Embolic Protection Systems

Balloon angioplasty, stent placement and a variety of other procedures used to open vascular blockages have become important standard methods for improving blood flow to the heart and brain, but these procedures also come with a large risk — the possibility of dislodging materials that can move to the heart or brain to produce heart attack or stroke or form other life-threatening embolisms in the vasculature. As with other technologies, these frequent side effects have resulted in the development of an important cardiovascular subsector: systems for capturing and removing these embolic materials and reducing the threat of these unwanted side effects.

Embolic protection systems have been developed in a broad range of innovative modalities to improve patient outcomes and reduce these frequent co-morbidities. For the most part, however, these systems are still in their infancy with the “gold standards” of these devices still to be developed.

Note: This section includes related technologies used in neurovascular procedures employed in and near the brain for the prevention of stroke, often similar to those systems used to protect embolisms in the cardiovascular system and peripheral vasculature.
Embolic protection systems —
corporate/product profiles


Product focus:

▼ ArteriA’s Parodi Anti-Emboli System (PAES) prevents emboli from traveling to the brain during angioplasty and stenting. The device differs from traditional filters by reversing blood flow in the carotid arteries. It works by occluding the common carotid, thus creating a negative pressure gradient distal to the balloon occlusion. This results in cerebral blood altering flow through the Circle of Willis and establishes retrograde flow down the internal carotid artery. The system establishes protection without touching the lesion, thereby avoiding the possibility of causing a stroke while navigating the device into place. The PAES leaves the internal carotid free of bulky devices that may get in the way during a therapeutic procedure. It has been used successfully in iliacs, subclavians, femorals and vertebrals.

▼ The next-generation PAES II has a simple and more user-friendly hub, is ergonomically designed, and is longer to accommodate taller patients, according to the company. In addition, the system also includes a dilator, introducer sheath, syringes and stop-cock.

Milestones:

♦ ArteriA in April 2002 presented results from a 100-patient clinical trial in Argentina using the PAES. In the study, all 100 cases were clinically and technically successful, and none of the patients suffered from an embolic event.

♦ Doctors from Montefiore Medical Center (New York) and Lenox Hill Hospital (New York) in September 2001 performed the first U.S. carotid angioplasty and stenting procedure with ArteriA’s PAES.

♦ The PAES has received the CE mark for prevention of cerebral embolization during angioplasty and stenting procedures and also is being used in Argentina, New Zealand and Australia.

♦ ArteriA in July 2001 received FDA IDE approval to conduct a clinical evaluation of PAES in conjunction with the investigational Carotid Wallstent Monorail Endoprosthesis system made by Boston Scientific (Natick, Massachusetts). The company said it plans to qualify the PAES for one of the larger, randomized studies being conducted in the United States that could lead to FDA approval of the CAS procedure as an alternative to open surgery.

♦ The ArteriA Parodi Catheter for Angiography was FDA-cleared in June 2001.

♦ ArteriA currently is involved in the Endarterectomy Versus Angioplasty in patients with Severe symptomatic carotid Stenosis (EVA03S) study in France.

**Product focus:**
- Boston Scientific EPI’s **FilterWire EX** technology is a low-profile filter designed to capture embolic particles, released during angioplasty and other vascular procedures, to prevent them from traveling to the brain. The device is incorporated into the interventional procedure by mounting on a rapid exchange deployment system.

**Milestones:**
- In June 2003, Boston Scientific EPI received 510(k) clearance to market the **FilterWire EX** embolic protection system to treat saphenous vein graft disease, and simultaneously launched the product in the United States.
- Also in June 2003, the company reported results from its FIRE clinical trial, which studied the **FilterWire EX** system. The objective of the trial was to establish the safety and efficacy of the **FilterWire EX** system during balloon angioplasty or stenting procedures in the treatment of SVGs. The multi-center study compared the **FilterWire EX** product to the PercuSurge GuardWire Plus system in a non-inferiority trial that enrolled 651 patients at 55 U.S. sites and four Canadian sites. The cumulative MACE incidence at 30 days was 9.9% for patients receiving treatment with the **FilterWire EX** system vs. 11.6% for those receiving treatment with the GuardWire Plus System.
- In February 2002, the company reported the first U.S. human use of its **FilterWire EX** embolic protection device and Carotid Wallstent Monorail device as part of an FDA-approved trial evaluating the benefits of stenting in conjunction with embolic protection to treat carotid artery disease. The procedure was performed at the Arizona Heart Institute and Foundation (Phoenix, Arizona). The trial was to enroll up to 775 patients at 40 U.S. sites.
- In 2000, Boston Scientific EPI received the CE mark for use of the **FilterWire EX** in the peripheral circulatory system, and in 2001, it received CE mark for use in coronary, SVG and peripheral vessels.


**Product focus:**
- Interventional Technologies (now Boston Scientific IVT) developed the **Cutting Balloon** for reduction of embolic events. The device features small blades, made of “aero-alloy” materials, that are attached to the balloon and cut away lesions in the vessel.
The Cutting Balloon Ultra2 device features tiny, longitudinally mounted atherotomes (microsurgical blades) that help reduce resistance of a lesion to expansion. The atherotomes create incisions that relieve stress in the artery as the balloon inflates, reducing the force necessary to expand the vessel. The device’s fold mechanism shields the atherotomes and protects the vessel wall as the catheter is passed to and from the treatment site. The Cutting Balloon Ultra2 device combines the company’s Maverick2 balloon catheter technology with Bioslide coating and enhancements to the balloon and microsurgical blades. As a result, the Cutting Balloon Ultra2 device’s blades are 25% more flexible, the enhanced tip provides for easier guidewire insertion while a newly applied laser bonding technique provides flexibility and crossability. The Cutting Balloon Ultra2 is designed to be used as a stand-alone treatment for complex lesions or as a predilatation device for the pre-treatment of lesions where stents will be placed.

The company’s Transluminal Extraction Catheter (TEC) system simultaneously excises and extracts plaque and thrombi. Studies show lower rates of distal embolization and myocardial injury when TEC is used before angioplasty as compared to balloon angioplasty alone.

Milestones:
♦ Boston Scientific IVT in August 2003 reported receiving FDA approval and the CE mark for the Cutting Balloon Ultra2 microsurgical dilation device. The company immediately launched monorail and over-the-wire versions of the device in both markets.
♦ In December 2002, Boston Scientific reported meeting “all revenue milestones” under its purchase agreement with Interventional Technologies, a $245 million deal made early in 2001 to acquire the Cutting Balloon technology.
♦ The company received FDA PMA clearance for the Cutting Balloon in early 2001, based on data reflecting 1,200 procedures.
♦ CardioTech International received a $100,000 grant from the National Heart, Lung and Blood Institute to test the feasibility of seeding endothelial cells on CardioPass CABGs.


Product focus:
♦ Edwards in May 2003 acquired the Embol-X intra-aortic embolic management system from Embol-X (Sacramento, California). The system features a small, expandable, polyester-mesh filtration system placed inside the aorta above the aortic clamp during open-heart surgery, in order to capture particles in the bloodstream. The intention is to prevent “embolic showers” which may result following the removal
of aortic cross-clamps and have the potential to cause neurocognitive complications. Edwards bills the device as the first of its kind in the United States.

(See Edwards Lifesciences Corp. also in “Atrial Fibrillation,” “Graft Technologies” and “Valve Technology.”)

Milestones:
♦ Edwards received FDA 510(k) clearance for the Embol-X system in February 2003 and was launched the following August.


Product focus:
▼ EndoTex Interventional Systems’ self-expanding carotid stent, NexStent, is designed to provide a minimally invasive approach for treating carotid artery disease. The NexStent acts much like a coronary artery stent in pushing the plaque back against the artery wall and restoring blood flow.

(See EndoTex Interventional Systems, Inc. also in “Stent Technology: Advanced Stenting.”)

Milestones:
♦ In May 2003, Boston Scientific (Natick, Massachusetts) made an equity investment in EndoTex and agreed to purchase the company if milestones are met.
♦ EndoTex has received FDA approval to begin a pivotal study, called Carotid Artery Revascularization using the Boston Scientific EP FilterWire EX and the EndoTex NexStent (CABERNET) trial. The trial is designed to evaluate the safety and efficacy of the NexStent and will enroll patients at high risk for surgical carotid endarterectomy across 30 U.S. and European clinical sites.


Product focus:
▼ In 2002, ev3 purchased EndiCor Medical, manufacturer of the X-Sizer catheter system, a pre-assembled, sterilized, disposable system designed to remove blood clots and soft tissue obstructions from coronary blood vessels. The device consists of a hand-held control module that houses a small motor, drive circuitry and various sensors and safety switches to guard against faulty operation. A catheter per
manently connected to the control module has a dual-lumen catheter shaft and contains a torque tube containing the guidewire lumen. It is connected to a hollow helical cutter. The outer lumen within the catheter body provides the path for excised debris to be aspirated from the lesion site. The use of vacuum pulls blood clots and soft, loose occlusive tissues into the catheter tip and aspirates tissue debris.

Through the purchase of Microvena, ev3 acquired that company’s **Trap Cardiovascular Filtration System** (CFS), **Trap Neurovascular Filtration System** (NFS) and **Trap Vascular Filtration System** (VFS), devices consisting of a nitinol-braided basket with a proprietary coating that captures embolic materials released during interventional procedures while providing perfusion. A recovery catheter then retrieves the basket and the embolic material is removed.

The **Spider Embolic Protection** device is designed to capture and remove dislodged embolic debris.

(See ev3 Inc. also in “Stent Technology: Advanced Stenting.”)

**Milestones:**

- A Phase II clinical trial of the **X-Sizer** was launched in March 2000 at 70 sites in the U.S. and Canada.
- In December 1999, EndiCor Medical completed the Phase I study of **X-Sizer** for Treatment of Thrombus and Atherosclerosis in Coronary Interventions Trial (X-TRACT) under an IDE approval in the U.S. The study was designed to determine the safety and efficacy of the **X-Sizer** for treating thrombus in native coronary arteries and treatment of degenerated SVGs.
- The **X-Sizer** is approved in all international markets, except Japan, for treating native coronary thrombus, failed coronary bypass grafts and in-stent restenosis.
- The company has received various CE mark approvals: for the **Trap CFS** for distal protection in SVG PTCA and stenting; for the **Trap NFS** for distal protection during carotid PTA and stenting; and for the **Trap VFS** for distal protection during percutaneous angioplasty and stenting interventions involving saphenous vein bypass grafts.
- A Phase II trial of the **Trap CFS** has been launched in the U.S. under an FDA IDE approval.
- The **Spider** device has received the CE mark to provide distal embolization protection in patients receiving carotid interventions such as PTA and CAS procedures.


**Product focus:**

- Kensey Nash’s **TriActiv Balloon Protected Flush Extraction Distal** system is designed to prevent heart attacks during the treat
ment of SVGs in patients who previously received coronary bypass surgery, but now have blockages in the grafts. The device incorporates three features to address the common problem of distal embolization: a balloon protection guidewire, a flush catheter and an extraction system to remove debris found in the grafts. The features work in combination to prevent the debris found in the graft from going downstream and causing a heart attack.

The company also developed the Angio-Seal device that seals and closes femoral artery punctures made during diagnostic and therapeutic cardiac catheterizations. Note: The Angio-Seal is FDA-approved and the product now is owned by St. Jude Medical (St. Paul, Minnesota).

(See Kensey Nash Corporation also in “Graft Technologies.”)

Milestones:

♦ In September 2002 Kensey Nash’s TriActiv Balloon Protected Flush Extraction System was used in a live case study during the Transcatheter Cardiovascular Therapeutics conference. The patient was a 63-year-old man with degenerative saphenous vein graft disease in a graft originally placed 12 years earlier.

♦ The company received the CE mark for its TriActiv Balloon Protected Flush Extraction System in January 2002.

♦ In 2001, Kensey Nash launched in the U.S. and Europe the PReduction during saphenous vein graft Intervention to prevent Distal Embolization (PRIDE) trial for its TriActiv Distal Protection system. In September 2002 data gathered to date showed a 6.8% MACE complication rate for patients treated with the protocols of the trial’s pilot phase. The in-hospital MACE rate for the overall patient subset treated with the TriActiv system was 15.3%. Other studies have indicated that such complication rates often run as high as 20% in non-protected vein graft procedures.


Product focus:

♦ MedNova has developed the Neuroshield and CardioShield devices. They are mounted on the distal tip of a guidewire and contain a pre-shaped nitinol expansion system. The filter guidewire is placed within the delivery catheter and passed to the target site. After deployment and completion of the procedure, the retrieval catheter is used to envelop and withdraw the filter.

Milestones:

♦ In May 2002 MedNova indicated it is sponsoring an 800-patient study on the CardioShield device against a currently available balloon device in angioplasty procedures. The trial is being conducted at the University of Pittsburgh Medical Center (Pittsburgh, Pennsylvania).

♦ MedNova’s first-generation filter products have received the CE mark.
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♦ MedNova’s first-generation filter products have received the CE mark.
In the United States, MedNova has launched the CAPTIVE trial of its filter systems at the Mayo Clinic (Rochester, Minnesota).


**Product focus:**

- Medtronic acquired the **PercuSurge Guardwire Plus Temporary Occlusion and Aspiration System** with its purchase of PercuSurge. The device is introduced at the start of an interventional procedure and then used to advance an angioplasty balloon or stent to the treatment site. A balloon at the distal tip is inflated to occlude the vessel, with embolic particles remaining suspended in the vessel until aspirated.

  (See Medtronic, Inc. also in “Atrial Fibrillation,” “Congestive Heart Failure,” “Defibrillation: Implantable Cardioverter Defibrillators [ICDs],” “Graft Technologies,” “Pacemaker Technology,” “Stent Technology: Advanced Stenting” and “Stent Technology: Drug-Coated and Drug-Eluting Stents.”)

**Milestones:**

- Medtronic in May 2002 launched the Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberalized Debris (EMERALD) trial, comparing use of the GuardWire system vs. percutaneous interventional therapy without embolic protection.

- Medtronic in June 2001 received FDA clearance for the PercuSurge GuardWire system.

- A study in *Circulation* reported a 42% reduction in adverse events using the GuardWire system in the 801-patient Saphenous Vein Graft Angioplasty Free of Emboli Randomized (SAFER) trial.


**Product focus:**

- Possis is focused on the development of thrombus and clot removal systems. The **Angiojet System** is a device employing micro-fine jets to send saline solution backward through a catheter, suctioning away blood clots prior to angioplasty while sparing healthy vasculature.

- The company’s **Angiojet Xpeedior** catheter uses patented Cross-Streat technology, which Possis says makes it three times more effective at removing wall adherent thrombus like that present in dialysis access grafts.

- The **XMI** catheter uses waterjet action to remove thrombus for rapid
restoration of flow in larger peripheral vessels.

**Milestones:**

♦ In August 2003, Possis halted the Thrombectomy in Middle cerebral artery Embolism (TIME 1) trial using the Angiojet Rheolytic thrombectomy system for the treatment of stroke, which was begun in May 2000, after the device did not demonstrate sufficient efficacy. The company said research into other possible remedies would continue.

♦ In December 2001, the FDA cleared the company’s 4 Fr XMI catheter for use in removing blood clots from native coronary arteries and coronary bypass grafts. In April 2002 the company submitted to the FDA a PMA supplement for marketing the XVG catheter next-generation versions of the XMI, for use in coronary SVGs and native conduits and focused on dealing with larger vessels, more distal vessels and older, more problematic clot burdens. AIMI’s hypothesis is that prompt removal of intracoronary thrombus with the AngioJet catheter results in improved myocardial tissue perfusion, reduced infarct size and reduced areas of stented vessel segments.

♦ In October 2001, Possis launched the Angiojet rheolytic thrombectomy In patients undergoing primary angioplasty for acute Myocardial Infarction (AIMI) study, a trial comparing the treatment of heart attack patients by means of Angiojet therapy followed by immediate, definitive percutaneous treatment vs. immediate percutaneous treatment only. The study involves the use of integrilin injection to determine if the device/drug combination produces the best patient outcomes.

♦ In April 2001, the company launched a multi-center trial studying the use of its AngioJet Xpeedior catheter in patients with acute lower extremity arterial thrombotic occlusions at six U.S. centers.

♦ The AngioJet System is approved by the FDA for removal of blood clots from dialysis access grafts, and in 1999 it won clearance under the agency’s expedited review program for dissolving blood clots in coronary arteries and bypass grafts.

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**Product focus:**

Rubicon Medical is focused on developing minimally invasive endovascular techniques and products. Its Rubicon Embolic Filter technology is a device under development for protection against embolic events in coronary and peripheral stent procedures. The Rubicon Embolic Filter is designed to be inserted into a blood vessel and allow blood to continue flowing during a surgical procedure, while blocking any particle large enough to cause damage to the body. The device is designed to prevent or reduce the possibility of serous or fatal embolization caused by particles loosened during surgery. The company said it believes the filter is the world’s smallest-profile embolic filtration device.
Milestones:
♦ Rubicon in August 2003 reported the first use of the Rubicon Filter in Germany in its European trial. The study will test the filter in SVGs, with the company projecting CE marking near the end of 2003. The company said it plans to begin the FDA approval process after completion of the European studies.
♦ The company reported successful use of its Rubicon Embolic Filter in feasibility testing at the Utah Artificial Heart Institute (Salt Lake City, Utah).
♦ In April 2003, three cardiologists featured the Rubicon Embolic Filter in separate conference presentations.
♦ In December 2002, the company said it was looking to sell or license its Guardian technology so that it could focus on development and eventual marketing clearance of its Rubicon Embolic Filter.

Also in this sector: * Scion Cardiovascular (Miami, Florida)
Table 9. AAA Endovascular Revenues Projections, 2001-2007

Source: Cardiovascular Device Update
### Table 3. Congestive Heart Failure/U.S. Market Size and Device Opportunity

<table>
<thead>
<tr>
<th>Heart Failure Class</th>
<th>Number Afflicted</th>
<th>Estimated Penetration Rate</th>
<th>Available Patient Pool</th>
<th>Average Selling Price</th>
<th>Resynchronization Device Mkt. Opp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>1.7 million</td>
<td>0%</td>
<td>0</td>
<td>$0</td>
<td>0</td>
</tr>
<tr>
<td>Class II</td>
<td>1.2 million</td>
<td>1%</td>
<td>12,000</td>
<td>$30,000</td>
<td>$360 million</td>
</tr>
<tr>
<td>Class III</td>
<td>1.5 million</td>
<td>10%</td>
<td>150,000</td>
<td>$20,000</td>
<td>$3.0 billion</td>
</tr>
<tr>
<td>Class IV</td>
<td>0.6 million</td>
<td>3%</td>
<td>18,000</td>
<td>$10,000</td>
<td>$180 million</td>
</tr>
<tr>
<td>Totals</td>
<td>5.0 million</td>
<td>3.6%</td>
<td>180,000</td>
<td>$20,000</td>
<td>$3.5 billion</td>
</tr>
</tbody>
</table>

Note: The blended average selling price for Class III patients assumes that half the patients would receive a device with ICD back-up at an average selling price of approximately $30,000, while the other half of patients would receive a device without ICD back-up at an average selling price of approximately $10,000.

Source: Thomas Weisel Partners LLC

### Table 4. Trends in Heart Failure Diagnosis

<table>
<thead>
<tr>
<th>Year</th>
<th>First-Listed Diagnoses</th>
<th>All-Listed Diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>880,000</td>
<td>2,672,000</td>
</tr>
<tr>
<td>1996</td>
<td>877,000</td>
<td>2,872,000</td>
</tr>
<tr>
<td>1997</td>
<td>966,000</td>
<td>3,070,000</td>
</tr>
<tr>
<td>1998</td>
<td>989,000</td>
<td>3,283,000</td>
</tr>
<tr>
<td>1999</td>
<td>975,000</td>
<td>3,135,000</td>
</tr>
<tr>
<td>2000</td>
<td>1,008,000</td>
<td>3,255,000</td>
</tr>
<tr>
<td>2001</td>
<td>1,000,000</td>
<td>3,292,000</td>
</tr>
</tbody>
</table>

Source: National Center for Health Statistics