Concepts in Stent Design, Carotid Access, and Embolic Protection

A review of technological developments aimed at establishing CAS as a suitable alternative to carotid endarterectomy.

BY MARK H. WHOLEY, MD

Technological developments in carotid artery stenting (CAS) have had a major setback after the denial of the approval process by the Centers for Medicare & Medicaid Services (CMS). Not only were patients with high surgical risk denied because of complex comorbidities, but even patients with anatomic high risk, who basically were not eligible for surgical carotid endarterectomy, were denied as well. This was despite published data with 30-day and 3-year results that were equivalent to, and in several parameters more favorable than, carotid endarterectomy and met the standards established by the American Heart Association (AHA).[1-3]

The failure to reimburse has also affected industry's interest in continuing research and, unfortunately, has turned entrepreneurial efforts in the United States to foreign markets. Fortunately, most investigators believe that with careful patient selection and operator experience, CAS is a desirable alternative to the surgically invasive endarterectomy. Since inception, the results have continued to show a decrease in procedural events, and early trials that reported 5% to 7% stroke, myocardial infarction, and death at 30 days in high-risk subsets have now reported as low as 1.5% all-event rates at 30 days. These results have stimulated a minority to continue research and development interests in improving the overall technology.[4]

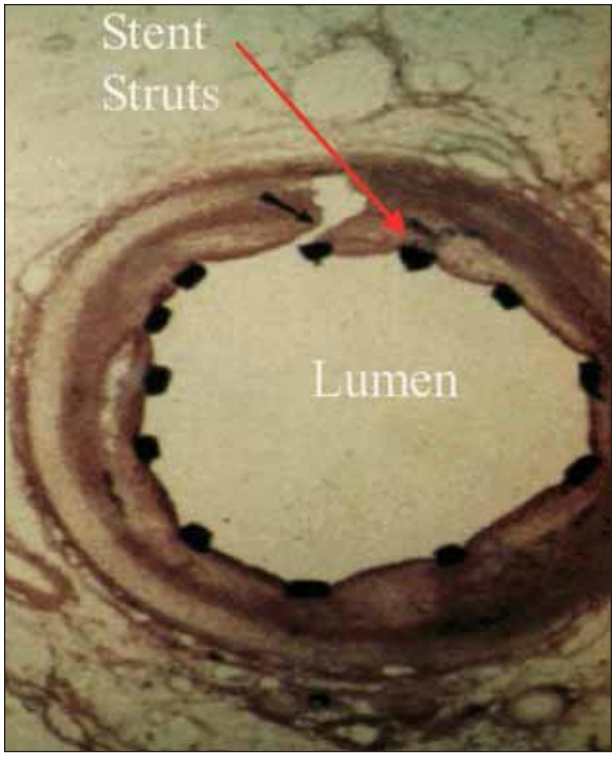


Figure 1. Basic stent functions include supporting tissue and plaque against the vessel wall, optimizing scaffolding, allowing for good angiographic outcomes, and preventing recoil and fracture over time.

STENT DESIGN

The initial stent design for carotid stenting was balloon-expandable stainless steel. The stent functioned satisfactorily and had all the components necessary for appropriate scaffolding, trackability, and adequate radial force (Figure 1). Unfortunately, because of its stainless structure, when positioned below the mandible, the stent could be compressed. Although only a 2% incidence of stent compression occurred with the balloon-

expandable stents, the events were cumulative, and it was only a matter of time before the Food and Drug Administration discouraged the use of the balloon-expandable stents in the carotid circulation.

The current standard for carotid stenting is nitinol, a shape-memory alloy, which is both crush resistant and self-expanding. The clinical outcomes relating to stent design are a function of performance attributes, such as axial and circumferential stiffness and strength, scaffolding, conformability, and side branch preservation. Deliverability, profile, and flexibility are all attributes that are considered. Optimizing parameters such as stent length, width, bridge configuration, and radial force are examples of the difficulty in optimizing the design. This does not include the variability of lesion characteristics and the radial forces (excessive force can result in plaque disruption in a vulnerable lesion), which also affect a device's performance. These engineering issues are more complex than the simple binary classification of open- or closed-cell stents. Cell size, surface area coverage, and pore size may be important, but whether or not it is closed or open may be less important, and current trial data have established this. An interventionist can create either open or closed with equivalent cell size. Trade-offs occur in flexibility, conformability, trackability, and scaffolding. It is appealing to think that closed cell might result in better scaffolding and open in better conformability, but again this only relates to cell size of the design. For example, the Precise (Cordis Corporation, Bridgewater, NJ) and Acculink (Abbott Vascular, Santa Clara, CA) stents are both open-cell designs but with different cell size, resulting in different characteristics; the Xact (Abbott Vascular) stent and carotid Wallstent (Boston Scientific

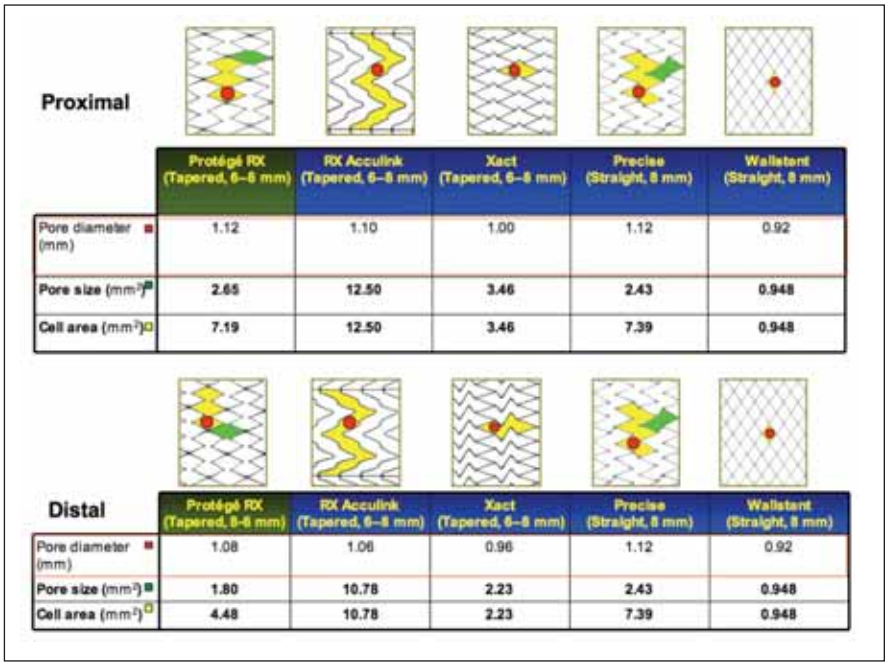


Figure 2. Commercially available stents, open- and closed-cell design. Note pore size diameter is similar whether the design is either large or small cell, open or closed.

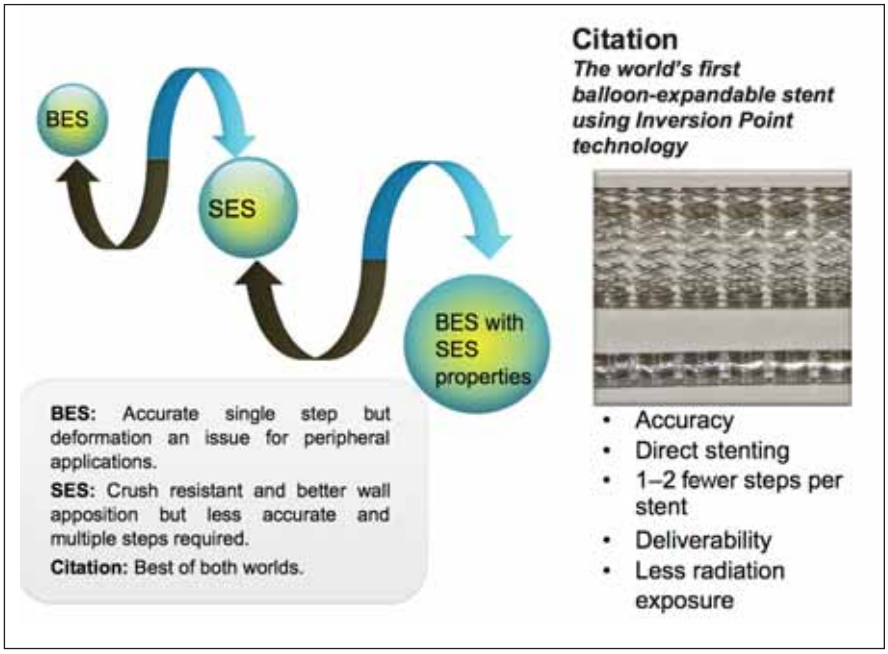


Figure 3. Stent design evolution, from the balloon-expandable stent to the self-expanding stent, to the current Inversion stent technology.

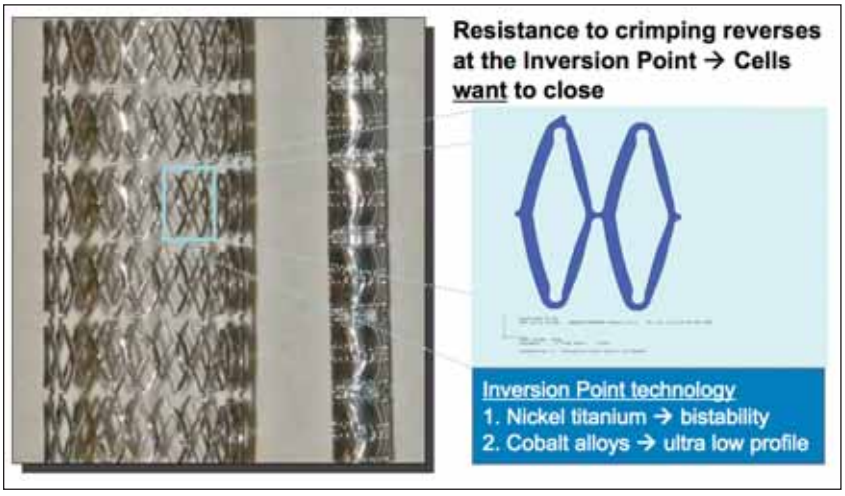


Figure 4. The Citation nitinol stent, which uses Inversion Point technology, in expanded and crimped form. This image shows the architecture of the stent after balloon expansion. The overlay represents a single cell.

Corporation, Natick, MA) endoprosthesis are closed designs, which also have different attributes (Figure 2).[5]

Through the years that followed, we learned to accept the foreshortening problems of elgiloy stents and the jumping/accuracy issues of nitinol stents, because these self-expanding stent disadvantages were counterbalanced by their benefits. An alternative stent design that has the desirable accuracy and single-step advantage of a balloon-expandable stent, while at the same time sharing the crush resistance of contemporary self-expanding stents, has recently been described (Citation stent [Nexeon MedSystems, Inc., Charleston, WV]) (Figure 3). The unique, proprietary architecture of the Citation stent's design enables the stent to crimp down onto a balloon delivery system when compressed, yet retain the flexible, crush-resistant characteristics of the standard nitinol stent when implanted. This design harnesses the shape-memory elastic qualities of nitinol and achieves stability in the expanded and crimped states (bistability) without ratchets or locking mechanisms that have failed in the past due to tissue interference. Along with achieving the accuracy of balloon-expandable stents, the stent enables the required three steps for placement of a traditional self-expanding stent to be combined into one, thereby simplifying the procedure and shortening the overall procedure time (Figure 4).

It is planned that the stent will be delivered on a 5-F platform with single balloon expansion, eliminating the poststenting balloon angioplasty that presently exists with conventional nitinol stents.

There is also current interest in a two-stage stent deployment system consisting of a conventionally designed closed-cell stent with a pore size of 1 mm^2, but an additional thin nitinol sheath is delivered as a covering (Attaché, Inc., San Antonio, TX). In this design, we can control emboli as small as 100 µm (Figure 5). In essence, the stent becomes its own filter. Pore size smaller than 100 µm is possible, but the stent's rigidity becomes a problem in flexibility. The design has the added advantage of not only emboli control but will

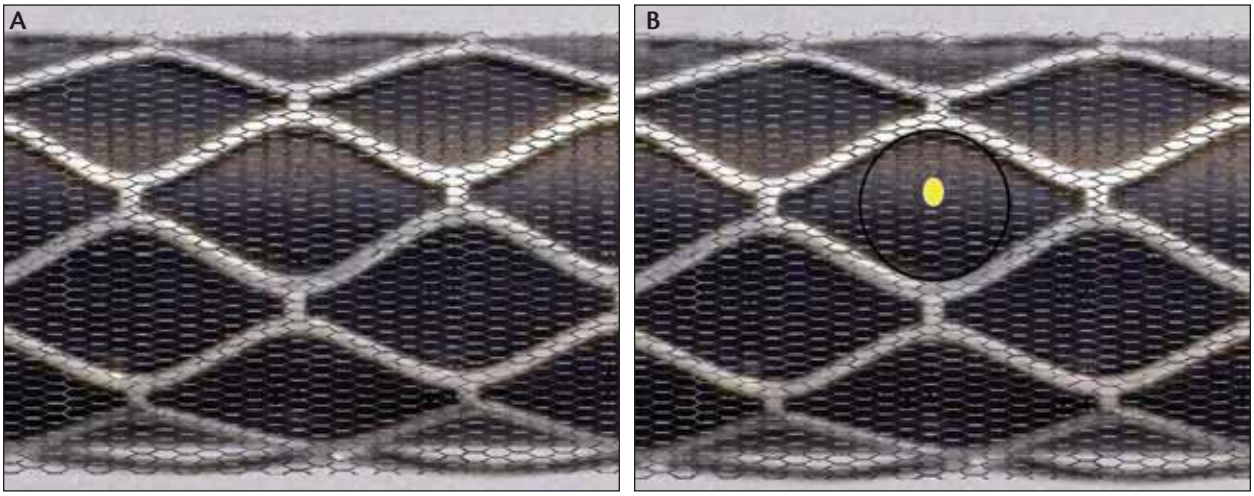


Figure 5. Self-expanding closed-cell nitinol stent, with an additional nitinol sheath that acts as a covering to prevent prolapse or emboli (A and B).

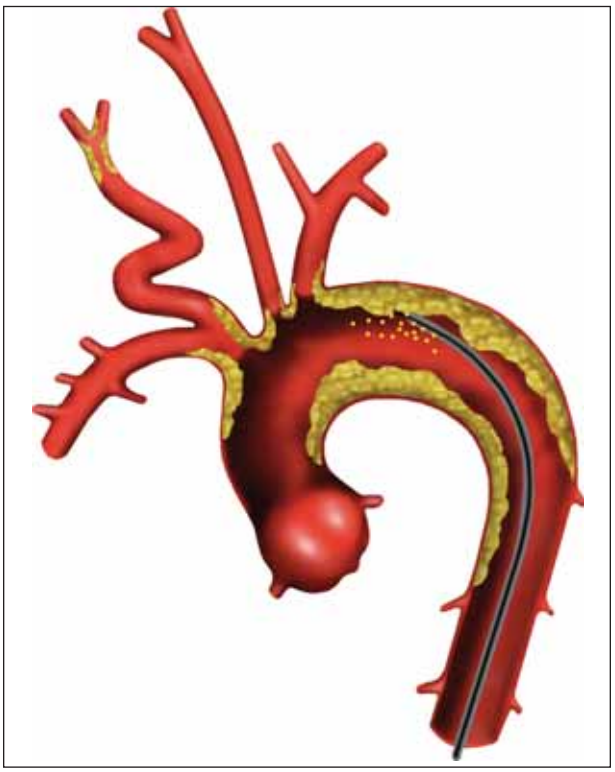


Figure 6. An illustration demonstrating the atherosclerotic changes in the aortic arch and the embolic potential from catheter manipulation.

also avoid plaque prolapse. With flow diversion to the internal carotid occurring, a reduced flow to the external carotid exists. Whether or not this might become an embolic source is to be established.[6]

ACCESS

The femoral access for carotid stenting is the primary access site in 95% of cases. Because 18% of the strokes during CAS are in the contralateral or posterior fossa circulation, there is a question as to whether these embolic events are originating from the aortic arch. The aortic arch is its own stroke risk predictor and has been the Achilles' heel of carotid stenting (Figure 6).

The complex type III atherosclerotic aortic arch requires excessive manipulation for accessing the carotid origin. Reforming catheters or excessive manipulation in the aortic arch is an additional risk that should be avoided. Failure to access the carotid origin within 20 minutes is an indication to abandon the procedure. These patients can be referred for surgery or direct carotid percutaneous stenting, assuming that the common carotid is not excessively calcified. Improvements in guides, sheaths, catheters, and wires have not solved the problem of the complex arch (Figure 7).

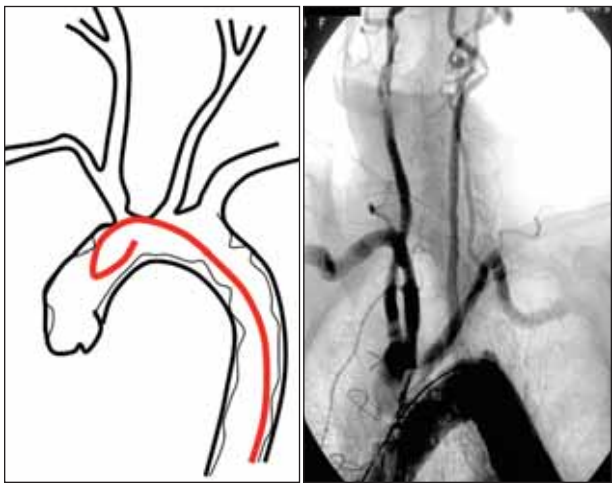


Figure 7. A complex type III aortic arch that represents a contraindication to carotid stenting from a femoral approach. It is best to avoid excessive catheter manipulation (especially with Simmons 1 and 2), as the aortic arch has its own set of embolic potential. These patients may be candidates for direct carotid access.

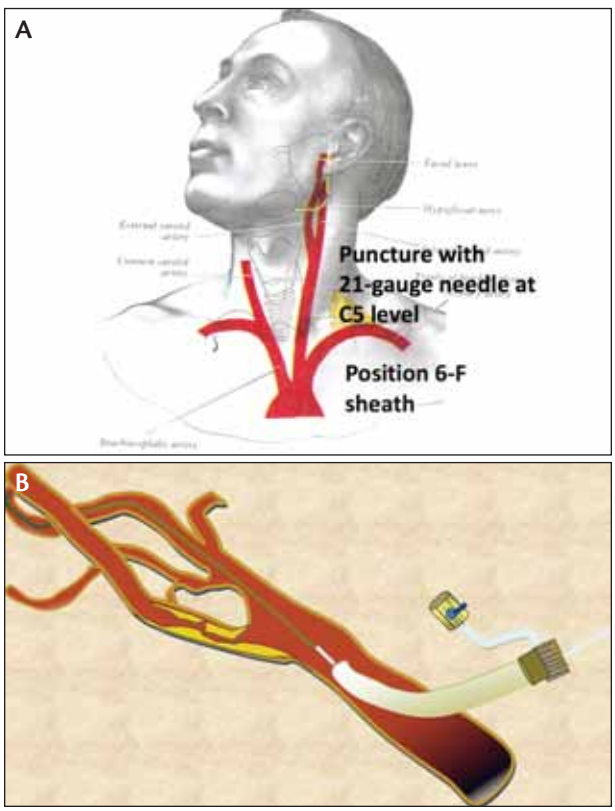


Figure 8. The Bergeron technique for direct carotid access: Puncture the common carotid at C5 and with a 21-gauge needle (A). Then, direct a Wholey Mini Wire to the external carotid, and insert a 6-F sheath, remove the wire, and insert the embolic protection filter (B).

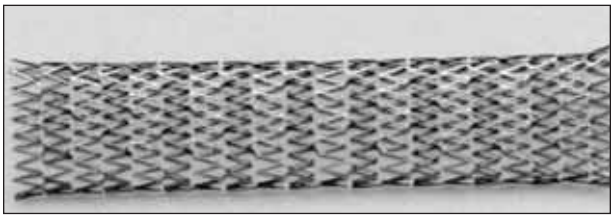
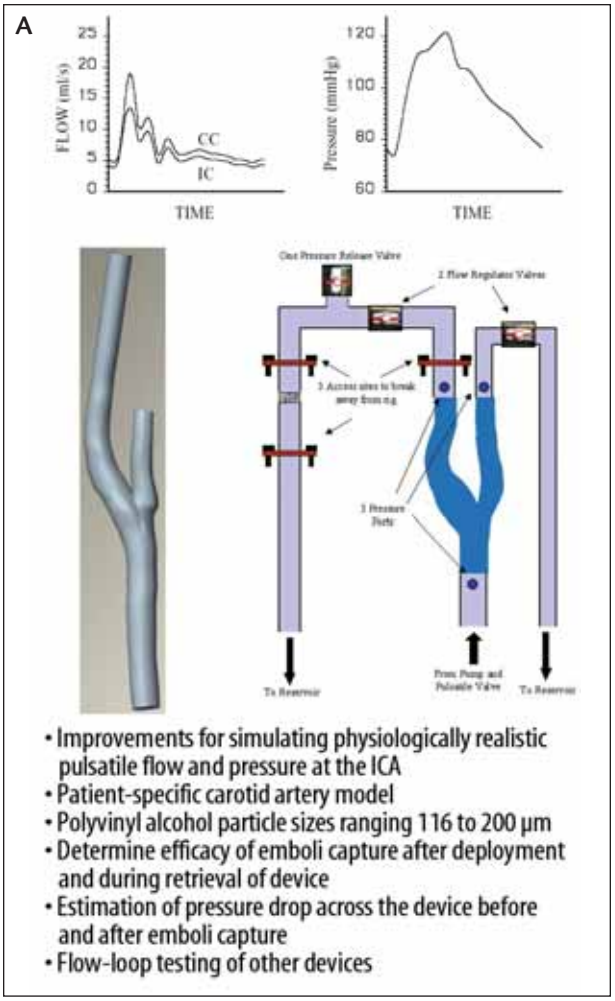


Figure 9. The Precise stent with nanoporous surface coating for drug elution.



B

DPF	Spider RX	FilterWire EZ	RX Accunet	FiberNet
Picture				
Material	Nitinol mesh	Nitinol frame / polyurethane membrane	Nitinol frame / polyurethane membrane	Polymer fibers
Pore Size (µm)	70-200	110	up to 150	down to 40

Figure 11. Benchtop testing of cerebral protection devices with a computational flow model (A). Pore sizes of commercially available filters, the Spider RX, FilterWire EZ, RX Accunet, and FiberNet (B). Abbreviation: DPF, distal protection filter.

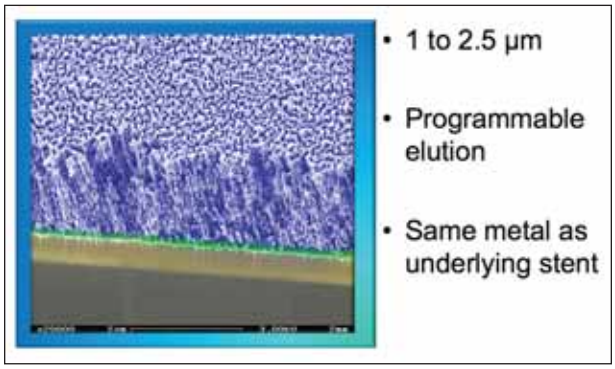


Figure 10. Controllable elution system: Cobalt chromium nanopore surface with 1- to 2.5-µm thickness for drug elution. The 1- to 2-µm-thin surface does not interfere with trackability or flexibility.

These problems have resulted in a renewed interest in direct percutaneous carotid access. Bergeron has pioneered this approach, and in his series of 150 patients, he reports no major strokes (oral communication with Patrice Bergeron, MD, November 2009).[3,7]

Direct carotid access procedural time varied from 10 to 15 minutes. The carotid puncture site was localized at C5, and the 0.035-inch wire was directed to the external carotid, followed by 6-F sheath insertion. The filter was positioned in the high cervical segment of the carotid, and the stent was deployed. The puncture site was closed with a Starclose vascular closure device (Abbott Vascular). In the series, there were no significant hematomas or complications that would require conversion. Complications at the aortic arch were eliminated, and octogenarians were not an issue. Direct carotid access could well be the answer to improving outcomes in these two difficult subsets, namely octogenarians and the complex atherosclerotic aortic arch. With the microsheaths and 21-gauge needle for puncture and acceptable closure, it is only a matter of time before this procedure is universally accepted and conceivably could become a procedure of choice (Figure 8).

CAROTID DRUG-ELUTING STENTS

Although restenosis after carotid stenting occurs in less than 5% of the patients, it presents a greater problem in patients with previous endarterectomy (7%). Nanotextured surfaces for controlled drug elution have been designed using a nonpolymeric metallic nanopore surface (ie, nitinol [nickel titanium]) on the nitinol struts (Figure 9). The porous nitinol surface may allow for a choice of drugs (Figure 10). Although this has not yet been tested in humans, in an experimental animal, there has been less inflammatory reaction at the intimal

	Average Number of Particles Missed by DPF (n = 10)			Capture Efficiency
	Small	Medium	Large	
Spider RX	14.6 ± 3.7	0.2 ± 0.4	0.0 ± 0.0	78.1%
FilterWire EZ	1.3 ± 1.8	0.1 ± 0.3	0.0 ± 0.0	98.1%
RX Accunet	0.2 ± 0.6	0.2 ± 0.6	0.0 ± 0.0	99.4%
FiberNet	3.6 ± 4.6	0.4 ± 1.0	0.0 ± 0.0	94.2%

Figure 12. The average number and standard deviation of particles missed and capture efficiency of the filters. Abbreviation: DPF, distal protection filter.

surface as well as less intimal hyperplasia (NanoMedical Systems, Mentor, OH).

DISTAL EMBOLIC PROTECTION

Distal embolic protection devices are a critical component in the CAS procedure. Filter efficiency varies in the commercially available systems. Using benchtop analysis with a computational flow model, the Spider RX (ev3 Inc., Plymouth, MN), FilterWire EZ (Boston Scientific Corporation), RX Accunet (Abbott Vascular), and FiberNet (Lumen Biomedical, Inc., Plymouth, MN, distributed by Invatec, Inc., Bethlehem, PA) embolic protection systems were evaluated (Figure 11). We had previously evaluated the AngioGuard emboli capture guidewire system (Cordis Corporation) and the Emboshield cerebral embolic protection system (Abbott Vascular), both of which had filter limitations in capture efficiency. In the computational model, the RX Accunet and FilterWire EZ systems were most efficient with all particles. With small particles ≤ 100 µm, the FiberNet, FilterWire EZ, and RX Accunet systems performed adequately and were also highly efficient in medium and large particles (Figure 12). The Spider RX system was less efficient with small particles. We also evaluated vascular resistance and flow rate beyond the filter. Filters with increased vascular resistance also had pressure gradients with decreased flow; the smaller the pore size, the greater the vascular resistance, and the higher pressure gradient across the filter. The highest vascular resistance was with the FiberNet and least with the Spider RX. The Spider RX has a 200-µm pore size proximally at the base, which accounts for the limitation in capturing small particles but also the high flow rate and the decreased vascular resistance. The Spider RX has conventional 100- to 120-µm pore size at the apex of its filter.[8]

CONCLUSION

Progress in technological improvements for CAS is being made but at a slower pace than anticipated. Fortunately, the developments are substantial and include new stent design concepts, more effective embolic protection, an antegrade percutaneous direct carotid access stenting technique, controlled drug elution, and the ability to understand the vulnerable carotid plaque, all in an effort to establish CAS as a desirable alternative to endarterectomy. ■

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