Designing the Ideal Stent

Stent cell geometry and its clinical significance in carotid stenting.

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Balloon-expandable closed-cell stents were introduced for carotid artery stenting (CAS) as early as 1995. At that time, the cell structure of these stents was intended to support tissue and plaque against the vessel wall. This provided the necessary scaffolding for the stented carotid artery, as it did for the coronary or other peripheral arterial stenotic lesions (Figure 1). The postprocedure angiograms demonstrated the precision in which these stents restored the vessel to its normal dimension. Unfortunately, there was a 2% incidence of stent collapse.[1] The stainless steel stent, when placed lower than the level of the mandible, could be externally compressed. For these reasons, the balloon-expandable stent for carotid occlusive disease was largely abandoned. Several valuable lessons, however, were learned from those early studies. Not only were radial rigidity and scaffolding important design features, but a range of expansion became a necessity. In the absence of articulation in the early designs, the flexibility and high profile of the stents prevented easy trackability. To improve the flexibility and the trackability, a connecting bridge between the two stents was integrated into the design (Figure 2). It was then observed that, depending on the length of the bridge, plaque prolapse could occur at the site. This observation would prove to be critical as we moved to the newer designs.

When the noncrushable memory alloy nickel titanium (NiTi) stent was introduced, there were already several established design improvements. Flexibility, trackability, device profile, and security were essential for the delivery system. The stent design concept included vessel conformability, scaffolding, side branch preservation, visibility, and recoil control to minimize migration and foreshortening. To evaluate expansion and prolapse analysis, tests were designed to measure the flexion (ie, radial forces) that could occur under controlled pressure.

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EMERGING DATA REGARDING STENT DESIGN

More recently, the question of indications, advantages, and limitations of an open-cell design versus a closed-cell stent has generated significant debate. As background, the Precise (Cordis Endovascular, a Johnson & Johnson company, Miami, FL) and Acculink

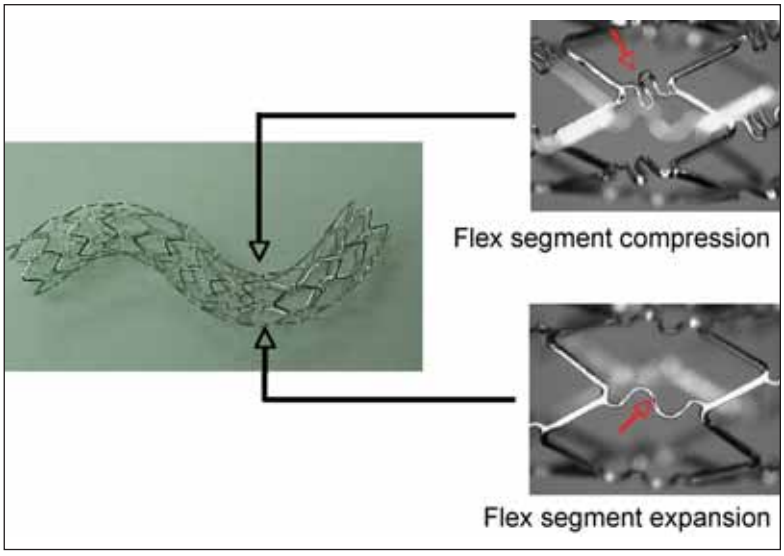

Figure 1. Closed-cell design with a detailed view of the bridge demonstrating the flexibility and conformability after expansion.

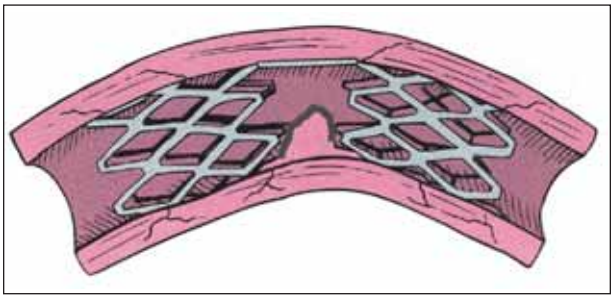

Figure 2. Early first-generation Palmaz-Schatz stent (Cordis) demonstrating the bridge that allows increased length with flexibility.

(Abbott Vascular, Santa Clara, CA) devices are open-cell stent designs, whereas the carotid Wallstent and NexStent (Boston Scientific Corporation, Natick, MA) and Xact stent (Abbott Vascular) devices are closed-cell designs; this concept will be discussed further later in this article. Bosiers et al[2] reported their observations in a retrospective dual-center study of 701 patients undergoing CAS with a binary categorization of open- or closed-cell stents. They indicate a stroke and death rate of 1.4%. When transient ischemic attacks (TIAs) were included, the total stroke, death, and TIA event rate was 3.7%; 4.6% was obtained in symptomatic patients and 3.7% in asymptomatic patients (Table 1).[2] In the open-cell–designed stents, there was an 11.1% stroke, death, and TIA event rate versus 3% in closed-cell stents. TIAs were largely responsible for the difference in outcomes. When TIAs were excluded, open-cell stent patients had 1.6% events versus 0.9% for the patients with closed-cell stents (Table 2).[2]

As even the investigators recognized, there are limitations to retrospective studies. For example, 74% of these patients received the carotid Wallstent; therefore, operator familiarity may have played a role. As might be expected, data from other retrospective reviews have provided different results. Recently, another retrospective analysis of more than 700 patients reported by Reimers et al[3] indicated that there were no statistically significant outcome differences at 30 days. Yet, numerically, the open-cell Precise outperformed all other stents. In addition, statistically significant results were obtained showing superiority of open-cell stents for restenosis at 1 year.[4] Also, in a comparative study of 3,000 patients enrolled in the CAPTURE postmarket surveillance study, using the open-cell Acculink stent with the Accunet filter, a stroke and death event rate of 5.7% was described.[5] The EXACT trial, using the closed-cell Xact stent and Emboshield filter, described a stroke and death rate of 5.1% (Table 3).[6] The difference between the open-cell Acculink and the closed-cell Xact stent stroke and death rate was not statistically significant. In another US postmarket study—the CASES-PMS trial with the open-cell Precise stent—all stroke and death at 30 days was measured at 4.5%.[7] Finally, in an analysis of 203 of our most recent patients at the Pittsburgh Vascular Institute who had an average 10.3-month follow-up and had undergone CAS with the Acculink stent and the Accunet (Abbott Vascular) filter, 1.6% presented restenosis; there was a 1% incidence for all strokes, 1% for myocardial infarction events, and a 7.8% all-deaths event rate. Although this is also retrospective and a small sample size, it does add to the debate of what plays a role in stent-related emboli.

ENGINEERING ASSESSMENT OF STENT DESIGN TRADEOFFS

The conflicting data and resulting debates raise important questions regarding cell size, surface area coverage, and the overall identification of the important factors in pre- and postperiprocedural embolic events. Clinical outcomes relating to any stent design are a function of performance attributes, such as axial and circumferential stiffness and strength, scaffolding properties, conformability, and side branch preserva-

TABLE 1. 30-DAY OUTCOMES

30-Day Outcome	Total (N=701)	Symptomatic	Asymptomatic
Stroke/death	1.4%	1.3%	1.5%
TIA, stroke, death	3.7%	4.6%	3%

NOTE: Data from a retrospective dual-center study of 701 patients undergoing CAS[2]: TIA, stroke, and death rates for symptomatic and asymptomatic patients.

TABLE 2. OUTCOMES AFTER TIA EXCLUSION

30-Day Events	Open Cell (N=63)	Closed Cell (N=235)
Stroke/death	1.6%	0.9%
Death	0%	0.4%
Stroke, death, TIA	11.1%	3%

NOTE: Data from a retrospective dual-center study of 701 patients undergoing CAS[2]: binary categorization of open- or closed- cell stents and their respective TIA and stroke and death rates.

tion. Stent designers attempt to balance such long-term performance attributes along with more acute considerations relating to deliverability and deployment, such as constrained profile and flexibility. All of these attributes must be balanced appropriately given the anatomical challenges and dynamic forces exerted by the vessel on the stent. Designers must select and optimize among numerous interrelated parameters, such as strut length and width, wire diameter and pitch, bridge configuration, material selection, and processing conditions to achieve optimal performance.

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Consider radial force as an example of the difficulty of assessing a performance attribute in stent design. The radial force required will be dependent on lesion characteristics and location. Aorto-ostial lesions may require more force than internal carotid artery stenoses. The radial strength of a carotid stent should provide adequate apposition and enough resistive force to prevent vessel wall recoil. Excessive force or rigid closed-cell designs might result in plaque disruption in a vulnerable unstable lesion. Most nitinol stents can be adjusted for cell size and still maintain satisfactory radial force.

As a result, given the aforementioned engineering considerations, it is important to anticipate that binary classifications, such as "open" versus "closed," may be too general for meaningful retrospective clinical analysis, especially when multiple varied stent designs are pooled within these two broad classifications. Reflecting on the comparative studies available, cell size and surface area coverage appear to be important. Whether open or closed may be less important than the actual cell size. For example, a closed cell with a diameter of 1,000 µm is more likely to be responsible for plaque prolapse and embolization than an open cell of 500 µm. Typically, the number and arrangement of bridge connectors differentiate open-cell designs from closed-cell designs (Figure 3). If adjacent ring segments are connected at every possible junction, the design is typically classified as closed cell. In closed-cell designs, these connections usually take the form of flexible bridge connectors, allowing some limited degree of flexion between adjacent rings (Figure 4). If some or all of the connecting junction points are removed, the design is typically classified as open cell. Such a design inherently allows for more flexion between adjacent rings, because fewer connection points allow for greater flexion and conformability. The flexion benefits of an open-cell design have a cost in scaffolding uniformity, just as the scaffolding benefits of a closed-cell design have a cost in flexion and conformability.

Many stent designs have been tried in clinical practice, with varying results. It is tempting to interrogate these results on the basis of binary attributes such as open cell versus closed cell, or one-dimensional attributes such as

TABLE 3. COMPARISON OF DATA FROM THE CAPTURE AND EXACT TRIALS

Event	CAPTURE (N=3,000)	EXACT* (N=900)	Difference 95% CI
Death, stroke, and MI†	6.4%	5.3%	-1.07% (-2.78%, 0.64%)
All stroke and death†	5.7%	5.1%	-0.62% (-2.28%, 1.04%)
Major stroke and death†	2.8%	2.1%	-0.69% (-1.80%, 0.42%)
Death	1.7%	1%	-0.70% (-1.50%, 0.10%)
All stroke	4.9%	4.4%	-0.42% (-1.97%, 1.13%)
Major stroke	1.9%	1.4%	-0.49% (-1.41%, 0.43%)
Minor stroke	3%	3%	0.00% (-1.27%, 1.27%)
MI	1%	0.2%	-0.74% (-1.21%, -0.28%)

*Preliminary results.
†Hierarchical: Includes only the most serious event for each patient and includes only each patient's first occurrence of each event.
Procedural event rates taken from Hart et al.[6] Comparison of data from the Capture and EXACT trials. All stroke and death rates were quite similar, with no statistical significant difference in the stroke and death rate between the Acculink open-cell and the Xact closed-cell stent designs.

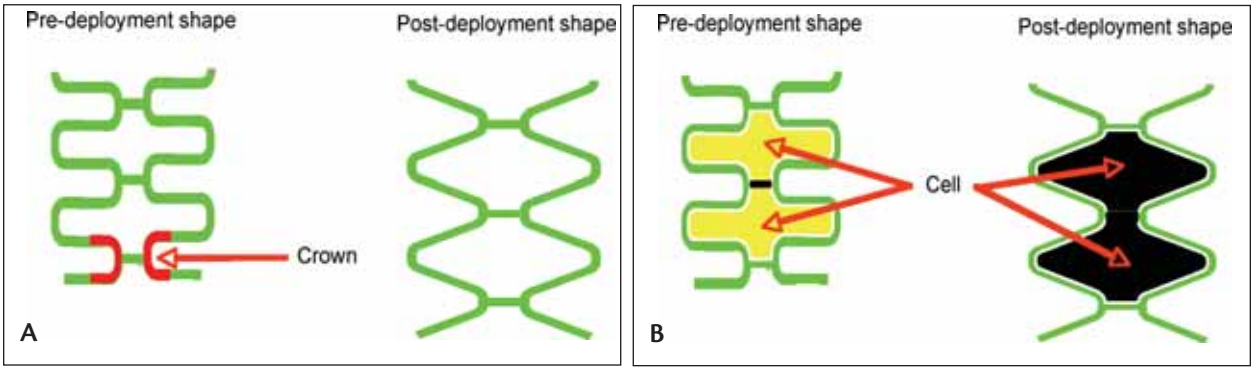

Figure 3. Closed-cell stent design demonstrating the diamond configuration with radial segments and bridge connection (A). Open-cell design with illustrated removal of a bridge connection (B).

wall thickness or cell size. Such analyses may be misleading, however, because of ambiguous definitions of these characteristics, or other important and often interrelated design characteristics that may not be considered. Open- versus closed-cell stent comparison serves as a good example of a chief analysis because it is entirely possible to design an open-cell stent with a cell size smaller than that of a closed-cell stent, thus rendering the distinction near meaningless. Similarly, a braided-wire stent and nitinol stent might both be classified as closed-cell, but they effectively share no meaningful design attributes. In stent design, just as in clinical investigations, single variables often suggest some meaningful insight, but we must be mindful that outcomes are driven not by single variables, but rather an interrelated system of variables.

As mentioned earlier, anatomy too plays an important role. If there are complex angulations at the carotid bifurcation where trackability becomes an issue, the flexibility of open-cell design may be required knowing that the potential of plaque prolapse will exist (Figure 5A). Reducing the size of the open cell, however, can control plaque prolapse. When cells open on the concave surface of an angulated carotid bifurcation, they are prone to having prolapse and fish scaling on the open surface (Figure 5B). This scaling can result in intimal disruption with contrast extending to the adventitia (Figure 5C).

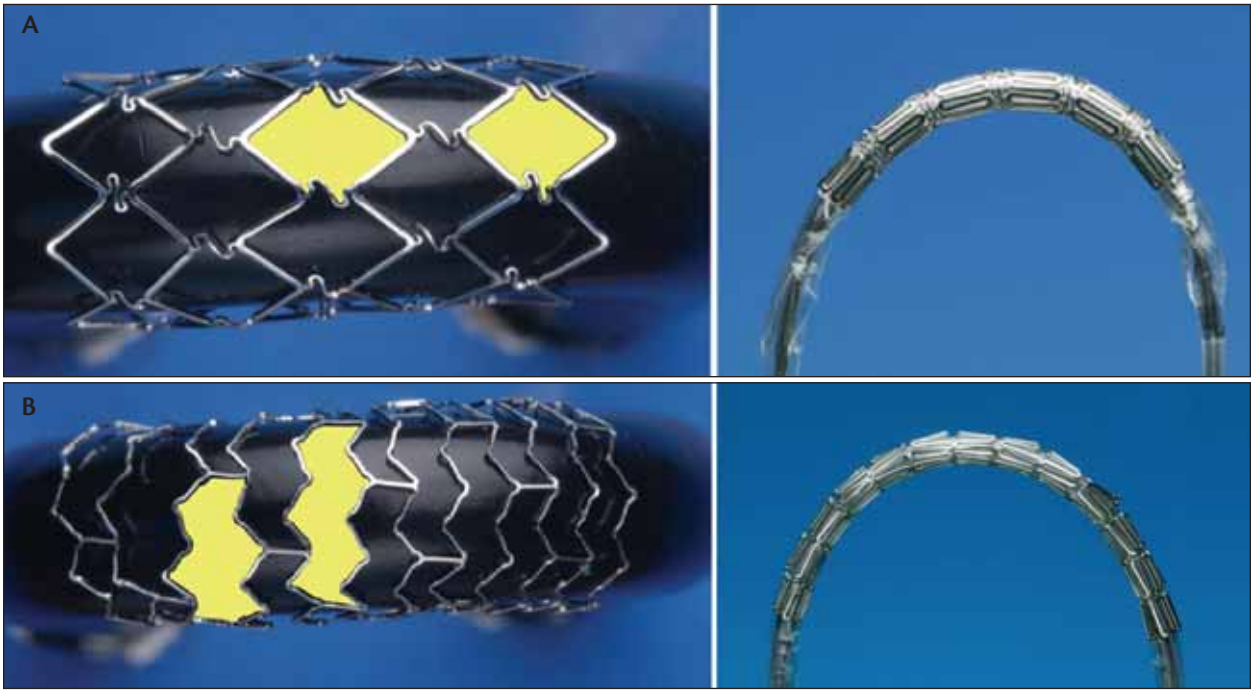

Figure 4. Fully supported closed-cell design (A) demonstrating comparable flexibility to the unsupported open-cell design (B).

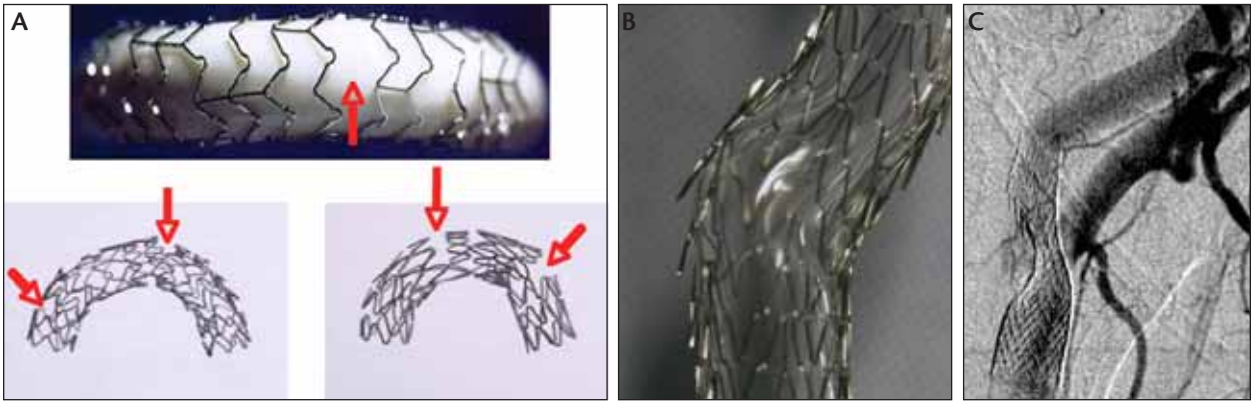

Figure 5. Larger open-cell–designed stents may not provide adequate scaffolding in a complex bend but do provide conformability (A). Open-cell design at the concave surface of the stent (B). Postprocedure angiogram demonstrating the open-cell struts extending beyond the intima with focal contrast extravasation to the adventitia (C).

The struts in the open-cell configuration can penetrate the intima and on occasion can extend to the adventitia. This raises the question of predisposition to restenosis or stent fracture at this site (Figure 6). Stretching of the cell size is exaggerated in the bend. There are, however, open-cell stents that meet the criteria of small cell size with cell conformability during flexion and consequently have acceptable scaffolding. Cell-size stability will prevent prolapse and possibly decrease embolic events in the long term. This in itself is important in that 20% of periprocedural events are in the poststenting period. This also explains the >2% stroke event (ipsilateral) in the 30-day versus 1-year stroke incidence noted in essentially all of the trials.

CONSIDERATIONS FOR THE FUTURE

With the recent introduction of intravascular ultrasound with virtual histology, it may be possible to better understand these lesion characteristics in determining the significance of cell size, stent flexibility and conformability, plaque prolapse, and thrombotically active plaque, all of which are stroke predictors. The angiographic anatomy may provide a better understanding of lesions more demanding of flexibility or scaffolding, whereas intravascular ultrasound with virtual histology might suggest lesions that are thrombotically active and not suited for stenting regardless of cell design (Figure 7).

It is not unreasonable that the cell structure, in itself, can be designed to act as its own filter. With virtual histology and the possibility of having a better understanding of the lesion characteristics, we may be better able to choose the most appropriate stent. Early clinical experience with the helically designed stents has also demonstrated excellent flexibility and kink resistance. The helical design allows uniform cell size at flexion points without scaling. In terms of clinical applications, the calcified and tortuous lesion may be best suited to the more conformable open- or helical-designed stents. For vulnerable plaque or ulcerative lesions with type C characteristics (high anatomical risk), greater scaffolding might be more appropriate.

It is clear that there remain unresolved clinical issues and room for improved product designs. While we await more robust data sets and device evolution, it is important that the interventional community remain mindful of the lessons of recent clinical trials in the US and Europe. The CAPTURE study observed that a difference existed between inexperienced versus experienced operators.[8] Major stroke and death occurred in 3.4% in the lesser-experienced operators versus a 1.1% event rate in the operators with significant experience.

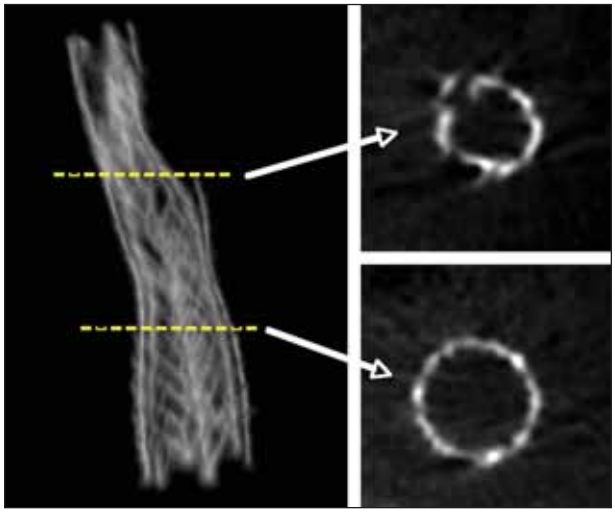

Figure 6. Postprocessing of a 3D reconstructed angiogram demonstrating a strut fracture in a nitinol carotid stent.

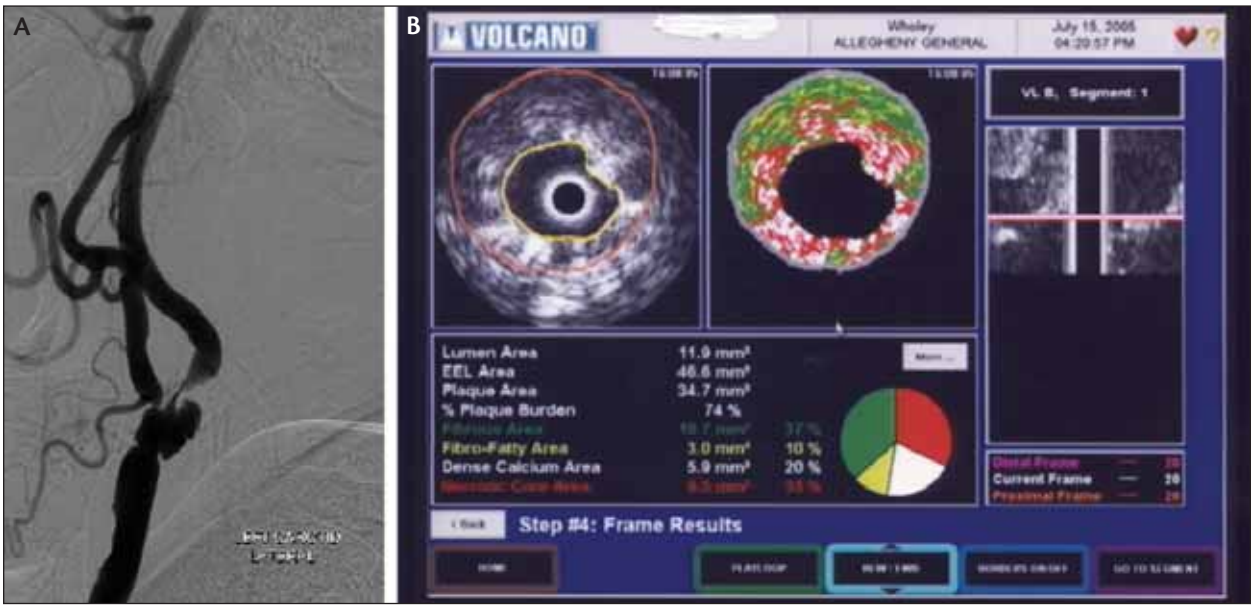

Figure 7. Angiogram and virtual histology of carotid artery occlusive disease. Preocclusive internal carotid lesion with complex ulceration and angulation (A). Virtual histology of that lesion obtained with a Volcano intravascular ultrasound demonstrating significant necrotic core and dystrophic calcification at the intimal surface (B). These lesion characteristics are best suited for endarterectomy.

Furthermore, an all-stroke and death rate comparison of inexperienced operators versus experienced operators also showed a difference with a 6.9% event rate with inexperienced operators versus a 4.6% rate in the high-level operators. Higher experienced operators had a 0% death rate, whereas inexperienced operators had a 2.3% death rate. The lesson is that doctors can and do achieve excellent stenting results when they are well trained in their devices and the procedure and select patients appropriate for the procedure.

CONCLUSION

The desired features of a carotid stent would include scaffolding that is adequate enough to control plaque prolapse but has acceptable levels of flexibility, conformability, and radial strength to track to the lesion, appose the vessel wall, and control recoil. Of course, no matter how tight the scaffolding, there is still no stent available to control embolic particles 100 µm and smaller. These small particles constitute most of the emboli produced during CAS. When used with an efficient distal protection filter and combined with a flow-reversal system, we may be able to control at least most of the embolic events occurring periprocedurally. Delayed postprocedure events, however, remain an enigma.[1] ■

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