Advantages and Disadvantages of Distal Protection Filter Devices

A comparative analysis of four current filter designs.

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Approximately 20 years ago, Jacque Theron suggested that embolic protection with balloon occlusion during carotid angioplasty could reduce procedure-related strokes.[1] This was documented in his report, with a >50% reduction in strokes when using distal balloon occlusion. Henry et al[2] described similar results using the PercuSurge balloon (Medtronic, Inc., Santa Rosa, CA) for distal protection. Clinical evidence suggested that not all patients tolerate the temporary interruption of blood flow caused by occlusion balloons and retrograde flow devices, as well as the possibility of the latter to cause carotid artery spasm during proximal occlusion. Müller-Hülsbeck et al[3] described the GuardWire (Medtronic) plus balloon occlusion in a comparative study with filters as having a 14% missed particle embolic event rate in their *in vitro* bench top model.

Nonetheless, there are now four systems with proximal balloon occlusion and reversal of flow and three systems with distal balloon occlusion. The most recent entry into distal protection is a .014-inch wire integrated with an expandable three-dimensional mesh of polyethylene terephthalate fibers (PET). This FiberNet distal protection device (Lumen Biomedical, Inc., Plymouth, MN) has both occluding and filter functions and in early studies has captured particles as small as 40 µm. At the present time, both distal and proximal balloon technology is limited to those patients with a functionally complete circle of Willis who will tolerate complete occlusion. There is also a question of emboli to the contralateral carotid and particle retention at the balloon junction with the arterial wall.

Proximal balloons are also encumbered by their large profiles. In spite of these criticisms, the occlusion flow reversal systems have the ability to capture particles smaller than 100 µm, and that in itself makes this category of emboli protection viable. Certainly, flow reversal systems have gained momentum and ideally should be integrated into dual-device development to include both a distal filter and a flow reversal system.

The notion of a filter-based protective device, rather than occlusion balloons, was described in 1987 when we invented a filter integrated with a 5-mm angioplasty balloon used during carotid angioplasty procedures.[4] When stents replaced balloons for managing carotid stenosis, several additional filter designs were introduced. Initially, the AngioGuard filter (Cordis Corporation, a Johnson & Johnson company, Miami, FL) was used as a system with the Precise stent (Cordis Corporation) for the landmark SAPPHIRE trial. This was followed by the Boston Scientific Embolic Protection Inc. (EPI) filter (Boston Scientific Corporation, Natick, MA) in the BEACH and CABERNET trials, the Accunet filter now distributed by Abbott Vascular (Abbott Park, IL) in the ARCHeR trial, and the Spider device (ev3, Inc., Plymouth, MN) for the CREATE trials.

There are eight filter-designed distal protection devices in either clinical practice or developmental stages. Distal protection filters have decreased the procedure-related stroke risk by 50% in several registries, including the multicenter World Registry that included 44 US and European sites.[5] Distal protection filter devices have their own significant inherent problems that, although rare, include dissection, filter detachment, and clot formation. Variation in profile, trackability, torqueability, and suboptimal capture efficiency also exist.

REVIEW OF BENCH TOP TESTING OF DISTAL PROTECTION FILTER DEVICES

The earliest study to report on the assessment of the effectiveness of a distal protection device (DPD) for carotid artery

stenting (CAS) was an *ex vivo* analysis performed with the first-generation Neuroshield filter (Mednova, Ireland) in a human carotid plaque specimen under steady flow conditions.[6] The investigators show that the device captured 88% of total particles released during CAS, and they also provide the first indications of design problems related to pore size, device recovery, and profile conformity of the device to the artery wall. A number of subsequent clinical studies were conducted to test the feasibility and safety of DPDs in severely stenosed carotids (>70% stenosis). Reimers et al[7] performed the first large consecutive series of CAS using the AngioGuard, Neuroshield (Abbott Vascular) and FilterWire EX (Boston Scientific Corporation) filters, reporting a 2.3% rate of major adverse events in a 30-day follow-up period. Castriota et al[8] showed a reduction of 79% in neurologic events with the use of DPDs in comparison with unprotected CAS in a consecutive series of 275 patients. They also detected vessel spasm of the intracranial carotid artery related to the protection device in 7.3% of the cases studied. In a more recent study, Bosiers et al[9] report a 92% procedural success with the FilterWire EX and 5% delivery failure due to severe internal carotid artery (ICA) angulation in 100 consecutive patients. However, these studies were aimed at evaluating the feasibility of DPD utilization in CAS and are not based on a performance comparison among DPDs in a clinical or experimental setting.

The consequence of emboli in relation to the potential neurologic events they can cause is somewhat controversial. Crawley et al[10] used transcranial Doppler to detect emboli released during carotid endarterectomy (CEA) and carotid angioplasty and were unable to find a positive correlation between the number of embolic particles and the rate of stroke associated with the procedures. The majority of particles released during CAS is smaller than 100 µm and occur during stent placement and balloon dilation.[11-14] It is noteworthy that current FDA-approved and other investigational DPD filters are manufactured with pore sizes that average more than 100 µm. The advantage of these DPD devices, however, is that they maintain continuous blood flow distal to the ICA, which may be compromised by designing filters with smaller pore sizes due to the risk of device occlusion.[15] The failure modes and complications that have emerged from the use of filters have been categorized by Ohki et al[16,17] and can be summarized as:

- compromise of emboli capture efficiency due to
  - inadequate pore size
  - particles flowing around the filter
  - loss of particles during filter retrieval
- difficulties in introducing and deploying the filter due to
  - large crossing profile
  - abrupt change in stiffness and torqueability

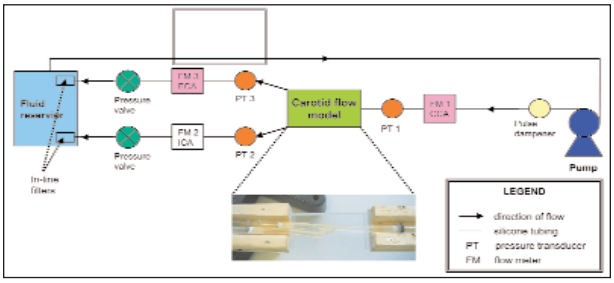


Figure 1. The *in vitro* flow-loop system with inset of a carotid artery flow model.

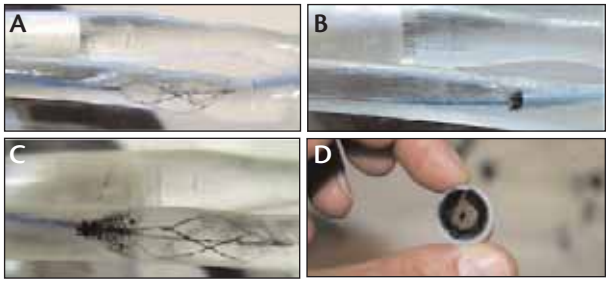
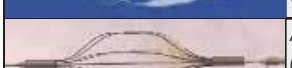
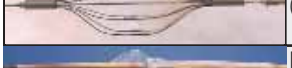


Figure 2. RX Accunet deployed within the ICA (A), basket filled with 200-µm microspheres (B), retrieval of filter with microspheres inside (C), particles collected by an in-line filter downstream of the ICA outlet (D).

TABLE 1. SUMMARY OF PROPERTIES FOR DISTAL PROTECTION DEVICES TESTED *IN VITRO*

Device		Material	Pore Size (mm)	Crossing Profile (F)	Sizes Available (mm)
	EmboShield (Abbott)	Nitinol frame and polyurethane membrane	140	2.9-3.3	3, 4, 5, 6
	RX Accunet (Guidant)	Nitinol frame and polyurethane membrane	115	3.5-3.7	4.5, 5.5, 6.5, 7.5
	AngioGuard XP (Cordis)	Nitinol frame and polyurethane membrane	100	3.2-3.9	4, 5, 6, 7, 8
	FilterWire EZ (Boston Scientific)	Nitinol frame and polyurethane membrane	110	3.2	One size fits all

- vessel injury induced by filter (spasm in the distal ICA)[18]
- difficulties in retrieving the filter
- other (detachment of filter components)

COMPARATIVE ANALYSIS OF FOUR CURRENT DISTAL PROTECTION FILTER DEVICES

Continuing our work in DPD flow analysis,[19-22] we have tested four distal protection devices (Table 1) in a patient-specific flow model, utilizing a thin-walled silicone model of a human carotid bifurcation with 70% stenosis at the internal carotid origin. Magnetic flow meters and pressure transducers were placed in the vicinity of the flow model to measure flow rate and intraluminal pressure (Figure 1). Quantitatively, the performance assessment is measured in the percentage of particles (200-µm diameter) missed by the device with respect to the total particles injected.

The outcome of the performance assessment of the four devices tested in terms of distal embolization is shown in Table 2, where M_{in} = mass of injected particles into the ICA (mg), M_{ICA} = mass of emboli distal to the ICA (mg), and R_A = % of emboli. Data are expressed as mean ±standard deviation and as a percentage of the injected particle mass in the ICA in parenthesis. M_{ICA} does not include emboli lost during retrieval of the device.

The RX Accunet device had the single best average filtration performance (P <.005, based on Student t test comparison with the appropriate Bonferroni correction to account for multiple comparisons made between two devices at a time in these experiments. No significant statistical difference (P >.005) was found between the capture efficiency of the RX Accunet and FilterWire EZ devices. Noteworthy is the significant embolization found distal to the ECA during testing of the RX Accunet device (Table 2), evidenced by the lower mass of microspheres that flowed through the ICA. We believe that the complex design of the basket in this device may have caused additional flow reversal observed proximal to the stenosis leading to the evident retrograde motion of emboli that eventually entered the ECA. Figure 2 illustrates four different phases of the experiment with the RX Accunet device.

The following observation can be made with respect to the performance assessment of the Emboshield device (Table 2). The large mass of particles missed by the device is in great part due to its migration distal to the ICA outlet during the injection of microspheres in the system, as illustrated in Figure 3. The added pressure gradient caused by injecting 6 mL of the embolized solution in the system created a normal force in the ICA large enough to overcome the friction force between the basket and the inner surface of the silicone flow model holding the device in place. Therefore, the basket, delivery catheter, and guidewire were displaced on average 5.5 cm distal to the original deployment site, yielding a larger percentage of emboli.

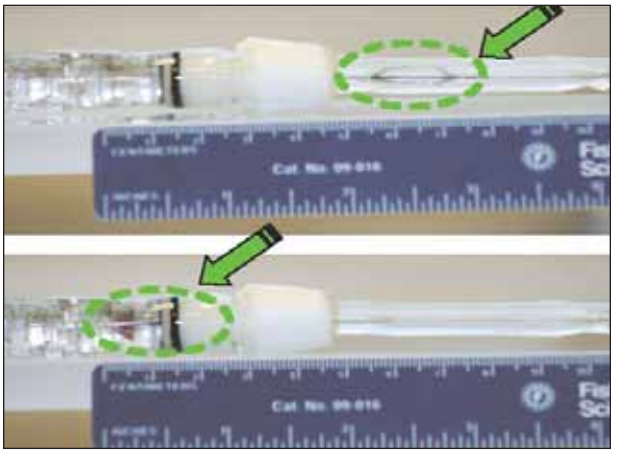


Figure 3. Distal migration of Emboshield device immediately after injection of 6 mL of embolized solution.

As part of an engineering evaluation of the devices tested, several design characteristics were determined to be likely to influence capture efficiency rates *in vitro*. The absence of a complex nitinol cage-like structure and the configuration of the inlet cross section of the basket at an angle with respect to the flow centerline in the FilterWire EZ device results in an improved apposition of the device against the ICA wall, with few to zero gaps for particles to flow through. The shape of the basket of the RX Accunet device, with its proximal triangular, nonporous, polyurethane membrane embedded with nitinol struts that are much thinner than the delivery guidewire, is also a favorable design characteristic that allows for better conformity of the basket upon deployment by providing adequate support to the distal porous membrane.

Although we have subjected selected filter devices to critical comparative analyses, we have not yet tested either distal or proximal balloon occlusion devices to similar

TABLE 2. AVERAGE MASS OF EMBOLIZED PARTICLES MISSED BY THE DEVICES

	RX Accunet	FilterWire EZ	AngioGuard XP	EmboShield
M_{in} (mg)	3.71±0.47	4.99±0.01	4.99±0.01	5.00±0.00
M_{ICA} (mg)	0.04±0.03	0.08±0.08	0.42±0.44	1.88±0.30
R_A	(1.1%)	(1.9%)	(14.0%)	(35.4%)

experimental flow model analyses. The clinical advantages in lesion characteristics that are better suited to proximal occlusion/flow reversal, therefore avoiding the need for crossing the target lesion, are appealing. It is also clinically significant that we capture particles in the 25 to 100 µm range that would not be captured in filters with pore sizes >100 µm. Ideally, it would appear that future-generation devices will have a system to integrate the distal filters with the proximal flow reversal system, all of which will be done in a simpler and lower-profile design than presently exists.

CONCLUSIONS

No wear or tear of the baskets was observed during the experimental trials. The primary evidence for subsequent distal ICA embolization in all the devices tested was the observed particles flowing around the basket. Therefore, an imperfect apposition of the device conforming to the noncircular arterial cross-section results in less than optimal assessment results. For reference, the inner cross-sectional area of the ICA flow model at the site of deployment is 20.75 mm^2, resulting in an average ICA characteristic diameter of 5.14 mm—appropriate for the sizes of the devices tested. These preliminary studies allow us to conclude that for embolic particles with a mean diameter greater than the average pore size of the device basket under constant luminal flow rate and pressure conditions in a compliant carotid artery model, the devices tested did not perform satisfactorily as to completely reduce the risk of embolization and prevent potential stroke. Therefore, we can infer that under *in vivo* conditions in which emboli would comprise smaller particles, the carotid artery can be tortuous and, with an asymmetric stenosis, the blood flow is pulsatile, and the performance of certain devices will be less than desirable in preventing adverse neurologic events.

In the high-surgical-risk, asymptomatic patient with 80% or greater stenosis, carotid stenting can be performed with a procedural stroke rate as low as 3% by experienced operators and careful patient selection. In the symptomatic patient and in octogenarians, the procedural stroke rate can be as high as 10% to 16%. Obviously, emboli are originating either at the aortic arch or the carotid lesion itself.[23] We know from our current study that distal filter devices have variable efficiency in terms of particle capture. We also know that most particles are less than 60 µm[6] and would pass through most filters. For CAS to be accepted as a universal procedure, we cannot exclude octogenarians and symptomatic patients. Flow reversal and balloon occlusion systems might control these emboli and, in combination with filters, could improve our existing limitations in avoiding procedural strokes.[24] ■

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