IVUS. Only 1 nonrecurrent lesion had a gap. In these 4 cases, the SES gap was not detectable angiographically, and it measured <1 mm in length by IVUS.

Among patients with recurrent ISR, the 1 asymptomatic patient did not undergo repeat revascularization. One patient underwent bypass graft surgery because of recurrent ISR and progression of other lesions. Nine patients underwent percutaneous revascularization; 4 patients were treated with balloon angioplasty, 1 with cutting balloon, 1 with γ-irradiation, and 3 with additional SESs. One patient, an 82-year-old female with insulin-treated diabetes, died 2 months after successful implantation of another SES.

TABLE 1. Baseline Clinical and Angiographic Characteristics and Postprocedural IVUS Findings

Characteristics	Values
Age, y	61.5±13.0
Male, n (%)	20 (74.1)
Diabetic, n (%)	6 (22.2)
Radiation failure, n (%)	18 (66.7)
Saphenous vein graft, n (%)	4 (13.3)
Angiography	
Lesion length, mm	16.2±8.6
Reference, mm	2.75±0.34
Preintervention MLD, mm	0.65±0.32
Postintervention MLD, mm	2.75±0.31
Mehran ISR classification, n (%)	
IA (gap)	0 (0)
IB (margin)	1 (3.3)
IC (focal body)	7 (23.4)
ID (multifocal)	7 (23.4)
II (diffuse intrastent)	2 (6.6)
III (proliferative)	11 (36.7)
IV (total occlusion)	2 (6.6)
IVUS	
MSA, mm^2	4.9±2.0
Average reference lumen CSA, mm^2	6.8±2.2
Persistent margins	
Distal lumen CSA, mm^2	5.7±2.2
Distal EEM CSA, mm^2	8.9±4.0
Distal plaque burden, %	36±15
Proximal lumen CSA, mm^2	8.2±2.9
Proximal EEM CSA, mm^2	13.7±5.6
Proximal plaque burden, %	40±19
Residual edge stenosis, n (%)	9 (30.0)
Gap between stents, n (%)	4 (13.3)

MLD indicates minimum lumen diameter; CSA, cross-sectional area; and EEM, external elastic membrane.

Discussion

The results of SES implantation to treat ISR are less impressive than de novo stent implantation. This report describes patients with ISR treated with SES implantation and compares the group with a successful result versus those cases who developed recurrent restenosis.

A recent IVUS study showed that an MSA <5.0 mm^2 was the optimal threshold to predict target-lesion revascularization 8 months after treatment of de novo lesions with SESs.[10] The predictive accuracy of this cutoff was 90%,

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TABLE 2. Individual Clinical, Procedural, and Angiographic Characteristics and IVUS Findings

	Patient No.											
	1	2	3	4	5	6	7	8	9	10	11	Total
Age, y	37	66	57	52	83	44	62	71	74	62	38	61±14
Gender	F	M	F	M	M	M	M	M	M	M	F	80% M
Symptoms	SA	SA	SA	SA	SA	SA	SA	SA	SA	SA	SA	
Diabetes	+	+	+	0	0	0	0	0	0	0	0	30%
Vessel	LCx	LM	RCA	LAD	SVG	LCx	DG	LAD	LCx	LAD	RCA	
Radiation failure	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	73%
Mehran classification	ID	IC	ID	III	II	IC	ID	III	ID	III	IC	...
Ostial	No	No	No	No	Yes	Yes	No	No	No	No	Yes	27%
No. of SESs	2	1	3	5	1	1	1	3	4	5	1	2.5±1.6
Total SES length, mm	35	18	54	55	8	18	18	47	76	96	18	40±28
Final balloon, mm	3.5	3.0	3.5	2.5	4.0	3.0	2.75	4.0	3.0	3.0	3.5	3.3±0.5
Postdilation with balloon ≥0.5 mm larger than SES	Yes	No	Yes	No	Yes	Yes	No	Yes	No	No	No	45%
Maximum inflation pressure, atm	16	18	20	28	14	16	20	14	16	18	20	18±3.9
IVUS	P	P/F	P	P/F	P	P	P/F	P/F	F	F	P	...
Residual edge stenosis	No	No	No	No	Yes	No	No	Yes	NA	NA	No	22%
Gap between stents	No	No	Yes	Yes	No	No	No	No	No	Yes	No	27%
MSA, mm^2	3.17	5.96	4.66	2.73	8.24	4.19	3.69	2.58	2.41	2.68	3.53	3.9±1.8
Follow-up IH area, mm^2	NA	3.68	NA	2.67	NA	NA	1.61	0.81	1.01, 1.57	3.97, 0.79, 1.67	NA	2.0±1.2
Follow-up												
Interval, d	72	286	234	137	186	150	133	175	284	272	275	200±74
Symptoms	UA	SA	SA	UA	SA	UA	SA	None	SA	SA	SA	...
Location of recurrence	Distal	In-stent	In-stent	In-stent	In-stent	Prox	In-stent	Distal	In-stent	Prox	In-stent	...
Mehran classification	ID	IC	ID	IA	IC	IB	IC	IB	ID	ID	IB	...
Treatment	CABG	PCI	PCI	PCI	PCI	PCI	PCI	0	PCI	PCI	PCI	...

F indicates female; M, male; SA, stable angina; LCx, left circumflex artery; LM, left main artery; RCA, right coronary artery; LAD, left anterior descending coronary artery; SVG, saphenous vein graft; DG, diagonal; P, post-SES; F, follow-up; NA, not available; IH, intimal hyperplasia; UA, unstable angina; Prox, proximal; and PCI, percutaneous intervention.

which indicates that SES underexpansion was the main reason for ISR. In the present study, 9 of 11 recurrences occurred in lesions with MSA <5.0 mm^2 despite the use of high inflation pressure (18±4 atm). In these, even a small amount of neointimal growth may compromise the lumen and lead to recurrent symptoms. Although aggressive stent expansion may not be necessary with SES, the present results indicate that adequate stent dimensions are still important. Thus, in selected patients, even higher inflation pressures may be needed (ideally, before SES implantation and controlled with IVUS guidance) to achieve a minimum acceptable stent area.

In 3 patients with recurrent lesions, IVUS identified a gap between multiple SESs. We speculate that sirolimus does not diffuse substantially from the edge of the stent to have a biological effect in the gap. Therefore, when ISR is treated with SES, it may be important to cover the entire length of previously implanted stents. This has been noted by others.[6,9]

Study Limitations

This is a small observational study. Follow-up angiograms and IVUS were not performed in all patients, and in 2 patients, IVUS was performed only at follow-up. However, previous IVUS studies have shown that stent dimensions do not change over time[11]; thus, stent areas at follow-up should be an accurate reflection of stent areas immediately after SES implantation.

Conclusions

Focal recurrence after SES treatment of ISR was observed in 25% of patients. IVUS showed that stent underexpansion, in particular, was associated with failure of SES implantation for the treatment of ISR.

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Information for Manufacturers Seeking Marketing Clearance of Diagnostic Ultrasound Systems and Transducers

This document is intended to provide guidance in the preparation of a regulatory submission. It does not bind the FDA or the regulated industry in any manner.

Computed Imaging Devices Branch
Division of Reproductive, Abdominal,
Ear, Nose, Throat and Radiological Devices
Office of Device Evaluation

Document Issued on September 30, 1997

While this guidance document represents a final document, comments and suggestions may be submitted at any time for Agency consideration by writing Robert A. Phillips, Ph.D., Center for Devices and Radiological Health, HFZ-470, 9200 Corporate Blvd., Rockville, MD 20850. For questions regarding the use or interpretation of this guidance, contact Robert Phillips at 240-276-3666 or by e-mail at RobertA.Phillips@fda.hhs.gov. This guidance replaces *Revised 510(k) Diagnostic Ultrasound Guidance for 1993* that was issued on February 17, 1993 .

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

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f) instructions for use,

g) summaries of clinical studies and

h) references.

4.8.1.1 Indications for use, contraindications, warnings, and precautions should be clearly stated. This includes (but is not limited to):

a) a precaution to perform a given ultrasound procedure prudently using the principle of ALARA (as low as reasonably achievable);

b) a statement, where applicable, cautioning that the device is "not intended for fetal use" (either in the operator's manual, individual transducer manuals, or on-screen labeling); and

c) a description of the means used to limit the surface heating of **invasive probes** to no more than 43 C in the event of a device malfunction.

At present, you may not promote or market your device for use in the following clinical applications:

- percutaneous umbilical blood sampling (PUBS)
- *in vitro* fertilization (IVF)

Specific diagnostic claims must be supported by appropriate data.

For new clinical or technological changes, it is advisable to check with the Office of Device Evaluation for guidance on the data necessary to support such changes.

4.8.1.2 Clinical instructions for the use of the device should be provided in either the system or transducer operator's manual. Indications for use should be specified.

4.8.1.3 Identify the device's compatible device accessories, kits and components in the operator's manuals. Provide the specifications for these accessories. Where use of probe sheaths is recommended, the user should be referred to FDA's Medical Alert on latex products (FDA 1991).

4.8.1.4 Provide the accuracy of each clinical measurement possible with the device and the range over which this accuracy can be expected to be maintained.

NOTE: The accuracy range possible for Doppler applications cannot exceed the range measured under 4.7.1.2.

4.8.1.5 Provide draft acoustic output labeling in the operator's manual, per Sec. 5.2 (Track 1) or Sec. 6.2 (Track 3).

4.8.1.6 Provide instructions for care of the device between uses, including storage, cleaning, disinfection, and sterilization of all components, as appropriate.

a) Labeling should recommend the use of sterile, when appropriate, market-cleared probe sheaths, for clinical applications of a semi-critical or critical nature (i.e., intraoperative, transrectal, transvaginal, transesophageal, biopsy procedures).

b) When recommending a procedure that uses a cleared liquid disinfecting or sterilizing agent, refer the user to the labeling instructions provided by the manufacturer of that product. At least one recommended procedure should use a cleared agent, if feasible. The ultrasound manufacturer will not need to validate these processes if they refer the user to the manufacturer's instructions.

c) When recommending a procedure other than liquid disinfection or sterilization, detailed instructions should be provided. These procedures should have been

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Appendix I: Slides from the presentation

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Percutaneous Circulatory Support During High-Risk PCI: A Multicenter Experience With Impella

JPS. Henriques[1], KD. Sjauw[1], PL. Danna[2], M. Viecca[2], C. Butter[3], HH. Minden[3], G. Pedrazzini[4], D. Wagner[5], S. Kerber[6], R. Schamberger[6], T. Engstrom[7], C. Hassager[7], J. Schofer[8], D.G. Mathey[8], T. Konorza[9], R. Erbel[9], K. Benali[10]

[1]Academic Medical Center, Amsterdam (Netherlands), [2]Sacco Hospital, Milano (Italy), [3]Heart Center Brandenburg in Bernau, Berlin (Germany), [4]Cardiocentro Ticino, Lugano (Switzerland), [5]Centre Hospitalier Luxembourg (Luxembourg), [6]Herz- und Gefäß-Klinik, Bad Neustad (Germany), [7]University Hospital of Copenhagen (Denmark), [8]Center for Cardiology and Vascular Intervention, Hamburg (Germany), [9]Universitat Klinikum Essen (Germany), [10]Abiomed, Danvers (USA)

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Study Objective

- ❑ Assess safety and feasibility of the use of Impella in the Cath-Lab
- ❑ In the largest European multicenter cohort using Impella LP2.5

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Methods

- Retrospective multicenter single arm study
- 9 participating centers in 6 European countries
- Total of N=109 patients undergoing PCI
- Circulatory support initiated with Impella LP2.5 in elective, urgent or emergent situations

- Safety and feasibility assessment based on:
  - Patient population profile
  - 30-day outcome
  - Adverse event rates

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Study Patients (N=109)

Patient Characteristics	Mean ± SD or %
Age (yrs)	72 ± 10
Age > 60 year old	88 %
Gender (Male in %)	80 %
BSA (m^2)	1.89 ± 0.2
BMI (Kg/ m^2)	26.2 ± 4.7
LVEF (%)	27 ± 10
LVEF <35% (%)	85 %
Non surgical candidate (Pt condition, Pt choice)	51 %
LMCA or last patent vessel	62 %
PCI Procedure (N=104, 5 were unknown):	
• Elective (n=80)	77 %
• Urgent (n=11)	11 %
• Emergent (n=13)	12 %

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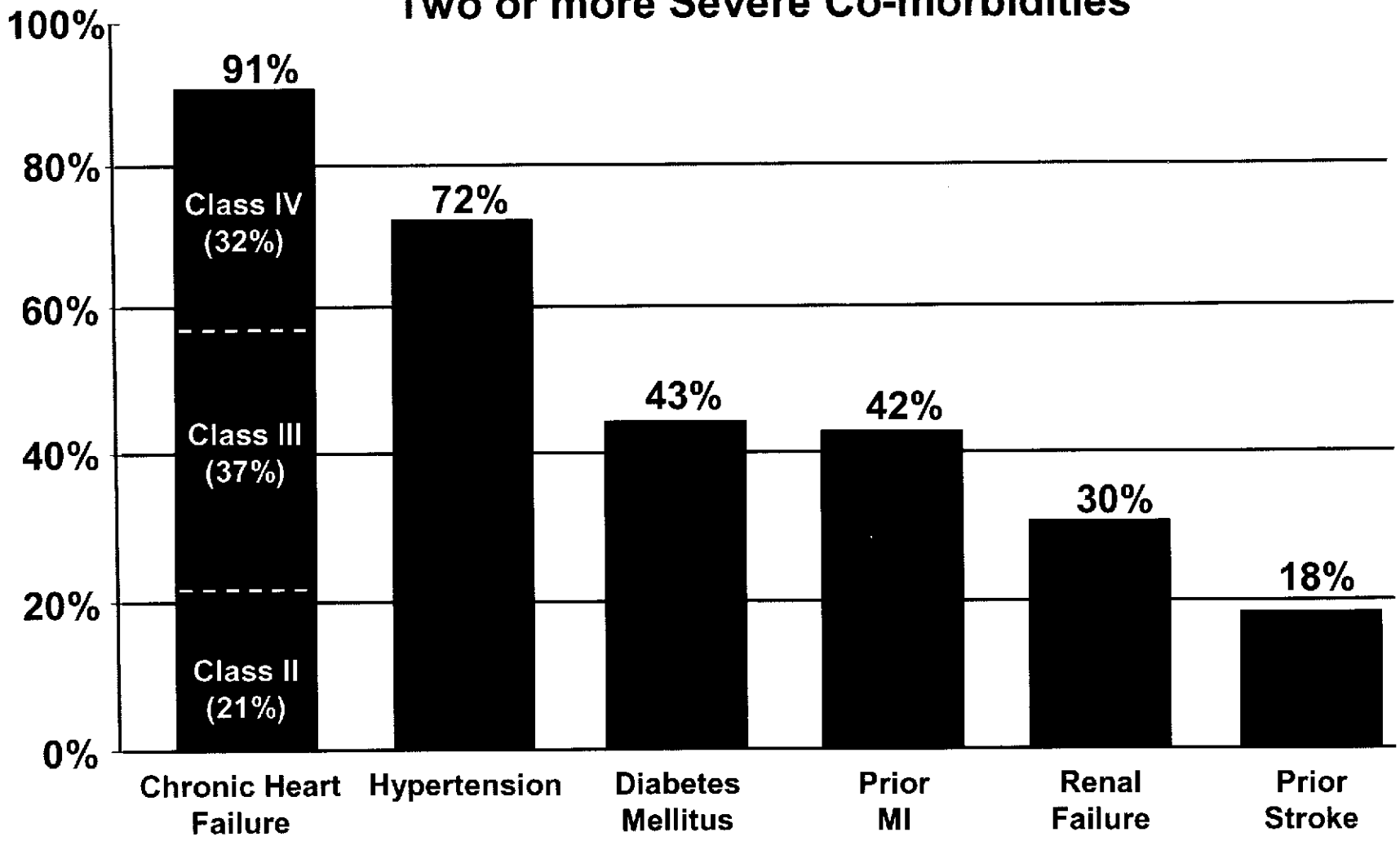
Study Patients (N=109)

~90% of the Patients Presented With Two or more Severe Co-morbidities



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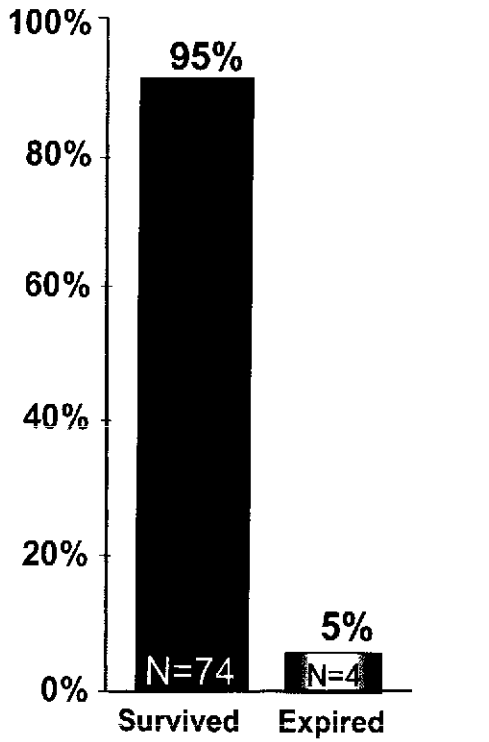
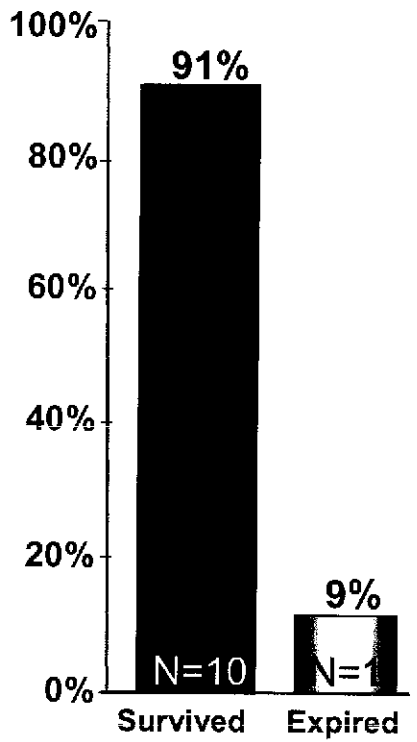
30-day Survival With Heart Recovery (N=101*)



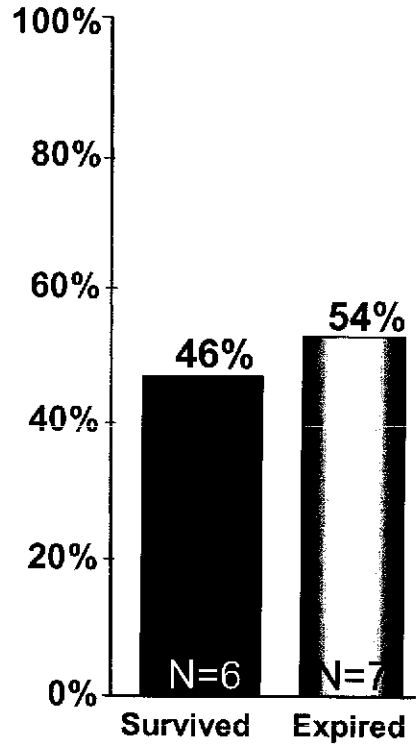
Elective High Risk PCI

Expected Mortality
10% to 15%**



Urgent PCI
(Pre-Shock NSTEMI)

Expected Mortality
Greater than 20%***



Emergent PCI
(Profound Cardiogenic Shock STEMI)

Expected Mortality
Greater than 80%****

**N=101 of 109 had 30-day outcome and PCI information available by the time of data collection*

*** Shreiber TL (1998); Vogel R et al. (2003), Sedlis SP et al (2004); STS and Euroscore Online Risk Calculators for similar patient population profile*
**** Klein LW et al. (2005); Kar B et al. (2006); Mehta RH et al. (2007), Burkhoff et al. (2006)*

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Low Event Rates (N=109)

In-hospital Adverse Event	n (%)
In hospital MACE:	
• Intra-procedural death	0 (0%)
• In-hospital Death (primary cause = Multi-organ failure)	12 (11%)
• Stroke	0 (0%)
• Emergency CABG	1 (1%)
• Myocardial Infarction	1 (1%)
Other In-hospital Adverse Events	
• Aortic valve injury	0 (0%)
• Bleeding (GI or ipsi/contralateral site) requiring transfusion	9 (8%)
• Mild/moderate bleeding without blood transfusion	7 (6%)
• Vascular complications (including non-device related)	10 (9%)
• Renal failure (contrast induced)	4 (4%)
• Sepsis (Impella groin)	1 (1%)
• Device malfunction	0 (0%)

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Summary

This multicenter retrospective study confirms:

Ease of use, safety and feasibility of Impella LP2.5 for elective, urgent and emergent circulatory support in the Cath-Lab

Studies warranted to expand the spectrum of clinical applications

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Appendix J: Echocardiograph Core Lab Analysis

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Appendix K: Revised 510(k) Summary

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Appendix L- Updated 510(k) Summary
(Prepared in accordance with 21 CFR Part 807.92)

a. Submitted

Applicant Name:	ABIOMED, Inc. 22 Cherry Hill Drive, Danvers, MA 01923
Contact Person:	Robert T.V. Kung, Ph.D.
Date Summary Prepared:	June 14, 2007

b. Device Information

Trade Name:	IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System
Common Name:	Percutaneous Cardiac Support System
Classification Name:	Pump, Blood, Cardiopulmonary Bypass, non roller type (classified under 870.4360) Catheter, Cannula and Tubing, Vascular, Cardiopulmonary Bypass (classified under 870.4210) Diagnostic intravascular catheter (classified under 870.1200)
Product Code:	74KFM, 74DWF, 74DQO

c. Legally Marketed Predicate Devices

- TandemHeart PTVA System – K991783, K052570 ,K924642 , K924643
- Vascular Solutions Langston Dual Lumen Catheter – K050168
- Shiley Femoral 12.5 F Left Ventricular Vent Catheter/ Shiley- K881734
- 20 F Adult Vent Catheter /DLP- K834352
- 18 F Malleable Vent Catheter/ CalMed- K981601
- 24 F Left Heart Vent Catheter with Pressure Monitoring Line, Medtronic- K012143
- StereoCath-Dx Electrophysiology (EP) Catheter, Boston Scientific- K940168
- Sonicath Ultra Imaging Catheter (9F/12 MHz)/ Boston Scientific- K902245

d. Device Description:

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System (IMPELLA RECOVER LP 2.5 System) provides circulatory support with the ability to deliver anticoagulant through an infusion system. The System is comprised of: 1) a catheter which contains an integrated pump motor/infusate lumen, integrated intravascular pressure lumen and integral cannula, 2) a controller/console and 3) infusion system designed to work together, and 4) accessories.

e. Intended Use:

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is

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intended for circulatory support using an extracorporeal bypass control unit. Intended duration of use is for periods appropriate to cardiopulmonary bypass, up to 6 hours. It is also intended to be used as an extracorporeal circulatory support system (for periods up to 6 hours) for procedures not requiring complete cardiopulmonary bypass (e.g., valvuloplasty, surgery of the aorta, high risk cardiac surgery, high risk patients undergoing non-surgical cardiac procedures, etc).

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System also provides for pressure measurements which are useful in determining intravascular pressure.

f. Technological Characteristics and Comparison to Predicate Device(s):

The technological characteristics of the IMPELLA RECOVER® LP 2.5 are the same as the TANDEM HEART systems and the Vascular solutions Langston catheter with the exceptions of the following differences:

- pump location
- certain materials of construction

g. Pre-clinical Test Results:

To validate the device design of the IMPELLA RECOVER® Percutaneous Cardiac Support System, ABIOMED performed the following *in vitro* testing:

With regard to sterilization, packaging, and shelf-life, the IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is sterilized using EtO gas with a SAL of 10^{-6}. The sterilization method/cycle was validated using EN 550 "*Sterilization of Medical Devices – Validation and Routine Control of Ethylene Oxide Sterilization.*" The EtO sterilization residual values for EO and ECH and are within the allowable limits of ISO 10993-7. The LAL test was used to ensure a pyrogen free determination. The packaging material has been validated to ensure its integrity.

Biocompatibility testing of all patient contacting materials was conducted on the finished sterilized devices in accordance with ISO-10993, "*Biological Evaluation of Medical Devices Part 1: Evaluation and Testing*". All testing results are acceptable.

The design and testing validation of the software contained in the IMPELLA MCS was conducted in compliance with the FDA 2005 guidance document entitled "*Guidance for Industry and FDA Staff: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices.*"

With regard to electromagnetic compatibility and electrical safety, the IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System was tested in accordance with EN 60601 and EN 61000 and their applicable subparts. The testing results demonstrate that the device is in conformance with these FDA recognized standards.

With regard to In vitro performance testing, ABIOMED conducted a full range of

testing demonstrating that the entire IMPELLA RECOVER® LP 2.5 System operates as intended. All tests were acceptable.

h. Conclusion:

The ABIOMED IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is substantially equivalent to the :

TandemHeart System as described:

- TandemHeart PTVA System and Control system (K991783)
- The TandemHeart Transseptal Cannula (K052570)
- The Medtronic Biomedicus 15F arterial cannula and introducer (K924642,K924643)

- The Vascular Solutions Langston Dual Lumen Catheter (K050168)
- Shiley Femoral 12.5 F Left Ventricular Vent Catheter-Shiley(K881734)
- 24 F Left Heart Vent Catheter with Pressure Monitoring Medtronic- (K012143)

- StereoCath-Dx Electrophysiology (EP) Catheter- Boston Scientific (K940168)

- Sonicath Ultra Imaging Catheter (9F/12 MHz)/ Boston Scientific- K902245

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December 18, 2007

ABIOMED, INC.
22 CHERRY HILL DR.
DANVERS, MA 01923
ATTN: ROBERT T. KUNG

510(k) Number: K063723
Product: IMPELLA RECOVER LP 2.5 PERCUTANEOUS CARDIAC SUPPORT

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

K063723 52

ABIOMED
Recovering hearts. Saving lives.

Abiomed, Inc.
22 Cherry Hill Drive
Danvers, MA 01923 USA
Phone 978-777-5410
Fax 978-777-8411
www.abiomed.com

FDA CDRH DMC

DEC 17 2007

Received

VIA OVERNIGHT MAIL

William J. Bolt
Sr. Vice President, QA/RA
22 Cherry Hill Drive
Danvers MA 01923
(p) 978-646-1451
(f) 978-739-0576

December 12, 2007

Documentation Mail Center (HFZ-401)
Office of Device Evaluation
Food and Drug Administration
Center for Devices and Radiological Health
9200 Corporate Boulevard
Rockville, MD 20850-3229

RE: 510 (k) K063723
Response to AI letter Dated October 3, 2007

Dear Sir/Madam:

Enclosed please find one original and three copies of a response to an additional information letter dated October 3, 2007 pertaining to ABIOMED 510(k) submission, K063723. An extension for our response was granted on 10/31/2007.

Thank you for your consideration in this matter. Please feel free to contact me with any questions or concerns.

Sincerely,

(b) (6) [redacted]

William J. Bolt

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

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K063723/52

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

FDA CDRH DMC
DEC 17 2007
Received

Abiomed, Inc.
c/o Mr. William J. Bolt
Senior Vice President
Cherry Hill Drive
Danvers, MA 01923

OCT - 3 2007

Re: K063723
Trade Name: IMPELLA RECOVER LP 2.5 Percutaneous Cardiac Support System
Dated: July 3, 2007
Received: July 5, 2007

Dear Mr. Bolt:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a legally marketed predicate device based solely on the information you provided. To complete the review of your submission, we require that you respond to the following concerns.

1. The IMPELLA 2.5 System is capable of up to 2.5 L/min of support. The TandemHeart predicate is capable of up to 5.0 L/min. You have not provided sufficient information to demonstrate that the partial support provided by your device would be sufficient for some of your indication claims, namely "high risk cardiac surgery." Please provide additional information from *in vivo* use (either animal or human) to demonstrate that the 2.5 L/min partial support is sufficient for the specific claims in your indication statement. Measures of interest would be demonstration that 2.5 L/min is sufficient to adequately perfuse the major organs of the body, including brain, liver and kidney. This could be demonstrated with functional measures (human) or histopathological assessments of adequate perfusion (animal). Please contact the Agency to discuss your approach before submitting a response to this item.

2. You acknowledged that there are several differences in the indication statement for your device compared to the TandemHeart predicate. You provided an explanation for the modifications in the clinical examples section. However, we believe that the technological differences between your device and this predicate necessitate additional information to demonstrate that the specified clinical examples can be performed with

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your device in place. Specifically, when inserted, the TandemHeart predicate catheter accesses the heart via the femoral vein, with the tip in the left atrium via transseptal puncture. Conversely, your device resides in the aorta, with the catheter tip inserted into the left atrium via the femoral artery and aortic valve. Please provide additional proof-of-concept information which supports your claim that valvuloplasty, surgery of the aorta, and high-risk cardiac surgery can safely be performed with your device in place. We believe this may require *in vivo* animal studies. Please contact the Agency to discuss your approach before submitting a response to this item.

3. You provided information from clinical experience to address the Agency's concerns regarding valve or aortic tissue damage, including published literature references, your European complaint history, and an echocardiography safety analysis from your IDE (G050017) feasibility study. Please address the following concerns:

   a. You referenced a published study involving 109 patients treated in Europe, which you state showed no evidence of aortic valve injury. However, it is unknown whether these patients were evaluated for chronic (>30 day) valve function to assess late-presenting injury, or worsening injury. Additionally, 11% of the patients died in-hospital. Please provide additional details regarding these deaths, including patient summaries and autopsy reports, if available.

   b. Although the information from your echocardiography study does show minimal effects on the aortic valve and surrounding structures, we do not feel that the small sample size of data (twenty patients at baseline with nine patients followed to 3 months) provides a reasonable assurance of safety with regard to aortic valve or tissue damage. Please provide an updated summary of all known animal and clinical data on adverse events attributable to support on the IMPELLA device.

   Please note that we believe that adequate demonstration of safety may ultimately require the results of a prospective clinical investigation. Please contact the Agency to discuss your approach before submitting a response to this item.

4. You have not provided hemolysis testing compared to a predicate device. The 510(k) regulations are based on equivalent performance to a chosen predicate device. Since your device has technological differences compared to the predicate CPB pumps, please perform side-by-side blood damage testing, inclusive of RBC, WBC and platelet counts, complement and platelet activation, and hemolysis studies. Testing conditions should be representative of worst case operating conditions, results should be evaluated regarding statistical significance, and your final conclusions should be discussed. Before conducting this additional testing, please provide your protocol for FDA review.

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

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The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device.

We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

You may not market this device until you have provided adequate information described above and required by 21 CFR 807.87(l), and you have received a letter from FDA allowing you to do so. If you market the device without conforming to these requirements, you will be in violation of the Federal Food, Drug, and Cosmetic Act (Act). You may, however, distribute this device for investigational purposes to obtain clinical data if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations.

If the information, or a request for an extension of time, is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days it will be considered and processed as a new 510(k)(21 CFR 807.87(l)); therefore, all information previously submitted must be resubmitted so that your new 510(k) is complete. Please note our guidance document entitled, "Guidance for Industry and FDA Staff FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the additional information request.

The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/cdrh/mdufma/guidance/1219.html.

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

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The requested information, or a request for an extension of time, should reference your above 510(k) number and should be submitted in duplicate to:

Food and Drug Administration
Center for Devices and
Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions concerning the contents of the letter, please contact Kathryn O'Callaghan at (240) 276-4182. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or at (240) 276-3150, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

M. G. Hillebrenner

for Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

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

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APPENDIX 1 – PRESS RELEASE in FEBRUARY 2006 CLAIMING FLOW INCREASES TO "Up to 5 L/M" DUE TO A "NEW INFLOW CANNULA THTC-EF". ORIGINAL INFLOW CANNULA GENERATED EQUIVALENT SYSTEM FLOW TO THE IMPELLA LP 2.5.

News

TandemHeart
PTVA System

Media Contact:
Dan Snyders
Armada Medical Marketing
303-623-1190 x230
dan@armadamedical.com

Monica Bush
CardiacAssist, Inc.
412-963-7770 x247
mbush@cardiacassist.com

FOR IMMEDIATE RELEASE
February 22, 2006

CardiacAssist Receives 510(k) Market Approval for New Transseptal Cannula

THTC-EF Cannula for TandemHeart® PTVA® System
increases percutaneous VAD blood flow to five liters per minute

PITTSBURGH – CardiacAssist, Inc., a Pittsburgh-based medical device company that develops, manufactures and markets cardiac assist devices, has received FDA 510(k) market approval for its new, high-flow cannula.

The TandemHeart Transseptal Cannula – Enhanced Flow (THTC-EF) enables the TandemHeart percutaneous ventricular assist device to provide blood flow of up to five liters per minute. The THTC-EF is positioned in the left atrium and is part of the TandemHeart Cannula Set, which connects the TandemHeart Pump to the human body. The TandemHeart System is used in critical care cardiology and helps heart failure patients survive heart attacks, high-risk procedures and other cardiac interventions.

"We've reached a new milestone in percutaneous blood flow," said CardiacAssist CEO Michael Garippa. "The percutaneous hemodynamic support capability of the TandemHeart System is changing the very nature of critical care cardiology."

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News

TandemHeart
PTVA System

Garippa added that reaching the five-liter-per-minute mark means that the TandemHeart System can take on even more challenging cardiac cases, giving patients and cardiologists more options and more hope when facing the most difficult heart procedures.

The THTC-EF was originally conceived as a product improvement to resolve occasional pliability of the currently marketed TandemHeart Transseptal Cannula (THTC). Although such problems are immediately noticed and easily resolved, Garippa said the company decided to provide a new-state-of-the art cannula to the market.

AREA OF EMPHASIS: NOTE COMMENT ABOUT "*TandemHeart System Flow* increase due to new inflow cannula"

The new cannula has a thinner wall which allowed CardiacAssist engineers to increase the inside diameter (ID) while keeping the same 21 French (7mm) outside diameter of the currently marketed THTC. The increased ID reduces resistance to flow and therefore the TandemHeart System flow increases from 4.0 liters per minute to a maximum of 5.0 liters per minute when used in conjunction with a 12 French arterial return cannula. The THTC-EF used in conjunction with a 15 French arterial return cannula provides a 30% increase in flow, from 3.5 liters to 4.5 liters.

To date, more than 525 uses of the system in 28 countries at 70 different facilities by 120 different physicians have been performed.

About CardiacAssist

Founded in 1996, CardiacAssist, Inc. is a privately held, Pittsburgh-based medical device company that develops, manufactures and markets innovative products designed to provide cardiologists and cardiac surgeons with
CardiacAssist, Inc.

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

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News

TandemHeart
PTVA System

minimally invasive solutions for treating weakened and failing hearts. Its vision is to help advance the treatment of heart disease by bridging gaps in current treatment methodologies.

This press release may contain certain forward-looking statements that relate to CardiacAssist's future business and financial performance. Such statements are subject to a number of risks and uncertainties that may cause the actual events or future results to differ from those discussed herein.

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ORIGINAL

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

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Draft Minutes from the FDA meeting – March 27, 2006

Attendees:

FDA

PARTICIPATING IN PERSON:
Kathryn O'Callaghan
Eric Chen, M.S.
Matt Hillebrenner, M.S.
William Riemenschneider, Biologist
Steve Hilbert, M.D., Ph.D.

PARTCIPATING VIA TELEPHONE:
Ileana L. Piña, M.D., FACC (joined meeting in progress)
Julie A. Swain, M.D.
Jean Rinaldi (joined meeting in progress)

PHYSICIANS (FOR ABMD, INC.)

PARTICIPATING IN PERSON:
José Henriques, M.D., University of Amsterdam, Netherlands, Academic Medical Center
Laura Mauri, M.D., MSc, Brigham & Women's Hospital and Harvard Clinical Research Institute
Stephanie Moore, M.D., Massachusetts General Hospital
William O'Neill, M.D., William Beaumont Hospital

PARTICPATING VIA TELEPHONE:
Bart Meyns, M.D., Ph.D., Katholieke Universiteit Leuven, University Clinic Gasthuisberg, Leuven, Belgium (joined meeting in progress)

ABIOMED, INC.

PARTICIPATING IN PERSON:

Karim Benali, M.D., Chief Medical Officer
William Bolt, VP Quality, Regulatory and Field Service
Robert T. V. Kung, Ph.D., Chief Scientific Officer
Thorsten Siess, Ph.D., Chief Technology Officer
Sheila Flaherty, General Counsel

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3:00 pm meeting begins.

Dr. K. Benali opened the meeting and turned it over to William O'Neill, MD who moderated the meeting. The ABMD team used a slide presentation to facilitate the discussion. The presentation is attached and incorporated herewith.

INCLUSION/EXCLUSION CRITERIA FOR PILOT STUDY FOR IMPELLA RECOVER 2.5

Dr. O'Neill reviewed the proposed inclusion criteria for the safety trial for the IMPELLA LP 2.5 that was submitted to the FDA in ABMD's Briefing Paper on the IMPELLA RECOVER LP 2.5 on February 17, 2006 and subsequently discussed during the March 9, 2006 conference call with FDA. He indicated that he would be responding to FDA inquiries regarding the patient profiles of the anatomic high risk PCI patient population ("AHR PCI") and the need for circulatory support.

Dr. O'Neill began a review of the physicians' experience with slide 8 and a discussion of his experience at Wm. Beaumont. He noted his view that AHR PCI patients provide a reasonable population size for this safety and feasibility study. The patient population with depressed left ventricular function supported at Wm. Beaumont had a high rate of co-morbidities and a mortality rate of approximately 10%.

Dr. Henriques next reviewed the European experience with this patient population (slide 9) at AMC and Bernau being treated with the IMPELLA 2.5. He pointed out that his patient population, as well as the one from Bernau hospital, has a similar co-morbidity profile to Dr O'Neill's patients. Dr. Moore and Dr. Mauri each discussed their experience at MGH and Brigham (based on 2005 data), respectively (also slide 9), with a similar patient cohort.

Dr. Swain inquired what the mortality figures were for the patients who were not treated with IABP in the MGH numbers (slide 9). Dr. Moore indicated that 52% of patients with unprotected left main were supported by IABP and 5 of the 7 deaths were treated with IABP, indicating that IABP alone provided insufficient support. Dr. Mauri indicated that, at Brigham, the numbers illustrated that 21 out of 2000 high risk PCI patients last year at her institution would be eligible for support with the IMPELLA 2.5. Dr. Mauri also indicated that for 2005, 80 patients at Brigham had ejection fraction ≤30% with multiple co-morbidities but did not undergo PCI or CABG because of their very high risk conditions. She added that some of these patients would have been eligible for IMPELLA support. Dr. Moore advised that 25 of the 1800 high risk PCI patients at MGH last year fell into this category and in response to FDA's inquiry about the patients at his institution, Dr. O'Neill advised that 3% of the high risk PCI patients at Wm. Beaumont would fall into this category and agreed that the proposed patient population for the safety trial was a small group. FDA noted that the defined high risk PCI patient group is 1% to 2% of the PCI population. Dr. Henriques later confirmed the same percentage.

Dr. Moore reviewed the Tandem Heart Registry (slide 12) and the number of high risk PCI patients. Eric Chen noted that the Tandem Heart was a different device than the IMPELLA. Dr. Swain noted that the Tandem Heart Registry defines high risk PCI differently than ABMD's proposed definition. Both ABMD and FDA concurred that there is no agreed upon definition of high risk. K. O'Callaghan noted that the duration of support for the Tandem Heart differs from the proposed duration for IMPELLA 2.5. (6 hours v. 5 days). Dr. Moore noted the registry illustrates that there is a patient population that needs support and that physicians are willing to use a device that has high risk for morbidities because they believe a mechanical assist device is required for this category of patients.

Dr. O'Neill reviewed the CPS registry (slide 13) and noted that prophylactic support improved outcomes and significantly improved mortality risk when compared to stand-by support. Without any kind of support, mortality would have been even higher than the 18% reported for stand-by support in the CPS registry. Dr. Swain agreed that an anatomic high risk patient population existed that could benefit from support, but wanted to look at specific inclusion criteria.
Dr. O'Neill responded with his view that low EF characterizes a high risk patient population (slide 14) because of the usual high rate of co-morbidities associated with a depressed ventricular function.

Dr. Moore reviewed the current literature and noted that a number of papers illustrate unprotected left main high risk PCI remains a challenge, even in the era of drug eluting stents. (Slide 16) Dr. Mauri concurred saying this is definitely a group of patients that the operators feel can benefit from support.

Dr. Henriques reviewed his experience using the IMPELLA 2.5 in Europe (slide 17), including the safety profile of the device in patients (slide 18). Dr Henriques mentioned that the slide only included data on the first 19 patients he treated with the IMPELLA LP 2.5 (published recently in Am. J. Cardiology), but his experience on 30 patients so far has been similar. He noted that in those patients that they looked at, there was no valve regurgitation.

Dr. Henriques provided a detailed case study of an unprotected left main PCI complicated by a large dissection and total occlusion (Slides 20 and 21). He noted that IMPELLA saved that patient from a probable large myocardial infarction, CABG or even death. He added that this case illustrates the potential benefit of the technology during high risk PCI.

Dr Swain summarized the experience of the ABMD physicians in high risk PCI and described the population profile as being:
Age: greater than 60 or 65
Unprotected left main
Queried whether the case reviewed was elective and the use of the STS to define non-emergent.

EF in the 20% range
Class III or IV NYHF
Multi-vessel disease

Dr. Moore compared IMPELLA RECOVER LP 2.5 for safety and efficacy to other approved devices (slide 22). Dr. O'Neill talked to the practicality of the different support devices in the table, noted that physicians disfavor and do not use CPS, and that Tandem Heart is very complex. Dr Swain stated that it looks like the analogy is more towards the IABP. Dr. O'Neill noted that the IABP will be the pivotal comparison.

Dr. Mauri stated that these patients were those with advanced heart failure and the only patients excluded were those in shock. Dr. Henriques noted that he felt a 30% EF was too low and it should be 35% or higher. Dr. O'Neill looked to the FDA for more guidance on the inclusion/exclusion criteria.

FDA responded as follows:
Change age criteria: 18 is too young, it should be 60 or above
EF with symptomatic heart failure
Unprotected left main
Not simply multi-vessel
Non-emergency, rather than elective

Dr. Moore reacted to the proposed age criteria and asserted that 60 was too old. She would be uncomfortable turning down patients in their 40s and 50s who could benefit from support. Dr. Henriques discussed the European experience and showed that the EF on average was greater than 30%.

FDA clarified the inclusion criteria it would find acceptable, as follows:
Minimum Age: greater than or equal to 40
Unprotected left main or last remaining conduit
EF≤ 35%
Non-emergent case

ABMD agreed on this last proposal. At this time, Drs. Piña and Swain exited the call. Jean Rinaldi joined the call. Dr. Meyns also joined the call.

FDA inquired about Dr. Henriques' experience with the IMPELLA in Europe and the duration of use and the pump speed. Dr. Henriques replied that the duration of use was up to three hours on the elective high risk PCI. S. Hilbert inquired if there was blood damage, when the pump speed was at maximum support (~51,000 rpms). Dr. Henriques noted that according to his experience, patients were supported at maximum rpm and blood damage has not been a concern. He also noted other patients in his institution presenting with acute MIs had been supported for up to 3.5 days with IMPELLA.

S. Hilbert inquired how the pump position is maintained. Dr. Henriques replied that it was very stable and maintaining the position was not a problem.

FDA inquired if the pump remains in position at high rpms. Dr Benali stated that a software feature controls rpm changes. The software increases/decreases rpm gradually from low to high or high to low speed in order to avoid expulsion of the pump from the ventricle.

FDA inquired about blood loss in Dr. Henriques' patient population. He responded that one elective case needed packed cells. That patient presented with anemia pre-procedure and had severe bleeding after the procedure from the groin. Dr. Henriques stated he had never needed to use platelets or plasma and there has been no suggestion of hemolysis.

S. Hilbert inquired if the software has the ability to tell if the pump is placed appropriately? Response: Yes.

VALVES

The discussion next turned to the question of potential adverse events involving the aortic valve. Dr. Meyns reviewed slide 25 and discussed his experience with animals. He described the limitations of the animal model. Next he discussed the European experience and the post mortem analysis performed and reported to FDA on 20 human autopsies, as well as a series of studies including a total of 78 patients supported with IMPELLA and undergoing valve function assessment under echocardiography. Dr. Henriques noted there were no visible lesions on the aortic valve, confirmed by post IMPELLA usage imaging.

FDA inquired about the duration of support for humans versus the duration with sheep in the animal studies (hours vs. days). Dr. Benali responded that the human experience reported in the literature ran from 2 hours to 19 days of IMPELLA support and referred to slide 35. He mentioned that this data has been provided to FDA as a part of the previously submitted briefing paper.

Dr. Meyns noted that European patients are generally supported between 2 to 8 days and 5 days is the mean. Dr. Meyns is confident that no lesions are due to the pump. Dr. Henriques concurred and noted that pre-discharge echocardiography confirm this statement in his experience.

E. Chen suggested that the clinical protocol include an echocardiography pre- and post-IMPELLA support for follow up to assess the functionality of the valves.
Dr. Moore suggested 3 month post-procedure echocardiography. FDA confirmed.

BLOOD COMPATIBILITY

K. O'Callaghan clarified a general misunderstanding and noted that ABMD has adequately addressed the question of complement activation. She noted that FDA's real concern with blood compatibility was the questions of thrombosis and hemolysis and

requested blood bench testing on the 2.5 (rather than just rely on the 5.0) because the gap and the rpms differ.

Dr. Kung noted that the 2.5 and 5.0 pumps have the same design and explained as follows: Although the diameter of the cannula and rpm differ, the shear rates of the 2.5 and the 5.0 are basically the same. Shear is governed by velocities and gap sizes. Since the 2.5 has a smaller pump it can run at higher rpms and still stay below shear rates that cause blood damage. The 5.0 runs at a lower rpm because it is larger, but the tip velocity of the two pumps is similar. Dr. O'Neill suggested doing blood testing for hemolysis in the 20 patients in the initial safety/feasibility study. FDA concurred but noted good clinical benchmarks were required. In addition, K. O'Callaghan requested any clinical information or literature on the low hemolysis rate. ABMD agreed.

K. O'Callaghan inquired about heat concentrations reported in one of the engineering tests and was concerned about potential risk of thrombosis induced by the pump. K. O'Callaghan asked whether on explant there was any thrombosis around the IMPELLA. Dr. Benali mentioned that the model proposed in the engineering test was not appropriate and a rational explanation will be provided. In addition, Dr Benali inquired if FDA would consider the clinical experience in terms of stroke rate and thrombosis rate as an additional argument to support safety of the pump with regard to heat and potential thrombosis issues. Dr Benali said the preliminary first experience with the IMPELLA pump in a multi-center randomized study (Meyns and al.) reported a stroke rate of 1.9%. In addition, the 13 other publications did not report stroke or thrombosis as being a complication associated with IMPELLA use. Mr. Bolt said there were no complaint reports from Europe on thrombosis and stroke. Dr. Meyns confirmed that he had no recent experience with thromboembolic events related to the IMPELLA. Dr. Henriques noted that he had no incidence of such events either.

ABMD inquired if autopsies and stroke rate data would address FDA's concerns regarding the heat question. K. O'Callaghan replied it would be sufficient as long as the autopsies and stroke data were not limited only to patients on a short duration of support. K. O'Callaghan also requested that ABMD inspect the pumps at explant and monitoring of blood parameters such as hemolysis during pump support.

FDA SUMMARY

K. O'Callaghan summarized the discussion and conclusions as follows:

Patient inclusion criteria:
Age: 40 - 80
EF≤ 35%
Change elective to non-emergent
Unprotected left main

Other protocol changes:
3 month follow up echocardiography to assess aortic valve function

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Collect blood data to measure hemolysis
Pump inspection after explant
Report of Stroke, TIA and thrombosis rates during safety trial

4:30 pm meeting concludes.

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PROTECT I

A Prospective Feasibility Trial Investigating the use of the IMPELLA® RECOVER® LP 2.5 System in Patients Undergoing High Risk PCI

IDE Number: G050017

Sponsor: ABIOMED, Inc.
22 Cherry Hill Drive
Danvers, MA 01923

Study Responsibility: Karim Benali, MD
Chief Medical Officer
ABIOMED, Inc.
22 Cherry Hill Drive
Danvers, MA 01923
(b) (4)

Principal Investigator: William O'Neill, MD

Study Centers:

- William O'Neill, MD – William Beaumont Hospital, MI
- Laura Mauri, MD – Brigham & Women's Hospital, MA
- Paul Teirstein, MD – Scripps Clinic, CA
- Judah Weinberger, MD - New York Presbyterian Hospital, NY
- Andrew Civitello, MD - Texas Heart Institute, TX

Date of Issue: May 25, 2006

Date(s) of Amendment(s):

This investigational plan contains confidential information for use by the Investigators and their designated representatives participating in this clinical investigation. It should be held confidential and maintained in a secure location.

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Protect I – ABIOMED Investigational Plan Approval Page

VERSION NUMBER: 3.0

I, the undersigned, have read and approve the investigational plan specified above and agree on its content:

Date

Karim Benali, MD
Chief Medical Officer
ABIOMED, Inc.
22 Cherry Hill Drive
Danvers, MA 01923

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Investigators' Signature Page

STUDY TITLE: PROTECT I: A Prospective Feasibility Trial investigating the use of the IMPELLA® RECOVER® LP 2.5 System in Patients Undergoing High Risk PCI.

STUDY CENTER: _____

VERSION NUMBER: 3.0

DATE:

I, the undersigned, have read and understand the investigational plan specified above and agree on its content. I agree to perform and conduct the study as described in the investigational plan and in accordance with the relevant parts of the ICH Guidelines for GCP, the Declaration of Helsinki, and the Code of Federal Regulations:

_____ _____

Principal Investigator Date

Print name: _____

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Investigational Plan Synopsis

Test Device	IMPELLA® RECOVER® LP 2.5 System
Primary Objective	The objective of this feasibility study is to demonstrate that the device is safe and potentially efficacious for use in patients undergoing high risk Percutaneous Coronary Interventions (PCI).
Study Design	This is a prospective single-arm feasibility study to be conducted at a maximum of seven institutions.
Enrollment	Patients will be considered enrolled in the study following consent and after the general inclusion/exclusion criteria are met.
Follow-Up Schedule	Patients will be followed through hospital discharge, at 30 days and three months postexplant of the IMPELLA RECOVER LP 2.5 System. The study will be considered complete in regard to the primary study endpoints after all subjects enrolled have completed their 30 day follow-up or been followed through discharge, (whichever is longer). Study follow-up will be complete when all subjects have been followed out to three months.
Number of Patients	Up to 20 subjects

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Appendices:

A Adverse Events

B Definitions and Acronyms

C Instructions for Use

D Sample Case Report Forms

E Sample Informed Consent Form

F Investigator's Agreement

G IMPELLA® RECOVER® LP 2.5 System Site Training Program

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1. Introduction

1.1. *Device Name*

The device under clinical investigation is the IMPELLA® RECOVER® LP 2.5 System.

1.2. *Background*

Cardiology practice in the catheterization laboratory has evolved rapidly over the last decade. Advanced technology and greater operator expertise have resulted in dramatic increases in the volume and complexity of procedures. Interventional cardiologists are tackling more complex and higher risk cases during Percutaneous Coronary Interventions (PCI) as device technology and adjunctive pharmacotherapy improve. However, cardiologists are still exposed to unusual challenges during high risk PCI because of procedure-related morbidity and mortality risks related to poor hemodynamic status or reserve [1,2]. Several approaches have been developed to provide hemodynamic support during these high risk PCI cases [3,4,5,6]. However, no single approach has attained a definitive consensus or received wide acceptance because of either the complexity of the techniques [4,6], their limited effectiveness during hemodynamic collapse [7,8],or due to device related complications [6,9,10].

In an attempt to address some of the limitations of current systems, ABIOMED developed a miniaturized catheter-based cardiac assist device, the RECOVER LP 2.5, that pumps up to 2.5 l/min of blood from the left ventricle to the systemic circulation across the aortic valve [11,12,13,14]. First clinical experience showed that RECOVER LP 2.5 potentially enables immediate and sustained unloading of the left ventricle while increasing the overall systemic cardiac output [14,15].

For this first pilot trial, ABIOMED would like to investigate the safety and potential effectiveness of RECOVER LP 2.5 in high risk PCI patient population. ABIOMED has provided a comprehensive analysis to FDA that justifies the need for a circulatory support for the proposed patient population (for further details, please refer to "Responses to FDA Questions" binder: (1) Appendix I- Briefing white-paper: pages 5-10; (2) Appendix II- ABIOMED presentation for March 27th 2006 meeting with FDA in Rockville: slides 7-23; (3) Appendix IV-

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Minutes of the March 27th 2006 meeting: pages 2-4). ABIOMED believes that such high risk patient population may benefit from an active circulatory support provided by RECOVER LP 2.5 in order to reduce the morbidity risk these patients are exposed to. As agreed upon during March 27th 2006, ABIOMED has modified some of the inclusion and exclusion criteria and proposes a patient population that follows FDA recommendations.

1.3. *Clinical Experience with the IMPELLA RECOVER LP 2.5*

The IMPELLA® RECOVER® LP 2.5 System is approved for 5 days of support in Europe under CE Mark and other parts of the world. We have been conducting a dynamic registry for IMPELLA products in Europe with regard to demographics, indications for use and patient outcomes. Between the date of the introduction of the RECOVER 2.5 in September 2004 and December 2005, 242 patients were treated. Of those, 78% were supported in the CathLab, 13% were supported in various care units (ICU, CCU, ER, etc.) and 9% were supported in the surgical suite.

Of all patients that underwent PCI in the CathLab under pump support, 78% were elective high risk PCI cases while 19% were emergent cases (cardiogenic shock post AMI, low output syndrome, etc.). The mortality rate for those patients was 6% and 35% respectively. The indication for support was not reported in 3% of the cases.

As IMPELLA RECOVER LP 2.5 usage continues to spread rapidly in Europe, the first indication for use remains high risk PCI. The experience has shown that most of the new centers would start first with some elective high risk PCI cases to better learn how to use the device, understand its performance and acquire more confidence with patient management.

In summary, based on the positive European clinical experience with RECOVER LP 2.5 [14,16,17] and the large patient population supported so far, we believe that the IMPELLA RECOVER LP 2.5 System can benefit patients in need of circulatory support.

2. Device Description and Intended Use

The IMPELLA® RECOVER® LP 2.5 System is intended to be used for up to five (5) days as a left ventricular cardiac assist device for patients undergoing high risk PCI procedures.

The system is comprised of the following components:

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- IMPELLA® RECOVER® LP 2.5 Catheter
- Mobile Pump Console (MPC)
- Power Supply
- Braun Vista® basic Infusion Pump
- Combitrans-Monitoring Set (CM-Set)
- Pressure Transducer Cable (Gray)
- Connector Cable (Black)
- Power Supply Cable
- Testplug Pump
- Introducer Set
- Boston Scientific Platinum Plus™ ST/.014mm/300cm Guidewire

Please refer to Appendix C "Instructions for Use" for complete information on the proper use and operation of the system.

Investigators and clinical site staff will be required to complete ABIOMED, Inc.'s IMPELLA® RECOVER® LP 2.5 Support System training program in order to be certified as an implanting center in the study. An overview of the training program is included in Appendix G.

3. Study Objective

The objective of the study is to demonstrate preliminary evidence that the IMPELLA® RECOVER® LP 2.5 System is safe and potentially effective for patients undergoing high risk PCI.

The proposed study is a prospective, single arm, multi-center feasibility study designed to examine the potential efficacy and the frequency of serious adverse events associated with use of the IMPELLA® RECOVER® LP 2.5 System in adult patients who are considered high risk for PCI procedures from the time of enrollment to the primary study endpoint of 30 days post device explant or through discharge (whichever is longer). The patients will be followed up to 3 months post device explant.

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4. Enrollment criteria

4.1. *Inclusion criteria*

For inclusion in the study, subjects must fulfill all of the following criteria:

1. Signed Informed Consent.
2. Patient is indicated for a NON emergent percutaneous treatment (please see Non emergent definition in Appendix B) of at least one de novo or restenotic lesion in a native coronary vessel or bypass graft.
3. Age Eligible ($40 \leq$ Age ≤ 80)
4. Patient has no child bearing potential or has a negative pregnancy test within 7 days prior to treatment.
5. Patient presents with Left Ventricular Ejection Fraction (LVEF) ≤35%

Subjects must also meet at least one of the following criteria:

a) Intervention on the last patent coronary conduit
b) Intervention on an unprotected left main coronary artery

4.2. *Exclusion Criteria*

1. ST Myocardial Infarction within 7 days
2. Pre-procedure cardiac arrest within 24 hours of enrolment requiring CPR.
3. Subject is in cardiogenic shock defined as

   - CI < 2.2 l/min/m^2 and PCWP > 15mmHg
   - hypotension (systolic BP < 90 mmHg for > 30 minutes or the need for supportive measures to maintain a systolic BP of greater than or equal to 90 mmHg) AND end organ hypoperfusion (cool extremities OR [a urine output of < 30 ml/hour AND a HR > 60 BPM]).

4. Mural thrombus in the left ventricle.
5. The presence of a mechanical aortic valve or heart constrictive device.
6. Documented presence of aortic stenosis (aortic stenosis graded as ≥ +2 equivalent to an orifice area of 1.5cm^2 or less).

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7. Documented presence of moderate to severe aortic insufficiency (echocardiographic assessment of aortic insufficiency graded as ≥ +2).
8. Severe peripheral arterial obstructive disease that would preclude RECOVER LP 2.5 System device placement.
9. Abnormalities of the aorta that would preclude surgery, including aneurysms and extreme tortuosity or calcifications.
10. Subject with renal dysfunction (creatinine ≥ 3.5mg/dL).
11. Subject has history of debilitating liver dysfunction with elevation of liver enzymes and bilirubin levels to ≥ 3x ULN or INR (Internationalized Normalized Ratio) ≥ 2.
12. Subject has severe pulmonary disease (FEV1≤1, etc.).
13. Subject has uncorrectable abnormal coagulation parameters (defined as platelet count ≤75,000/mm^3 or INR ≥2.0 or Fibrinogen ≤ 1.50 g/l.)
14. Subject has sustained or nonsustained ventricular tachycardia.
15. Active systemic infection.
16. History of recent (within 3 months) stroke or TIA.
17. Allergy or intolerance to heparin, aspirin, clopidogrel or contrast media.
18. Patients with documented heparin induced thrombocytopenia.
19. Participation in the active follow-up phase of another clinical study of an investigational drug or device.

5. Potential Benefits / Risks

The sponsor believes that the clinical trial is feasible because the potential benefits outweigh the possible risks.

5.1. *Potential Benefits*

The sponsor believes that potential benefits from the use of the IMPELLA RECOVER LP 2.5 System may include:

- Maintenance of hemodynamic stability during the PCI procedure
- Possible prevention of the following procedure-related events:
  - Ventricular fibrillation
  - Tachycardia requiring electrical cardioversion

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5.2. *Potential Risks*

Risks in participation in this study are similar to those associated with currently available circulatory assist devices including, but not limited to:

- Aortic Insufficiency
- Aortic Valve Injury
- Arrhythmia
- Atrial Fibrillation
- Bleeding
- Cardiac Tamponade
- Cardiogenic Shock
- Cerebral Vascular Accident (CVA) / Stroke
- Death
- Device Malfunction
- Hemolysis
- Hepatic Failure
- Insertion site infection
- Myocardial Infarction
- Perforation
- Renal Failure
- Respiratory Dysfunction
- Sepsis
- Thrombocytopenia
- Thrombotic Vascular (non-CNS) Complication
- Transient Ischemic Attack (TIA)
- Vascular Injury

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- Ventricular Fibrillation
- Ventricular Tachycardia

All efforts will be made to minimize these risks by selecting Investigators who are experienced and skilled in high risk PCI. In addition, appropriate training will be provided to investigators in the insertion and operation of the IMPELLA RECOVER LP 2.5 System.

Appropriate subjects will be selected, using clearly defined inclusion and exclusion criteria, to ensure that the treatment and follow-up of the subjects are consistent with current medical practices.

6. Study Endpoints

Data will be collected for each of the following endpoints for subjects enrolled in the study. The study endpoint for each patient will be at the 30 day follow-up visit or at hospital discharge, whichever is longer. Study follow-up will be complete when all subjects have been followed through three months.

Safety Endpoints:

1. Primary Endpoint:
   a) Major Adverse Cardiac and Cerebral (MACCE) events defined as death, new myocardial infarction, target vessel revascularization, urgent coronary artery bypass grafting procedure or cerebral vascular accident during and up to 30 days post-device explant or hospital discharge, whichever is longer.

2. Secondary Endpoint:
   a) Other intra-procedural and peri-procedural adverse events (listed in Appendix A).

Efficacy Endpoints:

1. Primary Endpoint:
   a) Freedom from Hemodynamic compromise during PCI procedure defined as: Mean Arterial Pressure (MAP) not falling below 60mm Hg for more than 10 minutes during the PCI procedure and additional pressor medication is not required.

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2. Secondary Endpoints:
   a) Freedom from the following procedural-related events:
      i. Ventricular fibrillation
      ii. Tachycardia requiring electrical cardioversion
   b) Angiographic success defined as residual stenosis <30% after stent implantation or <50% after balloon angioplasty.

7. Data to be collected

Data will be collected at baseline (i.e. pre-pump insertion), during the PCI procedure, immediately following the PCI procedure or device explant, in the ICU or the floor where the patient will spend the remainder of his or her hospital stay, at hospital discharge, at 30 days and at three (3) months post pump explant.

Clinical data will be collected according to the schedule on the following page:

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	BL	Pump Place-ment	During PCI	First 48 hours After PCI			48 hours through Pump Explant			Post Explant to D/C		30 Day (Or D/C)	3 Mo.
				Q4	Q8	Q24	Q8	Q12	Q24				
Physical	✓ Med. Hx									✓	Perform indicated testing Q24 hours when pt. in ICU Q48 hours when patient is in any other hospital unit	✓	✓
Pedal pulses & groin site exam	✓		Q15	Q30 minutes for the first 4 hours of pump operation. Thereafter Q1 hours until explant						✓		✓	✓
Neuro Exam	✓					✓			✓	✓		✓	✓
12 Lead EKG	✓					✓			✓				
Urine Output	✓					✓			✓	✓			
Hemodynamics													
Pump Parameters			Measure at balloon inflations & at pump speed changes	Q30 minutes for the first 4 hours post-PCI. Thereafter Q4 hours for 48 hours				✓					
Heart Rate	✓	✓						✓		✓		✓	✓
Blood Press.	✓	✓						✓		✓		✓	✓
PCWP, PAP, CVP		✓						✓					
Cardiac Index		✓						✓					
Imaging													
Echo	✓	✓		One echo postimplantation						One echo post postexplant		✓	✓
Blood Labs													
CBC	✓				✓			✓		✓	Perform indicated testing Q24 hours when pt. in ICU Q48 hours when patient is in any other hospital unit	✓	✓
Plasma Free Hgb	✓	1 hr. post-placement				✓			✓	3 days Post explant			
ACT		✓	Q30 minutes for the first hour Q60 minutes for the second hour Then Q4 hours up to explant (while on pump)										
Hemostasis	✓				✓			✓					
Complement	✓				✓			✓		✓			
Cardiac Enzymes	✓				✓			✓		✓			
Electrolytes	✓				✓			✓		✓		✓	✓
Blood Gases		✓			✓			✓					
Noncardiac Bloodwork	✓				✓			✓		✓		✓	✓
Medications	✓	Record all cardiac medications										✓	✓
Adverse Events	✓	Record all adverse events										✓	✓

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8. Study Methodology

8.1. *Eligibility of Patients, Exclusions, Missing Data and Removal of Patients*

All patients presenting for interventional cardiology procedures are potential study candidates and will be screened for eligibility. Patients who do not meet all inclusion/exclusion criteria will not be enrolled in the study. Once enrolled, withdrawal is strongly discouraged.

Management of dropouts and missing outcome data will depend on their frequency and the nature of the outcome measure. Outlier values will be evaluated for their validity; all data will be included unless judged to be invalid. Analysis of the distribution of prognostic factors between patients with data and those without data will be reviewed for significance to assess selection bias. Adjustments for missing data will be performed only if deemed necessary and will be described completely. All data will be reviewed and analyzed via methods appropriate to the type of data collected.

All patients enrolled in the study are considered follow-up eligible and will be required to adhere to the follow-up schedule outlined in this protocol. No patient will be removed from the study unless consent has been withdrawn prior to treatment or in those cases where no treatment was ever attempted.

Informed consent must be obtained for all patients who are potential study candidates prior to the pump implant procedure. If the patient is not capable of giving informed consent then the patient's next of kin or authorized representative may give consent for the patient at the time of need. If next of kin or the authorized representative is not available, the patient will not be enrolled in the study.

8.2. *Sample Size and Participating Institutions*

Up to (b) (4) will be treated at (b) (4) institutions. The first identified participating centers and corresponding investigators are:

(b) (4)

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(b) (4)

[redacted]

8.3. *Interim & Endpoint Analysis*

Since this is a feasibility study with the endpoints being assessed through 30 days post pump explant or discharge and at three months post removal, no interim analysis will be performed.

The study will be considered complete in regard to the study endpoints after all subjects enrolled have completed their 30 day follow-up or discharge (whichever is longer). Follow-up analysis will also be performed at three months. Study follow-up will be complete when all subjects have been followed out to three months.

8.4. *Medical Monitoring*

The study will utilize one or more independent physician Medical Monitor(s) that will be responsible for the review and validation of all complications that occur over the course of the study, and the subsequent classification of these complications as related to the device or procedure. During the review of the complications, the physician(s) will be blinded to the investigational sites. It is anticipated that meetings with the Medical Monitor(s) will be conducted as needed depending on the rate of patient accrual.

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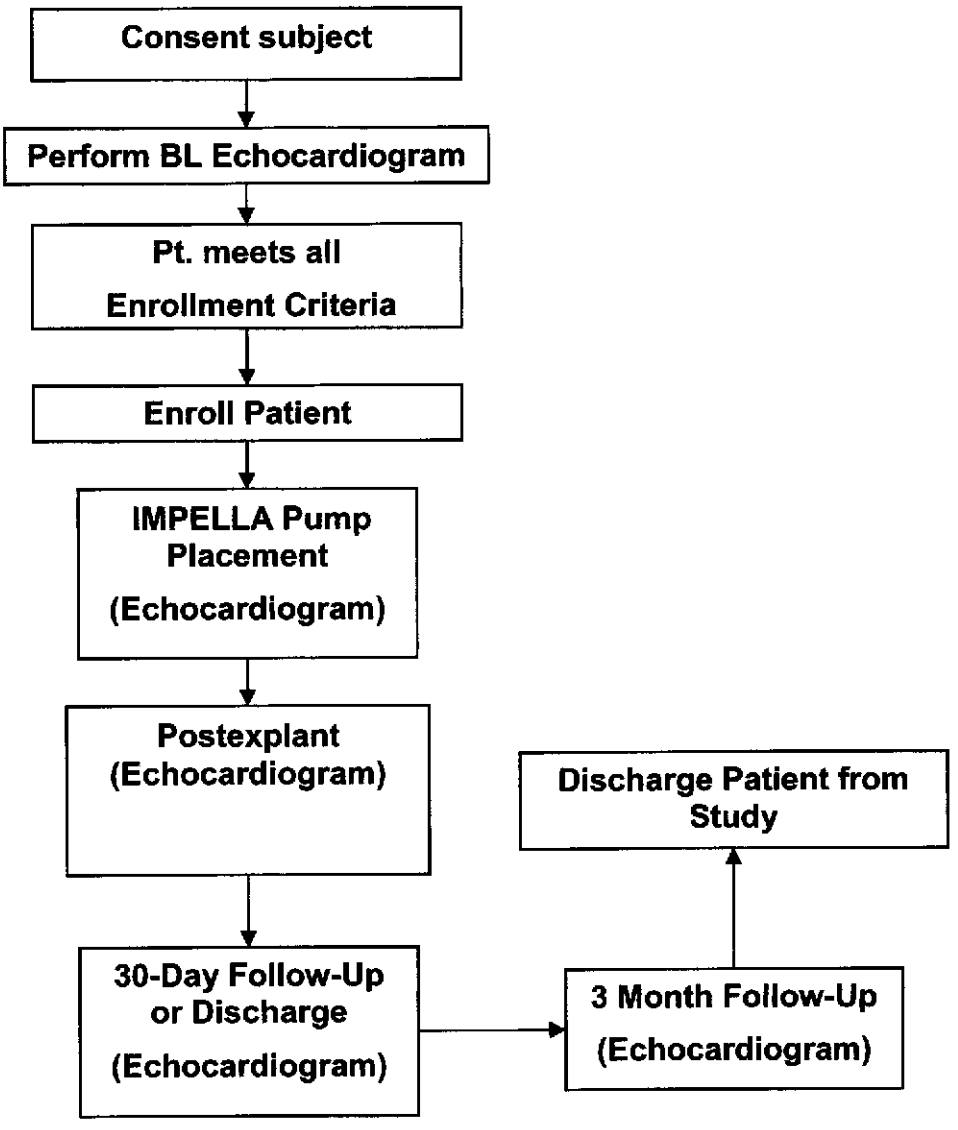
8.5. *Study Schematic*



8.6. *Length of Support provided by the IMPELLA RECOVER LP 2.5 System*

The IMPELLA RECOVER LP 2.5 System may be used to support patients for up to five (5) days post-implant. After five days the physician may choose to do the following: provide no additional hemodynamic support, initiate inotropic support, perform implantation of an IABP or implant a different FDA approved circulatory assist device. Following the 5 day period, the need for additional supportive treatment will be based on the best clinical practice as assessed by the attending investigator and the use of another IMPELLA device will not be permitted.

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8.7. *Study ProceduresPre-procedure*

Eligibility must be determined prior to study enrollment via review of the subject's record. Informed consent must be obtained for all subjects who are potential study candidates prior to the procedure. Since most of the potential candidates are those who are considered high risk for an elective PCI procedure, the subject should be able to sign the informed consent. If the subject is not able to do so, the consent should be signed by the subject's legal representative.

8.7.1. Within 24 Hours Prior to Pump Placement

- Medical history and physical examination including neurological assessment
- Summary of medical/surgical interventions including any blood product delivered
- Echocardiogram
- 12-lead ECG
- Peripheral pedal pulse assessment
- Baseline hemodynamics including:
  - Heart Rate
  - Blood Pressure (Systolic/Diastolic/Mean)
  - Cardiac Index
- Blood labs including:
  - Hematology
    1. WBC/RBC
    2. Platelets
    3. Plasma-free Hgb
    4. Hematocrit/Hemoglobin
  - Hemostasis
    1. INR or Prothrombin Time (PT) or Activated Partial Thromboplastin Time (aPTT)
  - Cardiac Enzymes
    1. CK
    2. CK-MB
    3. Cardiac Troponin

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- Electrolytes
    1. Potassium
    2. Chloride
    3. Phosphate
    4. Glucose
    5. Systemic Lactate
- Complement activation markers
    1. CRP
    2. C3
    3. C5a
    4. IL-6
    5. Granulocyte Elastase
- Noncardiac Blood work
    1. Total Bilirubin
    2. BUN
    3. Serum Creatinine
    4. LDH
    5. AST
- Urine output
- Record of current cardiac medications
- Adverse Events

8.7.1.1. Anticoagulation

For subjects implanted with the IMPELLA RECOVER LP 2.5 System, the subject should be anticoagulated with heparin prior to pump insertion to achieve an ACT between 250 to 500 seconds. Following discharge from the Cath lab and while on IMPELLA RECOVER LP 2.5 System support, subjects should have blood drawn Q30 minutes for the first hour, Q60 minutes for the second hour, then Q4 hours up until the time of pump explant in order to ensure that the ACT is between 160 and 180 seconds.

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8.7.1.2. Neurological Examination

Prior to placement of the IMPELLA RECOVER LP 2.5 System and at each follow-up time point thereafter a brief neurological examination must be performed. Neurological consultation will be obtained if a neurological examination at any time post-implant shows deficits not present at the baseline examination.

The brief neurologic exam will consist of the following evaluations:

a. Mental Status (N=Normal, A=Abnormal, U=Unable to Assess)

b. Pupils
   - i. Left Reactive
   - ii. Left Dilated
   - iii. Right Reactive
   - iv. Right Dilated

c. Sensory (N=No Sensory Loss, M= Mild/Moderate Loss, S=Severe to Total Loss)
   - i. Left Arm
   - ii. Left Leg
   - iii. Right Arm
   - iv. Right Leg

d. Motor (N=No Motor Loss, M=Mild/Moderate Loss, S=Severe to Total Loss)
   - i. Left Arm
   - ii. Left Leg
   - iii. Right Arm
   - iv. Right Leg

e. Cranial Nerves Examination
   - i. Olfactory
   - ii. Optic
   - iii. Oculomotor
   - iv. Trochlear
   - v. Trigeminal
   - vi. Abducens
   - vii. Facial

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viii. Vestibulocochlear

ix. Glossopharyngeal

x. Vagus

xi. Accessory

xii. Hypoglossal

8.7.1.3. Echocardiogram

Prior to placement of the IMPELLA RECOVER LP 2.5 System, an Echocardiogram shall be performed using institutional guidelines to evaluate the left ventricle for placement of the RECOVER LP 2.5 System. A transesophageal echo (TEE) or transthoracic echo (TTE) will assist the operator in ensuring that no contraindications are present at the time of pump placement. Echocardiogram can be used to assist in placement of the pump, as deemed necessary by the operator.

Follow-up echo exams will be used to assess aortic valve functional status.

8.7.2. Patient Monitoring Just Prior to or During Device Placement

- X-ray Fluoroscopy (for device placement)
- Echocardiogram (optional for placement)
- Heart rate
- Blood pressure (Systolic/Diastolic/Mean)
- PCWP
- PAP (Systolic/Diastolic)
- CVP
- CI
- Activated Clotting Time (ACT)
- Blood gases
    - a) PO2 arterial
    - b) PO2 venous
    - c) PCO2 arterial
    - d) PCO2 venous
    - e) HCO3

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f) pH venous

g) pH arterial

8.7.3. Patient Monitoring During the PCI Procedure

Patients shall be monitored while on pump support during the PCI procedure. The detailed list of tests, as shown on the Case Report Forms (CRFs), is provided below. Patient monitoring during the PCI procedure includes the following:

- Q15 minute peripheral pedal pulse assessment & groin site examinations.
- Echocardiogram once postimplantation to evaluate pump position
- ECG monitoring
- Hemodynamics (Measure during balloon inflations and pump speed changes):
  - Pump Parameters
  - Heart Rate
  - Blood Pressure (Arterial Pressure - Systolic/Diastolic/Mean)
- PCWP
- PAP
- CVP
- Cardiac Index
- Record of current cardiac medications
- Adverse Events

8.7.4. Patient Monitoring following discharge from the Cath Lab

Patients shall be monitored following their discharge from the Cath Lab whether or not the IMPELLA RECOVER LP 2.5 System has been explanted in the Cath Lab. The detailed list of labs, as shown on the Case Report Forms (CRFs), is provided below. In addition, during pump operation, the pump performance parameters shall be recorded on the CRFs and will be continuously monitored using the automated software in the MPC. Patient monitoring during pump support includes the following:

- Neurological assessment once every day until hospital discharge.
- Summary of medical/surgical interventions including any blood product delivered and inotropes/pressors used.

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- Peripheral pedal pulse assessment & groin site exam (Q30 minutes for the first 4 hours while on IMPELLA RECOVER LP 2.5 System support. Thereafter Q1 hour until explant.)
- 12-lead ECG Q24 hours
- Hemodynamics (Q30 for the first four hours of pump operation, then Q4 hours for up until 48 hours then Q12 hours until pump explant.):
  - Pump Parameters
  - Heart Rate
  - Blood Pressure (Arterial Pressure Systolic/Diastolic/Mean)
- PCWP (If available)
- PAP (If available)
- CVP (If available)
- Cardiac Index (If available)
- Blood labs (Q 8 hours for the first 48 hours, then Q12 until explant):
  - Hematology
    1. WBC/RBC
    2. Platelets
    3. Plasma Free Hgb one hour following pump start and Q24 hours thereafter until pump explant
    4. Hematocrit/Hemoglobin
  - Hemostasis
    1. INR or Prothrombin Time (PT) or Activated Partial Thromboplastin Time (aPTT)
  - ACT (Q30 minutes for the first hour of pump operation, then once during the second hour, then Q4 hours until pump explant)
  - Cardiac Enzymes
    1. CK
    2. CK-MB
    3. Cardiac Troponins

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- Electrolytes
    1. Potassium
    2. Chloride
    3. Phosphate
    4. Glucose
    5. Systemic lactate

- Complement activation markers
    1. CRP
    2. C3
    3. C5a
    4. IL-6
    5. Granulocyte Elastase

- Blood Gases (Q 8 hours for the first 48 hours, then Q12 until explant):
    1. PO2 arterial
    2. PO2 venous
    3. PCO2 arterial
    4. PCO2 venous
    5. HCO3
    6. pH venous
    7. pH arterial

- Noncardiac bloodwork (Q 8 hours for the first 48 hours, then Q12 until pump explant):
    1. Total Bilirubin
    2. BUN
    3. Serum Creatinine
    4. LDH
    5. AST

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- Urine Output
- Record of current cardiac medications
- Adverse Events

8.7.4.1. Device Removal / Recommended Weaning Protocol

Weaning the subject from the RECOVER LP 2.5 device is left up to the discretion of the physician. Patients may be supported with the RECOVER LP 2.5 device for up to 5 days.

The following is a weaning protocol that is provided as guidance only.

- ***Within the Cath Lab - post PCI***

  Weaning may be commenced in the Cath Lab if the subject demonstrates satisfactory hemodynamic status with minimal need for additional circulatory support following the PCI procedure.

  In this case, the physician may initiate "rapid weaning" by decreasing pump performance level in 2-steps (but never below P2 as long as the pump is in the ventricle) in intervals of 2 to 10 minutes. When the performance level has been reduced to P2, maintain the subject on P2 support for at least 10 minutes before discontinuing circulatory support. If the subject's hemodynamics remains stable, pull back pump into the aorta, stop the pump (P0) and explant the device.

- ***Post PCI and up to 5 Days post implant***

  If the subject can not be weaned in the Cath Lab, the IMPELLA RECOVER LP 2.5 System may remain implanted for up to 5 days. If stable hemodynamics are achieved within 5 days of implantation the physician may initiate weaning at his or her discretion.

  In this case, the physician may initiate "slow weaning" by decreasing pump performance level in 2-steps (but never below P2 as long as the pump is in the ventricle) in intervals of 2-3 hours. When the performance level has been reduced to P2, maintain the subject on P2 support for at least 2-3 hours before discontinuing circulatory support. If the subject's hemodynamics remain stable, pull back pump into the aorta, stop the pump (P0) and explant the device.

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If a significant dosage of inotropes are needed to maintain acceptable hemodynamics, the physician is advised not to initiate the "slow weaning" process until stable hemodynamic conditions can be achieved with no or low dose inotropes.

- ***5 Days post implant***

  The options available to subjects after 5 days include the following:

  1. Implantation of a different circulatory assist device such as an IABP or another FDA approved mechanical circulatory support device (if the patient still requires hemodynamic support).
  2. Removal without replacement of the IMPELLA RECOVER LP 2.5 System.

  It is not recommended that a single IMPELLA RECOVER LP 2.5 System remain in operation for more than 5 days.

8.7.4.2. Device retrieval

All used devices (IMPELLA RECOVER LP 2.5 System) will be gently rinsed with saline immediately upon removal from the subject. Any observation of gross deposits should be recorded on the Device Return Report. Photographs of the device should be taken and the device should then be returned to ABIOMED, Inc. in the biohazard packaging provided.

8.7.5. Patient Monitoring After Pump Removal

The patient will be monitored after pump removal up until discharge. The following assessments (except for plasma free hemoglobin measurements, pedal pulse assesment and echocardiography) shall be performed after pump removal on a Q24 hour basis while the patient is in the ICU and on a Q48 hour basis while the patient is in any other hospital unit other than the ICU:

Physical examination including neurological assessment

- Peripheral pedal pulse assessment & groin site exam
- Hemodynamic assessment including heart rate and arterial pressure (systolic/diastolic/mean)

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- Summary of medical/surgical interventions including any blood product delivered and inotropes/pressors used.
- Echocardiogram (once postexplant)
- Blood labs including:
    - Hematology
        1. RBC/WBC
        2. Platelets
        3. Plasma-free Hgb (once, three days postexplant)
        4. Hematocrit/Hemoglobin
    - Complement activation markers
        1. CRP
        2. C3
        3. C5a
        4. IL-6
        5. Granulocyte elastase
    - Cardiac Enzymes
        1. CK
        2. CK-MB
        3. Cardiac Troponins
    - Electrolytes
        4. Potassium
        5. Chloride
        6. Phosphate
        7. Glucose
        8. Systemic Lactate

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- Noncardiac bloodwork
    1. Total Bilirubin
    2. BUN
    3. Serum creatinine
    4. LDH
    5. AST

- Urine Output
- Record of current cardiac medications
- Adverse Events

8.7.6. Discharge

Complete the Discharge CRF. Telephone numbers should be obtained from the patient so he/she can be contacted after hospital discharge for scheduling of follow-up evaluations. Phone numbers should include home, work, primary physician's numbers, and numbers of a relative or friend.

8.7.7. Follow-Up at 30 Days (or Discharge) and at Three (3) Months

The following assessments shall be performed at 30 days (± 10 days) or at discharge (whichever is longer), and 3 months (± 30 days) post pump removal:

- Physical exam including neurological assessment
- Peripheral pedal pulse assessment & groin site examination.
- Hemodynamic assessment including heart rate and arterial pressure (systolic/diastolic)
- Echocardiogram
- Blood labs including:
    - Blood cell counts
        1. WBC/RBC
        2. Platelets
        3. Hematocrit

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- Electrolytes
    1. Potassium
    2. Chloride
    3. Phosphate
    4. Glucose
    5. Systemic Lactate
- Noncardiac bloodwork
    1. Total bilirubin
    2. BUN
    3. Serum creatinine
    4. LDH
    5. AST
- Record of current cardiac medications
- Adverse events

8.7.8. End of Study

Complete the end of study form when the patient has completed the 3 month follow-up or has been prematurely terminated from the study due to death or withdrawal.

8.8. *Withdrawal of Patients*

The subject always retains the right to withdraw from the study at any time, although withdrawal from the study is strongly discouraged after the subject has been enrolled. If a subject does not return for a scheduled visit, every effort should be made to contact her/him to complete follow-up. If possible, a complete, final examination should be performed on all subjects who withdraw from the study. At a minimum, every effort should be made to document subject outcome for every visit.

All subjects enrolled in this trial, including those subjects in whom the device(s) did not perform as intended, are subject to complete clinical follow-up and will be included in the analysis of safety. Patients who are entered into the study, but who fail to have a successful pump placement procedure will only be followed through to hospital discharge.

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In all cases of withdrawal, the reasons for withdrawal must be recorded on the CRF and in the subject's medical records. If more than one reason is cited for withdrawal, study personnel should identify the most significant reason.

8.9. *Post mortem examination*

The investigator is encouraged to request a postmortem examination for study subjects who expire within the 30 Day follow-up period or prior to discharge. Study personnel should request the following examinations be performed in addition to the routine post-mortem evaluations:

- Endocardial/myocardial injury
- Papillary muscle injury or chord injury
- Aortic or mitral valve injury
- Vascular trauma
- Evaluation of evidence of any other myocardial injury, valvular disease and non-cardiac diseases or trauma
- Introduction site
- End organ examination for necrosis or thrombosis

It is acknowledged that permission for autopsy is the right of the family, and although such permission will be requested postmortem for all subjects, it may not always be obtained.

9. Administrative Responsibilities

9.1. Data Collection Binders

Case Report Forms (CRFs) will be used to collect all subject data during the trial. CRFs must be fully completed for each subject, signed, and available for review by ABIOMED within 15 working days of the event they document. CRFs will be monitored following the guidelines established by the ABIOMED Standard Operating Procedures for monitoring investigational sites. The Investigator, or an individual designated by the Investigator, is responsible for recording all data from the trial on the CRFs supplied by ABIOMED.

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All Principal Investigator(s), Co-Investigator(s) and Study Coordinator(s) are required to sign the Site Personnel Signature Form correlating signatures, initials and dates of participation in the study. This signed form must be retained at the investigational site.

9.2. Investigational Plan Deviations

All departures from clinical study requirements, including ICH/GCP guidelines, will be considered deviations from the investigational plan. A 'serious' deviation is one that may affect the scientific soundness of the investigational plan or that would affect the rights, safety, or welfare of human subjects.

Patient-Level Deviations are those that occur in direct association with a specific study subject. These include, but are not limited to, deviations from Informed Consent procedures, inclusion/exclusion criteria, required clinical assessments, clinical assessment time frame infringements, clinical investigational plan procedures, device handling and usage, medication requirements, and source documentation or data completion.

Site-Level Deviations are those that occur at the study center, but are not directly related to a specific study subject. Those deviations include, but are not limited to, Institutional Review Board (IRB) approval and reporting; regulatory binder maintenance; device storage and accountability; facility, equipment, and staff qualification and maintenance; and general study log maintenance.

Documentation of deviations identified by the study center, the monitor, or other Sponsor representative(s) will be entered into the CRF by the study center representative for the purpose of tracking Investigator compliance in accordance with the Sponsor and ICH/GCP guidelines. The study center will be required to document actions taken to prevent recurrence of deviations; the Sponsor representative will initiate corrective actions consistent with the Sponsor guidelines based on individual deviations or trending reports, as appropriate.

10. Monitoring Procedures

Initiation visits will be conducted at each study center before the device is shipped to discuss the clinical investigational plan and review data collection procedures, AE monitoring and reporting procedures, and regulatory requirements. Monitors have been trained according to ABIOMED Clinical Research procedures. Monitors may include ABIOMED Clinical Field Monitors and/or

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Contract Research Organization (CRO) monitors. The Monitoring staff will be trained on the requirements of the ABIOMED Investigational Plan and the monitoring requirements specific to this study prior to commencing the monitoring for the study.

Authorized ABIOMED personnel and/or designees will review completed CRFs at the investigational site at intervals throughout the trial. The Investigator must permit inspection of the trial files, subject medical records and subject CRFs by such ABIOMED representatives and/or responsible government agencies.

10.1. Sponsor

ABIOMED, Inc. will serve as the Sponsor of the trial.

ABIOMED personnel responsible for the trial:

Karim Benali, MD
Chief Medical Officer
ABIOMED, Inc.
22 Cherry Hill Drive
Danvers, MA 01923

10.2. Monitoring and Auditing

Monitoring visits to the study centers will be made periodically during the study per the agreed upon monitoring plan, but no less than once per year, to ensure that all aspects of the current approved investigational plan/amendment(s) are followed. Source documents will be reviewed for verification of data on the Case Report Forms. The Investigator/institution guarantees direct access to source documents by designated ABIOMED personnel or their designees and appropriate regulatory authorities.

It is important that the Investigator and the relevant study personnel are available during the monitoring visits and possible audits and that sufficient time is devoted to the process.

10.3. Device Accountability

Device accountability records must be maintained at the study center. The number of devices delivered to and returned by the Investigator and the devices used to treat subjects will be

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recorded. Any accountability discrepancy must be explained in writing by the Investigator and reported to the Sponsor.

11. Adverse Events

11.1. Adverse Events and Adverse Device Effects

All complications, including any clinical event that results in prolonged hospitalization, death, cardiovascular- or trial-procedure-related injury, is considered an Adverse Event (AE). This definition includes events occurring during the hospital stay and the follow-up period specified in the investigational plan.

An Adverse Device Effect is a device-related Adverse Event. All Adverse Events (AE) and Adverse Device Effects (ADE) must be recorded in the Case Report Forms provided. A description of the event, including the onset date, duration, whether device related, any action taken and the outcome, should be provided, along with the Investigator's assessment of the relationship to the study treatment.

Elective hospitalization after the study procedure that was planned prior to subject enrollment in the study will not be regarded as an AE.

Underlying diseases are not reported as Adverse Events, but any deterioration in severity or exacerbation will be reported on appropriate Adverse Event Form(s).

Adverse Events must be monitored from the time of enrollment through the last follow-up visit. They may include, but are not limited to, the clinical events listed in the risk section of the investigational plan.

All reported defined Adverse Events (Appendix A) will be reviewed, adjudicated and categorized by the Clinical Reviewer, who has the authority to override the Investigator's final determination related to causality, severity and relationship to study device.

11.2. Reporting Events

The procedure for reporting any Adverse Events (Appendix A) or device-related AE is as follows:

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- Report any Adverse Event (Appendix A), and/or device related AE to ABIOMED within one working day of knowledge of the event by fax and to the IRB within 10 working days in writing.
- Complete the appropriate Case Report Form (CRF).
- Provide completed, signed copies of the Adverse Event Form and attachments to ABIOMED Clinical Research personnel.
- The Adverse Event Report must be signed and dated by the Investigator.
- Attach relevant physician/nurse notes or summaries about the event to the Adverse Event Report along with copies of source documentation when submitting the original AE to ABIOMED.
- Patient's identifiers (i.e., name, address, medical record #) should be made illegible on all copies of source documents.
- Completed Adverse Event Reports and attachments should be provided to ABIOMED within ten (10) working days of knowledge of the event.
- In case of death, the notification must include a brief statement of the pertinent details and be signed by the Investigator or Co-Investigator. A copy of the death records, death certificates and an autopsy report (if performed) must be sent to ABIOMED as soon as possible.

It is the responsibility of each Investigator to inform their Ethics Committee/Institutional Review Board (IRB) of Adverse Events and Adverse Device Effects as required by their Ethics Committee/IRB procedure and country law. ABIOMED is responsible for relaying adequate information on AEs to the other Investigators and regulatory authorities.

11.3. Clinical Events Review

An independent Medical Monitor will be responsible for adjudicating the Adverse Events listed in Appendix A of the protocol. The Medical Monitor will be a qualified physician experienced with VAD technology.

The Medical Monitor is also charged with the approval of the specific criteria used for the categorization of clinical events and clinical endpoints in the PROTECT I clinical trial. The

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Medical Monitor will approve explicit rules outlining the minimum amount of data required, and the procedure to be followed in order to adjudicate a clinical event.

The adjudication procedures that the reviewer will follow will be detailed in a separate document and will be made available to the FDA.

11.4. Device Failures and Malfunctions

A device malfunction is an unexpected change in study device performance that is contradictory to the labeling and/or negatively impacts the treatment when used according to the labeling.

All device failures and malfunctions will be documented on the CRF, and the device must be returned to ABIOMED within five (5) working days.

The report on the study results will include information on device failures and malfunctions. Instructions for returning the investigational device will be provided.

Device failures and malfunctions should also be documented in the subject's medical record and recorded as complaints according to ABIOMED complaint handling procedures.

12. Ethical Considerations

12.1. Relevant Guidelines and Regulations

The study will be performed in accordance with the relevant parts of the Code of Federal Regulations, ICH Guidelines for GCP, the Declaration of Helsinki, and all pertinent state and federal laws and regulations.

12.2. Institutional Review Board

Before enrollment of any subjects at a site, this investigational plan and the informed consent document must be reviewed and approved by the appropriate Institutional Review Board (IRB) where the trial is to be conducted in accordance with local requirements. Changes to the investigational plan that may increase the subject's risks, affect the scientific soundness of the study, or the rights, safety, or welfare of human subjects, require prior approval from ABIOMED, the FDA and the individual site IRB.

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The Investigator must notify the IRB of any deviations to the investigational plan or AEs occurring at their site. They must also submit any reports of adverse events received from ABIOMED.

It is the Investigators' responsibility to obtain and maintain written approval of the final investigational plan, including the Informed Consent, from the Institutional Review Board. It is also the Investigators' responsibility to inform the IRB and gain approval, if required, for all subsequent investigational plans and changes to the consent document.

Prior to receipt of investigational devices, a signed copy of the IRB approval letter addressing all of the required items must be submitted to ABIOMED certifying trial approval at the investigational site. Investigators are responsible for submitting and obtaining initial and continuing review (at intervals not greater than once a year) of the trial by their IRB. The approval should include study identification and the date of review.

All correspondence with the Institutional Review Board must be maintained by the Investigator with copies forwarded to ABIOMED.

12.3. Informed Consent

Informed consent is mandatory and must be obtained from all subjects (or their legal representative) prior to their participation in the PROTECT I trial. Informed consent must be obtained in accordance with the FDA regulation 21 CFR, Parts 50 and 812, and in accordance with IRB policies and procedures.

Prior to inclusion in the study, it is the responsibility of the Investigator to give each subject (or the subject's legally authorized representative) full and adequate verbal and written information about the objectives and the procedures of the study and the possible risks involved. The subjects must be informed about their right to withdraw from the study at any time and for any reason without sanction, penalty, or loss of benefits to which they are otherwise entitled and that withdrawal from the study will not jeopardize their future medical care. Furthermore, it is the responsibility of the Investigator to obtain a signed Informed Consent form from each subject prior to performing any study-related procedures. Informed consent documents should be written in language understandable to the subject or subject's legally authorized representative.

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The Informed Consent must be updated or amended whenever new information becomes available that may be relevant to the subject. The ABIOMED Informed Consent Form is included in Appendix E. Any modifications to the ABIOMED Informed Consent Form must be approved by ABIOMED. The institutional standard subject consent form does not replace the ABIOMED Consent Form. The site will use copies of this consent form to obtain subject consent signatures. IRB-approved modifications to the consent must be approved by ABIOMED, Inc. prior to use in the study.

A copy of the IRB- and ABIOMED- approved Patient Informed Consent Form along with a copy of each subject's signed consent form must be maintained by each Investigator. A signed copy of the consent form must be given to each subject.

12.4. Health Insurance Portability and Accountability Act (HIPAA)

All subjects enrolled in this study will be required to sign the Sponsor approved Clinical Trial HIPAA Authorization form that is incorporated as part of the informed consent document. This form must be signed by each subject enrolled into this study. Written HIPAA authorization is required at the time of study enrollment to ensure that the subject is aware and agrees to the use and disclosure of their study information by the institution and investigators to the Sponsor, their agents and representatives, the US Food and Drug Administration (FDA) and the Medical Monitor and other government agencies or review boards.

If the institution requires that an IRB specific HIPAA Authorization form be used, then the investigational site must provide a copy of this form to ABIOMED for review and approval. The institutional HIPAA authorization form may only be used in place of the Sponsor-approved form if prior written approval is granted by the Sponsor. This is to ensure that the content of the institutional version is consistent with the content of the ABIOMED Authorization form.

12.5. Amending the Investigational Plan

This investigational plan is to be followed by all parties. All changes affecting the scientific soundness of the study, or affecting subject's rights, safety or welfare require prior FDA and IRB approval. Amendments to the investigational plan must be written and approved in order to alter the investigational plan. Administrative changes that do not affect the subject benefit/risk ratio (e.g., editorial changes for clarity) may be made by ABIOMED without any further approvals.

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Any change that would require alteration of the Informed Consent Form must receive approval from all persons who approved the original investigational plan and from the IRB prior to implementation. Following approval, the investigational plan amendment(s) will be distributed to all investigational plan recipients with instructions to append them to the investigational plan.

13. Study Administration

13.1. Record Retention

In order to constitute evidence with respect to product safety or regulatory or legal compliance, the Investigator agrees to retain study-related documents in a location that is secure and to which ABIOMED can be gain access if required. The following documents must be archived: the Investigator's File containing all required GCP documents, including signed Informed Consent forms and subject-related materials, CRFs and Data Clarification Forms. The Investigator should retain records for at least two years after the IMPELLA RECOVER LP 2.5 System is no longer under an Investigational Device Exemption. ABIOMED retains the right to obtain these records after the two (2) year retention period. ABIOMED requires that the investigator provide the sponsor advanced notice before destroying such documents.

13.2. Criteria for Terminating Study

ABIOMED reserves the right to terminate the study, but intends only to exercise this right for valid scientific or business reasons or reasons related to subject safety. Investigators and associated IRBs will be notified in writing in the event of termination.

13.3. Criteria for Terminating a Study Center

ABIOMED reserves the right to stop the enrollment of subjects at a study center at any time after the study initiation visit if no subjects have been enrolled or if the center has multiple or serious investigational plan violations without justification or fails to follow remedial actions.

Possible reasons for terminating a study center include:

- Repeated failure to complete CRFs prior to scheduled monitoring visits.
- Failure to obtain Informed Consent.
- Failure to report (Appendix A) Adverse Events within 24 hours of knowledge.

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- Loss of (or unaccounted for) investigational product inventory.
- Repeated protocol violations.
- Failure to enroll an adequate number of subjects.

13.4. Notification/Application to Relevant Regulatory Authorities

According to the individual state law / regulation, the study will not be initiated before it has been approved by the relevant regulatory authorities or the relevant regulatory authorities have been notified as required by law / regulation.

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Appendix A

Adverse Event Definitions

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

AORTIC INSUFFICIENCY
Aortic regurgitation graded by echocardiographic measurement as ≥ 2 or an increase in aortic regurgitation by more than one assessment level on a 4-point scale as determined by echocardiographic measurement.

AORTIC VALVE INJURY
Injury to the aortic valve regardless of the cause as assessed by Doppler echocardiography versus baseline.

ARRHYTHMIA
Documentation of any one of the following: Atrial fibrillation/flutter (AF) requiring treatment, heart block, or sustained VT or VFIB requiring cardioversion and/or IV amiodarone

ATRIAL FIBRILLATION
New onset of atrial fibrillation/flutter (AF) requiring treatment. It does not include the recurrence of AF which had been present preprocedurally.

BLEEDING
Blood loss resulting in one of the following:

a) surgical exploration for resolution
b) any blood transfusion after 72 hours post-implantation

CARDIAC TAMPONADE
Accumulation of pericardial fluid resulting in hemodynamic compromise and requiring surgical intervention or catheter drainage.

CARDIOGENIC SHOCK

- CI < 2.2 l/min/m^2 and PCWP > 15mmHg
- Hypotension (systolic BP < 90 mmHg for > 30 minutes or the need for supportive measures to maintain a systolic BP of greater or equal to 90 mmHg) AND end organ hypoperfusion (cool extremities OR [a urine output of < 30 ml/hour AND a HR > 60 BPM]).

CEREBRAL VASCULAR ACCIDENT (CVA) / STROKE
Cerebral Vascular Accident (CVA) / Stroke defined as evidencethe persistence of a neurological deficit that persists > 24 hours or abnormal CT over 24 hours, or CAT scan or MRI demonstratinging ischemic or hemorrhagic changes in to the brain.

DEVICE MALFUNCTION
A device malfunction is an unexpected change in study device performance that is contradictory to the labeling and/or negatively impacts the treatment when used according to labeling.

HEMOLYSIS
Two plasma free hemoglobin values > 40 mg/dL with the two readings taken within a single forty-eight (48) hour period. If the second plasma free hemoglobin assessment is not performed within 48 hours following an initial determination of > 40 mg/dL, this would qualify as an adverse event.

HEPATIC FAILURE
Hepatic Failure is an increase in any two of the following hepatic laboratory values (total bilirubin, aspartate aminotransferase/AST and alanine aminotransferase/ALT) to a level greater than three times the upper limit of normal for the hospital, post-pump implant (or if hepatic failure is the primary cause of death) .

INSERTION SITE INFECTION
Clinical manifestation of infection at the IMPELLA RECOVER 2.5 LP System insertion site distinguished by such signs as pain, fever, elevated temperature, drainage and/or leukocytosis.

LIMB ISCHEMIA
New incidences of hypoperfusion of the leg requiring treatment and marked by such symptoms as decreased skin temperature of the limb or decreased peripheral pulses.

MAJOR ADVERSE CARDIAC AND CEREBRAL EVENTS (MACCE)
Defined as death, new myocardial infarction, target vessel revascularization, urgent coronary artery bypass grafting procedure or stroke during and up to 30 days post-index procedure. MACCE is adjudicated by the Medical Monitor of the study.

MYOCARDIAL INFARCTION
The presence of any two of the following:

a) CK-MB greater than three (3) times the normal range with positive MB fraction
b) Troponins greater than eight (8) times the normal range.
c) ECG with pattern or changes consistent with myocardial infarction
d) History and timing consistent with either of the above three events.

Myocardial Infarction is classified as follows:

- Q-wave MI: development of new (i.e., not present on the patient's ECG before allocation), pathological Q-waves in two (2) or more leads lasting 0.4 seconds or more with post procedure CK-MB levels elevated above normal.
- Non-Q-Wave MI: elevation of postprocedure CK levels to > 2.0 times normal with detectable CK-MB in the absence of pathological Q-waves; if no assay for CK-MB was performed, elevation of CK levels to > 2.0 times normal without new Q-waves is also considered a non-Q-wave MI.

PERFORATION
Vascular perforation requiring additional treatment (including efforts to seal the perforation or pericardial drainage), or resulting in significant pericardial effusion, abrupt closure, myocardial infarction, or death.

RENAL FAILURE
Abnormal kidney function requiring dialysis (including hemofiltration) in patients who did not require this treatment prior to PCI, or a rise in serum creatinine to a level ≥ 4 mg/dL sustained for over 48 hours.

RESPIRATORY DYSFUNCTION
Intubation or tracheostomy for respiratory distress, excluding reoperation or temporary intubation for diagnostic or therapeutic procedures.

SEPSIS
Evidence of systemic involvement by infection defined by any administration of presumptive antibiotics (not including prophylactic antibiotics).

THROMBOCYTOPENIA
Defined as a platelet count reading of less than 50,000/mm^3 taken more than 48 hours post-pump implant.

THROMBOTIC VASCULAR (non-CNS) COMPLICATION
Deficit in any noncerebrovascular organ system (pulmonary, renal, hepatic, splenic or limb) demonstrated through standard diagnostic assessment to be due to acute vascular occlusion.

TRANSIENT ISCHEMIC ATTACK (TIA)
TIA defined as a brief episode of neurological dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction.

VASCULAR INJURY
Any injury to the blood vessels that disrupts the anatomy or function of the blood vessel including vessel dissection, rupture, perforation, pseudoaneurysm, etc. and that requires intervention.

VENTRICULAR FIBRILLATION
Supraventricular tachyarrhythmia characterized by uncoordinated ventricular activation with consequent deterioration of ventricular mechanical function.

VENTRICULAR TACHYCARDIA
Tachycardia (> 120 bpm) with QRS duration greater than 110 msec lasting more than 60 seconds.

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Appendix B

Definitions and Acronyms

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

CALCIFICATION
Readily apparent densities seen within the artery wall and site of lesion either as an X-ray absorbing mass or as an echogenic and shadow generating mass in ultrasonic imaging.

CARDIAC TROPONINS
Cardiac specific protein used to evaluate detect and diagnose acute MI and reinfarction, and to monitor the severity of myocardial ischemia.

CASE REPORT FORM (CRF)
A record of the data and other information on each patient in the clinical study as defined by the protocol.

CREATINE KINASE (CK)
Creatine Kinase (CK). An enzyme used to evaluate possible causes of chest pain, to detect and diagnose acute MI and reinfarction, and to monitor the severity of myocardial ischemia.

CREATINE KINASE ISOENZYME MB (CK – MB)
An isoenzyme of CK with a distinct molecular structure specific as an indicator of myocardial cell injury. It is used to evaluate possible causes of chest pain, to detect and diagnose acute MI and re-infarction, and to monitor the severity of myocardial ischemia.

COMPLICATION
An undesirable clinical event that results in death, injury, or invasive intervention. Complications may or may not be related to the investigational product.

CARDIOPULMONARY RESUSCITATION (CPR)
Cardiopulmonary resuscitation (CPR) involves a combination of mouth-to-mouth rescue breathing or assisted ventilation and chest compression. CPR keeps oxygenated blood flowing to the brain and other vital organs until appropriate medical treatment can restore a heart rhythm.

END ORGAN PERFUSION
Assessment of end organ perfusion based on the following markers:
Renal function (urine output and creatinine), hepatic function (serum markers), hematologic markers including Hgb and platelets, and systemic lactate

FDA
Food and Drug Administration

HYPERCHOLESTEROLEMIA
Patient has a history of hypercholesterolemia diagnosed and/or treated by a physician with documentation of: a) Total Cholesterol > 200 mg/dL, b) LDL (Low-density lipoprotein) > 130 mg/dL, c) HDL (High-density lipoprotein) < 30 mg/dL or d) admission cholesterol > 200 mg/dl.

HYPERTENSION
Evidenced by one of the following: a) documented history of hypertension diagnosed and treated with medication, diet and/or exercise, b) blood pressure > 140 mm Hg systolic or > 90 mm Hg diastolic on at least two occasions, c) currently on antihypertensive medication.

HYPOTENSION
Abnormally low blood pressure, seen in shock but not necessarily indicative of it. MAP < 60mm Hg.

LACTATE (SERUM)
Lactate is measured to evaluate the presence of tissue damage and perfusion. The enzyme is elevated with the presence of damage to body tissues, especially the heart, liver, kidney, skeletal muscle, brain, blood cells, and lungs.

LEFT VENTRICULAR EJECTION FRACTION (LVEF)
A parameter of global ventricular function. The percentage of the blood emptied from the ventricle at the end of the contraction.

LEUKOPENIA
Leukopenia is defined as leukocyte count of less than 3.5 $x10^9$/liter for more than three days.

NON-EMERGENT PROCEDURE[1]
Defined as a procedure done on a patient who has:

- No ongoing ischemia including rest angina despite maximal medical therapy (medical and/or intra-aortic balloon pump [IABP])
- No acute evolving MI within the 24 hours before intervention
- No pulmonary edema requiring intubation
- No cardiogenic shock
- Not undergone CPR within 24 hours of admission to the Cath Lab.

NHLBI
National Heart, Lung, and Blood Institute.

NTG
Nitroglycerin

[1] Cannon CP, Battler A, Brindis RG, Cox JL, Ellis SG, Every NR, Flaherty JT, Harrington RA, Krumholz HM, Simoons ML, Van de Werf FJJ, Weintraub WS. ACC Key Elements and Data Definitions for Measuring the Clinical Management and Outcomes of Patients with Acute Coronary Syndromes: a report of the American College of Cardiology Task Force on Clinical Data Standards (Acute Coronary Syndromes Writing Committee). J Am Coll Cardiol 2001;38:2114 –30.

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NEW YORK HEART ASSOCIATION CLASSIFICATION (NYHA)

Class I: Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II: Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain.

Class III: Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity results in fatigue, palpitations, dyspnea, or anginal pain.

Class IV: Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

SERIOUS ADVERSE EVENT

Any undesirable clinical event that requires hospitalization, prolongs hospitalization, requires intervention, is life-threatening or terminal, or results in permanent disability.

SURVIVAL

Defined as patients who survived to 30 days or to discharge, whichever is longer.

WEANING

Defined as the explant of the IMPELLA RECOVER LP 2.5 device for this High Risk PCI group whether it is immediately post procedure or if a patient requires post-procedural support as determined by the attending physician.

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

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DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

May 19, 2008

ABIOMED, INC.
22 CHERRY HILL DR.
DANVERS, MA 01923
ATTN: ROBERT T. KUNG

510(k) Number: K063723
Product: IMPELLA RECOVER LP 2.5 PERCUTANEOUS CARDIAC SUPPORT

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

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

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

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K 063723/53

ABIOMED
Recovering hearts. Saving lives.

William J. Bolt
Sr. Vice President of QA/RA
22 Cherry Hill Drive
Danvers, MA 01923
(p) 978-646-1451
(f) 978-739-0576

MAY 15 2008

May 15, 2008

Office of Device Evaluation
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, MD 20850

K063 723

Re: Response to AI letter for K062723

Dear Madam/Sir:

Enclosed please find three copies of a response to an Additional Information letter dated 1/16/2008 pertaining our 510(k) submission, K062723.

Thank you for your consideration in this matter. Please contact me with any comments or concerns.

Sincerely,

(b) (6) [redacted]

William J. Bolt
Sr. Vice President, QA & RA

K39

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

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Response to the FDA January 16, 2008 Additional Information Letter

ABIOMED, Inc.

IMPELLA® RECOVER® LP 2.5 Percutaneous Cardiac Support System

FDA Reference: K062723

Table of Contents

Section- Description	Submitted Informally	Reference Date
Executive Summary-Overview of Formal Response to AI letter of 1/16/08	No	-
1- FDA Additional Information (A.I.) Letter (1/16/2008)	NA	-
1a- Response to labeling issues (Deficiencies 1, 2 in 10/3/2007 A.I. Letter)	No	-
2- Response to Remaining Deficiency #4 in 1/16/2008 A.I. Letter- Summary	Yes	3/19/2008
2a- Comparative Testing- In vitro RBC, WBC, Platelet Counts and PFH- Executive Summary	No	-
2a1- In Vitro Blood Component Damage Test Report & Protocol	Yes	3/19/2008
2a2- Flow Curve for TandemHeart from previous submission	Yes	3/19/2008
2a3- Report- Worst Case Test Conditions for in vitro Blood Damage Testing	Yes	3/19/2008
2a4- FDA Email (4/25/2008) Requesting Additional Information for Blood Damage Testing	NA	-
2a5- ABIOMED clarification regarding previous 37 degree testing	Yes	5/8/2008
2a6- ABIOMED Response to FDA email (4/25/2008)	Yes	5/12/2008
2a7- Minutes of 5/14/2008 Teleconference of FDA Acceptance of Blood Damage Test Results	Yes	5/15/2008
2b- Comparative Testing- Complement Activation Testing- Summary	No	-
2b1- Complement Activation Test Report and Protocol	Yes	3/19/2008
2b2- FDA Email (4/11/2008) requesting additional clarification for complement activation testing	N/A	-
2b3- Additional Complement Activation testing information from Nelson Labs	Yes	4/15/2008
2b4- FDA Acceptance of Complement Test Results (email communication)	NA	5/8/2008
2c- Platelet Activation Testing and OUS Experience- Summary	No	-
2c1- In Vitro Comparison Tests and Protocols	Yes	3/31/2008
2c2- OUS Analysis	Yes	4/12/2008
2c3- FDA Acceptance of Platelet Activation Testing (4/25/2008 email)	NA	-
Appendix A- Final Updated Labeling- Instructions for Use	No	-
Appendix B- Final 510k Summary and Indications for Use Statement	No	-
Appendix C- Human Data Review "Platelet Activation and the LP 2.5 – A Review of the IDE Safety Study" by Dr. Mark Slaughter, including full IDE Safety Report	Yes	3/25/2008

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

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JAN 1 6 2008

COPY

Abiomed, Inc.
c/o Mr. William J. Bolt
Senior Vice President
Cherry Hill Drive
Danvers, MA 01923

Re: K063723
IMPELLA RECOVER LP 2.5 Percutaneous Cardiac Support System
Dated: December 12, 2007
Received: December 17, 2007

Dear Mr. Bolt:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a legally marketed predicate device because you did not completely respond to the deficiencies listed in our October 3, 2007 letter. To complete the review of your submission, we require that you respond to the following concerns.

1. In response to deficiencies 1 and 2, you propose to remove references to "high-risk cardiac surgery" and specific procedures ("valvuloplasty, mitral valve re-operation, surgery of the vena cava and/or aorta, liver transplant, etc.") from the Indications For Use. We agree with this proposal, with a slight modification to clarify the degree of support provided by your device. Please revise your Indications For Use to state the following:

   "The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is intended for partial circulatory support using an extracorporeal bypass control unit, for periods up to 6 hours. It is also intended to be used to provide partial circulatory support (for periods up to 6 hours) during procedures not requiring cardiopulmonary bypass.
   The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System also provides pressure measurements which are useful in determining intravascular pressure."

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

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2. In response to deficiency 4, you proposed to address concerns regarding the blood compatibility of your device using clinical data in place of the bench comparison studies we requested. This alternative approach was discussed with the Agency during a teleconference on October 3, 2007. As we noted then, although clinical data could potentially provide useful information to address this concern, the acceptability of this approach depends on the availability of a reasonable comparator in order to establish substantial equivalence. In this regard, the clinical information you provided does not adequately address our concerns regarding blood compatibility of your device. In fact, your clinical data actually support our original concern that this new technology may introduce significant potential for hemolysis. The clinical data is not acceptable for the following reasons:

    a. the average support time was only 1.7 hours;
    b. the data was collected post-implant (with initial readings collected 6 hours post-implant);
    c. at least 3/20 patients had significantly high hemolysis rates (>40mg/dl) – e.g., patients 002-001, 005-001, and 006-006;
    d. the data provided give us no indication of the hemolysis incurred during support; and
    e. no control data was provided to determine whether standard of care produces equivalent hemolysis results.

    Therefore, since your device may have significant potential for blood damage (such as hemolysis), please perform side-by-side comparison blood studies as previously requested, including red blood cell (RBC), white blood cell (WBC), and platelet counts; complement and platelet activation; and hemolysis studies. Testing conditions should be representative of worst case operating conditions, results should be evaluated regarding statistical significance, and your final conclusions should be discussed. The Agency has provided you with recommendations regarding test methods for some of the requested *in vitro* blood studies (emails dated November 27 and December 4, 2007).

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device.

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

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We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

You may not market this device until you have provided adequate information described above and required by 21 CFR 807.87(l), and you have received a letter from FDA allowing you to do so. If you market the device without conforming to these requirements, you will be in violation of the Federal Food, Drug, and Cosmetic Act (Act). You may, however, distribute this device for investigational purposes to obtain clinical data if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations.

If the information, or a request for an extension of time, is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days it will be considered and processed as a new 510(k)(21 CFR 807.87(l)); therefore, all information previously submitted must be resubmitted so that your new 510(k) is complete. Please note our guidance document entitled, "Guidance for Industry and FDA Staff FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment." If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the additional information request.

The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/cdrh/mdufma/guidance/1219.html.

The requested information, or a request for an extension of time, should reference your above 510(k) number and should be submitted in duplicate to:

Food and Drug Administration
Center for Devices and
Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

If you have any questions concerning the contents of the letter, please contact Kathryn O'Callaghan at (240) 276-4182. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or at (240) 276-3150, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

M. G. Hillebrenner

Matthew G. Hillebrenner, M.S.E.
Chief, Circulatory Support and
Prosthetics Branch
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

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

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Response to Labeling Issues
(Concern 1 in 1/16/2008 A.I. Letter)

Per FDA recommendations, the references to "high risk cardiac surgery" and specific procedures ("valvuplasty, mitral valve re-operations, surgery of the vena cava and/or aorta, liver transplant, etc.") have been removed from the Indications for Use. Furthermore, as suggested by the FDA, the Indications for Use now states (copied directly from 1/16/2008 A.I. Letter):

> "The IMPELLA RECOVER® LP 2.5 Percutaneous Support System is intended for partial circulatory support using an extracorporeal bypass control unit, for periods up to 6 hours. It is also intended to be used to provide partial circulatory support (for periods up to 6 hours) during procedures not requiring cardiopulmonary bypass. The IMPELLA RECOVER® LP 2.5 Percutaneous Support also provides pressure measurements which are useful in determining intravascular pressure."

All of labeling has been modified for consistency with the revised Indication for Use given above. The final labeling, the Instructions for Use, are provided in Appendix A. Besides the change in the Indications or Use, the final Instructions for Use are identical in content to that included in the original 510 submission. In addition, the final versions of the 510k Summary Statement and the Indications for Use are both given in Appendix B. The 510k Summary has been updated to include additional predicates added during the FDA review, and the new Indications for Use given above. Likewise the Indications for Use have been updated to match the Indications for Use given above.

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

ABIOMED attests that the information provided in this section is identical to that submitted to the FDA for informal review on 3/19/2008. No changes have been made.

Signed,

(b) (6) [redacted] May 15, 2008

William J. Bolt
Senior Vice President, QA & RA
ABIOMED, Inc.

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Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

ABIOMED attests that the information provided in this section is identical to that submitted to the FDA for informal review on 3/19/2008. No changes have been made.

Signed,

(b) (6) [redacted] 5/15/2008

William J. Bolt
Senior Vice President, QA & RA
ABIOMED, Inc.

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Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

ABIOMED attests that the information provided in this section is identical to that submitted to the FDA for informal review on 5/15/2008. No changes have been made.

Signed,

(b) (4) [redacted] 5/15/08

William J. Bolt
Senior Vice President, QA & RA
ABIOMED, Inc.

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

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

FDA TELECONFERENCE MINUTES

DATE/TIME: Wednesday, 5/14/2008 at 2:30 PM ET

Purpose: Follow-up to 5/2/2008 call and preceding a planned 5/15/2008 meeting at FDA offices

Participants:

Mike Minogue
Bill Bolt
Bob Kung
Matt Hillebrenner
Katie O'Callaghan
Richard Malinauskas

ABIOMED and the FDA team had a phone conference regarding the Impella LP 2.5 510k. It was designed to be a review of the remaining questions or concerns from the ABIOMED response to the FDA letter of April 25th and the phone conference of May 2

Matt Hillebrenner commented that the answers provided in the May 12th response adequately addressed the remaining FDA concerns and that there were no more questions to be answered. ABIOMED had satisfied the concern of blood damage raised in Deficiency #4 from the October 3, 2007 letter and a follow-up January 16, 2008 letter from the FDA. No further testing was necessary . All deficiencies identified by FDA in the October 3, 2007 letter and the January 16, 2008 letter have been resolved.

FDA stated that ABIOMED has cleared all remaining deficiencies and that the FDA will be granting the Impella 2.5 510(k) clearance upon receipt and processing of the formal submission. .

The next phase for formal submission was discussed. The following actions were requested of ABIOMED:

1) Provide Ms. Katie O'Callaghan a draft "Table of Contents" of the formal response to the January 16, 2008 AI letter. This letter should serve as the starting point for this formal response since all other formal responses through January 16, 2008 covering the submission requirements are already on file with the FDA . The Table of contents should contain the relevant documents that were used by the FDA in its informal review to satisfy the remaining concerns on Complement Activation, Platelet activation and hemolysis testing.

2) Provide a statement for each section of the formal submission that the information provided in this section has not changed since FDA reviewed this section in the informal review process and add a date referencing when the informal information was sent to the FDA.

3) Provide an updated final 510(k) summary and final labeling reflecting the agreed to Intended Use Statement from the January 16, 2008 letter in the formal submission.

The FDA review should be expedited if we can provide the statements verifying that each section is identical to those reviewed in the informal process mentioned above. Matt Hillebrenner replied that he would get back to ABIOMED on a timeline to complete the processing of the final submission after checking with Richard Malinauskas and Katie O'Callaghan.

Rich had some interest in maintaining a scientific dialogue on the topics we have been dealing with. It was agreed that at some mutually convenient time after 510(k) clearance,

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

ABIOMED would like to visit with FDA and discuss the scientific issues around test methodology.

ABIOMED thanked FDA for their work on this file and their persistence in working with the company to address the issues they deemed necessary for device clearance.

The call ended at 3:15 PM.

(b) (4)

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

ABIOMED attests that the information provided in this section is identical to that submitted to the FDA for informal review on 3/19/2008. No changes have been made.

Signed,

(b) (4) [redacted] May 15, 2008

William J. Bolt
Senior Vice President, QA & RA
ABIOMED, Inc.

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

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Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

From: O'Callaghan, Kathryn (b) (4) [redacted]
Sent: Friday, April 11, 2008 1:18 PM
To: Bolt, William
Cc: Hillebrenner, Matthew
Subject: RE: Complement Activation Comparison

Hi Bill,

Here are our comments on your complement activation testing:

Statistical comparison was done to the Tandem Heart predicate. Please list any statistically significant differences between the test samples and the serum or polypropylene negative controls. This will aid in assessing the level of complement activation induced by the test sample.

(b) (4) [redacted]

Please let me know if you have any questions.

Katie O'Callaghan
Division of Cardiovascular Devices
(b) (4) [redacted]
(240) 276-4182

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From: Bolt, William [(b) (4)]
Sent: Tuesday, April 15, 2008 3:03 AM
To: Hillebrenner, Matthew ; O'Callaghan, Kathryn
Subject:

Dear Katie and Matt,

Below is the response to the FDA's questions on Complement Activation we received on Friday afternoon. These answers were provided by the person listed below. (b) (4)

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

(b) (4) [redacted]

[redacted] Please let me know if there are any other questions.

Thanks

Bill Bolt

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www.abiomed.com

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

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From: O'Callaghan, Kathryn [mailto:kathryn.ocallaghan@fda.hhs.gov]
Sent: Thursday, May 08, 2008 2:16 PM
To: Bolt, William
Cc: Hillebrenner, Matthew
Subject: Re: Complement Activation Comparison

Bill,

You have adequately addressed the complement activation issue for the purposes of this submission.

Please note that for future submissions, the Division recommends that direct contact testing should be conducted instead of using extracts.

With Regards,

Katie O'Callaghan
Division of Cardiovascular Devices
kathryn.ocallaghan@fda.hhs.gov
(240) 276-4182

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

(b) (4)

Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

ABIOMED attests that the information provided in this section is identical to that submitted to the FDA for informal review on 3/31/2008. No changes have been made.

Signed,

(b) (4) [redacted] 5/15/08

William J. Bolt
Senior Vice President, QA & RA
ABIOMED, Inc.

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

(b) (4)

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INTERNATIONAL STANDARD

ISO 10993-1

Third edition
2003-08-01

Biological evaluation of medical devices —

Part 1: Evaluation and testing

Évaluation biologique des dispositifs médicaux —
Partie 1: Évaluation et essais

Reference number
ISO 10993-1:2003(E)

© ISO 2003

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

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Table 1 — Initial evaluation tests for consideration

Medical device categorization by			Biological effect							
Nature of body contact (see 4.2)		Contact duration (see 4.3) A — Limited (< 24 h) B — prolonged (24 h to 30 days) C — permanent (> 30 days)	Cytotoxicity	Sensitization	Irritation or intracutaneous reactivity	Systemic toxicity (acute)	Subacute and subchronic toxicity	Genotoxicity	Implantation	Hæmocompatibility
Category	Contact									
Surface device	Skin	A	x	x	x					
		B	x	x	x					
		C	x	x	x					
	Mucosal membrane	A	x	x	x					
		B	x	x	x					
		C	x	x	x		x	x		
	Breached or compromised surface	A	x	x	x					
		B	x	x	x					
		C	x	x	x		x	x		
External communicating device	Blood path, indirect	A	x	x	x	x				x
		B	x	x	x	x				x
		C	x	x		x	x	x		x
	Tissue/bone/dentin	A	x	x	x					
		B	x	x	x	x	x	x	x	
		C	x	x	x	x	x	x	x	
	Circulating blood	A	x	x	x	x				x
		B	x	x	x	x	x	x	x	x
		C	x	x	x	x	x	x	x	x
Implant device	Tissue/bone	A	x	x	x					
		B	x	x	x	x	x	x	x	
		C	x	x	x	x	x	x	x	
	Blood	A	x	x	x	x	x		x	x
		B	x	x	x	x	x	x	x	x
		C	x	x	x	x	x	x	x	x

NOTE This table is a framework for the development of an assessment programme and is not a checklist (see Clause 6).

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American National Standard

ANSI/AAMI/ISO 10993-4:2002
(Revision of ANSI/AAMI/ISO 10993-4:1993)

Biological evaluation of medical devices— Part 4: Selection of tests for interactions with blood

Approved 1 October 2002 by
Association for the Advancement of Medical Instrumentation

Approved 31 October 2002 by
American National Standards Institute, Inc.

Abstract: This standard gives guidance to agencies, manufacturers, research laboratories, and others for evaluating the interactions of medical devices with blood.

Keywords: biological evaluation, blood, coagulation, *ex vivo*, hematology, medical devices, thrombosis

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TAT thrombin-antithrombin complex

TCC terminal complement complex

TT thrombin time

VWF von Willebrand factor

5 Types of devices in contact with blood (as categorized in ISO 10993-1)

5.1 Non-contact devices

An *in vitro* diagnostic device is an example of a non-contact device.

5.2 External communicating devices

These are devices that contact the circulating blood and serve as a conduit into the vascular system. Examples include but are not limited to those in ISO 10993-1.

a) External communicating devices that serve as an indirect blood path include but are not limited to

— cannulae,

— extension sets,

— blood collection devices,

— devices for the storage and administration of blood and blood products (e.g., tubing, needles, and bags), and

— cell savers.

b) External communicating devices in contact with circulating blood include but are not limited to

— atherectomy devices,

— blood monitors,

— catheters,

— guidewires,

— intravascular endoscopes,

— intravascular ultrasound,

— intravascular laser systems,

— retrograde coronary perfusion catheters,

— cardiopulmonary bypass circuitry,

— extracorporeal membrane oxygenators,

— hemodialysis/hemofiltration equipment,

— donor and therapeutic apheresis equipment,

— devices for absorption of specific substances from blood,

— interventional cardiology and vascular devices, and

— percutaneous circulatory support systems.

5.3 Implant devices

Implant devices are placed largely or entirely within the vascular system. Examples include but are not limited to

— annuloplasty rings,

— mechanical or tissue heart valves,

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

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Records processed under FOIA Request #2015-278; Released by CDRH on 10-22-2015

ABIOMED attests that the information provided in this section is identical to that submitted to the FDA for informal review on 4/12/2008. No changes have been made.

Signed,

(b) (6) [redacted] May 15, 2008

William J. Bolt
Senior Vice President, QA & RA
ABIOMED, Inc.

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Complement Activation Package
(Received via email dated 3/19/2008 with attachments 2a, 2ai and 2aii)

FDA comments provided previously via email dated 4/11/2008; we are currently reviewing your responses to those comments received via email dated 4/15/2008.

Thrombogenicity Package

- Comparative *in vitro* static testing (received via email dated 3/31/2008 with 1 merged attachment = tabs 3a – 3aii2 in hard copy)
- US clinical experience (received via email dated 3/25/2008 with attachments 3b and 3bi)
- OUS clinical experience (received via email dated 4/12/2008 with 2 attachments)

(b) (4) [redacted].

***In Vitro* Blood Damage Package**
(Received via email dated 3/25/2008 with attachments 1ai, 1aii, 1aiii, and 1b)

Questions for 25°C condition:

1. It is unclear from your report whether you normalized the data using the individual platelet and white blood cell (WBC) counts in each test loop at time zero. Typically, the initial count for each loop is set to 100% and the decrease over time is expressed as a percentage. Please re-evaluate this data for both platelet and WBC values.

2. You did not provide blood temperature data. The test loop figure does not provide sufficient details for FDA to determine whether the actual temperature of the blood was measured during the testing, or if only the external flow loop tubing temperature was measured. Please clarify.

3. The lack of raw data inhibits FDA from checking the measurements and calculations you performed in your testing. Please provide raw data in your formal submission for our review. Please ensure that the raw data addresses the following questions:

    a. What were the absolute plasma free hemoglobin concentrations for both blood draws at all times in each test loop?

    b. How much hemodilution compensation was necessary due to the infusion systems of the two devices?

(b) (4) [redacted]

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

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FDA feedback
Emailed 4/25/2008

(b) (4)

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Change to Labeling- Instructions for Use Manual

The Instructions for Use Manual in the following section for the IMPELLA LP 2.5 Percutaneous Cardiac Support System is identical to that submitted in the original 510k submission with the one exception. Specifically, as requested by the FDA, the page in the Instructions for Use containing the Indications for Use (Page 2.2) has been replaced to the final version:

> "The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is intended for partial circulatory support using an extracorporeal bypass control unit, for periods up to 6 hours. It is also intended to be used to provide partial circulatory support (for periods up to 6 hours) during procedures not requiring cardiopulmonary bypass.
>
> The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System also provides pressure measurements which are useful in determining intravascular pressure."

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

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ABIOMED

Recovering hearts. Saving lives.

Impella RECOVER LP2.5
Percutaneous Cardiac Support System

Instructions for Use

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Impella® RECOVER® LP2.5
Percutaneous Cardiac Support System

Instructions for Use

ABIOMED, Inc.
22 Cherry Hill Drive
Danvers, MA 01923 USA

978-777-5410
978-777-8411 (fax)
clinical@abiomed.com (email)
www.abiomed.com

24-Hour Emergency Hotline: N. America 1-800-422-8666

December 2006
Document No. 0046-9004 Rev. 1 **DRAFT**

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

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IMPORTANT NOTICE: Read this ***entire*** manual before using the Impella® RECOVER® LP2.5 Percutaneous Cardiac Support System (LP2.5 System). The LP2.5 System is to be used only in accordance with this manual. This manual is only applicable within the U.S.A.

Information contained in this document is subject to change without notice.

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

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

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Introduction

This manual provides instructions for use of the Impella® RECOVER Circulatory Support System LP2.5 (LP2.5 System). The following summarizes the contents of each section:

- **Section 1 (Warnings and Cautions)** discusses the warnings and cautions pertaining to the use of the LP2.5 System.
- **Section 2 (Indications, Contraindications, and Potential Adverse Events)** discusses indications for use of the System and potential adverse events that may be associated with it.
- **Section 3 (The LP2.5 System)** provides an overview of the System and describes its major components.
- **Section 4 (Using the Impella® MPC)** describes the controls and connections of the Impella Mobile Pump Console.
- **Section 5 (Using the LP2.5 System)** provides the procedures for using the System.
- **Section 6 (Cleaning and Storage)** provides instructions on cleaning and storing System components.
- **Section 7 (Abbreviations and Symbols)** provides the abbreviations and symbols used on System components and packaging.
- **Section 8 (System Specifications)** lists technical information pertaining to the System.
- **Section 9 (MPC Alarms and Warnings)** provides an alphabetical listing of Mobile Pump Console alarms and warnings, as well as information on what to do to resolve them.

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1 Warnings and Cautions

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Warnings

NOTE: A warning indicates a situation that could result in injury or death.

- The LP2.5 System is intended for use only by personnel trained in accordance with the Abiomed Training Program.
- The sterile components of the LP2.5 System can be used only if the sterilization indicators show that the contents have been sterilized, the packaging is not damaged, and the expiration date has not elapsed.
- Do ***NOT*** resterilize or reuse the LP2.5 Catheter. It is a disposable device and is intended for single use only. Do ***NOT*** autoclave the Catheter.
- Retrograde flow will occur across the aortic valve if the pump is set at performance level P0.
- Fluoroscopy ***MUST*** be used for the insertion of the Impella guidewire and LP2.5 Catheter.
- To prevent failure of the 13F peel away introducer, remove the 13F peel away introducer prior to transport. The ACT should also be less than 150 seconds to ensure that the patient is not anticoagulated.
- The Braun Vista® basic Infusion Pump provided by Abiomed must ***NOT*** be used in conjunction with any products other than Impella products.
- Do ***NOT*** support a patient with the LP2.5 System for more than 5 days. Operation of this System for more than 5 days can lead to malfunction of the System and result in injury or death.
- Do ***NOT*** use an LP2.5 System if any part of the System is damaged.
- Take care to avoid over-inserting the Catheter and possibly impinging the Catheter tip against the vessel/ventricular/atrial walls.

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- Do ***NOT*** advance or withdraw an intravascular device against resistance without determining the cause of the resistance by fluoroscopy. Failure to do so can result in separation of the Catheter or guidewire tip, damage to the Catheter, or vessel or ventricular perforation.

- To prevent the risk of explosion, do not operate the LP2.5 System near flammable anesthetics.

- To prevent malfunction of the locking mechanism of the 13F peel away introducer, do ***NOT*** hold the hemostatic valve while inserting into the artery.

- Do ***NOT*** apply negative pressure to the infusion line with a syringe to remove an air bubble. This can cause blood to be introduced into the pump bearing area and may result in pump failure.

- Changing to the backup MPC will stop the pump.

- Be sure that the stopcock is always kept in the closed position or is connected to pressure tubing. Significant bleedback can result if the stopcock is open.

- Do ***NOT*** use alcohol-based fluids for lubrication.

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Cautions

NOTE: A caution indicates a situation in which equipment may malfunction, be damaged, or cease to operate.

- Use only original accessories and replacement parts supplied by Abiomed.
- Refer to the Instructions for Use supplied with the Braun Vista® basic Infusion Pump ***before*** using the Pump with the LP2.5 System.
- Holding down the MPC's ON key for longer than 3 seconds during operation will cause the MPC to go into emergency stop mode.
- During the MPC Function Test, if a pressure value of 50 (± 4) mmHg does not appear or the speed is not within the specified range of 23,000 to 25,000 revolutions per minute (rpm), do ***NOT*** use the MPC.
- Do ***NOT*** use damaged or contaminated connector cables.
- To prevent device failure, do not start the LP2.5 Catheter until the guidewire has been removed.
- To troubleshoot Vista basic alarms not listed in this manual, refer to the Vista basic Instructions for Use.
- When the Braun Vista® Pump Set in the Braun Vista basic Infusion Pump is to be replaced, the replacement process must be completed within 2 minutes. The LP2.5 Catheter may be damaged if replacement takes longer than 2 minutes.
- Protect the MPC and the Power Supply from direct sunlight and exposure to excessive heat (max. 40°C) to prevent malfunction.
- To prevent overheating and improper operation, do ***NOT*** block the cooling vents of the Power Supply while it is operating. Do ***NOT*** place the MPC on top of the Power Supply.

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- Do not kink or clamp the LP2.5 Catheter or the 13F peel away introducer.

- The Li-Ion batteries must be charged for 10 hours prior to system operation. After being unplugged, the MPC will operate for a minimum of 60 minutes after the batteries have been fully charged.

- Minimize exposure of LP2.5 System components to sources of electromagnetic interference (EMI). Exposure to sources of EMI, such as cell phones and two-way radios, may cause operational interference. To clear interference, either increase the distance between System components and the EMI source or turn off the EMI source.

- Operation of LP2.5 System components may interfere with the operation of other devices. If interference occurs, increase the distance between the device and System components.

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2 Indications, Contraindications, and Potential Adverse Events

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Indications

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is intended for partial circulatory support using an extracorporeal bypass control unit, for periods up to 6 hours. It is also intended to be used to provide partial circulatory support (for periods up to 6 hours) during procedures not requiring cardiopulmonary bypass.

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System also provides pressure measurements which are useful in determining intravascular pressure.

Contraindications

- Mechanical aortic valve or heart constrictive device.
- Aortic stenosis (graded as ≥ +2 equivalent to an orifice area of 1.5 cm^2 or less).
- Moderate to severe aortic insufficiency (echocardiographic assessment of aortic insufficiency graded as ≥ +2).
- Severe peripheral arterial obstructive disease that would preclude LP2.5 System device placement.

Potential Adverse Events

- Death
- Cerebral vascular accident (CVA) / Stroke
- Aortic insufficiency
- Aortic valve injury
- Arrhythmia

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- Atrial fibrillation
- Bleeding
- Cardiac tamponade
- Cardiogenic shock
- Device malfunction
- Hemolysis
- Hepatic failure
- Insertion site infection
- Myocardial infarction
- Perforation
- Renal failure
- Respiratory dysfunction
- Sepsis
- Thrombocytopenia
- Thrombotic vascular (non-CNS) complication
- Transient Ischemic Attack (TIA)
- Vascular injury
- Ventricular fibrillation
- Ventricular tachycardia

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3 The LP2.5 System

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Overview

The LP2.5 System consists of the following components:

- LP2.5 Catheter (Catheter)
- Impella® Power Supply
- Impella® Mobile Pump Console (MPC)
- Braun Vista® basic Infusion Pump (Vista basic)

LP 2.5 Catheter

The LP 2.5 Catheter (see Figure 1) is an intravascular microaxial blood pump that delivers up to 2.5 liters of blood per minute from the left ventricle and into the aorta for up to 5 days.

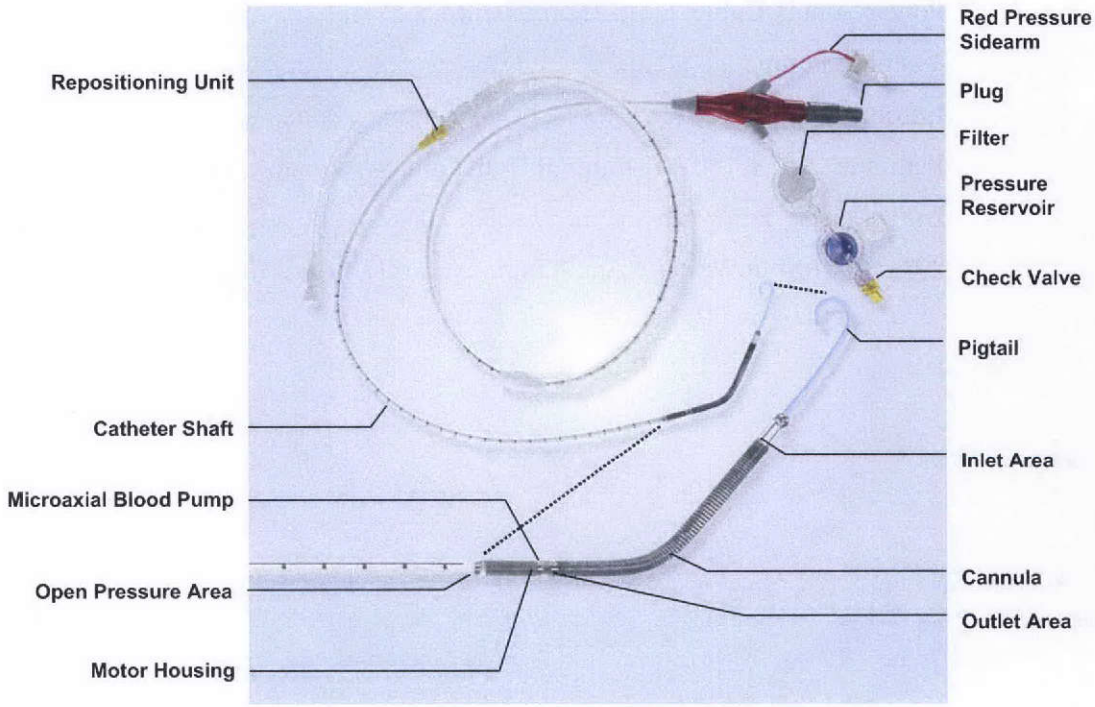

Figure 1 RECOVER LP 2.5 Catheter

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Pigtail

A 6F pigtail is attached to the cannula at the distal end of the inlet area. The pigtail assists with stabilizing the Catheter in the correct position in the left ventricle.

Cannula with Inlet and Outlet Area

The cannula is 12F in diameter and has a spiral-shaped reinforced body. The body of the cannula is shaped in a 45-degree angle.

The inlet area, where the blood enters the cannula, is located at the distal tip. The proximal end of the cannula is attached to the outlet area where the blood exits the cannula.

Microaxial Blood Pump

The microaxial blood pump is located between the cannula and the Catheter. The motor housing is 12F in diameter and consists of a completely encapsulated motor.

Open Pressure Area

The open pressure area is an opening located between the motor housing and the distal end of the Catheter.

A pressure lumen transitions from the open pressure area and runs the length of the Catheter into the plug. A pressure sensor is located in the plug and enables the pressure to be displayed on the MPC.

Catheter Shaft

A 9F catheter shaft is located between the motor housing and the plug. A purge lumen, a pressure measurement lumen, and a pump monitoring cable are contained within the lumen of the catheter shaft.

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The catheter shaft has longitudinal and transversal marks. The longitudinal marks are placed on the side of the inner radius of the cannula and show the position of the curved, flexible cannula. The transversal marks are placed 1 cm apart and aid in proper positioning.

Plug

The plug, which is the section of the Catheter that connects to the MPC through a connector cable, is located at the proximal end of the Catheter. There are two sidearms attached to the plug:

- A clear sidearm that leads to the filter, the pressure reservoir, and the check valve. This is attached to the Braun Vista basic infusion pump.
- A red pressure sidearm for priming the line of the pressure measurement system. This is attached to a standard pressure bag.

Filter, Pressure Reservoir, and Check Valve

An infusion filter, pressure reservoir, and check valve are located off of the clear sidearm from the plug.

The filter prevents bacterial contamination and prevents air from entering the Catheter.

The yellow check valve ensures that purge fluid does not flow in the reverse direction when a purge solution is exchanged.

The pressure reservoir includes a flexible rubber diaphragm that provides additional filling volume by means of an expansion chamber during purge solution change.

Repositioning Unit

The repositioning unit consists of an introducer (graduated from 9F to 12F) located on the catheter shaft and an anticontamination sleeve with an anchoring ring.

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The introducer (with hemostatic valve) allows repositioning of the Catheter.

The anchoring ring of the anticontamination sleeve is used for securing the catheter sheath to the introducer.

Impella® Mobile Pump Console (MPC)

The Impella® Mobile Pump Console (MPC) controls the microaxial blood pump and monitors the LP 2.5 System (see Figure 2). The Console weighs 7 lbs. and can operate on its internal battery for a minimum of 60 minutes when fully charged.

MPC operation is described in detail in Section 4 of this manual.

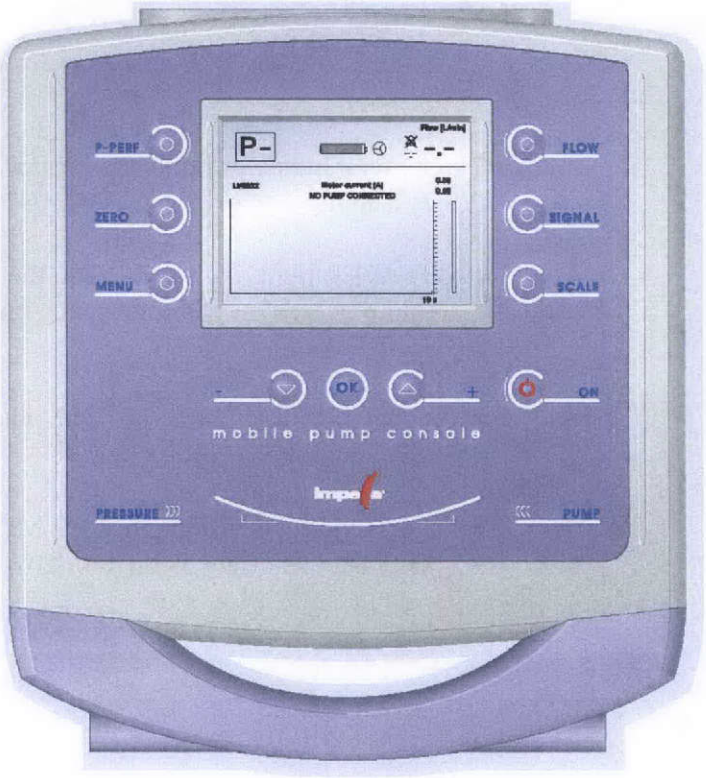

Figure 2 Impella® Mobile Pump Console (MPC)

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Impella® Power Supply

The Impella® Power Supply provides power to and charges the battery within the MPC (see Figure 3).

The Power Supply is a multivoltage power source for use with voltages within a range of 100 to 240 V at line frequencies of 50 and 60 Hz. The integrated charging circuit can fully charge the MPC's Li-Ion batteries in about 10 hours.

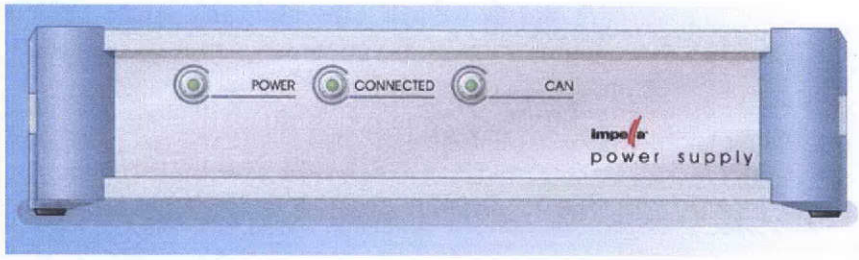

Figure 3 Impella® Power Supply

Three green indicator lights are located on the front panel of the Power Supply:

- POWER light – turns on when the unit is connected to AC power and powered on with the switch on the rear panel. (The power switch is illuminated.)
- CONNECTED light – turns on when the MPC is connected to the switched-on Power Supply.
- CAN light – turns on when the MPC is connected and powered on; is not as bright as the other two lights.

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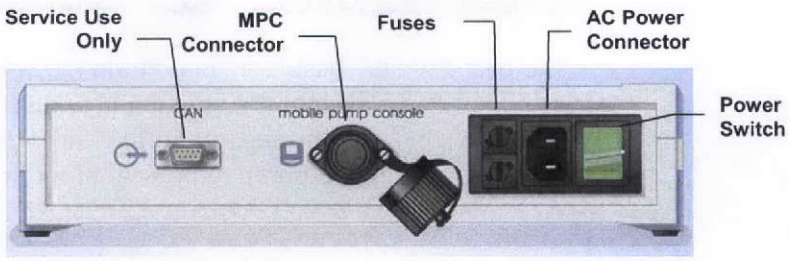

Figure 4 Impella® Power Supply Rear Panel

The following items are located on the rear panel (see Figure 4) of the Power Supply:

- Power switch (lights up when ON)
- Connector for AC power cable
- Fuses
- Connector for cable to the MPC
- CAN-Bus interface for data transfer to an external device (for Abiomed service use only)

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Braun Vista® basic Infusion Pump

The Braun Vista® basic Infusion Pump (see Figure 5) is compatible with the LP 2.5 System. Its function is to deliver purge fluid (20% Dextrose solution plus heparin 50 I.U. /mL) through the Catheter to the microaxial blood pump to prevent blood from entering the motor.

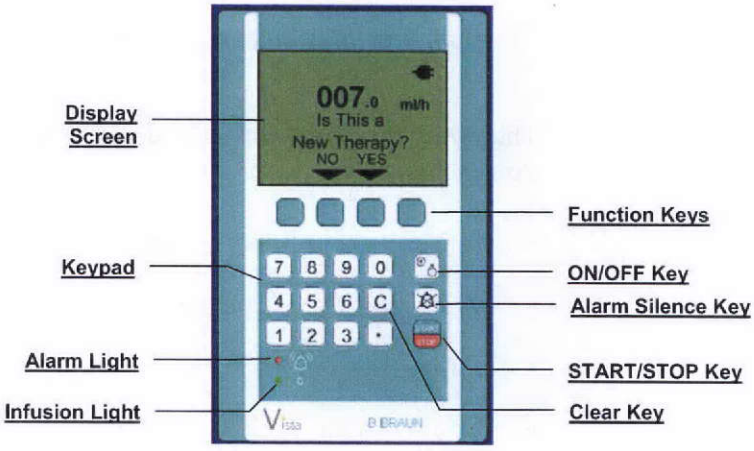

Figure 5 Braun Vista® basic Infusion Pump

- Display screen – green backlighting turns on when the unit is connected to AC power. In battery operation, the backlighting turns on when a key is pressed.
- Keypad – used to enter infusion settings.
- Alarm light – turns on when an alarm condition occurs. The display flashes "AAA.A".
- Infusion light – turns on when the Pump is infusing.
- Function keys – allow selection of on-screen options.
- ON/OFF key – used to turn power on and off.
- Alarm silence key – silences the alarm for approximately 2 minutes.
- START/STOP key – used to start and stop infusion.
- Clear key – used to reset a value to zero.

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Accessories

Impella® Combitrans-Monitoring Set (CM-Set)

The CM-Set (see Figure 6) is connected to the Braun Vista® Pump Set (Vista pump set) and is used to measure the purge pressure in the purge lumen of the Catheter. The purge pressure measurement is displayed on the MPC and must be within the range of 300 to 700 mmHg.

The CM-Set is connected to the MPC with the pressure transducer cable.

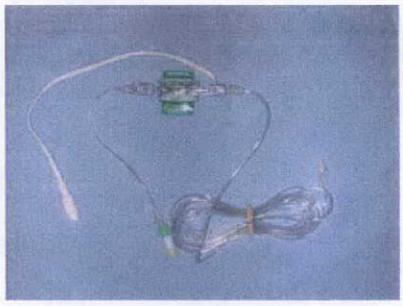

Figure 6 Impella® Combitrans-Monitoring Set (CM-Set)

Pressure Transducer Cable

The pressure transducer cable connects the CM-Set to the MPC (see Figure 7). The cable is reusable and nonsterile.

The plug with the red hub at the end of the cable is inserted into the pressure connector socket on the left-hand side of the MPC. The plug at the opposite end is connected to the CM-Set.

Figure 7 Pressure Transducer Cable

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Connector Cable

The connector cable connects the Catheter to the MPC (see Figure 8).

The Catheter plug is connected to the socket at the PATIENT end of the cable. The plug labeled CONSOLE at the opposite end of the cable is inserted into the pump connector socket on the right-hand side of the MPC. A retainer at the end of the connector cable prevents inadvertent removal of the cable from the MPC.

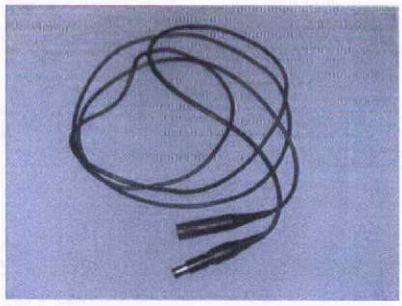

Figure 8 Connector Cable

Power Supply Cable

The power supply cable connects the MPC to the Power Supply (see Figure 9).

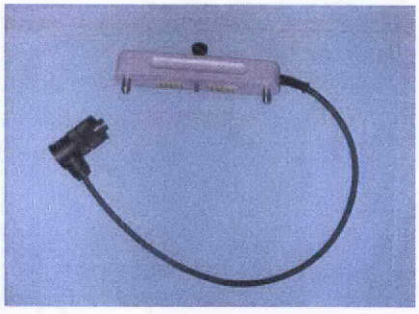

Figure 9 Power Supply Cable

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Testplug Pump

The Testplug Pump is a test device used to confirm the functionality of the MPC prior to operation (see Figure 10).

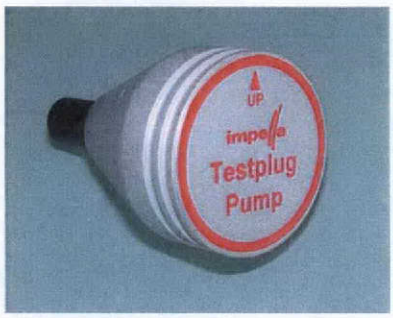

Figure 10 Testplug Pump

Introducer Kit

See Figure 11.

- 13F peel away introducer with hemostatic valve
- 13F dilator
- 7F introducer with dilator
- 18G Seldinger needle
- 10 cc syringe
- 150 cm 0.035" guidewire

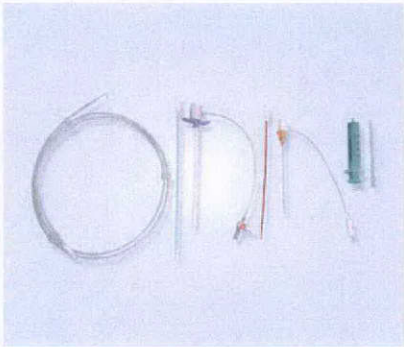

Figure 11 Introducer Kit

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Platinum PLUS™ ST/0.014"/300 cm Guidewire

The Platinum PLUS wire is used for the placement of the Catheter (see Figure 12). The guidewire has a radiopaque, shapeable tip.

Figure 12 Platinum PLUS™ ST/0.014"/300 cm Guidewire

Braun Vista® Pump Set

The Braun Vista Pump Set is the required infusion tubing used in the Braun Vista® basic Infusion Pump. The infusion tubing connects to the yellow check valve off of the LP 2.5 Catheter.

20% Dextrose in Water

20% Dextrose solution with heparin concentration of 50 I.U./mL is used as the purge fluid that is infused by the Braun Vista basic Infusion Pump through the Catheter.

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4 Using the Impella® MPC

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MPC Function Keys

There are 10 function keys located around the MPC display (see Figure 13):

- P-PERF key – used to change the performance level of the pump (P0 to P9).
- ZERO key – not active.
- MENU key – used to access the following functions:

  With the Catheter connected:

  - Low Flow Limit: **Set Default** sets limit to approximately 0.3 L/min below currently displayed mean flow; **Change Limit** allows adjustment of the limit in 0.1 L/min steps; **Off** deactivates flow limit monitoring.
  - Information: pump type, pump ID, MPC software version, pump operating hours.
  - Repositioning Guide: displays recommended steps for repositioning the Catheter.
  - Disable Position Monitoring: disables the Positioning Monitoring function. It is recommended that this option may only be used with the assistance of a trained Abiomed representative.

  With no Catheter connected:

  - Language: German, English.
  - Switch Off Console
- ▼ and ▲ keys – used to decrease or increase selected parameters or to select a menu item.
- OK key – used to acknowledge an entry value or command.
- FLOW key – not active.

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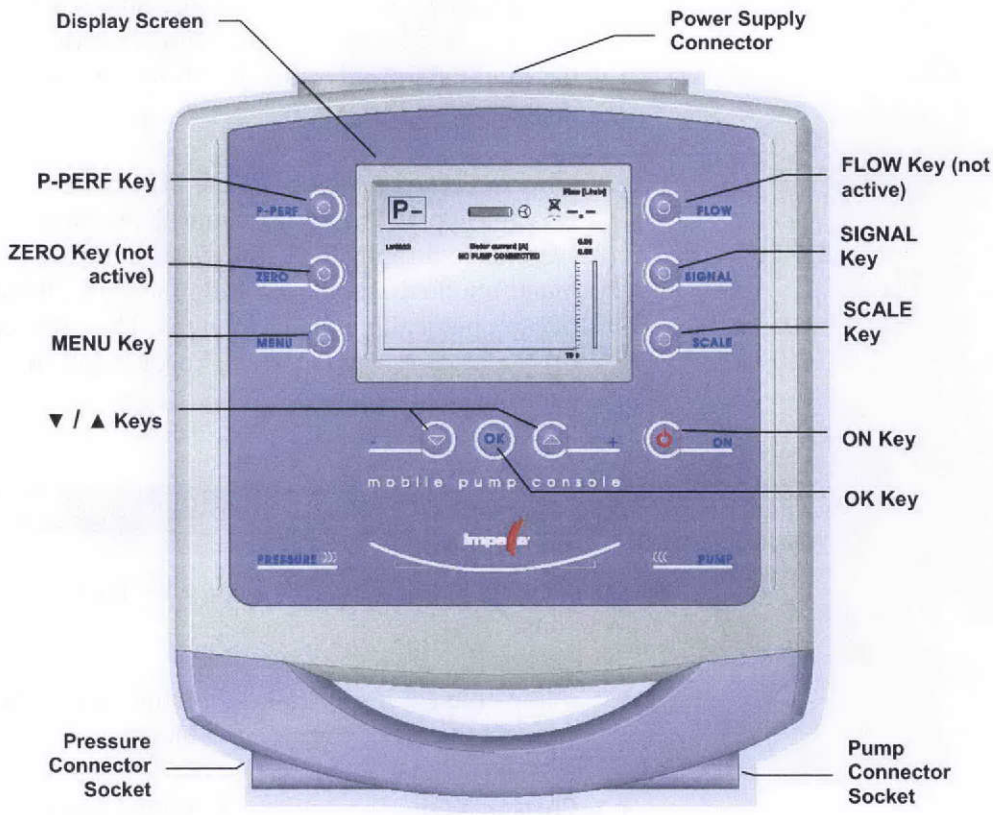

Figure 13 MPC Function Keys

- SIGNAL key – allows viewing of the following screens:
  - Placement Signal (mmHg)
  - Purge Pressure (mmHg)
  - Motor Current (A)
  - Speed (rpm x 1000)
  - Flow Rate (L/min)
  - Dual Signal (Motor Current and Placement Signal)
  - Placement Monitoring (Graphic Display)

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- SCALE key – selects one of three time windows: 10 seconds, 5 minutes, or 5 hours. The corresponding value is displayed as a bar graph in the vertical axis. Minimum and maximum values appear above the axis.

- ON key – used to power up the MPC when not connected to the Power Supply. The ON key must be pressed and held for 3 seconds to turn the MPC on. To turn the MPC off, the Catheter must first be disconnected from the MPC, which will then turn off automatically after 10 minutes. The MPC can also be turned off by: (1) pressing the Menu key, (2) selecting "Switch Off Console" and (3) pressing OK.

MPC Connections

Connections to the MPC (see Figure 13) are made at the following locations:

- Pump connector socket – right-hand side of the MPC; used to connect the black connector cable.

- Pressure connector socket – left-hand side of the MPC; used to connect the gray pressure transducer cable.

- Power Supply connector – at the top of the MPC; connects to the Power Supply by a cable. Data is also transferred from the MPC to the CAN-Bus interface in the Power Supply through this connection.

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MPC Display

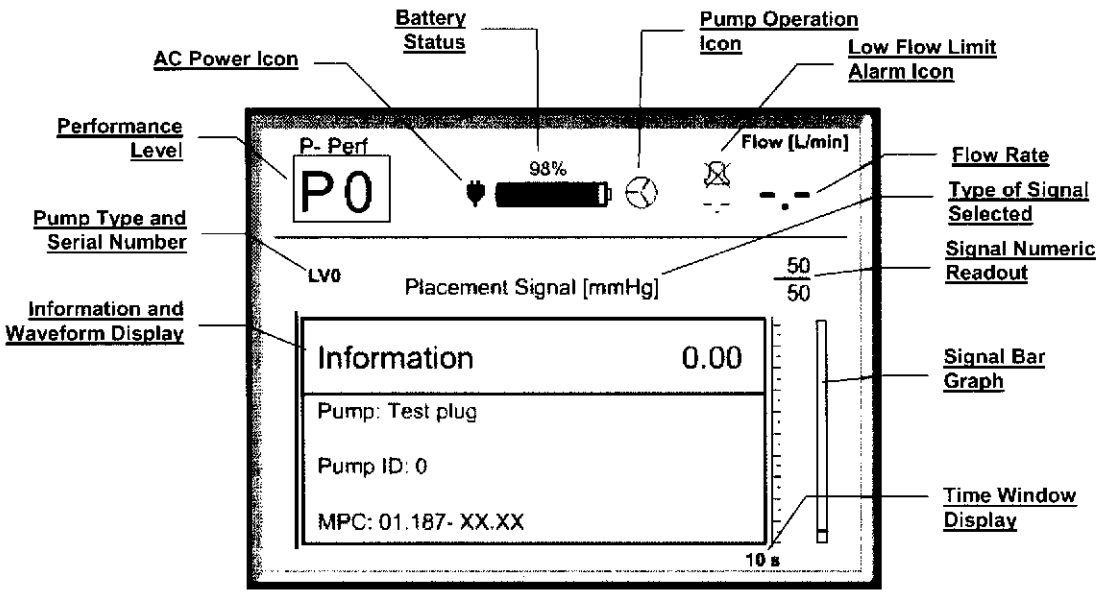

Figure 14 MPC Display

- Information and waveform display – shows information during the startup procedure; shows waveforms during Catheter operation.
- Pump type and serial number – indicates whether the Catheter is left ventricular or right ventricular; also displays the Catheter serial number.
- Performance level – indicates the performance level (P0 to P9) at which the Catheter is operating.
- AC power icon – appears when the MPC is connected to the Power Supply.
- Battery status information – bar graph and numeric readout (percentage) show the approximate battery charge level. During battery operation, the bar graph flashes when the charge level is less than 50%. When the battery is charging, the bar graph flashes between the present charge level and 100%.

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- Pump operation icon – rotates when the pump is operating.
- Low flow alarm limit icon – indicates whether the alarm is enabled or disabled. Enabled: bell symbol and numeric alarm limit are displayed. Disabled: bell symbol is crossed out as shown.
- Flow rate – indicates the calculated pump flow (0 to 2.6 liters per minute [L/min]).
- Type of signal selected – title of the signal shown.
- Signal numeric readout – corresponds to the selected signal. Example: Placement Signal screen shows aortic or ventricular pressure.
- Signal bar graph – corresponds to the selected signal.
- Time Window display – indicates the type of window displayed (10 seconds, 5 minutes, or 5 hours).

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Selecting Performance Levels

Ten different performance levels (P0 to P9) can be selected (see Table 1).

Table 1 Performance Level Flow Rates

Performance Level	* Flow Rate (L/min)	Revolutions Per Minute (rpm)
P0	0.0 – 0.0	0
P1	0.0 – 0.5	25,000
P2	0.4 – 1.0	35,000
P3	0.7 – 1.3	37,000
P4	0.9 – 1.5	40,000
P5	1.2 – 1.8	43,000
P6	1.4 – 2.0	45,000
P7	1.6 – 2.2	47,000
P8	1.9 – 2.5	50,000
P9	2.1 – 2.6	51,000

* Flow rate can vary due to suction or incorrect positioning.

- P0 – microaxial blood pump is stopped.
- P1 – flow rate is not displayed but the pump is rotating at 25,000 rpm.
- P2 to P9 – flow rate is displayed; increases as the performance level is increased.
- P8 – recommended ***maximum performance level for continuous use.***
- P9 – used to verify Catheter position; can be used to provide maximum flow for up to 5 minutes. (The MPC will automatically default to P8 after 5 minutes.)

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Positioning Aids

Placement Signal (mmHg)

The Placement Signal screen shows a pressure measurement that corresponds to the location of the open pressure area of the Catheter. The Placement Signal is used to verify the position of the pump by evaluating the current pressure waveform as an aortic or ventricular waveform (see figures below).

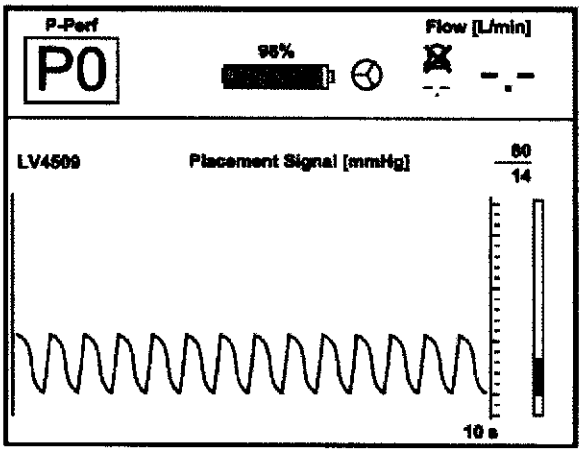

Figure 15 Ventricular Waveform on Placement Signal Screen

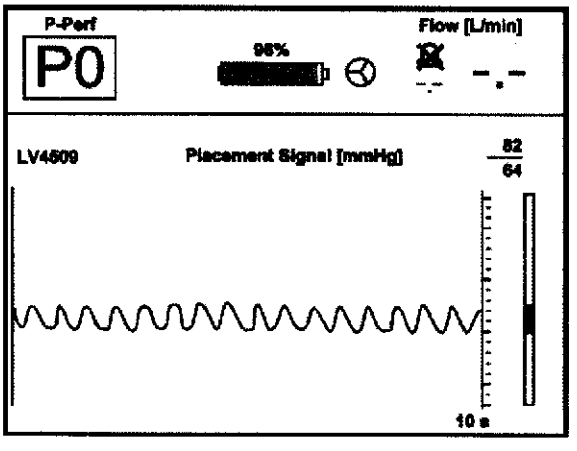

Figure 16 Aortic Waveform on Placement Signal Screen

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Motor Current (Amps)

Motor Current is a measurement of the energy intake of the pump motor. This measurement is directly related to the delivery of blood volume (motor current increases as flow rate increases). The Motor Current screen is important in diagnosing pump status (see Figure 17).

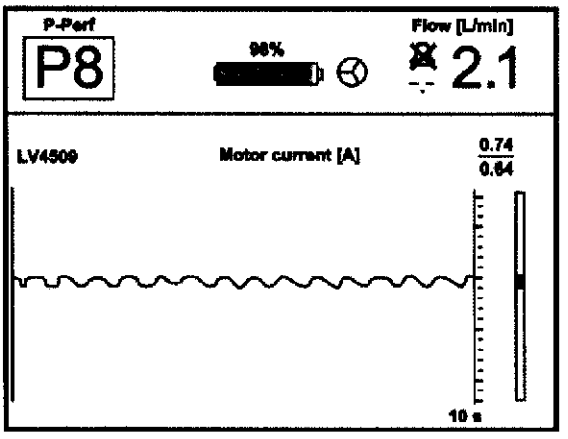

Figure 17 Motor Current Screen

Placement Monitoring

The Placement Monitoring screen shows the approximate location of the pump position across the aortic valve (see Figure 18).

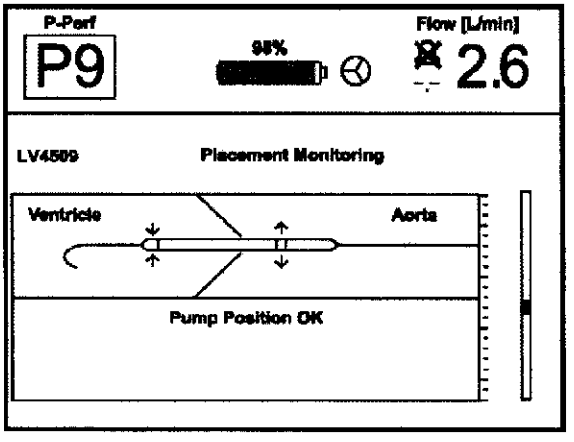

Figure 18 Placement Monitoring Screen

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Dual Signal

The Dual Signal screen (see Figure 19) shows the Motor Current and Placement Signal waveforms simultaneously. The Motor Current is the upper waveform.

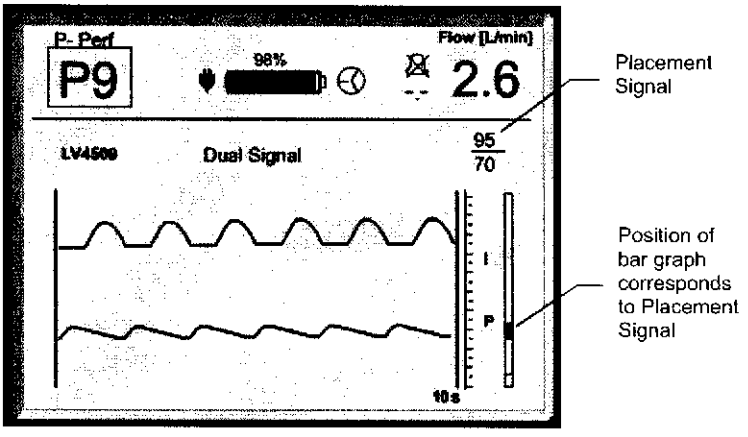

Figure 19 Dual Signal Screen

Mobile Operation

The MPC can be operated on internal battery power when it is not connected to the Impella® Power Supply:

1. Disconnect the MPC from the Power Supply by disconnecting the power supply cable from the top of the MPC.
2. The MPC beeps once to alert the user that the MPC is on battery power.
3. When connected back to the Power Supply, the MPC beeps once to alert the user that the MPC is on main power.

NOTE: If it is necessary to turn the MPC on under mobile operation, the ON key must be held for 3 seconds to power up the MPC.

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5 Using the LP 2.5 System

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MPC Function Test 5.4
Preparing the Connector Cable 5.5
Preparing the LP 2.5 Catheter 5.6
Deaerating the LP 2.5 Catheter 5.8
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Replacing the Braun Vista® Pump Set 5.20
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Startup

WARNING: Do ***NOT*** use an LP 2.5 System if any part of the System is damaged.

CAUTION: Protect the MPC and the Power Supply from direct sunlight and exposure to excessive heat (max. 40°C) to prevent malfunction.

CAUTION: To prevent overheating and improper operation, do ***NOT*** block the cooling vents of the Power Supply while it is operating. Do ***NOT*** place the MPC on top of the Power Supply.

CAUTION: The Li-Ion batteries must be charged for 10 hours prior to system operation. After being unplugged, the MPC will operate for a minimum of 60 minutes after the batteries have been fully charged.

CAUTION: Holding down the MPC's ON key for longer than 3 seconds during operation will cause the MPC to go into emergency stop mode.

1. Place the Impella® Power Supply and the MPC next to each other on a horizontal surface or on the optional MPC cart.
2. Connect the power cable to the socket on the rear panel of the Power Supply and to an AC outlet.
3. Connect the MPC to the Power Supply with the Power Supply cable (see Figure 20).

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Figure 20 Connecting the Power Supply Cable

4 Turn the Power Supply ON using the power switch located on the rear panel of the Power Supply. The MPC is powered up automatically when the Power Supply is turned on.

5 Make sure that the Power Supply is functioning properly by checking for ***all*** of the following conditions:

- ON/OFF switch is illuminated.
- Power Supply fan is running.
- Green POWER and CONNECTED lights on the Power Supply are on.
- AC power icon appears on the MPC display.

NOTE: If the CONNECTED light is not on, turn the Power Supply OFF and ON. If this does not solve the problem, turn the Supply OFF and ON again. Do not use the Supply if the CONNECTED light is not on after two attempts.

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MPC Function Test

CAUTION: During the MPC Function Test, if a pressure value of 50 (± 4) mmHg does not appear or the speed is not within the specified range of 23,000 to 25,000 rpm, do ***NOT*** use the MPC.

Before use, the MPC must complete a Function Test using the Testplug Pump.

1 Insert the Testplug into the pump connector socket at the right-hand side of the MPC's handle. Insertion is acknowledged with a single beep and then a series of three beeps. The MPC displays the MPC Function Test Screen (see Figure 21).

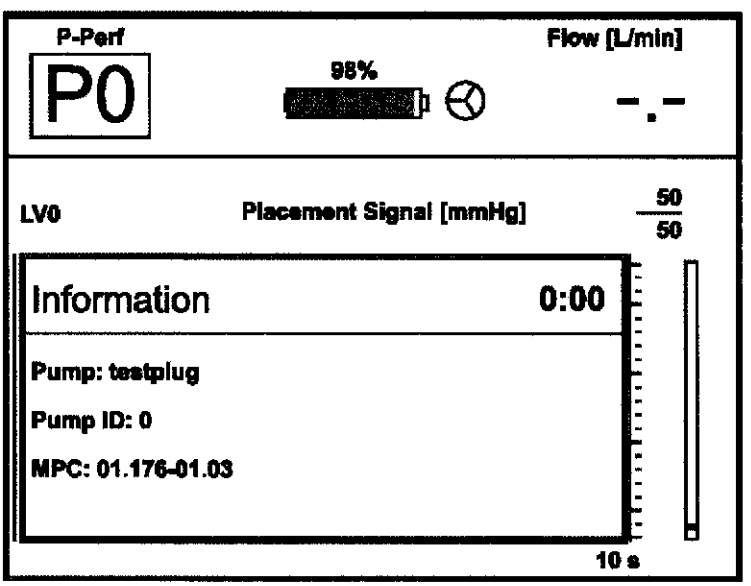

Figure 21 MPC Function Test Screen

2 Confirm that the following items are displayed (see Figure 21):

- P-Perf: P0
- Pump: testplug
- Pump ID: 0

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- Flow (L/min): -.-
- Pressure value of ***50 (± 4) mmHg*** (above the right-hand diagram axis)

3 The MPC displays the Placement Signal screen.

4 Press the Signal key three times to open the Speed screen (Speed [RPM]).

5 Press and hold P-PERF until two blinking vertical bar graphs appear next to the P0 display.

6 Set the performance level to P5 by pressing ▲ and acknowledging within 10 seconds by pressing OK. Confirm that the speed lies within the range of ***23,000 to 25,000 rpm***.

7 Return the performance level to P0 by pressing P-PERF, OK, and ▼ before the Testplug is removed. Remove the Testplug.

8 The MPC Function Test is now complete. Continue the procedure under sterile conditions.

Preparing the Connector Cable

1 Remove the connector cable (black) from its package using sterile technique.

2 Inspect the cable for damage.

3 Inspect the socket end (patient end) of the cable for contamination.

4 Secure the PATIENT end of the cable to the sterile field.

5 Insert the plug labeled CONSOLE into the pump connector socket on the right-hand side of the MPC (see Figure 22).

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Figure 22 Connector Cable

Preparing the LP 2.5 Catheter

WARNING: The sterile components of the LP 2.5 System can be used only if the sterilization indicators show that the contents have been sterilized, the packaging is not damaged, and the expiration date has not elapsed.

CAUTION: Do not kink or clamp the LP 2.5 Catheter or the 13F peel away introducer.

1. Remove the LP 2.5 Catheter from its package using sterile technique.
2. Insert the Catheter plug into the connector cable socket (patient end, see Figure 23). The tab and the slot must be aligned during connection (see Figure 24).

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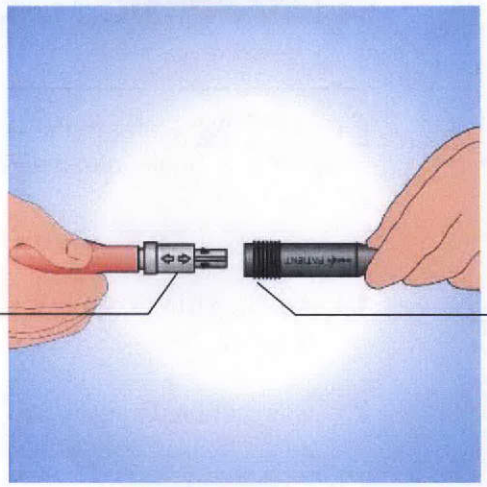

Figure 23 Inserting the Catheter Plug

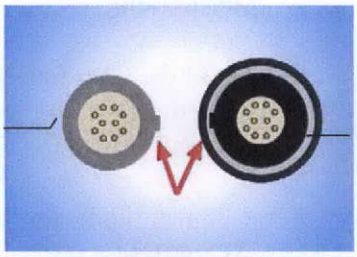

Figure 24 Location of Tab and Slot

3 Connection is confirmed by a single beep and then a series of three beeps. Pull back on the connection to make sure that the plug has snapped into place.

4 Snap the plastic hook (located on the pressure reservoir of the clear sidearm) to the connector cable.

5 The display screen on the MPC shows: the Pump Type (LP 2.5), Pump ID, and MPC software version.

6 The MPC automatically initiates the startup procedure for the LP 2.5 System and displays "Infusion Configuration OK?" The Catheter is now ready to be deaerated.

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Deaerating the LP 2.5 Catheter

CAUTION: Refer to the Instructions for Use supplied with the Braun Vista® basic Infusion Pump ***before*** using the Pump with the LP 2.5 System.

1. Add heparin to achieve 50 I.U. heparin/mL in 20% Dextrose solution.
2. Connect the Braun Vista® Pump Set (Vista pump set) into the 20% Dextrose solution.
3. Flush the Vista pump set manually and close the roller clamp.
4. Using sterile technique, open the Impella® Combitrans-Monitoring Set (CM-Set) and secure the male luerlock to the sterile field.
5. Hand the CM-Set's green pressure transducer off the sterile field and connect it to the Vista pump set. Open the roller clamp and manually flush the CM-Set. Close the roller clamp.
6. Connect the Braun Vista basic Infusion Pump (Vista basic) to an AC outlet.
7. Turn the Vista basic ON by pressing the ON/OFF key.
8. Open the Vista basic door by pressing the Door Open button at the top right corner. Push and hold open the clamp at the top of the fluid path.
9. Insert the Vista pump set tubing into the clamp and release it. Thread the tubing down the fluid path, making sure the tubing is pressed into the Air-in-Line detector at the bottom of the fluid path. (The roller clamp should be below the Vista basic. The pinch clamp should be open and positioned between the drip chamber and the Vista basic.) Close the door and open the roller clamp.

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10 The Vista basic displays "Is This a New Therapy?" Press the Yes key to confirm.

11 The Vista basic displays "Enter Infusion Rate". Enter a rate of 7 mL/h.

12 Press VTBD (Volume To Be Delivered) and enter the bag volume in mL. Press OK.

13 Connect the CM-Set to the yellow check valve (on the filter unit) of the Catheter.

14 Press START/STOP to begin the infusion. The screen displays a rate of 7 mL/h.

15 Confirm "Infusion Configuration OK?" on the MPC by pressing OK.

16 The MPC displays "Pressure Transducer Connected?" Connect the gray pressure transducer cable to the white cable of the CM-Set.

17 Connect the pressure transducer cable (end marked with the red hub) to the pressure connector socket on the left-hand side of the MPC (see Figure 25).

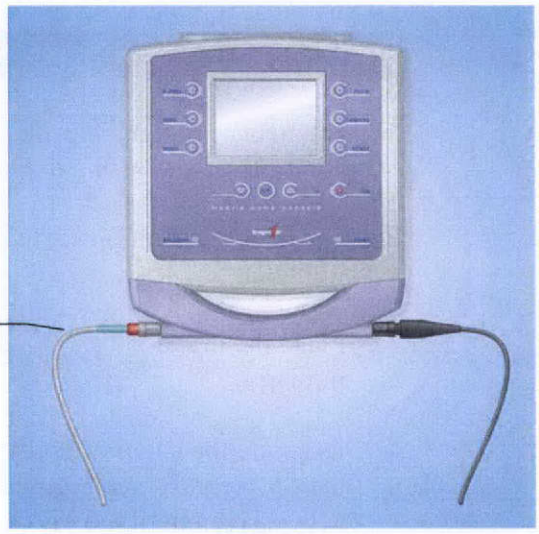

Figure 25 Connecting the Pressure Transducer Cable

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18 The MPC displays "Deaerate with Infusion Pump".

19 On the Vista® basic, press BOL and enter a bolus release of 8 mL. Press OK to start the bolus.

20 The MPC beeps when the purge pressure reaches 500 mmHg. When the beep occurs, press Stop on the Vista basic screen. The infusion rate of 7 mL/h continues to run. The MPC displays "Deaeration Complete?"

NOTE: If the bolus is not stopped prior to reaching 700 mmHg, the MPC will alarm due to a High Purge Pressure. The Vista basic will alarm and stop the bolus at 1000 mmHg.

---

21 Wait until fluid is discharged from the outlet area of the Catheter (approximately 1 minute). Gently tap the Catheter against a dry, sterile cloth to determine whether or not fluid has already been discharged from the outlet area.

22 When fluid is discharged from the pump, the Catheter is fully deaerated.

23 The MPC displays "Deaeration Complete? Infusion ON?" Press OK on the MPC.

Preparing the Open Pressure Measurement

1 Connect a sodium chloride (0.9% NaCl) infusion bag to a solution set and prime the set.

2 Connect the solution set to the red pressure sidearm of the Catheter.

3 Place the infusion bag in a pressure bag and inflate to 300 to 400 mmHg.

4 Deaerate the solution set by squeezing the white flush valve for at least 5 seconds (see Figure 26). Follow the moving bar on the MPC screen until the MPC beeps and displays "Pump Covered with Test Fluid?"

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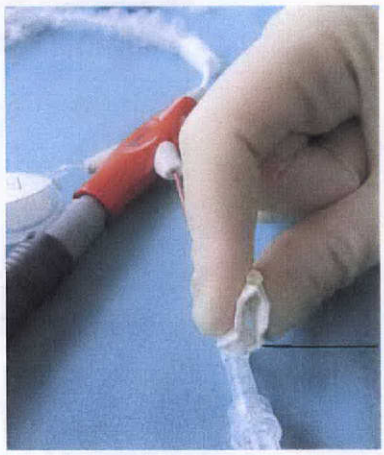

Figure 26 Red Pressure Sidearm with White Flush Valve

LP 2.5 Catheter Function Test

1 Completely submerge the motor housing and the cannula into a pan filled with sterile isotonic solution (see Figure 27).

Figure 27 Submerging the Motor Housing and the Cannula

2 Press OK on the MPC to confirm that the pump is covered with test fluid (see Figure 28).

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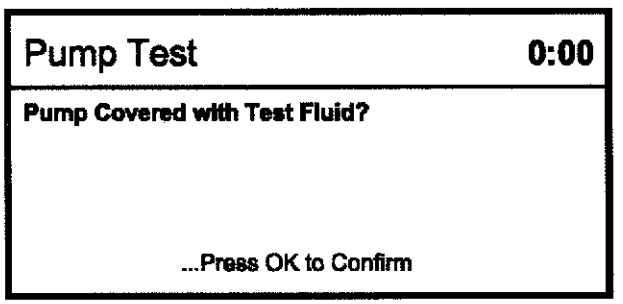

Figure 28 Catheter Function Test Screen

3 The pump automatically starts at performance level P1.

4 Make sure the pump delivers fluid out of the pump outlet area.

5 Press OK to acknowledge successful pump testing and to stop the pump.

6 The Catheter is now ready for use. Remove the Catheter from the sterile isotonic solution and set it aside using sterile technique.

7 Press OK. The Placement Monitoring screen appears.

Inserting the LP 2.5 Catheter

WARNING: To prevent malfunction of the locking mechanism of the 13F peel away introducer, do ***NOT*** hold the hemostatic valve while inserting into the artery.

CAUTION: Do not kink or clamp the LP 2.5 Catheter or the 13F peel away introducer.

NOTE: After insertion of the Catheter (and until explant), ACT should be maintained at 160 to 180 seconds.

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1. Obtain access to the femoral artery.

2. Insert a 7F introducer and administer heparin to achieve an ACT of 250 to 500 seconds.

3. After an ACT of 250 to 500 seconds is achieved, remove the 7F introducer over the .035 guidewire (provided) and insert the 13F peel away introducer with dilator (see Figure 29). While inserting the 13F introducer, hold the shaft of the introducer to slide it into the artery.

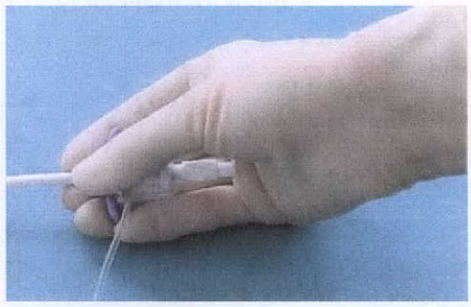

Figure 29 Inserting the 13F Peel Away Introducer

4. Remove the 13F dilator and insert the 7F introducer with dilator over a guidewire and into the 13F peel away introducer. Remove the 7F dilator.

5. Insert a 6F diagnostic catheter (Judkins Right or Multipurpose recommended, see Figure 30) into the 7F introducer and advance it over a diagnostic .035 or .038 guidewire into the left ventricle.

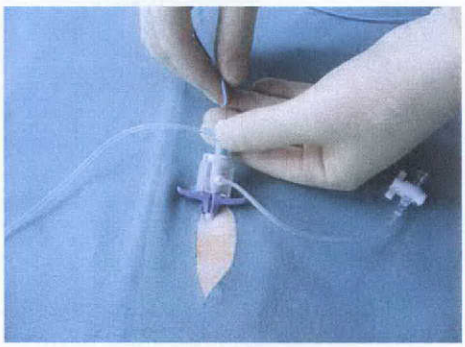

Figure 30 Inserting the 6F Diagnostic Catheter

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6 Remove the diagnostic guidewire and insert the supplied .014 Platinum PLUS™ guidewire.

7 Advance the .014 guidewire into the left ventricle until the floppy end and 3 to 4 cm of the stiffer part of the guidewire are visible in the left ventricle.

8 Remove the 6F diagnostic catheter and 7F introducer.

9 Wet the cannula and backload the pigtail section of the Catheter onto the .014 guidewire. Straighten the cannula to ensure that the guidewire exits on the inner radius of the cannula (see Figure 31).

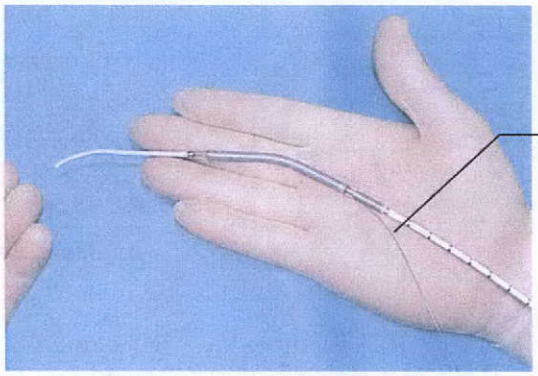

Figure 31 Exiting of the .014 Wire from the Catheter

10 Advance the Catheter through the hemostatic valve into the femoral artery (see Figure 32) and along the .014 guidewire into the left ventricle. Follow the Catheter under fluoroscopy as it is advanced into the left ventricle.

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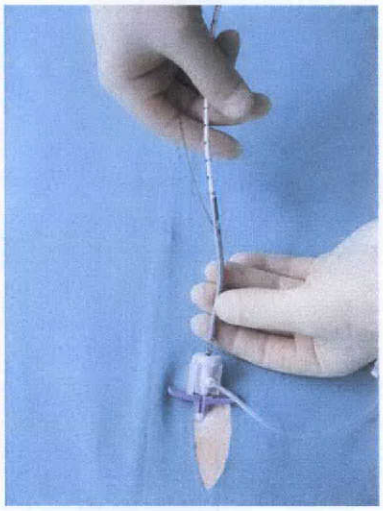

Figure 32 Inserting the LP 2.5 Catheter

11 Remove the .014 guidewire.

CAUTION: To prevent device failure, do not start the LP 2.5 Catheter until the guidewire has been removed.

12 Confirm that a ventricular waveform is displayed on the MPC.

Positioning and Starting the LP 2.5 Catheter

WARNING: Retrograde flow will occur across the aortic valve if the pump is set at performance level P0.

1 Place the Catheter plug at the same level as the patient's heart.

2 Confirm that a ventricular waveform is displayed on the MPC (see Figure 33). If a ventricular waveform is not present, gently advance the Catheter forward until a ventricular waveform is present on the Placement Signal screen.

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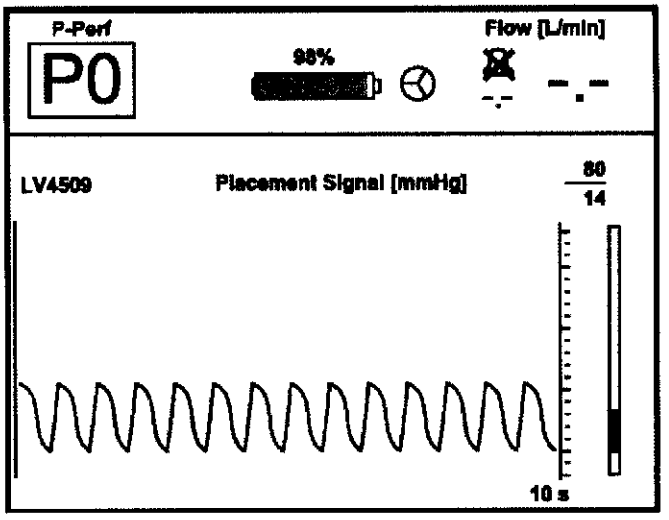

Figure 33 Ventricular Waveform on Placement Signal Screen

3 Pull the Catheter back until an aortic waveform is present on the Placement Signal screen (see Figure 34).

4 When the aortic waveform is present, pull the Catheter back an additional 4 cm. (The distance between adjacent markings on the Catheter is 1 cm.) The pump should now be centered across the aortic valve.

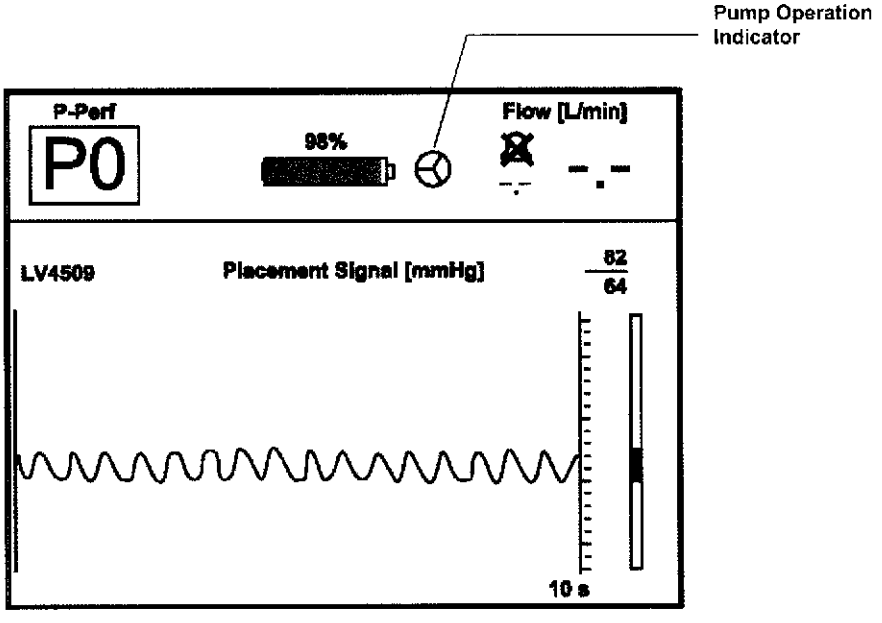

Figure 34 Aortic Waveform on Placement Signal Screen

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5 Increase the performance level from P0 to P1. Check that the pump operation indicator (see Figure 34) is rotating to ensure that the pump is now operating.

6 Increase the performance level to P9 to confirm correct and stable placement. Placement should be verified with fluoroscopy and with the Placement Monitoring screen.

7 After correct placement has been achieved, decrease the performance level to the desired flow rate. Performance level P9 will default back to P8 after 5 minutes.

8 Reposition the Catheter as necessary.

Use of the Repositioning Introducer and the 13F Peel Away Introducer

WARNING: To prevent failure of the 13F peel away introducer, remove the 13F peel away introducer prior to transport when ACT is less than 150 seconds.

1 Flush the sidearm of the repositioning introducer located on the catheter shaft.

2 Carefully remove the 13F peel away introducer out of the artery over the catheter shaft (see Figure 35) and apply manual pressure above the puncture site.

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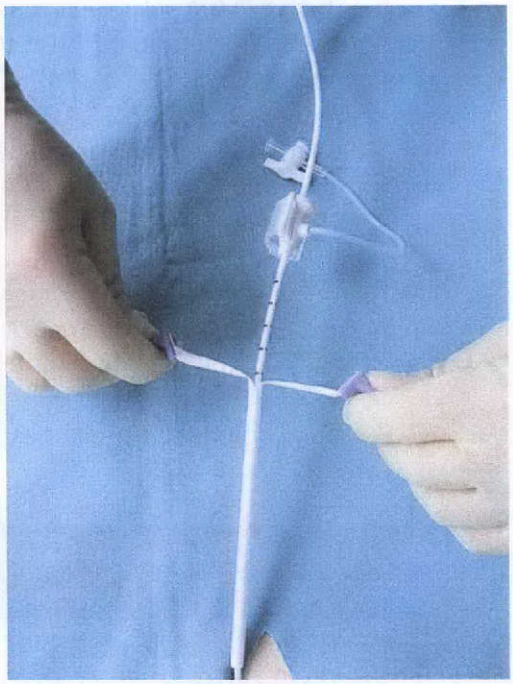

Figure 35 Removing the 13F Peel Away Introducer

3 Grasp the purple "wings" and peel away the 13F introducer off of the catheter shaft.

4 Disconnect the hemostatic valve by sliding the clear section forward (see Figure 36). The white section disconnects into two pieces (see Figure 37).

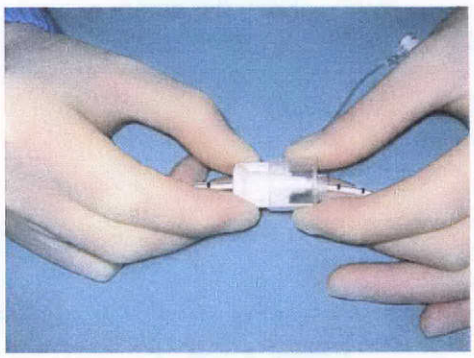

Figure 36 Sliding the Clear Section Forward

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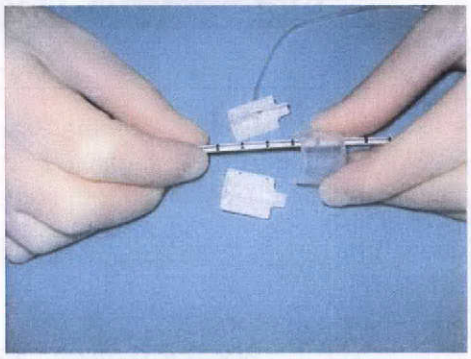

Figure 37 Hemostatic Valve Disconnected

5 Slide the repositioning introducer over the catheter shaft and advance it into the artery to the yellow eyelet.

6 Secure the yellow section of the repositioning introducer by suturing it to the skin using the provided eyelet.

7 Slide the proximal end of the anticontamination sleeve onto the yellow section of the repositioning introducer. Lock the anchoring ring in place by turning it clockwise. Secure the catheter shaft in place by tightening the connected anchoring ring.

8 Carefully extend the anticontamination sleeve to maximum length and secure the end by tightening the distal anchoring ring.

9 Prepare a pressurized, heparinized 0.9% NaCl infusion setup and connect it to the sidearm of the repositioning introducer. The 0.9% NaCl solution must be at room temperature. Ensure that all the air is expelled from the IV tubing prior to connecting to the introducer.

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Replacing the Braun Vista® Pump Set

CAUTION: When the Braun Vista® Pump Set in the Braun Vista® basic Infusion Pump is to be replaced, the replacement process must be completed within 2 minutes. The LP 2.5 Catheter may be damaged if replacement takes longer than 2 minutes.

NOTE: ABIOMED recommends replacing the Braun Vista Pump Set and CM-Set ***every 24 hours***.

1. Prepare a 20% Dextrose solution with 50 I.U. heparin/mL.
2. Connect a new Braun Vista Pump Set (Vista pump set) and CM-Set to the 20% Dextrose solution.
3. Flush the Vista pump set and CM-Set manually and close the roller clamp.
4. Press BOL on the Vista basic and enter a bolus release of 8 mL. Press OK to start the bolus.
5. When the purge pressure on the MPC reaches 600 mmHg, stop the bolus by pressing Stop on the Vista basic.
6. Close the roller clamp on the current Vista pump set. Interrupt the infusion by pressing Stop.
7. Disconnect the CM-Set from the Catheter at the yellow check valve.
8. Open the Vista basic door. Remove the current Vista pump set.
9. Load the new prepared Vista pump set into the Vista basic.
10. Close the Vista basic door and open the roller clamp completely.
11. Connect the CM-Set to the Catheter at the yellow check valve.

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12 Press START/STOP to resume the infusion.

13 Press BOL on the Vista® basic and enter a bolus release of 8 mL. Press OK to start the bolus.

14 When the purge pressure on the MPC reaches 600 mmHg, press Stop on the Vista basic to stop the bolus.

Troubleshooting the Braun Vista® basic Infusion Pump

CAUTION: To troubleshoot Vista basic alarms not listed in this manual, refer to the Vista basic Instructions for Use.

Low Purge Pressure

If the purge pressure falls below 300 mmHg, the MPC displays the alarm message shown in Figure 38.

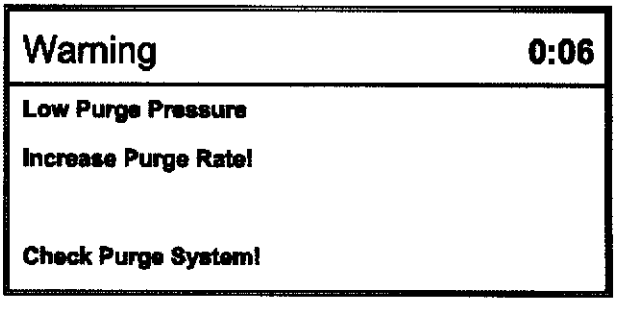

Figure 38 Low Purge Pressure Screen

1 Press BOL on the Vista basic and enter a bolus release of 8 mL. Press OK to start the bolus.

2 Inspect the purge system for leaks.

3 If there are no leaks, increase the purge pressure by increasing the infusion rate by 1 mL/hr (not to exceed a 12 mL/hr infusion rate) on the Vista basic until the purge pressure is within the range of 300 to 700 mmHg.

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High Purge Pressure

If the purge pressure exceeds 700 mmHg, the MPC displays the alarm message shown in Figure 39.

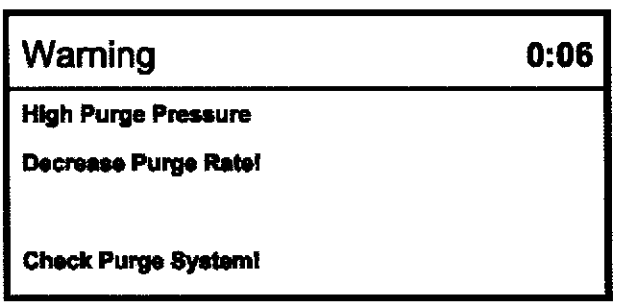

Figure 39 High Purge Pressure Screen

1. Inspect the purge system for kinks in the tubing.
2. If there are no kinks, slowly decrease the infusion rate by 1 mL/hr (do not decrease to less than a 4 mL/hr infusion rate) until the purge pressure is within the range of 300 to 700 mmHg.

Downstream Occlusion

If a "downstream occlusion" alarm occurs on the Vista® basic (see Figure 40), the purge fluid flow stops.

1. Inspect the Braun Vista® Pump Set for any kinks or defects.
2. Make sure the roller clamp is not closed.
3. Press Start to resume the infusion.
4. If the alarm persists, open the Vista basic door and inspect the tubing down the fluid path. Close the door and press Start to resume the infusion.

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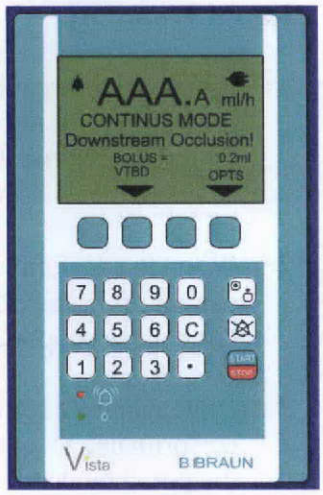

Figure 40 Downstream Occlusion Alarm

Patient Weaning

WARNING: Do ***NOT*** support a patient with the LP 2.5 System for more than 5 days. Operation of this System for more than 5 days can lead to malfunction of the System and result in injury or death.

Weaning the patient from the LP 2.5 System is at the discretion of the physician. Patients can be supported with the System for up to 5 days.

The following weaning protocol is provided as ***guidance only***.

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Rapid Weaning

1. Initiate rapid weaning by decreasing pump performance level in 2-level steps at intervals of several minutes (for example, P6 to P4 to P2). Do ***not*** decrease performance level below P2 as long as the pump is in the ventricle.

2. When the performance level has been reduced to P2, maintain the patient on P2 support for at least 10 minutes before discontinuing circulatory support.

3. If the patient's hemodynamics remain stable, decrease the performance level to P1, pull the Catheter into the aorta, and stop the pump by decreasing the performance level to P0. Explant the Catheter.

4. Remove the 13F peel away introducer if it is still in place and follow institutional guidelines for percutaneous arterial closure.

5. Disconnect the connector cable from the MPC and the Catheter by sliding back the locking sleeves (at the <= => markings) and removing the plugs. Do ***not*** twist the plugs because the contact pins may be damaged.

6. Press MENU. Select "Switch Off Console" and press OK.

7. Return all used, opened, or malfunctioned Catheters to Abiomed.

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Slow Weaning

1. Initiate slow weaning by decreasing pump performance level in 2-level steps at intervals of 2 to 3 hours (for example, P6 to P4 to P2). Do ***not*** decrease performance level below P2 as long as the pump is in the ventricle.

2. When the performance level has been reduced to P2, maintain the patient on P2 support for at least 2 to 3 hours before discontinuing circulatory support.

3. If the patient's hemodynamics remain stable, decrease the performance level to P1, pull the Catheter into the aorta, and stop the pump by decreasing the performance level to P0. Explant the Catheter, including the repositioning introducer.

4. Follow institutional guidelines for percutaneous arterial closure.

5. Disconnect the connector cable from the MPC and the Catheter by sliding back the locking sleeves (at the <= => markings) and removing the plugs. Do ***not*** twist the plugs because the contact pins may be damaged.

6. Press MENU. Select "Switch Off Console" and press OK.

7. Return all used, opened, or malfunctioned Catheters to Abiomed.

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6 Cleaning and Storage

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Cleaning

Cleaning the MPC, the Testplug, and the Cables

Clean the MPC, the Testplug, and the cables by wiping them down with disinfectant. Do not allow any fluids to enter the connector sockets.

Disinfecting and Resterilizing the Connector Cable

- Remove any contamination from the connector cable by wiping it with a disinfectant.
- If necessary, the cable can be submerged in a disinfectant bath. Make sure that the plugs are allowed to dry thoroughly after removal from the bath.
- The connector cable can be resterilized by autoclaving for 4 minutes at 134°C (273°F).
- Disinfection and resterilization can be repeated up to 100 times.

Storing the MPC and the Power Supply

CAUTION: The Li-Ion batteries must be charged for 10 hours prior to system operation. After being unplugged, the MPC will operate for a minimum of 60 minutes after the batteries have been fully charged.

- Place the MPC on a horizontal surface to prevent falling.
- Connect the AC power cable from the Power Supply to an AC outlet.
- The battery may be destroyed if the MPC is stored with a depleted battery.
- Cover the MPC if it will not be used for an extended period of time.

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7 Abbreviations and Symbols

SN	Serial number
REF	Order number
V	Volt
Hz	Hertz
VA	Volt ampere (Watt)
	Protect from moisture!
	Date of manufacture
	Defibrillator-proof type CF equipment
+10°C +25°C	Storage temperature

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	Protect from sunlight!
	Use-by date
	Do not reuse
	Attention, consult accompanying documents
	Class II equipment
STERILE EO	**Sterilized with ethylene oxide**

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8 System Specifications

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

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Ambient Conditions

During Operation

	MPC	Pump
Max. temperature	40°C (104°F)	Ambient conditions that prevail within the human body
Min. temperature	10°C (50°F)	
Max. rel. atmospheric humidity	75%	

During Storage

	MPC	Pump
Max. temperature	40°C (104°F)	25°C (77°F)
Min. temperature	10°C (50°F)	10°C (50°F)
Max. rel. atmospheric humidity	75%	

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Pump Parameters

Speed range	0 to 51,000 rpm
Power consumption	less than 0.99 A
Voltage	max. 18 V
Flow-Maximum	2.3 ± 0.3 L/min
Purging the LP 2.5 Catheter Recommended purge fluid Purge pressure Infusion rate	 20% Dextrose solution with heparin concentration of 50 I.U. per mL 300 to 700 mmHg 4 to 12 mL/h
Maximum duration of use	5 days
Dimensions of LP 2.5 Catheter Length of invasive portion (w/o catheter) Diameter	 130 ± 3 mm max. 4.2 mm (nom. 4.0 mm)
Classification per DIN EN 60601-1	Safety class II, degree of protection: CF (MPC and pump)
Classification per MDD/93/42/EEC	Class III

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

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MPC and Power Supply Parameters

Accuracy of calculated flow rates	± 10% (relative to maximum flow rate)
Characteristic values	
Nominal voltage	100/240 V (at 50/60 Hz)
Max. nominal current under load	1.1 A
Max. power consumption under load	120 VA
Device fuse	2x2 A slow-blow
Running time without Power Supply with fully charged batteries	60 minutes (charging duration of at least 10 hours)
Classification per DIN EN 60601-1	Safety Class II, degree of protection: CF
Classification per MDD/93/42/EEC	Class IIb
Electromagnetic compatibility	tested in accordance with DIN EN 60601-1-2
MPC dimensions	
Height	55 mm
Width	260 mm
Depth	305 mm
Weight	3.35 kg (7.38 lbs.)
Power Supply dimensions	
Height	75 mm
Width	305 mm
Depth	265 mm
Weight	3.2 kg (7.0 lbs.)

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Connector Cable (Black)

Length	2.5 m
Service life	100 sterilization cycles
Resterilization	autoclave for 4 minutes at 134°C (273°F)

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

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9 MPC Alarms and Warnings

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

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MPC Alarms

Header	Message	Cause	Action
Alarm	**Battery Completely Discharged** **Sudden Pump Stop Possible** **Change Console Immediately!**	The battery is depleted.	1. Change the MPC immediately. 2. Notify Abiomed.
Alarm	**Battery Discharged** **Change Console or Connect Power Supply!**	The battery is depleted.	1. Immediately connect the MPC to the Power Supply to recharge the MPC batteries. 2. Connect the Power Supply to AC power and switch it on. 3. If the AC power icon does not appear, replace the Power Supply and the connection cable. 4. If the alarm is still present or the AC power icon still does not appear, change the MPC.
Alarm	**Battery Temperature too High** **Change Console Immediately!**	The temperature of the MPC batteries is dangerously high.	1. Change the MPC immediately. 2. Notify Abiomed.
Alarm	**Keyboard not Available** **Change Console!** **Inform Service!**	The MPC keypad is defective. The pump can no longer be controlled with the MPC.	1. Change the MPC. 2. Notify Abiomed.
Alarm	**No External Pressure Signal** **Check Cable and Transducer!**	The purge pressure measurement is faulty.	1. Check all cable and plug connections. 2. If connections are secure, replace the pressure transducer cable. 3. If the alarm is still present, change the MPC. 4. Notify Abiomed.

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Header	Message	Cause	Action
Alarm	**Please Release ON Key!** **Do NOT Use ON to Switch off!** **Emergency Shut Down of Console!** **Using ON May Cause Data Loss!**	During operation the ON key was pressed and held. The MPC will turn off if the ON key is held for longer than 3 seconds. Data saved on the MPC may be lost.	Press "OK" to confirm the alarm message or if the MPC is off press "ON" to turn the MPC back on.
Alarm	**Pump Disconnected while Running** **Check Connection!**	The Catheter was disconnected during operation, or the connection to the pump was interrupted.	Check the Catheter connection and all cable and plug connections.
Alarm	**Pump Plug Defect** **Use New Pump!**	Error reading in pump data.	1. Replace the Catheter. 2. Notify Abiomed.
Alarm	**Pump Stopped** **Console Defect** **Change Console Immediately!**	The pump has stopped due to an MPC error.	1. Change the MPC immediately. 2. Notify Abiomed.
Alarm	**Pump Stopped** **Console Shows Last Performance Value** **Confirm or Change Value!**	A pump that was operated previously at a performance level greater than P0 has been plugged in again.	1. Press OK on the MPC to restart the pump at the previous performance level. 2. To restart the pump at a different level, use the +/- keys to select the desired level. Press OK to confirm.
Alarm	**Pump Stopped** **Restart Pump!** **Monitor Motor Current!**	The pump-specific motor current limit has been exceeded. The pump stopped. This may be the result of electrical or mechanical causes.	1. Try to restart the pump at performance level P2. 2. Replace the Catheter if the pump does not start up after the third attempt.
Alarm	**System Error** **Pump Stopped** **Pump Restarted!**	The pump stopped but is now running again.	Notify Abiomed.
Alarm	**System Error** **Pump Stopped** **Restart Pump!**	The pump has stopped due to an error.	1. Try to restart the pump at performance level P2. 2. If the pump cannot be restarted, change the MPC. 3. Notify Abiomed.

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MPC Warnings

Header	Message	Cause	Action
Warning	**Console Running On Battery** **Remaining Time "__" Minutes**	The remaining battery capacity is less than 50%. The MPC displays the estimated remaining run-time.	Observe remaining run-time.
Warning	**Could not Hold Target Performance** **Pump Still Running**	The selected performance level cannot be attained. The pump is not running at full power.	1. Change the MPC. 2. If the warning is still present, replace the Catheter. 3. Notify Abiomed.
Warning	**Data Storage not Available** **Please Inform Service!**	The MPC's data logging function is not working.	Notify Abiomed.
Warning	**Deaeration of Pressure Line Insufficient** **Repeat Deaeration!**	The pressure lumen was not deaerated completely.	Repeat deaeration by squeezing the white valve at the red pressure lumen for 5 seconds. Make sure the pressure bag is at 300 to 400 mmHg.
Warning	**Flow Below Low Flow Limit** **Check Flow Rate!** **Monitor Pump Signals!**	The flow rate has fallen below the low flow limit value selected by the user.	1. If the performance level has been reduced, adjust the low flow limit value accordingly. 2. If attachment due to suction has occurred, reduce the performance level first.
Warning	**High Battery Temperature** **Please Cool Console!**	The temperature of the MPC has increased to a dangerous level.	Do not place the MPC on top of the Power Supply.
Warning	**High Motor Current Value** **Pump Still Running** **Monitor Motor Current!**	The pump has mechanical problems. The motor current limit for the selected performance level has been exceeded. The pump may stop if the motor current continues to increase.	1. Observe motor current characteristics. 2. If the current continues to increase, replace the Catheter if possible. 3. Notify Abiomed.

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Header	Message	Cause	Action
Warning	**High Purge Pressure** **Decrease Purge Rate!** **Check Purge System!**	The purge pressure has increased to greater than 700 mmHg.	1. Inspect the purge system for kinks. 2. Reduce the purge flow rate at the infusion pump by 1 mL/hr. Do not decrease the flow rate to less than 4 mL/hr. 3. If the problem persists, replace the BRAUN Vista basic.
Warning	**Low Purge Pressure** **Increase Purge Rate!** **Check Purge System!**	The purge pressure has decreased to less than 300 mmHg.	1. Inspect the purge system for leaks. 2. Increase the purge flow rate at the infusion pump by 1 mL/hr. Do not exceed 12 mL/hr. 3. If the problem persists, replace the BRAUN Vista basic.
Warning	**No Pump Connected** **Console will be Switched off**	No Catheter has been plugged into the MPC. The MPC will operate for 10 minutes and then shut down automatically.	Plug in a Catheter or switch the MPC off by pressing OK twice.
Warning	**Pump Plug Defect** **Flow Calculation not Possible**	Error reading flow rate performance data from the pump plug.	Replace the Catheter.
Warning	**Pump Position Wrong** **Pump Outlet Blocked** **Pull Pump Back 1 cm**	Pump is too deep in the ventricle. The outlet may be at the level of the aortic valve.	Pull Catheter back 1 cm.
Warning	**Pump Position Wrong** **Reposition Pump!** **Apply MENU for Reposition!**	A wrong pump position was detected.	1. Reposition the pump according to the Repositioning Menu. 2. If step 1 does not provide correct positioning, check the pump position by imaging methods.
Warning	**Pump Repositioning Function has been canceled**	The placement guide was canceled because of a fault. A measuring signal (placement signal) is outside the validity range.	Select the placement guide again using the MENU key. If the placement guide cancels again, use imaging procedures as assistance for repositioning.

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Header	Message	Cause	Action
Warning	**Pump Stopped** **Reverse Flow!** **Restart Pump!**	Retrograde flow will occur because the pump has stopped.	Unless the pump is being explanted, restart the pump immediately. Do not restart the pump during explantation.
Warning	**Real Time Clock Error** **Missing Time Information** **Please Inform Service!**	The MPC's internal clock is defective. Data is being recorded without a time stamp.	Notify Abiomed.
Warning	**Sensor Value not Reliable**	Defective pressure sensor or signal interference.	1. If the warning occurs while deaerating the pressure lumen, check that the pressure bag is at 300 to 400 mmHg. 2. If signal interference is suspected, either increase the distance between LP 2.5 System components and the EMI source or turn off the EMI source. 3. If the warning is still present, replace the Catheter.
Warning	**Suction Likely** **Decrease Performance Slowly!**	The MPC has detected pump suction.	1. Reduce the performance level. 2. Check the filling of the left ventricle. 3. If there are no filling problems, check the pump for correct positioning. 4. Try to increase the performance level to reach the intended level of support.
Warning	**Time Out Reposition Guide Function has been canceled**	The placement guide has been canceled because of timeout.	If the incorrect positioning persists, select the placement guide again using the MENU key.

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510(k) Summary (Prepared in accordance with 21 CFR Part 807.92)

a. Submitted

Applicant Name:	ABIOMED, Inc.
	22 Cherry Hill Drive, Danvers, MA 01923
Contact Person:	William J. Bolt
Date Summary Prepared:	May 15, 2008

b. Device Information

Trade Name:	IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System
Common Name:	Percutaneous Cardiac Support System
Classification Name:	Pump, Blood, Cardiopulmonary Bypass, non roller type (classified under 870.4360)
	Catheter, Cannula and Tubing, Vascular, Cardiopulmonary Bypass (classified under 870.4210)
	Diagnostic intravascular catheter (classified under 870.1200)
Product Code:	74KFM, 74DWF, 74DQO

c. Legally Marketed Predicate Devices

- TandemHeart PTVA System – K991783, K052570 ,K924642 , K924643
- Vascular Solutions Langston Dual Lumen Catheter – K050168

d. Device Description:

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System (IMPELLA RECOVER LP 2.5 System) provides circulatory support with the ability to deliver anticoagulant through an infusion system. The System is comprised of: 1) a catheter which contains an integrated pump motor/infusate lumen, integrated intravascular pressure lumen and integral cannula, 2) a controller/console and 3) infusion system designed to work together, and 4) accessories.

e. Intended Use:

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is intended for partial circulatory support using an extracorporeal bypass control unit, for periods up to 6 hours. It is also intended to be used to provide partial circulatory support (for periods up to 6 hours) during procedures not requiring cardiopulmonary bypass.

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System also provides pressure measurements which are useful in determining intravascular pressure.

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f. Technological Characteristics and Comparison to Predicate Device(s):

The technological characteristics of the IMPELLA RECOVER® LP 2.5 are the same as the TANDEM HEART systems and the Vascular solutions Langston catheter with the exception of the following differences:

- pump location
- certain materials of construction

g. Pre-clinical Test Results:

To validate the device design of the IMPELLA RECOVER® Percutaneous Cardiac Support System, ABIOMED performed the following *in vitro* testing:

With regard to sterilization, packaging, and shelf-life, the IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is sterilized using EtO gas with a SAL of 10^{-6}. The sterilization method/cycle was validated using EN 550 "*Sterilization of Medical Devices – Validation and Routine Control of Ethylene Oxide Sterilization.*" The EtO sterilization residual values for EO and ECH and are within the allowable limits of ISO 10993-7. The LAL test was used to ensure a pyrogen free determination. The packaging material has been validated to ensure its integrity.

Biocompatibility testing of all patient contacting materials was conducted on the finished sterilized devices in accordance with ISO-10993, "*Biological Evaluation of Medical Devices Part 1: Evaluation and Testing*". All testing results are acceptable.

The design and testing validation of the software contained in the IMPELLA MCS was conducted in compliance with the FDA 2005 guidance document entitled "*Guidance for Industry and FDA Staff: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices.*"

With regard to electromagnetic compatibility and electrical safety, the IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System was tested in accordance with EN 60601 and EN 61000 and their applicable subparts. The testing results demonstrate that the device is in conformance with these FDA recognized standards.

With regard to In vitro performance testing, ABIOMED conducted a full range of testing demonstrating that the entire IMPELLA RECOVER® LP 2.5 System operates as intended. All tests were acceptable.

h. Conclusion:

The ABIOMED IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is substantially equivalent to the TandemHeart PTVA System and Control system (K991783), the TandemHeart Transseptal Cannula (K052570), the Medtronic Biomedicus 15F arterial cannula and introducer (K924642, K924643) and the Vascular Solutions Langston Dual Lumen Catheter – K050168

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Indications for Use

510(k) Number (if known): K063723

Device Name: IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System

Indications for Use:

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System is intended for partial circulatory support using an extracorporeal bypass control unit, for periods up to 6 hours. It is also intended to be used to provide partial circulatory support (for periods up to 6 hours) during procedures not requiring cardiopulmonary bypass.

The IMPELLA RECOVER® LP 2.5 Percutaneous Cardiac Support System also provides pressure measurements which are useful in determining intravascular pressure.

Prescription Use __X_____ AND/OR Over-The-Counter Use_____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

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ABIOMED attests that the information provided in this section is identical to that submitted to the FDA for informal review on 3/25/2008. No changes have been made.

Signed,

May 15, 2008

William J. Bolt
Senior Vice President, QA & RA
ABIOMED, Inc.

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

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