Published in final edited form as:

J Vasc Interv Radiol. 2008 October ; 19(10): 1467–1476. doi:10.1016/j.jvir.2008.07.007.

Vascular Resistance in the Carotid Artery: An In Vitro Investigation of Embolic Protection Filters

Gail M. Siewiorek, BS, Mark H. Wholey, MD, and Ender A. Finol, PhD

Biomedical Engineering Department (G.M.S.) and Institute for Complex Engineered Systems (E.A.F.), Carnegie Mellon University; and Department of Radiology (M.H.W.), University of Pittsburgh Medical Center–Shadyside, Pittsburgh, Pennsylvania

Abstract

Purpose—To assess in vitro performance of four embolic protection filters (EPFs) with a varying mass of injected particles. Evaluation is based on capture efficiency, pressure gradient, flow rate, and vascular resistance.

Materials and Methods—A bench-top flow apparatus was used for in vitro testing of four devices (Spider RX, FilterWire EZ, RX Accunet, and Emboshield). A silicone phantom with average human carotid artery dimensions and a 70% symmetric internal carotid artery (ICA) stenosis was used to model the carotid bifurcation. A blood-mimicking solution (glycerol/deionized water) was circulated at the time-averaged mean peak velocity for the common carotid artery. Five and 10 mg of 200- or 300- μ m-diameter microspheres were injected into the ICA to evaluate the capture efficiency of the devices. The normalized pressure gradient, flow rate, and vascular resistance in the ICA were calculated from measured values of pressure and flow rate.

Results—The Spider RX captured the most particles (99.9% for 5 mg, 98.4% for 10 mg) and was associated with the slightest increase in pressure gradient (+8%, +15%) for both masses of microspheres injected. The Spider RX and FilterWire EZ were associated with the slightest decreases in flow rate (Spider RX, –1.9% and –12.1%; FilterWire EZ, –3.5% and –8.2%) and the slightest increases in vascular resistance (Spider RX, +10.1% and +33.0%; FilterWire EZ, +20.5% and +32.7%). The device-specific porosity was calculated, and the Spider RX was found to have the greatest at 50.4%; the Emboshield had the lowest at 2.2%.

Conclusions—The Spider RX and FilterWire EZ had the best overall performances. Design features such as porosity and pore density are important parameters for improving the effectiveness of EPFs. Vascular resistance in the ICA is a flow-derived variable indicative of device performance and affected by the filter design features.

A narrowing of the carotid artery resulting from atherosclerotic plaque accounts for 20%–30% of all cases of stroke, the third leading cause of death in the United States. Carotid artery stenting (CAS), a relatively new minimally invasive procedure, is quickly becoming a prominent alternative treatment for patients with a severely stenosed carotid artery. However, there is skepticism regarding the efficacy of CAS because of the possibility of periprocedural distal plaque embolization. The widespread acceptance of CAS is dependent

Address correspondence to E.A.F., Institute for Complex Engineered Systems, Carnegie Mellon University, Hamburg Hall 1205, 5000 Forbes Ave., Pittsburgh, PA 15213; finole@cmu.edu.

M.H.W. serves as a consultant to Cordis (Miami Lakes, Florida), Abbott/Guidant (North Chicago, IL), Medrad (Indianola, Pennsylvania), Boston Scientific (Natick, Massachusetts), Edwards Life Sciences (Irvine, California), and Mallinckrodt Medical (St. Louis, Missouri). E.A.F. has received grant/research funding from the Pennsylvania Infrastructure Technology Alliance (PITA), a partnership of Carnegie Mellon University, Lehigh University, and the Commonwealth of Pennsylvania Department of Community and Economic Development. G.M.S. has identified no conflicts of interest.

on its comparable efficacy to the surgical approach of carotid endarterectomy (CEA). According to the North American Symptomatic Carotid Endarterectomy Trial (1), the 30-day death and stroke rate was 5.8% with CEA. The first major multi-center trial comparing CEA and CAS, the Carotid And Vertebral Artery Transluminal Angioplasty Study (2), reported no statistical difference in stroke and death rate between the two treatments in a randomized study of 504 patients (5.9% vs 6.4%). Concern for the risk of distal plaque embolization has led to the development of cerebral protection devices to improve the efficacy of CAS. The World Registry (3) has reported that, in 4,221 cases of protected CAS, the stroke and procedure-related death rate was 2.23%, compared with 5.29% for unprotected CAS.

There are three types of cerebral protection devices: distal balloon occlusion devices, proximal balloon occlusion devices, and embolic protection filters (EPFs). EPFs were selected for this investigation because of their advantage of allowing distal perfusion during CAS, which allows angiograms to be obtained during the procedure (4). EPFs usually consist of a 0.014-inch wire with a basket frame made of nitinol and a porous polyurethane membrane over the frame, a delivery sheath, and a retrieval sheath. Recently, new EPF designs have used a nitinol mesh or polymer fibers as the material of choice for the filter basket. Pore sizes for EPFs typically vary between 40 μm and 200 μm .

In the present investigation, we evaluated the effect of emboli mass on the performance of four EPFs (Spider RX [ev3, Plymouth, Minnesota], FilterWire EZ [Boston Scientific, Natick, Massachusetts], RX Accunet [Guidant, St. Paul, Minnesota], and Emboshield [Abbott Vascular, Santa Clara, California]) in an anatomic model of a human carotid artery with a stenosis in the internal carotid artery (ICA). The objectives of conducting this study were to (i) assess the performance of the devices based on the percentage of particles (a) missed after particle injection and (b) lost during device retrieval, and (ii) the effect device performance has on the change in normalized (a) pressure gradient, (b) flow rate, and (c) vascular resistance in the ICA. The clinical relevance of objective (i.a) is a measure of each device's ability to capture emboli larger than the pore size and a quantifiable measure of wall apposition; the smaller the percentage of particles missed, the greater the wall apposition, and thus the potential for more favorable clinical outcomes for the patient. Objective (i.b) is a measure of the ability of each device to retain emboli during removal of the filter from the patient's body; it also implies that the smaller the percentage of particles released, the more favorable the clinical outcome. Objective (ii) measures the blood flow blockage resulting from the use of an EPF; the lower the pressure gradient and vascular resistance and the greater the flow rate, the more favorable the clinical outcome. The authors' original contribution to this field of study is based on incorporating physiologically realistic features for testing EPFs, which include navigation of the device through a stenosis, pressure and flow measurements proximal and distal to the device, use of a blood-mimicking fluid in the flow model, indirect assessment of device wall apposition, and variability in the injected mass of embolized plaque particles.

Materials and Methods

Experimental Setup

The in vitro flow loop used in this investigation is illustrated in Figure 1. It consists of Tygon tubing (inner diameter, 0.25 inches) and a silicone carotid artery bifurcation model (Shelley Medical Imaging Technologies, London, Ontario, Canada). The carotid bifurcation model is an average representation of 62 human carotid arteries with a 70% symmetric stenosis in the ICA (5). Three low-flow magnetic flow meters (SeaMetrics, Kent, Washington) and three pressure transducers (Honeywell Sensotec, Columbus, Ohio) are placed adjacent to the common carotid artery (CCA), ICA, and external carotid artery

(ECA). A blood-mimicking solution (viscosity, 3.5 cP) consisting of 36% glycerol and 64% deionized water was circulated at 737 mL/min by a peristaltic pump (Ismatec, Wertheim-Mondfeld, Germany) and using a pulse damper. This flow rate was calculated on the basis of the mean peak velocity averaged over one cardiac cycle for the human CCA (6). Pressure valves maintained physiologic CCA pressure (average, 97 mm Hg).

The EPFs tested have been described previously (4,7). The Spider RX device has a nitinol wire filter basket with pore sizes ranging from 70 μm to 200 μm , with the largest and smallest pores located at the proximal and distal ends of the basket, respectively. The FilterWire EZ device has a nitinol wire frame and a polyurethane membrane with a pore size of 110 μm . It comes in one size that fits vessels 3.5–5.5 mm in internal diameter. The RX Accunet device also has a nitinol wire frame and polyurethane membrane with a pore size of 115 μm . The Emboshield device has a pore size of 140 μm in its polyurethane membrane (Table 1).

Protocol

The local ethics committee did not require an approved research protocol or informed consent for this investigation. Each device was inserted in the bench-top apparatus by means of its deployment catheter and delivery sheath according to manufacturer instructions. Pressure and flow rate were measured at the CCA, ICA, and ECA after flow stabilization via a data acquisition system (DAQ 6224 and LabVIEW 7.1; National Instruments, Austin, Texas) for the initial condition. The device was then deployed 5 cm distal to the stenosis. Pressure and flow rate were again measured after flow stabilization at the CCA, ICA, and ECA for the empty filter condition. A syringe was filled with dyed polymer microspheres (Duke Scientific, Palo Alto, California), 5 mL of deionized water, and 1 mL of Tween-20 (Fisher Scientific, Fair Lawn, New Jersey). The embolization solution was then injected directly into the ICA flow model. The microspheres selected for testing had a nominal diameter of 200 μm , larger than the pore size of any of the devices. The exception was the Spider RX, with pores ranging in size from 70 μm to 200 μm , which was tested with particles with a nominal diameter of 300 μm . Because each vial contained particle sizes within a specified range (coefficients of variation were 3.3% for the 300- μm microspheres and 5.5% for the 200- μm microspheres, as reported by the manufacturer), some of the 200- μm particles were smaller than the Spider RX's largest pores. Therefore, if the microspheres injected have the potential to pass through the pores of the device, a statement on the wall apposition of the device cannot be made. This justifies the use of microspheres larger than all device pores in the present work. During previous testing of the Emboshield device, it was observed that the filter and guide wire migrated approximately 6 cm downstream from the initial placement after particle injection (8). We have not seen this phenomenon reported in the literature before. In our clinical practice, the position of the filter is fixed by controlling the guide wire, so we conducted the present experiments by securing the Emboshield device to the frame of the flow loop. Clamping the device does not have a significant effect on the capture efficiency of the device ($P > .05$) (8).

The particles missed by the devices after injection were captured distal to the carotid bifurcation model in two polyurethane in-line mesh filters (pore size, 40 μm). The pressure and flow rate were then measured after flow stabilization at the CCA, ICA, and ECA for the full filter condition. The in-line filters distal to the carotid bifurcation were consequently replaced by new ones. The device was retrieved and the particles lost during device retrieval were captured by the new in-line filters. This protocol was repeated for 10 trials each for two masses of microspheres (5 mg and 10 mg) per device. The particles missed by the device after injection and during retrieval were counted and their mass was calculated (rather than the particles being weighed, as a result of the formation of glycerol residue), with the diameter and density representative of each vial having been provided by the manufacturers.

Statistical Analysis

The four devices were compared in pairs with a two-sample two-tailed Student t test at an $\alpha = 0.05$ significance level. The significance level is the probability of making a type I error, or concluding that the null hypothesis is false when it is actually true (ie, concluding that there is a difference in the ability of each device to capture particles, or $H_0 = \bar{R}_{\text{missed}} = \bar{R}_{\text{retrieve}}$, when there actually is not). In addition, a one-way analysis of variance was performed to determine if the difference between the 5-mg and 10-mg groups is larger than the differences within each group at an $\alpha = 0.05$ significance level. The null hypothesis is each sample is drawn from the same probability distribution. A significance level of less than 0.05 is the probability of concluding the two groups are statistically different when they are not.

High-resolution Imaging of Device Baskets

To adequately visualize the device pores, the filter membranes were removed from the nitinol struts and mounted flat on a microscope slide with deionized water. The four images were obtained with a Microfire Microscope Digital CCD camera (Optronics, Goleta, California) mounted on an Olympus BX51 upright microscope through a 4 $\times$ UplanFl objective (Olympus, Center Valley, Pennsylvania) with a numeric aperture of 0.13. Mosaic images were acquired with use of an automated stage controlled with the software package Neurolucida (version 5; MicroBrightfield, Williston, Vermont). The resulting pixel resolution was 1.83 $\mu\text{m}/\text{pixel}$. Images of the FilterWire EZ, RX Accunet, and Emboshield devices were acquired with autofluorescence of the polyurethane under an excitation light of 488 nm. The Spider RX, which is not autofluorescent, was imaged with transmitted light.

We have defined porosity as the ratio of the surface area of all pores to the total surface area of the filter basket. The latter was estimated by tracing the perimeter of the filter basket in the high-resolution images (Fig 2) with ImageJ software (version 1.38x; National Institutes of Health, Bethesda, Maryland). The surface area of the pores for FilterWire EZ, RX Accunet, and Emboshield devices was calculated by counting the number of pores and using the manufacturer-reported diameter of the circular pores. Pores of the Spider RX device were individually measured by tracing the outline of each pore. We have defined pore density as the ratio of the number of pores to the total surface area of the basket. Basket length was measured excluding portions of the nitinol struts not covered by the filter membrane, if applicable.

Results

Particles Missed after Injection

The percentage of particles missed after injection was estimated by calculating the ratio of the mass of particles missed by the device (found in the ICA in-line filter after injection) to the mass of particles that traveled through the ICA (ie, mass of particles found in the ECA in-line filter after injection subtracted from the total mass of particles injected). Negligible embolization into the ECA after particle injection allowed the average mass of particles that traveled through the ICA to be nearly identical to the actual mass injected (5-mg experiments, 5.00 mg $\pm$ 0.01; 10-mg experiments, 9.99 mg $\pm$ 0.02). None of the devices tested were able to completely prevent embolization in the ICA (Table 2). All devices missed more particles after injection of 10 mg of particles than with 5 mg. The Spider RX device missed the lowest percentage of particles in the 5-mg and 10-mg experiments ($\bar{R}_{\text{missed}}$ 0.06% and 1.6%, respectively). The Emboshield device missed the most particles in the 5-mg and 10-mg experiments ($\bar{R}_{\text{missed}} = 28.3\%$ and 48.4%, respectively).

Particles Lost during Retrieval

The percentage of particles lost during device retrieval was estimated by calculating the ratio of the mass of particles that escaped the device basket during retrieval (ie, particles found in the ICA in-line filter after removal of the device from the system) to the mass of particles captured in the basket after injection (ie, the mass calculated previously to estimate the percentage of particles missed after injection). The percentage of particles lost during retrieval ($\bar{R}_{\text{retrieve}}$) is dependent on the percentage of particles missed after injection ($\bar{R}_{\text{missed}}$). None of the devices tested were able to contain all particles in the filter basket during the collapse of the device into the recovery sheath and removal of the sheath from the flow model (Table 3). All devices except the Spider RX lost a higher percentage of particles during retrieval in the 10-mg experiments than in the 5-mg experiments. Although the percentage of particles lost during device retrieval in the 10-mg experiments with the Spider RX device was lower than that in the 5-mg experiments, the mass of microspheres lost was the same between sets of trials. The Spider RX device lost the lowest percentage of particles during retrieval of all devices for 5-mg and 10-mg experiments ($\bar{R}_{\text{retrieve}} = 0.55\%$ and 0.3% , respectively). The Emboshield device lost the most particles during retrieval in the 5-mg and 10-mg experiments ($\bar{R}_{\text{retrieve}} = 2.8\%$ and 13.6% , respectively).

Pressure Gradient in the ICA

The change in the normalized pressure gradient across the ICA was calculated as the ratio of the difference between the measured pressures at the CCA and ICA to the difference in the CCA and ICA pressures at initial conditions (see Eq [1]). The pressure difference across the ICA was calculated for all conditions and normalized with the trial-specific pressure difference at the initial condition; hence, the initial condition–normalized pressure difference for all devices was equal to 1. The results were averaged over all trials ($N = 10$). The normalized pressure gradient in the ICA is dependent on the mass of particles captured by the device. All devices tested were subject to an increase in the normalized pressure gradient in the ICA in the full filter condition compared with the initial condition (Fig 3). All devices were subject to a greater increase in the normalized pressure gradient in the 10-mg experiments than in the 5-mg experiments. The Spider RX device had the smallest increase in normalized pressure gradient at 5 mg and 10 mg (1.08 and 1.15, respectively), whereas the Emboshield device had the largest increase in the 5-mg and 10-mg trials (1.51 and 1.58, respectively).

$$\Delta P^* = \frac{P_{CCA} - P_{ICA}}{(P_{CCA} - P_{ICA})|_{IC}} \quad (1)$$

Flow Rate in the ICA

The normalized volume flow rate in the ICA was calculated as the ratio of the fraction of flow rate in the ICA (ie, fraction of flow from the CCA into the ICA) to the fraction of flow rate at initial conditions (see Eq [2]). Similar to the normalized pressure gradient, the normalized flow rate was calculated for initial, empty, and full-filter conditions for each trial and averaged over all trials ($N = 10$); all devices therefore had an initial condition–normalized flow rate equal to 1. The normalized flow rate is also dependent on the mass of particles captured by the device. All devices tested had a decrease in the normalized flow rate in the ICA in the full-filter condition compared with the initial condition (Fig 4). All devices also had a greater decrease in normalized flow rate in the 10-mg experiments than in the 5-mg experiments. The Spider RX device had the smallest decrease in the normalized flow rate at 5 mg (0.981), and the FilterWire EZ had the smallest decrease at 10 mg (0.918). Injection of more particles into the FilterWire EZ had the least effect on the normalized flow

rate (decreasing from 0.965 to 0.918). The Emboshield device was associated with the greatest decrease for both masses, maintaining approximately the same normalized flow rate regardless of the mass injected (0.524 and 0.522, respectively). For reference, the fraction of flow rate in the ICA at initial condition was measured at 0.397.

$$Q^* = \frac{Q_{ICA}/Q_{CCA}}{(Q_{ICA}/Q_{CCA})|_{IC}} \quad (2)$$

Vascular Resistance in the ICA

Vascular resistance is the flow impedance when the frequency of oscillatory motion is zero (ie, fluid is moving steadily) (9). The percent increase in resistance to flow in the ICA was calculated as the ratio of the pressure gradient in the ICA to the flow rate in the ICA at full-filter conditions (see Eq [3]). All devices were subject to a greater vascular resistance in the 10-mg experiments than in the 5-mg experiments (Table 4). The Spider RX device had the slightest increase at 5 mg (10.1%) and the FilterWire EZ had the slightest increase at 10 mg (32.7%). The Emboshield device had the greatest increase for the 5-mg and 10-mg experiments (194% and 250%, respectively). For reference, the vascular resistance in the ICA at initial conditions was measured at 278 mm Hg/L min⁻¹.

$$R^* = \frac{\left(\frac{P_{CCA} - P_{ICA}}{Q_{ICA}}\right)|_{FF}}{\left(\frac{P_{CCA} - P_{ICA}}{Q_{ICA}}\right)|_{IC}} \quad (3)$$

Design Characteristics

Pore size, porosity, pore density, and length of the filter basket are all design characteristics that affect the performance of an EPF. The size of the pores in each of the devices is reported by the manufacturer, but no indication of what percentage of the basket surface contains pores is given. Therefore, porosity can have a large effect on the flow properties in the ICA during CAS with cerebral protection. If the porosity can be correlated to the pressure gradient, flow rate, and vascular resistance, it can be an important design parameter to assess in vitro EPF performance.

The Spider RX device had the highest porosity (50.4%) and is also the only device porous throughout the entire surface of the basket (Table 5). The Emboshield had the lowest porosity (2.2%) and pore density (1.4 pores/mm²). The FilterWire EZ had the highest pore density (13.6 pores/mm²). The Spider RX and Emboshield had the deepest baskets (17.3 mm and 17.2 mm, respectively).

Statistical Analysis

Three sets of statistical tests were conducted to (i) compare each device pairwise for the percentage of particles missed after injection for 5-mg and 10-mg experiments, (ii) compare each device for the percentage of particles lost during retrieval for 5-mg and 10-mg experiments, and (iii) compare each percentage for a single device across masses (Tables 6,7,8). The Spider RX device, which missed the lowest percentage of particles after injection, had a significantly different performance from all the other devices tested for both masses ($P < .05$) (Table 5). The Emboshield device, which captured the fewest particles after injection, was also significantly different from all other devices tested for both masses

($P < .05$). The FilterWire EZ and RX Accunet performed equally well after particle injection and were not significantly different from each other for the 5-mg experiments only ($P > .05$). The RX Accunet and Emboshield captured significantly fewer particles after injection of the two different masses. The FilterWire EZ did not miss a significantly different percentage of particles after injection.

Because there are more than two samples available for analysis within each group, a one-way analysis of variance was conducted for percentage of particles missed after injection and lost during device retrieval. An analysis of variance was conducted for all devices injected with the same mass of plaque emboli for the percentage of particles missed after injection and lost during retrieval. The percentages of particles missed after injection was statistically different between the two masses injected for each device (Table 7). These results agree with the results of the t test conducted except in the case of the FilterWire EZ (Table 6). The percentage of particles lost during retrieval was statistically different for the RX Accunet and Emboshield devices ($P < .05$), but not the Spider RX and FilterWire EZ ($P > .05$). These results also agree with the results of the t test except for the FilterWire EZ. For the devices that yielded significant results, it is likely that the two groups are from different populations.

Discussion

Various in vitro and ex vivo studies have been conducted by previous investigators (10–13) to evaluate the capture efficiency, pressure gradient, flow rate, and vascular resistance of cerebral protection devices. Müller-Hülsbeck and associates (10–12) investigated in vitro the capture efficiency of two previous-generation versions of the EPFs evaluated in the present work (Neuroshield [first-generation Emboshield; Abbott Vascular] and FilterWire EX [predecessor to FilterWire EZ; Boston Scientific]). They found that the Neuroshield missed the lowest percentage of synthetic and human plaque particles (3.5% and 0.8%, respectively) (10,11), whereas we have found that this device missed the most particles (28.3% for 5 mg, 48.4% for 10 mg). Ohki and associates (13) found in an ex vivo study that the Neuroshield missed 12% of plaque particles. Order and colleagues (12) found that the FilterWire EX missed the lowest percentage of small, medium, and large particles (5.81%, 2.99%, and 1.20%, respectively) in a severely tortuous idealized ICA in vitro. To our knowledge, the capture efficiency of the RX Accunet and Spider RX devices has been reported only by our laboratory (8,14–16). The present investigation correlates well with our previous in vitro work with vessels with constant cross-sections. The RX Accunet had the smallest percentage of particles missed in vessels sized 5.0 mm, 5.5 mm, and 6.0 mm in diameter (0.42%, 0.16%, and 2.13%, respectively) (14,15). The FilterWire EZ also performed equally well for the 5.0-mm and 5.5-mm vessels (1.07% and 1.01%, respectively).

Hendricks and associates (17) found a significant correlation between pressure gradient and flow reduction of a blood-mimicking fluid through a single tube in vitro. Of the EPFs we have tested in common with Hendricks et al (17) (FilterWire EZ, RX Accunet, and Spider RX), the FilterWire EZ had the greatest pressure gradient (7.95 mm Hg) and the Spider RX the smallest (1.65 mm Hg). We have also found that the Spider RX has the lowest normalized pressure gradient in the empty filter condition, followed by the Emboshield. The RX Accunet and FilterWire EZ devices have equally high normalized pressure gradients in the empty filter condition. This discrepancy with the work of Hendricks et al (17) could result from the way flow diverts in a carotid phantom model with a 70% symmetric stenosis, rather than in a single straight silicone tube with a constant cross-section, as used by Hendricks et al (17). The bifurcation and change in cross-section resulting from a stenosis affect how the flow diverts, influencing the pressure and flow rate in the ICA.

Casslerly and associates (18) observed via in vivo angiograms a significant reduction in antegrade flow in the ICA proximal to the EPF, which they referred to as a “slow-flow phenomenon.” They hypothesized that the slow-flow phenomenon is a result of clogging of EPF pores by plaque emboli. Patients in whom the slow-flow phenomenon was observed had a higher incidence of stroke or death within 30 days of the procedure than patients with normal blood flow (9.5% vs 2.9%). It should be noted that a significant percentage of embolic debris (by number of particulates) is smaller than the pore size of EPFs, and these have the potential to occlude distal capillary beds. Therefore, the slow-flow phenomenon can occur even if the filter basket is not full.

The clinical significance of plaque embolization is not clear in regard to the effectiveness of CAS. Thus far, a correlation between microemboli and periprocedural stroke rate has not been found (19). In addition, the critical amount of embolized plaque that can be tolerated by patients (20,21) and the type of plaque that is susceptible to embolization (22–25) is not known. Therefore, it is beneficial to investigate the effects of different masses of particles on the performance of EPFs. In general, we have found that as mass increases, the capture efficiency decreases, pressure gradient increases, flow rate decreases, and vascular resistance increases.

The Spider RX device captured significantly more microspheres after injection ($P < .05$). Because of the low percentage of missed particles, we have hypothesized that the Spider RX has a greater wall apposition than the other devices tested. Yet this device had the smallest effect on the normalized pressure gradient and flow rate as a result of the distribution of pores along the entire surface of the basket varying from smaller pores (70 μm) at the distal end of the basket to larger pores (200 μm) at the proximal end of the basket. The Spider RX had the greatest porosity, which may contribute to the minimal effect this device had on the pressure and flow rate in the ICA. It is worth noting that this device was tested with 300- μm particles whereas the other devices were tested with 200- μm particles. The rationale is that all particles used in this investigation had to be larger than the pore size of the devices to allow a valid statement to be made about wall apposition. However, one limitation of selecting this particle size is that no conclusive statement can be made for debris ranging from 200 μm to 300 μm in size; it is possible for these particles to pass between the device and the wall. Preliminary studies conducted in July, 2006 by Siewiorek (results not reported here) have indicated that testing the Spider RX device with 200- μm -diameter particles (4.7% coefficient of variation) yields a significantly greater percentage of particles missed (48.3% vs 0.06% for 5 mg, $P < .05$; 57.7% vs 1.6% for 10 mg, $P < .05$), indicating that, for this device, particles slightly smaller than the largest pore on the basket are not captured in an efficient manner. This is likely a result of the design of the device enabling the flow of microspheres in suspension to exit through the proximal end of the basket rather than traveling downstream toward the distal end, where the cell size of the nitinol mesh is significantly smaller than 200 μm .

The Spider RX and FilterWire EZ devices had similar ability to retain microspheres during device retrieval. Interestingly, the Spider RX had the deepest filter basket among the devices tested and the FilterWire EZ had the shallowest. However, it should be noted that the basket depth is uniform for the entire filter of the Spider RX and FilterWire EZ (Table 1), unlike the RX Accunet and Emboshield devices. The RX Accunet has triangular sections that artificially lengthen the basket depth.

The Emboshield device had the poorest capture efficiency and the greatest effect on the normalized pressure gradient and flow rate. The Emboshield had the smallest number of pores and the lowest porosity and pore density. These design characteristics of the Emboshield contributed to this device's association with the largest pressure gradient and

flow rate decrease. A high-speed video filmed during injection of microspheres into the Emboshield device shows the clogging of pores by individual microspheres. After the pores were clogged, the fluid had difficulty passing through the device. Fluid builds up in the basket of the device, allowing fewer particles to be captured. The clogged device elongates and decreases its basket diameter to allow fluid to pass between the device and the vessel wall. All other devices tested in this investigation performed significantly better than the Emboshield ($P < .05$). This clogging phenomenon likely explains the poor capture efficiency and high vascular resistance of the Emboshield device.

The use of a constant flow rate instead of pulsatile flow is a simplification of the bench-top tests that affects the performance of EPFs. Pulsatile flow introduces the potential of particles entering and exiting the basket periodically, possibly affecting device performance over time. A silicone carotid bifurcation model does not exhibit the same soft-tissue mechanics as a human carotid artery. Damage to the endothelium and spasm resulting from device deployment cannot be observed in synthetic flow models. Vascular resistance in the ICA was calculated with the pressure gradient and flow rate as dependent variables. Setting the pressure gradient or flow rate as an independent variable would provide a more accurate measure of vascular resistance. Although there is a stenosis in the carotid bifurcation model used in this investigation, it is an idealized geometry. Plaque lesions are not always navigable clinically, and crossing the lesion with an EPF has the potential to disrupt plaque. In addition, wall apposition varies widely depending on the patient-specific geometry; in this investigation, the EPF was deployed in a nearly circular cross-section, which will ideally conform to the device the best.

The use of EPFs can reduce the risk of stroke and death during CAS. The performance of the devices is affected by the capture efficiency, pressure gradient across the device, flow rate through the device, and vascular resistance. In the present investigation, we injected two different masses of microspheres into a patient-based silicone carotid phantom to simulate the various amounts of mass that can be embolized during CAS. We found that, overall, the Spider RX device had the best performance for the lower mass of particles injected, but the FilterWire EZ performed equally well for both masses. In particular, the vascular resistances of the Spider RX and FilterWire EZ devices were nearly identical for the larger mass of particles. The particles injected had a diameter greater than the pore size of the filter basket, so it was inferred that the Spider RX had the best wall apposition. The Spider RX had the highest porosity. The Emboshield device had the worst performance by missing the most particles after injection, losing the most particles during retrieval of the lower mass of particles, and increasing the vascular resistance the most. We have found that pore size is not the only important design consideration to take into account with EPFs, but porosity and pore density are also important. The devices with the best ability to retain particles have a uniform basket depth. We believe that the increase in ICA vascular resistance obtained with a distal protection device in a constant flow rate scenario is an important consequence of filter design that needs to be taken into consideration for future generations of EPFs. In pulsatile flow, vascular impedance is expected to play an important role in the assessment of EPF performance.

Acknowledgments

The authors thank Dr. Justin C. Crowley and Mr. Corey J. Flynn of Carnegie Mellon University's Department of Biological Sciences and Center for the Neural Basis of Cognition for their invaluable assistance in the acquisition of the high-resolution filter images.

Abbreviations

CAS	carotid artery stenting
CCA	common carotid artery
CEA	carotid endarterectomy
ECA	external carotid artery
EPF	embolic protection filter
ICA	internal carotid artery

References

1. NASCET Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;325:445–453. [PubMed: 1852179]
2. CAVATAS Investigators. Endovascular versus surgical treatment in patients with carotid stenosis in the carotid and vertebral artery transluminal angioplasty study (CAVATAS): a randomised trial. *Lancet* 2001;357:1729–1737. [PubMed: 11403808]
3. Wholey MH, Al-Mubarek N, Wholey MH. Updated review of the global carotid artery stent registry. *Cathet Cardiovasc Interv* 2003;60:259–266.
4. Eskandari MK. Design and development of mechanical embolic protection devices. *Expert Rev Med Devices* 2006;3:387–393. [PubMed: 16681459]
5. Smith RF, Rutt BK, Fox AJ, Rankin RN, Holdsworth DW. Geometric characterization of stenosed human carotid arteries. *Acad Radiol* 1996;3:898–911. [PubMed: 8959179]
6. Holdsworth DW, Norley CJ, Frayne R, Steinman DA, Rutt BK. Characterization of common carotid artery blood-flow waveforms in normal human subjects. *Physiol Meas* 1999;20:219–240. [PubMed: 10475577]
7. Kasirajan K, Schneider PA, Kent KC. Filter devices for cerebral protection during carotid angioplasty and stenting. *J Endovasc Ther* 2003;10:1039–1045. [PubMed: 14723572]
8. Siewiorek GM, Wholey MH, Finol EA. In vitro performance assessment of distal protection devices for carotid artery stenting: effect of physiological anatomy on vascular resistance. *J Endovasc Ther* 2007;14:712–724. [PubMed: 17924739]
9. Nichols, WW.; O'Rourke, MF. McDonald's blood flow in arteries: theoretic, experimental and clinical principles. 3rd. Philadelphia: Lea & Febiger; 1990. Vascular impedance; p. 283–324.
10. Müller-Hülsbeck S, Jahnke T, Liess C, Glass C, Grimm J, Heller M. Comparison of various cerebral protection devices used for carotid artery stent placement: An in vitro experiment. *J Vasc Interv Radiol* 2003;14:613–620. [PubMed: 12761315]
11. Müller-Hülsbeck S, Jahnke T, Liess C, et al. In vitro comparison of four cerebral protection filters for preventing human plaque embolization during carotid interventions. *J Endovasc Ther* 2002;9:793–802. [PubMed: 12546580]
12. Order BM, Glass C, Liess C, Heller M, Müller-Hülsbeck S. Comparison of 4 cerebral protection filters for carotid angioplasty: an in vitro experiment focusing on carotid anatomy. *J Endovasc Ther* 2004;11:211–218. [PubMed: 15056017]
13. 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;30:1034–1044. [PubMed: 10587387]
14. Finol EA, Scotti CM, Verdinelli I, Amon CH, Wholey MH. Performance assessment of embolic protection filters for carotid artery stenting. *Model Med Biol* 2005;8:133–142.
15. Finol EA, Siewiorek GM, Scotti CM, Wholey MH, Wholey MH. Wall apposition assessment and performance comparison of distal protection filters. *J Endovasc Ther* 2008;15:177–186. [PubMed: 18426268]

16. Gaspard, S.; Siewiorek, GM.; Finol, EA. Performance assessment of a cerebral protection device by in vitro testing and computational fluid dynamics. Presented at the ASME Summer Bioengineering Conference; June 21-25, 2006; Amelia Island, Florida.
17. Hendriks JM, Zindler JD, van der Lugt A, et al. Embolic protection filters for carotid stenting: differences in flow obstruction depending on filter construction. *J Endovasc Ther* 2006;13:47–50. [PubMed: 16445323]
18. Casserly IP, Abou-Chebl A, Fathi RB, et al. Slow-flow phenomenon during carotid artery intervention with embolic protection devices: predictors and clinical outcome. *J Am Coll Cardiol* 2005;46:1466–1472. [PubMed: 16226169]
19. Crawley F, Clifton A, Buckenham T, Loosemore T, Taylor RS, Brown MM. Comparison of hemodynamic cerebral ischemia and microembolic signals detected during carotid endarterectomy and carotid angioplasty. *Stroke* 1997;28:2460–2464. [PubMed: 9412633]
20. Hayashi K, Kitagawa N, Morikawa M. Observing the carotid debris aspirated during carotid stenting: technical note. *Neurol Res* 2005;27:22–26. [PubMed: 15829154]
21. Quan VH, Huynh R, Seifert PA, et al. Morphometric analysis of particulate debris extracted by four different embolic protection devices from coronary arteries, aortocoronary saphenous vein conduits, and carotid arteries. *Am J Cardiol* 2005;95:1415–1419. [PubMed: 15950562]
22. Chen CI, Iguchi Y, Garami Z, et al. Analysis of emboli during carotid stenting with distal protection device. *Cerebrovasc Dis* 2006;21:223–228. [PubMed: 16446534]
23. de Weert TT, Ouhlous M, Zondervan PE, et al. In vitro characterization of atherosclerotic carotid plaque with multidetector computed tomography and histopathological correlation. *Eur Radiol* 2005;15:1906–1914. [PubMed: 15806368]
24. Golledge J, Greenhalgh RM, Davies AH. The symptomatic carotid plaque. *Stroke* 2000;31:774–781. [PubMed: 10700518]
25. Rapp JH, Pan XM, Yu B, et al. Cerebral ischemia and infarction from atheroemboli <100 μ m in size. *Stroke* 2003;34:1976–1980. [PubMed: 12855822]

Figure 1.
Schematic of flow loop system with inset of carotid artery model. (Available in color online at www.jvir.org.)

Figure 2. High-resolution images of EPF baskets removed from nitinol frame and mounted on microscope slides: **(a)** Spider RX, **(b)** FilterWire EZ, **(c)** RX Accunet, **(d)** Emboshield. (Available in color online at www.jvir.org.)

Figure 3.

Change in normalized pressure gradient (ΔP^*) with y error bars in the ICA for 5-mg and 10-mg plaque emboli: **(a)** Spider RX, **(b)** FilterWire EZ, **(c)** RX AccUNET, **(d)** Emboshield. IC = initial condition (ie, before device deployment). EF = empty filter condition (ie, device deployed). FF = full filter condition (ie, device filled with particles). ΔP^* = change in the normalized pressure gradient in the ICA with respect to initial condition. (Available in color online at www.jvir.org.)

Figure 4.

Change in normalized flow rate (Q^*) with y error bars in the ICA for 5 mg and 10 mg plaque emboli: (a) Spider RX, (b) FilterWire EZ, (c) RX Accunet, (d) Emboshield. Q^* = change in the normalized fractional flow rate in the ICA with respect to IC. (Available in color online at www.jvir.org.)

Table 1
Embolic Protection Filters Tested In Vitro: (A) Spider RX, (B) FilterWire EZ, (C) RX
Accunet, (D) Emboshield

	DPD	Pore Size (microns)	Device Size (mm)
A		70-200	3, 4, 5, 6, 7
B		110	3.5-5.5 (one size fits all)
C		115	4.5, 5.5, 6.5, 7.5
D		140	3, 4, 5, 6

Table 2
Mean Mass and Percentage of Particles Missed after Injection of Plaque Emboli

Outcome	Spider RX	FilterWire EZ	RX Accunet	Emboshield
5 mg				
Particles that traveled through ICA (mg)	5.00 ± 0.01	4.99 ± 0.01	5.00 ± 0.00	5.00 ± 0.01
Particles missed by device (mg)	0.01 ± 0.01	0.20 ± 0.13	0.12 ± 0.09	1.42 ± 0.31
Particles missed (%) *	0.06	3.9	2.5	28.3
10 mg				
Particles that traveled through ICA (mg)	10.0 ± 0.0	10.0 ± 0.0	10.0 ± 0.0	9.98 ± 0.03
Particles missed by device (mg)	0.16 ± 0.14	0.76 ± 0.35	1.46 ± 0.51	4.83 ± 0.90
Particles missed (%) *	1.6	7.6	14.6	48.4

* Average of the ratio of 10 trials.

Table 3
Mean Mass and Percentage of Particles Lost during Device Retrieval

Outcome	Spider RX	FilterWire EZ	RX Accunet	Emboshield
5 mg				
Particles in basket of device before retrieval (mg)	4.99 ± 0.01	4.80 ± 0.13	4.88 ± 0.09	3.58 ± 0.31
Particles lost by device during retrieval (mg)	0.03 ± 0.02	0.02 ± 0.02	0.09 ± 0.07	0.04 ± 0.03
Particles lost during device retrieval (%) *	0.55	0.45	1.8	1.1
10 mg				
Particles in basket of device before retrieval (mg)	9.81 ± 0.14	9.24 ± 0.35	8.53 ± 0.51	5.15 ± 0.90
Particles lost by device during retrieval (mg)	0.03 ± 0.04	0.22 ± 0.17	0.35 ± 0.23	0.73 ± 0.57
Particles lost during device retrieval (%) *	0.3	2.4	4.1	13.6

* Average of the ratio of 10 trials.

Table 4
Percent Change in Vascular Resistance in ICA at Full-filter Condition

Device	Vascular Resistance (%)	
	5 mg	10 mg
Spider RX	+10.1%	+33.0%
FilterWire EZ	+20.5%	+32.7%
RX Accunet	+40.6%	+57.2%
Emboshield	+194%	+250%

Table 5

Design Characteristics of the Four EPFs Tested

EPF	Pore Size (μm)	No. of Pore	Pore Surface Area (mm^2)	Basket Surface Area (mm^2)	Porosity (%)	Pore Density (pores/ mm^2)	Basket Length (mm)
Spider RX	70–200	1,563	78.8	157	50.4	10.0	17.3
FilterWire EZ	110	2,576	24.5	190	12.9	13.6	13.4
RX Accuret	115	912	9.47	208	4.5	4.4	15.1
Emboshield	140	400	6.16	282	2.2	1.4	17.2

Note.—Basket length excludes any metal struts not covered by the polyurethane membrane.

Table 6
Particles Missed after Injection and Lost during Device Retrieval

Pairwise Comparison		Mass Injected (mg)	<i>P</i> Value *	
			After Particle Injection	During Device Retrieval
Spider RX	FilterWire EZ	5	<.05	>.05
		10	<.05	<.05
Spider RX	RX Accunet	5	<.05	<.05
		10	<.05	<.05
Spider RX	Emboshield	5	<.05	<.05
		10	<.05	<.05
FilterWire EZ	RX Accunet	5	>.05	<.05
		10	<.05	>.05
FilterWire EZ	Emboshield	5	<.05	<.05
		10	<.05	<.05
RX Accunet	Emboshield	5	<.05	>.05
		10	<.05	<.05

* Student *t* test.

Table 7
Particles Missed after Injection and Lost during Device Retrieval for a Single Device for All Plaque Emboli

EPF	<i>P</i> Value *	
	After Particle Injection	During Device Retrieval
Spider RX	<.05	>.05
FilterWire EZ	>.05	<.05
RX Accunet	<.05	<.05
Emboshield	<.05	<.05

* Student *t* test.

Table 8
Particles Missed after Injection and Lost during Device Retrieval for a Single Device for All Plaque Emboli

EPF	<i>P</i> Value *	
	After Particle Injection	During Device Retrieval
Spider RX	<.05	>.05
FilterWire EZ	<.05	>.05
RX Accunet	<.05	<.05
Emboshield	<.05	<.05

* One-way analysis of variance.