

## REVIEW ARTICLES

Richard P. Cambria, MD, Section Editor

# Current update of cerebral embolic protection devices

Albeir Y. Mousa, MD, John E. Campbell, MD, Ali F. AbuRahma, MD, and Mark C. Bates, MD, *Charleston, WV*

Carotid artery stenting (CAS) has evolved into a viable alternative to carotid endarterectomy. Although CAS outcomes have improved during the last decade, the associated stroke rate remains higher when compared with carotid endarterectomy. Therefore, the pivotal role of embolic protection devices (EPDs) in minimizing stroke risk cannot be underestimated as a vital component of CAS. As technology advances, EPDs continue to be refined, and each device currently on the market has its own advantages and disadvantages. This review provides an overview of the current status of EPDs and highlights the unique features of each device, followed by suggestions for application in specific clinical scenarios. (*J Vasc Surg* 2012;56:1429-37.)

Stroke is the third most common cause of death worldwide. Thirty percent of strokes have been attributed to atherosclerotic disease of the extracranial carotid artery. There is level 1 evidence confirming that carotid endarterectomy (CEA) decreases the risk of stroke in symptomatic and asymptomatic patients.<sup>1-3</sup> Carotid artery stenting (CAS) has evolved as an alternative therapy for carotid atherosclerotic disease in high-risk patients. The efficacy of this technique has been validated in multiple studies, including randomized controlled studies.<sup>4-9</sup>

The Carotid Revascularization Endarterectomy vs Stenting Trial (CREST) investigators<sup>9</sup> showed that CEA and CAS are comparable procedures. This multicenter, well-designed, prospective, randomized controlled study examined the primary end points of stroke, myocardial infarction (MI), and death in 2502 patients. Evaluation was initiated in the preoperative period and extended to 4 years after randomization. Although no significant differences were found between CEA and CAS in the composite end points, as defined by periprocedural ( $\leq 30$  days) death, stroke, or MI, strokes were more frequent after CAS (4.1%

vs 2.3%;  $P = .01$ ). Respected authorities agree that the lower risk of MI and cranial nerve injury with CAS compared with CEA is counterbalanced by an increased risk of ipsilateral stroke events.

Because stroke is the most feared complication of CAS, there is a great need for continued efforts to develop the ideal embolic protection device (EPD) to minimize embolic events during CAS before this treatment modality can replace CEA. The basics of filter design began with the interpretation of animal studies<sup>10</sup> conducted many years ago to evaluate the size of particles that may contribute to intracerebral arteriolar occlusion by injection of microspheres of different sizes into the intracranial arterial vessels. Interestingly, only 2% of 15- $\mu$ m-diameter embolic spheres were shunted to the cerebral venous circulation, suggesting that even microembolic particles can occlude cerebral arteriolar inflow. The average filter has 100- $\mu$ m pores; therefore, microembolization phenomena may occur with the use of all currently available filters.

Theron et al<sup>11</sup> performed the first carotid artery angioplasty with an EPD in 1990. The EPD they used was a distal balloon occlusion (DBO) system that allowed most of the trapped debris to be removed with an aspiration catheter. This was one of the first EPD devices to become available, and in their initial report, the stroke rate was reduced by  $>50\%$ . DBO subsequently fell out of favor due to intolerance and difficulty in procedural technique. Nevertheless, EPDs have continued to evolve, with various engineering strategies to increase efficacy and deliverability.

The selection of an EPD is mainly guided by a patient's anatomy and operator preference. Although vascular specialists have not reached a consensus regarding the ideal EPD, there is a consensus that routine use of an EPD during CAS is beneficial and mandatory.<sup>12</sup> Indeed, multiple studies have demonstrated the feasibility of EPD use,<sup>13-16</sup> with a decrease in the 30-day stroke rate (Fig 1). Traditionally, the most common access is the femoral ap-

From the Department of Vascular and Endovascular Surgery and the Department of Surgery, Robert C. Byrd Health Sciences Center, West Virginia University.

Author conflict of interest: Dr Campbell is on the Speakers Bureau for Abbott Vascular. Dr Bates had patents owned by Boston Scientific, Nexon MedSystems and Gore Medical, but has no active financial conflict to report in the last 5 years or presently.

Reprint requests: Albeir Y. Mousa, MD, Department of Vascular and Endovascular Surgery, Robert C. Byrd Health Sciences Center/West Virginia University, Charleston Area Medical Center, 3110 MacCorkle Ave, SE, Charleston, WV 25304 (e-mail: [amousa@hsc.wvu.edu](mailto:amousa@hsc.wvu.edu)).

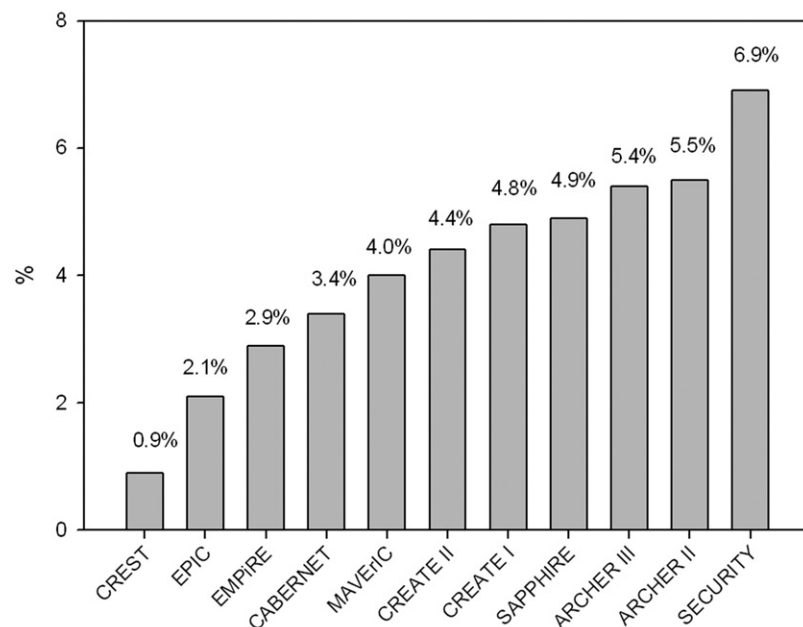
The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214/\$36.00

Copyright © 2012 by the Society for Vascular Surgery.

<http://dx.doi.org/10.1016/j.jvs.2012.05.077>

## 30 Days Stroke Risk in Major Clinical Trials



**Fig 1.** Bar graph demonstrates the 30-day stroke rate in all current studies of carotid artery stenting; the stroke rate decreases along the time line for these studies. *ARCHER II*, Acculink for Revascularization of Carotids in High-Risk Patients trial II; *ARCHER III*, Acculink for Revascularization of Carotids in High-Risk Patients trial III; *CABERNET*, Carotid Artery Revascularization Using the Boston Scientific EPI FilterWire EX/EZ and the EndoTex NexStent; *CREATE II*, Carotid Revascularization with ev3 Arterial Technology Evolution; *CREST*, Carotid Revascularization Endarterectomy vs Stent Trial; *EMPIRE*, Embolic Protection with Flow Reversal; *EPIC*, FiberNet Embolic Protection System in Carotid Artery Stenting Trial; *MAVERIC*, Evaluation of the Medtronic AVE Self-Expanding Carotid Stent System with Distal Protection in the Treatment of Carotid Stenosis; *SAPPHIRE*, Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy; *SECURITY*, A Registry Study to Evaluate the Neuroshield Bare Wire Cerebral Protection System and Xact Stent in Patients at High Risk for Carotid Endarterectomy.

**Table I.** Technical details of selected embolic protection devices (EPDs)

Type of EPD	Device name	Manufacturer	Pore size (μm)	Vessel size (mm)	Crossing profile (F)
Distal filter	RX AccUNET (Fig 4)	Abbott Vascular	150	3.25-5.0	3.5-3.7
	Angioguard RX (Fig 6)	Cordis Corp	100	4.5-7.5	3.2-3.9
	Emboshield Nav6 (Fig 5)	Abbott Vascular	140	2.5-7.0	2.8-3.2
	FiberNet (Fig 7)	Medtronic Inc	<40	3.5-7.0	1.7-2.9
	FilterWire EZ (Fig 3)	Boston Scientific Corp	110	3.5-5.5	3.2
	SpiderFX (Fig 2)	Covidien	50-300	3.0-7.0	3.2
Distal occlusion	GuardWire	Medtronic Inc	...	3.0-5.5	2.8
Proximal occlusion	Gore NPS	W. L. Gore & Assoc	...	...	...
	Mo.Ma Ultra	Medtronic Invatec	...	...	...

proach, but recent advances in the profile of EPDs has allowed some to use the radial artery as an alternative approach for CAS.<sup>17</sup>

### CATEGORIES OF EPDs

Three types of cerebral EPDs are currently available (see Table I for more details).

#### 1. Flow preservation devices: distal filters (DFs)

#### 2. Distal occlusion devices (DODs): DBOs

#### 3. Proximal protection devices:

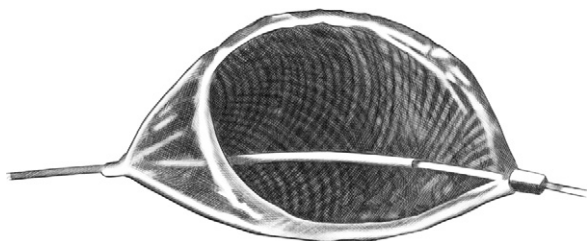
- Mo.Ma Ultra Proximal Protection System (Medtronic Invatec, Frauenfeld, Switzerland)
- Gore Flow Reversal System (W. L. Gore and Associates, Flagstaff, Ariz)

Each category is associated with advantages and disadvantages (Table II).

**Table II.** Recommended application and advantages/disadvantages of various embolic protection devices (EPDs)

Type of EPD	Recommended applications	Advantages	Disadvantages
Distal filter	Standard lesion Cannot tolerate occlusion Stenosis not preocclusive	Preserves antegrade flow Interval arteriography Real-time debris capture Contrast imaging possible throughout intervention	Higher crossing profile Too stiff for tortuous vessel May clog with debris Difficult to steer Filter entrapment in stent May not capture all debris Delivery/retrieval catheters may embolize
Distal occlusion	Preocclusive lesion ICA or CCA tortuosity	Low profile High flexibility Universal size	Flow cessation Risk of ICA dissection No angiogram during stent
Proximal occlusion	Fresh thrombus at bifurcation Crescendo TIAs Severe distal ICA tortuosities Intracranial stenosis	Avoid embolization during procedure Protects before crossing Treats preocclusive lesions Uses guidewire of choice Reversal of flow in ICA	Large sheath Risk of CCA injury Cerebral blood flow reversed Stagnant flow and difficulty with imaging during intervention

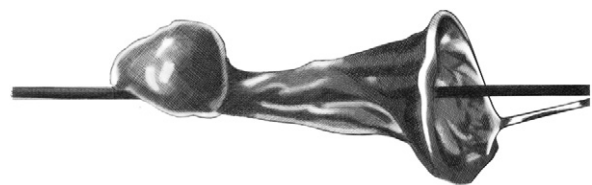
CCA, Common carotid artery; ICA, internal carotid artery; TIA, transient ischemic attack.



**Fig 2.** Diagram of a Spider FX (Covidien, Mansfield, Mass) embolic protection device (EPD).

**Flow preservation devices (DFs).** This type of protection is the most commonly used neuroprotection today. The DF allows antegrade cerebral flow during the entire procedure, with a lower risk of intolerance compared with proximal protection devices and DOD systems, while allowing intraprocedural angiograms and minimal deviation from standard balloon angioplasty techniques. Filter designs vary: some can be advanced over a 0.014-inch wire, and others are attached to a steerable wire tip. Crossing profiles range from the 1.7 F FiberNet (Lumen Biomedical Inc, Plymouth, Minn) to the 3.9 F Angioguard RX (Cordis Corp, Bridgewater, NJ).

The main limitations of DFs are related to the need to cross the lesion with the wire and filter before initiating protection. In addition, the escape of particles with filter bias and malapposition, along with microembolic risk inherent to the pore size of 100 to 150  $\mu\text{m}$  needed to maintain flow, are significant considerations during use of a DF. Data from multiple studies showed that 60% of the typical embolic load can be  $<60 \mu\text{m}$ , with resultant embolic load to the distal vascular system of up to 60,000 particles. The average arteriolar diameter is 12 to 16  $\mu\text{m}$ ; therefore, there is a significant theoretic risk of microembolic intracerebral arteriolar occlusion, even with the current DFs.<sup>10,18</sup> Although there is the inherent disadvantage



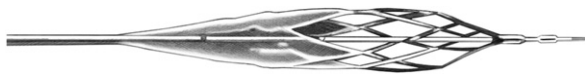
**Fig 3.** Diagram of a FilterWire EZ (Boston Scientific Corp, Natick, Mass) embolic protection device (EPD).

of particles  $<60 \mu\text{m}$  escaping to the target organ, most experts still believe that DFs are more efficacious devices than DODs, given the risk of particles  $>60 \mu\text{m}$  escaping when the balloon is deflated if adequate aspiration cannot be performed secondary to the watershed area present at the margin of the balloon.<sup>18-20</sup>

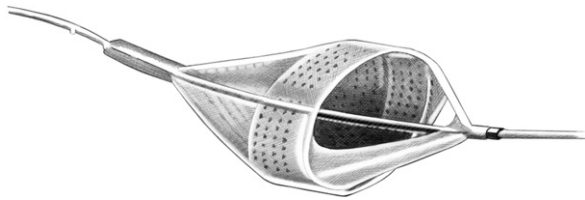
Moody et al<sup>21,22</sup> described a decrease in cognitive function in patients after coronary artery bypass grafting and found in postmortem studies that microemboli were typically  $<70 \mu\text{m}$ . Interestingly, the patients in Moody's series had clinically silent events, with no evidence of stroke postoperatively, only to have the embolic event discovered subsequently when the indolent symptoms of cognitive function issues surfaced during follow-up. Accordingly, we believe special attention must be exercised when considering CAS patients with poor cognitive function or reserve.

Currently, six DF devices are predominately in use: SpiderFX (Covidien, Mansfield, Mass; Fig 2), FilterWire EZ (Boston Scientific Corp, Natick, Mass; Fig 3), RX Accunet (Abbott Vascular, Santa Clara, Calif; Fig 4), Emboshield Nav6 (Abbott Vascular; Fig 5), Angioguard RX (Cordis Corp, Bridgewater, NJ; Fig 6), and FiberNet EPD (Lumen Biomedical, Inc; Fig 7). Table II summarizes the main characteristics of each DF.

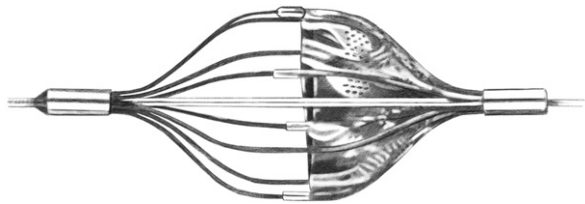
**The DODs.** The GuardWire Temporary Occlusion and Aspiration System (Medtronic Corp, Minneapolis, Minn) is a DOD that has a 3- to 6-mm diameter and uses a



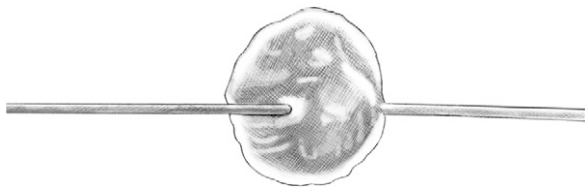
**Fig 4.** Diagram of an RX AccUNET (Abbott Vascular, Santa Clara, Calif) embolic protection device (EPD).



**Fig 5.** Diagram of an Emboshield Nav6 (Abbott Vascular, Santa Clara, Calif) embolic protection device (EPD).



**Fig 6.** Diagram of an Angioguard RX (Cordis Corp, Bridgewater, NJ) embolic protection device (EPD).



**Fig 7.** Diagram of a FiberNet (Lumen Biomedical Inc, Plymouth, Minn) embolic protection device (EPD).

0.014-inch system with a compliant balloon. DODs are characterized as having a low profile, requiring a very short landing zone, and having the ability to be deployed in tortuous vessels. They also have the ability to allow the aspiration of embolic particles  $<100 \mu\text{m}$ .

Inflation of the compliant balloon is achieved through a 0.014-inch wire inflation system. The proximal portion of the wire is designed with an inflation device that allows balloon inflation when the window is opened. Once the balloon is inflated and complete occlusion is confirmed on the angiogram, the wire can be used as a rail for the rest of the procedure. Careful observation is required after balloon deployment to rule out any leaks. After CAS is completed, an export aspiration catheter is advanced into the cul-de-sac to evacuate any debris, followed by deflation of the balloon.

The main concern with the DOD is intolerance, secondary to circulation arrest in the internal carotid artery; therefore, careful preoperative evaluation of the circle of

Willis and the status of the contralateral carotid artery is essential. In addition, the occlusion balloon is inflated to a point of occlusion, which causes the obvious disadvantage of the inability to adequately visualize the lesion secondary to cessation of antegrade flow in the target vessel. Angiograms can be performed, but embolic material can reflux and escape the target vessel into the external carotid artery (ECA) or, in extreme cases, into the thoracic aorta. This can lead to stroke if the ECA collaterals connect to the cerebral circulation or if embolic material refluxes into the contralateral carotid artery.

Another potential issue is the inability to remove all of the embolic material from the watershed area on either side of the balloon. Finally, there is potential for spasm or even dissection of the artery at the site of deployment if there is movement of the DOD system or if the balloon is overinflated.

**Proximal protection devices.** These include the Mo.Ma Ultra and the Gore Flow Reversal System. These are the newest advancements in EPDs, allowing embolic protection before the lesion is crossed using flow stasis and flow reversal. The Mo.Ma uses common carotid and ECA balloons in a single-delivery catheter, whereas the Gore Flow Reversal System creates a flow circuit between the carotid artery and femoral vein to initiate gradient-driven flow reversal. The main advantage of these devices is that no interaction with the plaque occurs until the reversal/stagnation of flow is initiated.

Some reports have indicated that 15% of cerebral emboli occur during the initial crossing of the lesion,<sup>18</sup> and these devices also provide protection during the most critical time of the highest burden of cerebral emboli, which is during poststenting balloon angioplasty.<sup>23</sup> Using the Coulter Counter technique (Beckman Multisizer 3; Beckman Coulter Inc, Fullerton, Calif) for particle analysis in an ex vivo model, Coggia et al<sup>10</sup> recorded  $>40,000$  microemboli during guidewire passage and thousands of microemboli during stent placement.

A recent prospective single-center trial, the Silk Road Medical Embolic PROtectiOn System: First-In-Man (PROOF) study, evaluated the MICH neuroprotection system (Silk Road Medical Inc, Sunnyvale, Calif).<sup>24</sup> This novel technique uses controlled reverse flow through an 8 F transcervical approach. The anticipated advantages are to provide short and direct access for balloon and stent delivery, in addition to all of the perceived benefits of flow reversal, to minimize microemboli and macroemboli from reaching the cerebral circulation. This study included 44 patients with a primary composite end point of major stroke, MI, or death  $\leq 30$  days perioperatively. Embolic brain injury was assessed with diffusion-weighted magnetic resonance imaging (DW-MRI), which was performed 24 hours before the procedure. Within the first 48 hours, 31 patients underwent DW-MRI, and 16% of those had evidence of a new ischemic brain injury; however, all remained clinically asymptomatic. Transient flow-reversal intolerance was encountered in 9% of patients, who were treated by minimizing the duration of flow reversal. This study points



out the feasibility and safety of transcervical CAS using the MICH neuroprotection system. In addition, DW-MRI demonstrates that controlled reverse flow may provide an equivalent embolic protection to CEA.

In another recent retrospective analysis, Alvarez et al<sup>25</sup> evaluated early- and medium-term outcomes of transcervical CAS with flow reversal in 219 patients aged >70 years who were at high risk for CEA. The main objective of their study in using the transcervical approach was to avoid arch manipulation and its associated risks, such as atheroembolism, and the higher incidence of difficult anatomy in the elderly population. For the entire group, 30-day combined stroke/death/MI rate was 2.2% (stroke, 1.8%; MI, 0.45%); however, in symptomatic patients (44%), the combined stroke/death/MI rate was 5.1% (stroke, 4.1%). In the meantime, none of the asymptomatic patients suffered stroke, MI, or death postoperatively. Technical failure was 3.7%, mainly secondary to an inability to cross the lesion. The incidence of >70% restenosis was 3% at 1 year and 8% at 2 and 3 years. Only one patient experienced an ipsilateral stroke during follow-up. The overall survival rate was 94% at 1 year and 90% at 2 and 3 years. The authors concluded that the transcervical approach with flow reversal is a safe technique for treating carotid stenosis in patients aged >70 years old, and avoiding all aortic arch manipulations, especially in those patients with tortuous supra-aortic vessels, augments the favorable results in this study.<sup>25</sup>

From these observations, proximal protection has been recommended for the following indications<sup>26-28</sup>:

1. Symptomatic carotid ulcerative plaque/filling defect in patients who are not candidates for open surgery
2. Symptomatic patients with abnormal transcranial echoes with reduced cognitive function

These indications may be broadened to include all symptomatic patients if randomized trials confirm that microemboli using DFs has an effect on cognitive function.

## LITERATURE REVIEW

An interesting ex vivo model<sup>26</sup> examined the differences between DF and proximal occlusion with flow reversal (POFR). This model used intact carotid plaques removed from patients en bloc. When DF devices were used in 6-mm-diameter polytetrafluorethylene tubes, the percentage of trapped emboli was poor (up to 27.8%). There was no difference between the devices regarding capture of embolic material; however, capture capability function of these filters improved with oversizing the filter, from 22% (same size) to 51.4% (oversize;  $P < .001$ ). However, POFR efficiency improved with increasing back pressure and with repeated aspirations. When the efficiency of POFR was assessed with forward flushing volumes, similar to those used for DF, the efficiencies were similar.

Another model<sup>27</sup> was used to evaluate capture efficiency, pressure gradient, flow rate, and vascular resistance of four EPDs; namely, the SpiderFX, FilterWire EZ, RX Accunet, and Emboshield. The model used a silicone phantom with 70% stenosis at the proximal internal carotid

artery, in which a blood-mimicking solution (glycerol/deionized water) was circulated at a mean peak velocity for the common carotid artery. The SpiderFX trapped the most particles and was associated with the slightest increase in pressure gradient for both masses of microspheres injected. The SpiderFX and FilterWire EZ were associated with the slightest decreases in flow rate and the slightest increases in vascular resistance. The SpideRX had the greatest device-specific porosity, at 50.4%, and the Emboshield had the lowest, at 2.2%. This study concluded that the SpiderFX and the FilterWire EZ had the best overall performances; however, these data do not apply to the new version of the Emboshield, the Emboshield Nav6, that was released after this study and is currently available. This study demonstrated that design features, such as porosity and pore density, are important parameters for improving the effectiveness of EPDs.

A large retrospective multicenter study<sup>28</sup> evaluated 3160 CAS procedures, using nine types of EPDs. The risk of adverse procedural events was 0.9% in protected and 2.3% in unprotected procedures ( $P = .12$ ). Compared with the most frequently used device (FilterWire), there was no significant difference in the risk of procedural adverse events for any of the other EPDs. A pairwise comparison of proximal occlusion balloons vs filters, distal occlusion balloons vs filters, and proximal vs distal occlusion balloons revealed no significant difference in the risk of procedural or 30-day adverse events. There was no significant difference in the risk of procedural events between eccentric and concentric filters; however, the relative risk of eccentric compared with concentric filters at 30 days was 0.59 (unadjusted 95% confidence interval [CI], 0.38-0.92;  $P = .04$ ). This difference was still apparent after adjustment for risk factors (relative risk, 0.61; 95% CI, 0.39-0.95,  $P = .06$ ) but not after adjustment for risk factors and open-cell vs closed-cell stent type (relative risk, 0.76; 95% CI, 0.47-1.22;  $P = .51$ ). The authors concluded that the use of EPDs is associated with a lower risk of adverse procedural events and that there was no significant difference in risks of adverse procedural events between different devices and types of devices.

The investigators of the Carotid Acculink/Accunet Post-Approval Trial to Uncover Unanticipated or Rare Events (CAPTURE)<sup>29</sup> indicated that CAS is safe with the use of EPDs. In a prospective multicenter registry, 353 physicians at 144 sites enrolled 3500 patients. The 30-day primary end point event rate was 6.3% (95% CI, 5.5%-7.1%), and the difference between the experience levels of the three operators (5.3%, 6.0%, and 7.4%) from most to least experienced was not significant ( $P = .31$ ). A trend was noted, however, and a statistical difference might have been present with a larger patient population. Outcomes did not differ among physician specialties when adjusted for case-mix, and no unanticipated device-related adverse events occurred.

**Efficacy of EPDs.** The efficacy of EPD protection is not just limited to macroembolization but also extends to microembolization, which can be of great concern as well.

As we learned from the coronary literature, the National Institutes of Health coma scale cannot precisely evaluate microembolization, yet these tiny particles can affect cognitive function to some extent. One study that evaluated the efficacy of EPDs found subclinical microembolization occurred with particles ranging from 10 to 70  $\mu\text{m}$ .<sup>21</sup> Transcranial Doppler (TCD) monitoring during CEA has demonstrated that particles sized <10  $\mu\text{m}$  do not contribute to a large clinical stroke but are associated with cognitive deterioration.<sup>30</sup>

The two main diagnostic tools to examine cerebral emboli during CAS are TCD and DW-MRI.<sup>31,32</sup> A recent study<sup>33</sup> examined the periprocedural embolic events related to CAS detected by DW-MRI, which was used to assess 44 patients (mean age, 68 years) who underwent protected CAS and had DW-MRI before and after intervention. A proximal EPD was deployed in 25 patients (56.8%) and a DF in 19. A symptomatic target lesion was found in 15 patients (60.0%) who had proximal protection, and 10 (52.6%) were symptomatic in the distal protection group. Significant abnormalities were detected when DW-MRI was performed after CAS with DF, which augmented the concern of silent cerebral injury from the microemboli.<sup>34</sup> Although most of the embolic events were clinically silent, new lesions were seen on the postinterventional DW-MRI in seven of 25 patients (28.0%) in the proximal EPD group vs six of 19 (32.6%) with a DF, which was not significant. No significant differences were noted in the T2 appearance of the new lesions or in the number of new lesions observed away from the vascular territory of the stented artery.

**Perceived difference between filter and DODs.** Zahn et al<sup>35</sup> evaluated 1734 patients in a prospective CAS registry. Of these patients, 729 were treated with an EPD, including 553 (75.9%) with a DF and 176 (24.1%) with a DOD. Patients treated with DODs were more likely to be treated for symptomatic stenosis (64.5% vs 53.4%,  $P = .011$ ). The carotid lesions in patients treated with a DOD seemed to be more complicated, as expressed by a higher proportion of ulcers ( $P = .035$ ), severe calcification ( $P = .039$ ), a longer lesion length ( $P = .025$ ), and a higher preinterventional grade of stenosis ( $P < .001$ ). The median duration of the CAS intervention was 30 minutes in the DOD group, compared with 48 minutes in the DF group ( $P < .001$ ). No differences in clinical event rates were observed between the two groups of EPD patients. A multivariate analysis on the occurrence of the combined end point of in-hospital death or stroke found no difference between DF and DOD. This study concluded that although DF is currently the preferred method of EPD in clinical practice, DF-EPD and DOD seem to be equally effective during CAS.

## PITFALLS OF EPDs

### Pitfalls of DFs

**Selective protection.** We use this term to remind the reader that embolic particles sized <100  $\mu\text{m}$  will escape

through the filter's pores. This may be an issue in patients with decreased cognitive function or poor reserve.

**Filter occlusion or flow stagnation.** This occurs secondary to thrombosis of the filter or when a large embolic load overwhelms the capacity of the filter. Special attention to preprocedural antiplatelet and anticoagulation status before navigation through the carotid lesion is an important preventive measure. Regardless of the cause, any slowing of flow or flow stagnation should prompt the operator to urgently perform aspiration, which can be done with any number of aspiration catheters. Failure to perform angiography before filter removal could result in missed filter occlusion, and embolic stroke can occur during filter retrieval.

Casserly et al<sup>36</sup> observed cases where there was angiographic evidence of a significant reduction in antegrade flow in the internal carotid artery proximal to the filter device, which is referred to as "slow-flow" phenomena. In 414 patients who underwent 453 carotid artery interventions using DF, slow flow occurred in 10% and most commonly occurred after poststent balloon dilatation (71.4%). A multivariate logistic regression analysis identified predictors of slow flow as recent history (<6 months) of stroke or transient ischemic attack, increased stent diameter, and increased patient age. The 30-day incidence of stroke or death was 9.5% among patients with slow flow compared with 2.9% in patients with normal flow ( $\chi^2 = 4.73$ ;  $P = .03$ ). This study demonstrated that slow flow is a predictor of worse patient outcomes and that late complication risks may be related to plaque prolapse between the stent struts in this complex patient subset having a high burden (large vessel) of soft plaque (recent symptoms).

**Filter entanglement.** Filter entanglement can occur when the filter is inadvertently withdrawn and becomes entangled in the distal portion of the stent or when the filter wire is trapped over the edge of the stent. This dreaded complication might require open surgical extrication. Careful management of the wire and fluoroscopy can avoid this during advancement of all catheters because the sheath can prolapse into the aorta. The tip of the sheath/guide should be visualized during all steps of the procedure and never out of the field of view. Also, the use of a "floating filter" can give the operator some leeway for wire movement when compared with a filter attached to the wire.

Another issue in this category reported by our group is the "marriage" between the filter system and the balloon catheter, which is due to inadvertent aggressive interaction between the balloon catheter and the filter during poststenting balloon angioplasty. This also can have a disastrous outcome because the filter cannot be retrieved with the traditional method. Our group has reported a technique for endovascular retrieval if this occurs, but obviously, the best prevention is to closely watch the catheters during exchange and avoid the complication from occurring.<sup>37</sup>

**Filter tear.** To compress the filter into a low-profile delivery system, the polymer membrane is very thin. In patients with complex, large calcified captured material, the

filter can tear on closure, which can cause release of the material or difficulty with extrication.

### Pitfalls of DBOs

**Intolerance.** Ischemia occurs in 20% of patients with occlusion of the ipsilateral carotid artery, and understanding collateral cerebral blood flow is critical; thus, preoperative knowledge concerning the circle of Willis and extracranial collateral vessel patency is imperative. Patients with an intact circle of Willis and patent inflow vessels generally remain asymptomatic throughout the intervention. Patients with subclavian steal syndrome, intracranial disease, or an incomplete circle of Willis often have symptoms, which can range from a gradual decrease in communication to hemiparesis and seizure. In our experience, minimizing the occlusion time to <8 minutes decreases the risk of cerebral ischemia.

**Watershed embolic zones around the proximal portion of the occlusion balloon.** As described by Zahn et al,<sup>35,38</sup> the distal balloon in smaller vessels will likely have larger angles with more chance for retained particles at these angles. They recommended advancing the export catheter for aspiration during balloon deflation. In larger vessels, angles around the balloon are less prominent with less chance of retained particles (Fig 8).

**Particle reflux.** This will occur when blood in the cul-de-sac is replaced with contrast during “test injections.” These particles will reflux into the ECA with a chance of collateral embolization or paradoxical stroke. Avoiding injections after angioplasty can reduce this complication.

**Premature deflation.** Special attention should be considered to prevent inadvertent pulling on the proximal end of the wire when the balloon is inflated, because this can contribute to accidental separation of the occluding inner core mechanism and premature balloon deflation.

**Vessel mismatch.** When the target vessel diameter is larger than the balloon, the balloon can be overinflated by disconnecting the wire from the inflation device with the port closed and reloading the system with additional volume. However, this is outside the instructions for use for that device and should be avoided, if possible.

**Vessel injury.** This can occur if the balloon is oversized for the target vessel or if the balloon is inadvertently withdrawn during the procedure.

### Pitfalls of proximal protection

**Intolerance.** The biodynamics of this is similar to the distal occlusion balloon; however, in the reversal system, there is more opportunity to evacuate the debris-filled cul-de-sac at any time. Understanding the flow circuit is crucial to the procedure. If the patient starts to have cerebral symptoms, discontinuation of reversal or resumption of antegrade flow is imperative. Unlike with DBO, antegrade flow can be quickly established in the flow reversal model because the cul-de-sac is always maintained clear of debris. In the case of static proximal occlusion, maneuvers must be done when symptoms start, including completion of the step in process and export of embolic material.

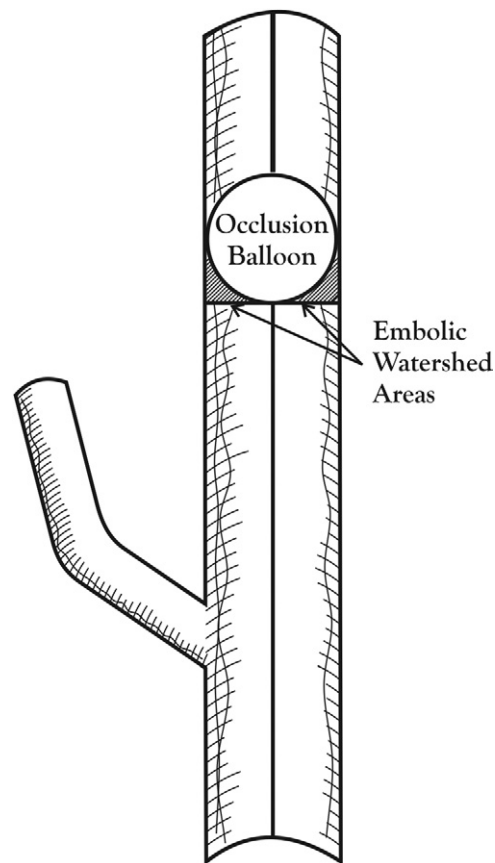


Fig 8. Diagram demonstrates the watershed area when a distal balloon occlusion device is used for embolic protection.

**Higher risk of access complication.** This complication is present with both proximal protection systems secondary to the large sheath size required. Also, with the flow reversal system, arterial and venous access are both required, which can lead to venous access complications as well.

**Carotid vacuum effect.** This can occur during active flow reversal, which can result in elongation and constriction of the deployed stent.

**Anatomic variants.** The normal anatomic variant of a separate origin of the superior thyroid artery from the ECA can contribute to incomplete flow control/reversal.

### Pitfalls for all EPDs

**Vasospasm.** This can contribute to periprocedural stroke, especially in patients with an incomplete circle of Willis or contralateral carotid artery occlusion<sup>39-41</sup> and is more likely to be encountered during distal occlusion or filter placement. Vasospasm is secondary to vessel trauma, and caution has to be exercised when deploying a filter or distal balloon. Theoretically, floating filters may be less traumatic to the carotid artery than fixed filters and cause less vessel spasm. Also, slow distal balloon inflation or deflation is recommended with DBO devices. Intra-arterial

papaverine or nitroglycerine injection may be needed to relieve spasm, and rarely, low-pressure balloon inflation is needed to release the spasm if the patient is having ischemic symptoms.

**Arterial dissection.** Again, this is more common with DBO and DF placement. Flow-limiting dissection can be treated with self-expanding stents. If not flow-limiting, anticoagulation and imaging follow-up is recommended.

**Prolonged intervention time.** The use of EPDs has extended the intervention time by an average of 10 minutes. Carotid angioplasty takes a median of 45 minutes with the use of an EPD vs 35 minutes without ( $P < .001$ ).<sup>38</sup>

**Equipment failure.** Equipment failure can include but is not limited to partial or complete DF fracture/embolization, unwanted occlusive balloon deflation, or the inability to deflate the occlusion balloon.

**Trapped guidewire.** Trapped guidewire occurs in 0.2%.<sup>8</sup>

**Fasciculations.** Muscle twitching occurs in 15% with OPD.<sup>8</sup>

**Difficult retrieval.** This occurs especially with an increase in the tortuosity index  $>80^\circ$  and with calcified plaque.<sup>42</sup>

## CONCLUSIONS

Improvements in technology and a better understanding of the pathology of carotid plaque have contributed to a significant decrease in the stroke risk associated with CAS. Embolization occurs during all transcatheter interaction with atherosclerotic plaque, and the brain is unforgiving. The intuitive benefit of EPDs amplifies the ethical concerns about a randomized trial because withholding embolic protection in the control arm seems unethical. Accordingly, few controlled randomized data are available to confirm the reduced stroke risk with EPDs, but the compelling preclinical data and improvement in outcomes through time support the current expert consensus that EPDs are mandatory in the domain of CAS.

There is no panacea for protection: filters may have microemboli, volume threshold, and entanglement; distal occlusion has intolerance and paradoxical embolization; and proximal flow occlusion has intolerance and a higher access profile. The ideal device has yet to be defined; however, understanding the feasibility and limitations of these devices is crucial for better usage by vascular specialists.

## AUTHOR CONTRIBUTIONS

Conception and design: AM

Analysis and interpretation: AM, MB

Data collection: Not applicable

Writing the article: AM, JC, MB

Critical revision of the article: AM, JC, AA, MC

Final approval of the article: AM, JC, AA, MB

Statistical analysis: Not applicable

Obtained funding: Not applicable

Overall responsibility: AM

## REFERENCES

- Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med* 1998; 339:1415-25.
- Moore WS, Young B, Baker WH, Robertson JT, Toole JF, Vescera CL, et al. Surgical results: a justification of the surgeon selection process for the ACAS trial. The ACAS investigators. *J Vasc Surg* 1996;23:323-8.
- Naylor AR. The asymptomatic carotid surgery trial: bigger study, better evidence. *Br J Surg* 2004;91:787-9.
- Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;351:1493-501.
- Keldahl ML, Phade SV, Eskandari MK. Carotid artery stenting using proximal balloon occlusion embolic protection. *Perspect Vasc Surg Endovasc Ther* 2010;22:187-93.
- Matsumura JS, Gray W, Chaturvedi S, Gao X, Cheng J, Verta P, et al. CAPTURE 2 risk-adjusted stroke outcome benchmarks for carotid artery stenting with distal embolic protection. *J Vasc Surg* 2010;52: 576-83, 583 e571-583 e572.
- Silver FL, Mackey A, Clark WM, Brooks W, Timaran CH, Chiu D, et al. Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). *Stroke* 2011;42:675-80.
- Cremonesi A, Manetti R, Setacci C, Castriota F. Protected carotid stenting: clinical advantages and complications of embolic protection devices in 442 consecutive patients. *Stroke* 2003;34:1936-41.
- Brott TG, Hobson RW 2nd, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010;363:11-23.
- Coggia M, Goñau-Brissonnière O, Duval JL, Leschi JP, Letort M, Nagel MD. Embolic risk of the different stages of carotid bifurcation balloon angioplasty: an experimental study. *J Vasc Surg* 2000;31: 550-7.
- Theron J, Courtheoux P, Alachkar F, Bouvard G, Maiza D. New triple coaxial catheter system for carotid angioplasty with cerebral protection. *AJNR Am J Neuroradiol* 1990;11:869-74; discussion 875-7.
- Lam RC. Contemporary review of embolic distal protection strategies in carotid artery stenting. *J Invasive Cardiol* 2009;21:413-4.
- Veselka J, Cerná D, Zimolová P, Martinkovicová L, Fiedler J, Hájek P, et al. Feasibility, safety, and early outcomes of direct carotid artery stent implantation with use of the FilterWire EZ embolic protection system. *Catheter Cardiovasc Interv* 2009;73:733-8.
- Ansel GM, Jaff MR. Carotid stenting with embolic protection: evolutionary advances. *Expert Rev Med Devices* 2008;5:427-36.
- Saratzis N, Saratzis A, Melas N, Lioupis A, Lykopoulos D, Ginis G, et al. Carotid artery stent placement with embolic protection: single-center experience. *J Vasc Interv Radiol* 2007;18:337-42.
- Eskandari MK, Najjar SF, Matsumura JS, Kibbe MR, Morasch MD. Technical limitations of carotid filter embolic protection devices. *Ann Vasc Surg* 2007;21:403-7.
- Trani C, Burzotta F, Coroleu SF. Transradial carotid artery stenting with proximal embolic protection. *Catheter Cardiovasc Interv* 2009;74: 267-72.
- Ohki T, Roubin GS, Veith FJ, Iyer SS, Brady E. Efficacy of a filter device in the prevention of embolic events during carotid angioplasty and stenting: an ex vivo analysis. *J Vasc Surg* 1999;30:1034-44.
- Ohki T, Parodi J, Veith FJ, Bates M, Bade M, Chang D, et al. Efficacy of a proximal occlusion catheter with reversal of flow in the prevention of embolic events during carotid artery stenting: an experimental analysis. *J Vasc Surg* 2001;33:504-9.
- Ohki T, Marin ML, Lyon RT, Berdejo GL, Soundararajan K, Ohki M, et al. Ex vivo human carotid artery bifurcation stenting: correlation of lesion characteristics with embolic potential. *J Vasc Surg* 1998;27:463-71.
- Moody DM, Brown WR, Challa VR, Stump DA, Reboussin DM, Legault C. Brain microemboli associated with cardiopulmonary bypass: a histologic and magnetic resonance imaging study. *Ann Thorac Surg* 1995;59:1304-7.



22. Moody M, Panerai RB, Eames PJ, Potter JF. Cerebral and systemic hemodynamic changes during cognitive and motor activation paradigms. *Am J Physiol Regul Integr Comp Physiol* 2005;288:R1581-8.
23. Orlandi G, Fanucchi S, Fioretti C, Acerbi G, Puglioli M, Padolecchia R, et al. Characteristics of cerebral microembolism during carotid stenting and angioplasty alone. *Arch Neurol* 2001;58:1410-3.
24. Pinter L, Ribo M, Loh C, Lane B, Roberts T, Chou TM, et al. Safety and feasibility of a novel transcervical access neuroprotection system for carotid artery stenting in the PROOF study. *J Vasc Surg* 2011;54:1317-23.
25. Alvarez B, Matas M, Ribo M, Maeso J, Yugueros X, Alvarez-Sabin J. Transcervical carotid stenting with flow reversal is a safe technique for high-risk patients older than 70 years. *J Vasc Surg* 2012;55:978-84.
26. Rapp JH, Zhu L, Hollenbeck K, Sarkar R, Velez PM, Reilly LM, et al. Distal filtration versus flow reversal: an ex vivo assessment of the choices for carotid embolic protection. *J Vasc Surg* 2009;49:1181-8.
27. Siewiorek GM, Wholey MH, Finol EA. Vascular resistance in the carotid artery: an in vitro investigation of embolic protection filters. *J Vasc Interv Radiol* 2008;19:1467-76.
28. Iyer V, de Donato G, Deloose K, Peeters P, Castriota F, Cremonesi A, et al. The type of embolic protection does not influence the outcome in carotid artery stenting. *J Vasc Surg* 2007;46:251-6.
29. Gray WA, Yadav JS, Verta P, Scicli A, Fairman R, Wholey M, et al. The CAPTURE registry: results of carotid stenting with embolic protection in the post approval setting. *Catheter Cardiovasc Interv* 2007;69:341-8.
30. Brown WR, Moody DM, Challa VR, Stump DA. Histologic studies of brain microemboli in humans and dogs after cardiopulmonary bypass. *Echocardiography* 1996;13:559-66.
31. Sakai H, Sakai N, Higashi T, Iihara K, Takahashi J, Kogure S, et al. [Embolic complications associated with neurovascular intervention: prospective evaluation by use of diffusion-weighted MR imaging]. *No Shinkei Geka* 2002;30:43-9.
32. Lövblad KO, Plüschke W, Remonda L, Gruber-Wiest D, Do DD, Barth A, et al. Diffusion-weighted MRI for monitoring neurovascular interventions. *Neuroradiology* 2000;42:134-8.
33. El-Koussy M, Schroth G, Do DD, Gralla J, Nedeltchev K, von Bredow F, et al. Periprocedural embolic events related to carotid artery stenting detected by diffusion-weighted MRI: comparison between proximal and distal embolus protection devices. *J Endovasc Ther* 2007;14:293-303.
34. Jaeger H, Mathias K, Drescher R, Hauth E, Bockisch G, Demirel E, et al. Clinical results of cerebral protection with a filter device during stent implantation of the carotid artery. *Cardiovasc Intervent Radiol* 2001;24:249-56.
35. Zahn R, Ischinger T, Mark B, Gass S, Zeymer U, Schmalz W, et al. Embolic protection devices for carotid artery stenting: is there a difference between filter and distal occlusive devices? *J Am Coll Cardiol* 2005;45:1769-74.
36. Casserly IP, Abou-Chebl A, Fathi RB, Lee DS, Saw J, Exaire JE, et al. Slow-flow phenomenon during carotid artery intervention with embolic protection devices: predictors and clinical outcome. *J Am Coll Cardiol* 2005;46:1466-72.
37. Campbell JE, Bates MC, Elmore M. Endovascular rescue of a fused monorail balloon and cerebral protection device. *J Endovasc Ther* 2007;14:600-4.
38. Zahn R, Mark B, Niedermaier N, Zeymer U, Limbourg P, Ischinger T, et al. Embolic protection devices for carotid artery stenting: better results than stenting without protection? *Eur Heart J* 2004;25:1550-8.
39. Cardaioli P, Giordan M, Panfilì M, Chioin R. Complication with an embolic protection device during carotid angioplasty. *Catheter Cardiovasc Intervent* 2004;62:234-6.
40. Tsutsumi M, Kazekawa K, Onizuka M, Aikawa H, Nii K, Kodama T, et al. Spasm induced by protection balloon during carotid artery stenting. *Radiat Med* 2007;25:335-8.
41. Vijayvergiya R, Otaal PS, Bagga S, Modi M. Symptomatic carotid vasospasm caused by a distal-protection device during stent angioplasty of the right internal carotid artery. *Tex Heart Inst J* 2010;37:226-9.
42. Lian X, Liu W, Li M, Lin M, Zhu S, Sun W, et al. Risk factors and complications associated with difficult retrieval of embolic protection devices in carotid artery stenting. *Cardiovasc Intervent Radiol* 2012;35:43-8.

Submitted Mar 19, 2012; accepted May 16, 2012.