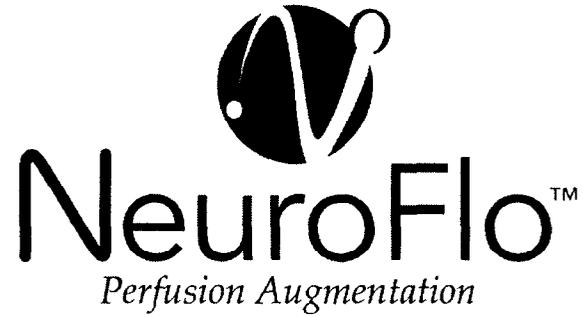


LABELING



Instructions For Use

Humanitarian Device. Authorized by Federal Law for use in the treatment of cerebral ischemia resulting from symptomatic vasospasm following aneurismal subarachnoid hemorrhage secured by either surgical or endovascular intervention for patients who have failed maximal medical management. The effectiveness of this device for this use has not been demonstrated.

REF: XXXX
(Version 3.0 3/3/2005)



It is important to thoroughly read the entire Instructions for Use prior to using this device

STERILE	EO
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Sterile: This device is provided sterile. Sterilized using ethylene oxide gas.

Single Use: This device is intended for SINGLE USE ONLY.

Caution: Federal law restricts this device to sale by or on the order of a physician.

Contents

One (1) NeuroFlo™ Catheter

Device Description

The NeuroFlo™ Catheter is a multi-lumen device with two balloons mounted near the distal tip. The catheter is inserted over a guide wire through a vascular introducer sheath placed in the femoral artery. The device has a working length of approximately 62 cm and is coated with a hydrophilic coating containing heparin. A multi-port manifold at the proximal end of the device allows balloon inflation, guide wire insertion and attachment of a pressure monitoring line. Each balloon can be inflated independently to a variable diameter to control blood flow in the descending aorta. The device has three marker bands to aid in balloon placement. The catheter is EtO sterilized and is intended for single use only.

Indications For Use

The CoAxia NeuroFlo™ Catheter is intended for the treatment of cerebral ischemia resulting from symptomatic vasospasm following aneurismal subarachnoid hemorrhage, secured by either surgical or endovascular intervention for patients who have failed maximal medical management.

Contraindications

- Patients with significant left ventricular dysfunction
- Patients with aortic aneurysm including those which have been treated with endovascular grafts
- Patients with a history of bleeding disorders
- Pregnant women

Warnings

- This device should be used only by physicians properly trained in percutaneous interventional procedures.
- This device should not be used in patients with International Normalized Ratio (INR) > 1.7.
- This device should not be used in patients with activated clotting time (ACT) > 300 sec.
- The device should not be used in patients with endovascular grafts that are implanted to treat aneurysms above or below the renal arteries.
- This device contains heparin. This device should not be used in patients with sensitivity to heparin or who cannot be anticoagulated or infused with heparinized saline.
- This device should not be used in patients with systolic blood pressure (SBP) > 200 mmHg at time of device insertion. The safety of the device has not been evaluated in patients with uncontrolled hypertension (SBP > 200 mmHg).
- Only one procedure using the device should be performed on any given subject. Repeated application of the device in any one individual has not been evaluated.
- The device should not be implanted and deployed for more than one hour. The safety of the device when used for longer periods of time has not been evaluated or established and may lead to increased complications.
- The inflated balloon diameter(s) must not exceed the diameter of the vessel at the intended occlusion site. Verify the aortic diameter under fluoroscopy to confirm that the balloon diameters do not exceed the diameter of the vessel.
- Do not exceed the maximum recommended inflation volume as balloon rupture may occur.
- Do not use air, or any gaseous media, to inflate the balloon due to risk of gas embolization.
- Deflate the balloon(s) slowly. Rapid deflation of the balloon(s) may lead to rebound hypotension or cerebral hypoperfusion.
- Do not use MRI while the NeuroFlo catheter is in the body because of the risk of burn from significant temperature rise due to the presence of the device.
- Careful monitoring of a patient's renal function should be performed during and after the procedure in patients with acute or chronic renal insufficiency.

Precautions

- Do not advance the catheter against resistance until the source of resistance is identified under fluoroscopy
- The hydrophilic coating on this device contains heparin. The activity and quantity of heparin in the coating has not been defined. No testing has been done to demonstrate increased thromboresistance due to the presence of the coating.
- Use an inflation medium consisting equal parts of contrast and saline
- Use only the recommended size sheath and guidewire
- Do not use if packaging is opened or damaged.

Storage

Store the catheter inventory in a cool, dry area.

Adverse Events

Observed adverse effects:

In an uncontrolled clinical trial, nineteen patients with cerebral vasospasm following aneurismal subarachnoid hemorrhage (symptomatic=16, asymptomatic=2, compassionate use = 1) were treated with the NeuroFlo device. The compassionate use patient was in a barbiturate coma and was treated based on imaging evidence of vasospasm. Adverse events are summarized in the table below for all 19 patients.

**Summary Table
Adverse Events in 19 Patients**

Adverse Event	N (%)
Death	6 (32)
Neurological deterioration	4 (21)
Hydrocephalus	2 (10)
Anemia	1 (5)
Sepsis	1 (5)
Psychomotor excitation	1 (5)
Groin hematoma	1 (5)
Cervical spontaneous edema	1 (5)
Urinary tract infection	1 (5)
Dyspnea	1 (5)
Transient arrhythmia	1 (5)
Coagulopathy	1 (5)
Acute Respiratory Distress Syndrome	1 (5)
Renal failure	1 (5)
Cardiogenic shock	1 (5)
Pulled out sheath	1 (5)

N = number of patients experiencing event

Potential Adverse Effects:

Although not reported during the clinical trial, other potential adverse effects associated with the NeuroFlo procedure may include:

- aortic dissection
- aortic rupture
- cardiac arrhythmias
- cardiac failure
- femoral bleeding
- hemodynamic deterioration
- intracranial hemorrhage
- renal failure
- thromboembolism
- tissue ischemia

Clinical Information

The study of the NeuroFlo catheter for treatment of cerebral vasospasm following aneurismal subarachnoid hemorrhage was conducted at three institutions in Mexico, Argentina, and Brazil between May 2002 and April 2003. Nineteen patients were treated with 20 procedures performed (one patient having received two procedures); sixteen patients had symptomatic vasospasm, two patients had asymptomatic vasospasm and one patient who was in a barbiturate coma and was treated based on imaging evidence of vasospasm (compassionate use). Data regarding outcome is presented for the 16 patients with symptomatic vasospasm per the indication for this HDE. Adverse events were supplied for all 19 patients.

Patients who had failed maximal medical therapy for vasospasm were screened against the following criteria:

Inclusion criteria:

- 1) Age > 18.
- 2) Clinical evidence of vasospasm with angiographic confirmation OR
- 3) A perfusion deficit on Xenon CT, MRI perfusion scan or parenchymogram.
- 4) Informed Consent

Exclusion criteria:

- 1) Unsecured aneurysm(s)
- 2) Symptoms attributable to other causes (metabolic, infection, etc.)
- 3) Large infarct on CT scan
- 4) Hydrocephalus thought to be the cause of symptoms
- 5) Intracranial hemorrhage (not due to the aneurysm rupture)
- 6) Coagulopathy
- 7) Aortic diameter not between 12-23cm below the renal arteries and 12-27 above the renals
- 8) Aortic aneurysm
- 9) Renal insufficiency (creatinine 2x normal)
- 10) History of myocardial infarction, congestive heart failure or angina or ejection fraction < 40%
- 11) Femoral artery stenosis precluding device placement
- 12) Pregnancy

Patient Demographic:

Characteristics	Mexico	Argentina	Brazil	All Sites
Number	1 (s) 1 (a)	14 (s) 1 (a) 1 (c)	1 (s)	19
Age range (yrs)	56 & 61	31-63	30	30 - 63
Gender: Male/Female	1/1	5/11	1/0	7/12

s = symptomatic a = asymptomatic c = compassionate use

NeuroFlo treatment was administered by placing the device balloons under fluoroscopy on either side of the renal arteries. The infrarenal (IR) balloon was inflated first to 70% occlusion for 5 minutes, followed by inflation of the suprarenal (SR) balloon to 70% occlusion for an additional 40 minutes. At the end of the 45 minute inflation cycle, the balloons were slowly deflated.

Patients were administered an NIH Stroke Scale (NIHSS) test prior to NeuroFlo treatment, upon completion of treatment, at 24 hours and at 30 days. Clinical improvement was defined as a ≥ 3 point decrease in NIHSS.

Results

Information on clinical outcome (i.e., NIHSS) is provided in Table 1. Table 1 stratifies patients based on their Fisher score (a scale from 0-4 of the severity of the subarachnoid hemorrhage (SAH), 4 being most severe) compared with their baseline, post-procedural, 24 hour and 30-day NIHSS scores. The Fisher score was taken upon presentation to the hospital at the time of SAH; the baseline NIHSS was taken once a patient was accepted for NeuroFlo treatment – an average of 9 days post-SAH.

Assuming that a decrease of ≥ 3 points in NIHSS from baseline to immediately post-treatment represents a significant neurologic improvement, 8/16 patients (50%) demonstrated such a clinically relevant response to NeuroFlo treatment that was sustained at 24 hours; of these 8, 7 had a presenting Fisher score of 4. Ten of 16 patients (63%) had a 3 point or greater decrease in NIHSS at 30 days. In all but 2 cases, patients who received the NeuroFlo treatment had failed to respond to Triple-H (i.e., hypertension, hypervolemia, and hemodilution) therapy and/or other medical therapies to treat their vasospasm.

There were 6 deaths total (32%); 4 occurred in the symptomatic group (25%). Adverse events leading to death included hydrocephalus with neurological deterioration (2), sepsis (1), neurological deterioration (1), stroke (1) and arrhythmia and organ failure (1). Other adverse events included anemia and neurological deterioration. Due to the small sample size, the reliability of these numbers is unknown.

Table 1
Outcome of Sixteen Patients with Symptomatic Vasospasm

Presenting Fisher	Baseline NIHSS	Immediate Post-Deflation NIHSS	24-Hour NIHSS	30-Day NIHSS
1	1	0	0	0
2	17	ND-Sedated	ND	ND-Died @ 84 hours
3	6	ND	9	0
3	10	2	2	1
3	2	2	1	See second Treatment
Second Treatment	3	1	3	0
4	15	12	13	5
4	8	1	1	0
4	21	19	18	ND-Died @ 8 Days
4	7	5	5	1
4	9	9	23	ND-Died @ 9 Days
4	6	2	0	0
4	11	7	5	ND-Died @ 4 Days
4	17	7	4	2
4	14	4	6	4
4	3	1	1	1
4	9	6	6	2

ND = not done

When the outcome data is stratified by baseline NIHSS (see Table 2), good outcome at 30 days, as defined by a ≥ 3 -point drop in NIHSS Score, was seen in 70% of patients with a good presenting score (10 or less) where as poor outcome was seen in 50% of patients with NIHSS > 10. The literature on SAH supports that the likelihood of a good outcome in the patients presenting with less severe disease is higher than for those presenting in worse neurologic condition. Therefore, the individual 30 day results shown could be related to the expected outcome in patients due to the natural history of the disease, and unrelated to treatment with the NeuroFlo device.

Table 2
Outcome Data Stratified by Baseline NIHSS Score

NIHSS	Total number of patients	Average group NIHSS	Good outcome	Poor outcome
0-10	10	6.5	7	3
>10	6	16	3	3

Compatibility

The NeuroFlo device is designed to be compatible with a 9F (0.121" ID) introducer sheath and guide wires ≤ 0.035 " in diameter.

Procedural Materials Required:

Quantity	Item
1	NeuroFlo™ Catheter
2	Three-way stopcocks
1	20cc syringe
As Req'd	50/50 contrast/saline inflation medium
1	≤ 0.035 " guide wire at least 150cm long
1	$\geq 9F$ introducer kit
2	Inflation devices with volume measurements and a three-way stopcock
2	Pressure monitoring lines and transducers
As Req'd	Sterile heparinized saline

Device Preparation

1. Carefully remove the catheter from the package and inspect for any signs of damage. If damage is noted, do not use the device.
2. Attach a three-way stopcock to each of the two balloon ports.
3. Prepare each balloon with inflation medium (50% contrast / 50% saline mixture) in the following manner:
 - a. Load a 20cc syringe with 5cc of inflation medium.
 - b. Attach the syringe to one of the balloon ports and pull vacuum for 15 seconds.
 - c. Release the vacuum and re-apply for an additional 15 seconds.
 - d. Rotate the stopcock to lock the catheter under vacuum.
 - e. Remove the syringe.
 - f. Repeat steps 3a – 3e for the second balloon.
4. Flush the guidewire lumen with heparinized saline until fluid drains from distal tip of the catheter.

Device Use

1. Prior to device introduction, an aortogram must be performed to determine the minimum aortic diameter for each balloon and location of the renal arteries. The renal arteries should be landmarked for the purpose of catheter positioning during the procedure.
2. Place a guidewire in the descending aorta so the tip extends above the renal arteries.
3. Insert the proximal end of the guidewire through the distal lumen of the catheter. Advance the catheter over the wire until the distal tip is near the introducer sheath.
4. Rinse the two balloons on the catheter with sterile saline. This will activate the hydrophilic coating, which will aid in device introduction.
Caution: Do not attempt to wrap the balloons prior to insertion in the introducer sheath as this may damage the balloons and/or catheter.
5. While holding the guidewire stationary, advance the catheter until the center marker band reaches the midline between the renal arteries.
Caution: Do not force advancement of the catheter if significant resistance is observed.
Note: The location of the proximal shaft relative to the sheath should be recorded once the catheter is properly positioned.
6. Remove the guidewire and attach a three-way stopcock and pressure monitoring line to the central lumen to measure SR pressure. Evacuate the air from the lines and flush the central lumen with heparinized saline following standard techniques.
7. Attach a pressure monitoring line to the side arm of the introducer sheath to measure IR pressure. Evacuate the air and flush the lumen with heparinized saline following standard techniques.
8. Fill two (2) inflation devices each with 15cc of inflation medium and attach one to each balloon port stopcock.
Note: It may be helpful to label the inflation devices for supra renal and infra renal balloons.
9. Purge air out of each stopcock and inflation device by expelling 2cc of inflation medium.
10. Secure the proximal shaft of the NeuroFlo to the patient's leg using surgical tape or a commercially available catheter securement device.
Note: It is very important to secure the device prior to inflation so that catheter does not move during or after balloon inflation.
Note: If used in conjunction with the StatLock Universal Plus securement device, lock the StatLock around the black strain relief on the catheter shaft.

11. To inflate the balloons, open the stopcock and gradually infuse inflation medium into the balloon. Note the infused volume (cc) of inflation medium. Refer to Table 3 for the infusion volume to obtain 70% occlusion at various aortic diameters.
12. Using fluoroscopy, verify proper balloon placement and inflation.
13. While the balloons are inflated, blood pressure may be monitored distal and proximal of the balloons, utilizing the attached pressure lines.
Note: Pressure lines should be flushed periodically to ensure accurate measurements.
14. To deflate a balloon, gradually withdraw inflation medium into the inflation device.
Warning: Rapid deflation of the balloons may lead to rebound hypotension or cerebral hypoperfusion. Balloons should be deflated at a rate of 1cc/min until 50% of the inflation volume has been removed. The balloons may then be deflated with full vacuum.
15. After each balloon has been deflated and is under vacuum, turn off the stopcock to the device.
16. Remove the catheter by withdrawing the catheter through the introducer sheath.

Treatment Recommendation

1. Perform an aortic angiogram or abdominal CT scan to determine the minimum aortic diameter 6cm above and 6 cm below the midpoint of the renal arteries.
2. Inflate the IR balloon to occlude 70% of the aortic cross-sectional area as measured below the renal arteries. [See Table 3 for balloon volume/% occlusion information.] Confirm a 5-10 mmHg pressure drop between SR and IR MAP readings.
3. At approximately 5 minutes from the IR balloon inflation, inflate the SR balloon to 70% occlusion using the same technique. Confirm an additional 5-10 mmHg pressure drop (10-20 mmHg total) between the SR and IR MAP readings.
4. Maintain inflation for 40 minutes. If the SR blood pressure increases more than 30% above baseline or above 220mmHg systolic, modify balloon inflation as required for blood pressure management. Assessment of the lower extremities should be made frequently to verify appropriate circulation. Reduction of the SR balloon volume may be considered if limb ischemia is noted.
5. Deflate the SR balloon slowly per the instructions above.
6. Deflate the IR balloon slowly per the instructions above.

**Table 3 - NeuroFlo Model: 1017
Inflation Volume vs. Aortic Occlusion Area**

Aorta Diameter (mm)	Volume for 70% Occlusion (cc)	Aorta Diameter (mm)	Volume for 70% Occlusion (cc)
12.0	2.5	18.5	6.2
12.5	2.7	19.0	6.7
13.0	2.8	19.5	7.2
13.5	2.9	20.0	7.7
14.0	3.1	20.5	8.3
14.5	3.4	21.0	8.9
15.0	3.6	21.5	9.4
15.5	3.9	22.0	10.0
16.0	4.2	22.5	10.7
16.5	4.5	23.0	11.4
17.0	4.9	23.5	12.1
17.5	5.3	24.0	12.9
18.0	5.8		

Nominal working range

Warning: Do not inflate the balloon with more than 13cc of inflation medium.



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(Version 3.1 3/21/2005)

CoAxia NeuroFlo™ Catheter

Patient Information

HUMANITARIAN USE DEVICE:

Authorized by Federal Law for use in the treatment of cerebral ischemia resulting from symptomatic vasospasm following aneurismal subarachnoid hemorrhage secured by either surgical or endovascular intervention for patients who have failed maximal medical management. The effectiveness of this device for this use has not been demonstrated.

Caution: Federal law restricts this device to sale by or on the order of a physician.

INTENDED USE

The CoAxia NeuroFlo™ Catheter is intended for the treatment of cerebral ischemia resulting from symptomatic vasospasm following aneurismal subarachnoid hemorrhage, secured by either surgical or endovascular intervention for patients who have failed maximal medical management.

PROCEDURE

Your doctor has determined that you have suffered a bleed in your brain and that you are having symptoms from spasm of arteries in your brain (symptomatic vasospasm*). Your doctor feels that you might benefit from the use of the NeuroFlo Catheter. The NeuroFlo Catheter* is a device with two balloons attached near the end of the catheter or tube. The catheter is placed in the large blood vessel (Aorta) that leads from your heart to the lower part of your body, through a small hole in the upper part of your leg. The balloons on the catheter are inflated for approximately 45 minutes. The assumption is that during this time, blood flow to the lower part of your body will be reduced while that to your upper part, including your brain, will be increased. When the procedure is completed, the catheter is removed.

RISKS AND PROBABLE BENEFITS OF USING THE NEUROFLO CATHETER

There is the risk that use of the NeuroFlo catheter can make your vasospasm and/or neurological condition worse or cause other complications like brain swelling, irregular heart rhythm, kidney failure, fluid in your lungs or death. There is a risk that the NeuroFlo device could fail causing damage to the large blood vessel. If the damage to the aorta is severe, an emergent procedure or surgery may be required to repair the damage. You could also have bleeding problems from the small hole in your upper leg; these bleeding problems can range from mild to serious. During the procedure you will receive a blood thinner called heparin. This may increase the risk of bleeding at the insertion site or elsewhere. Because the NeuroFlo is used only by your doctor, and you will be in the

hospital before and after its use, there are no special instructions for you to follow with regard to the NeuroFlo device.

There is the chance that the NeuroFlo could improve your vasospasm and/or neurological condition. In a study of the NeuroFlo conducted at three institutions in Mexico, Argentina, and Brazil between May 2002 and April 2003, 8/16 (50%) patients with symptomatic vasospasm had improvement in their neurological status within 24 hours. However, due to the small sample size, the reliability of this number is unknown. Also unknown is the long term benefit of this device.

ALTERNATIVE PRACTICES AND PROCEDURES

Currently there are not any approved device *treatments* for symptomatic vasospasm. The only FDA approved therapy is oral Nimodipine, a drug which is used as a preventive measure for vasospasm following subarachnoid hemorrhage. Your doctor can tell you what he/she currently uses as a treatment for vasospasm. Some common therapies being used are percutaneous transluminal angioplasty*, intra-arterial vasodilators* and Triple-H therapy* (i.e., hypertension, hypervolemia, and hemodilution). The safety and efficacy of these therapies for the treatment of vasospasm has not been evaluated by the FDA.

GLOSSARY OF TERMS

Words with an (*) next to them are defined below:

- Symptomatic vasospasm – squeezing down of a blood vessel [in the brain] that results in symptoms of a stroke such as difficulty in talking, weak arms or legs or the inability to move your eyes from side to side
- NeuroFlo catheter – a long, stiff tube with two small balloons on one end that is used to partially block blood flow in large blood vessels
- Percutaneous transluminal angioplasty – a minimally invasive procedure where spastic vessels are dilated mechanically using a balloon catheter
- Intra-arterial vasodilators – drug or chemical agents that causes dilation of the blood vessels
- Triple-H therapy – a procedure for increasing blood flow through narrowed vessels in the brain through increased pressure and volume of fluid to the patient who had symptomatic vasospasm