Parent Vessel Size and Curvature Strongly Influence Risk of Incomplete Stent Apposition in Enterprise Intracranial Aneurysm Stent Coiling

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Endovascular embolization using a stent-assisted technique has proved to be an effective option in the treatment of wide-neck intracranial aneurysms.1-4 Stents serve as a physical barrier to prevent coil protrusion into the parent vessel during coiling of wide-neck or fusiform lesions. Follow-up imaging of patients who have undergone stent-mediated coil embolization procedures has traditionally focused on the presence or absence of residual filling in the dome.5 Despite excellent laboratory evaluations of stent conformation in vitro,6,7 data on visualization and strut configuration of stents deployed in the intracranial circulation remain scant. Several studies have evaluated the architecture of stents within coronary vessels and have noted the presence of ISA to the vessel wall.8-10 Because this finding may be associated with adverse clinical events such as late stent thrombosis10,11 in the coronary circulation, we sought to identify the presence of any ISA within the intracranial circulation in patients undergoing stent-mediated coiling by using the self-expanding intracranial EN (Cordis, Miami Lakes, Florida). Correlating our findings with angiographic FPCT, we describe here a new crescent-shaped flow signal intensity external to the stent struts on 3T-MRA as a marker for ISA in EN-treated aneurysms and describe the morphologic characteristics of target vessels that predispose to poor stent—vessel wall apposition.

Materials and Methods

Patient Selection
Since January 2009, all patients undergoing stent-mediated coiling in our service have routinely undergone prospective 3T-MRA postprocedurally. All aneurysm stent-coiling procedures using ENs in the intracranial vasculature from January 2009 to September 2010 with 3T-MRA performed within 3 days of stent deployment, totaling 33 cases, were included. An additional 6 patients who underwent prospective 3T-MRA imaging within 3 days of EN deployment between June 2007 and September 2008, as part of a pilot study on the utility of 3T-MRA in randomly selected patients following stent-coiling, were also included in the study. Cases of off-label use of ENs such as the waffle-cone technique12 were not included. The use of the EN and the current study were approved by the institutional review board.

Embolization Procedure
Patients were pretreated with clopidogrel (75 mg by mouth daily) and aspirin (325 mg by mouth daily) for at least 3 days before the proce-
Stent-mediated coiling by using the EN (4.5 mm diameter by 14, 22, 28, or 37 mm length) was performed according to the manufacturer’s instructions for use via a Prowler Plus Select 0.021-inch microcatheter (Codman Neurovascular, Raynham, Massachusetts). Stent coiling was performed either by using the sequential or jailing technique. In the former, the EN is first deployed, and then a separate 0.014-inch microcatheter (Excelsior SL-10; Boston Scientific, Natick, Massachusetts) is used to catheterize the aneurysm dome through the stent interstices followed by coiling. In the jailing technique, the aneurysm is first selected by the SL-10 microcatheter, followed by EN deployment, thereby pinning the coiling microcatheter between the stent and vessel wall while coiling proceeds. The stent was deployed by stabilizing the delivery microwire and then unsheathing the stent by withdrawal of the Prowler Plus Select microcatheter. All patients were treated with intravenous anticoagulation for a target partial thromboplastin time of 55–70 seconds for 24 hours following the procedure.

**Angiographic Analysis and MR Imaging Methods**

A single calibrated flat-panel biplanar DSA system (Artis; Siemens, Erlangen, Germany) was used for all procedures. 3D-RA and angiographic C-arm FPCT were performed (DynaCT; Siemens) during the embolization procedure. Acquisitions were reconstructed and analyzed by using the Leonardo software package (Siemens).

Patients underwent 3T-MRA of the brain within 3 days of the initial procedure by using a 3T Achieva unit (Philips Healthcare, Best, the Netherlands). MRA was performed by using a 3D time-of-flight technique with a TR of 25 ms, TE of 3.45 ms, flip angle of 20°, FOV of 20 cm, with 1-mm phase-encoding, reconstructed to 512 × 512 (voxel size 0.39 × 0.39 × 0.5 mm). The volumetric 3D datasets obtained from 3T-MRA and FPCT source images were visualized in 3D by using 3D MPR and maximal intensity projection by using OsiriX software (64-bit, Version 3.8; Pixmeo, Bernex, Switzerland).

**Morphologic Feature Measurement**

The measurements of the morphologic features were performed in 3D by using MPR of the 3D volumetric dataset obtained from the 3D reconstruction of the post–stent deployment or post–stent coiling rotational angiographic runs. The 3D volumetric dataset was exported from the workstation and analyzed by using MPR visualization by using OsiriX. The radius of curvature was measured as a feature of the parent vessel in which the stent was deployed by obtaining the radius of a circle fitted through the centerline of the carotid artery curved segment. The parent vessel diameter was measured as the average of the diameter at the distal and proximal stent-deployment sites. The stent-subtended arc angle, measured independent of the radius of vessel curvature, was evaluated on the basis of the angle at which the stent was deployed in the parent vessel.

Morphologic feature measurements were made individually and independently by both authors in a blinded fashion (without knowledge of ISA status), on separate occasions, and on different computers by using the same datasets. The interobserver correlation coefficient r values for vessel curvature, stent-subtended angle, and vessel diameter were each >.90. Values reported for each sample point are averages of each observer’s measurements.

**Statistical Analysis**

The differences in characteristics between subtypes were evaluated by using 1-way analysis of variance, stepwise-regression modeling, χ² testing, and ORs for categoric values by using JMP, Version 8 (SAS, Cary, North Carolina). Statistical significance was assumed for P < .05.

**Results**

**Detection of ISA by 3T-MRA**

During surveillance imaging in a number of EN stent-mediated aneurysm embolization procedures in which stent positioning was thought to be paramount, high-resolution FPCT imaging was performed and evaluated for the quality of stent apposition to the vessel wall (Fig 1). In a number of patients in whom ENs were deployed around curved segments of the ICA (Fig 1), the stent exhibited central crimping and ovalization with luminal loss and the outer and/or inner stent struts were noted not to be in contact with the vessel wall, resulting in significant ISA. FPCT imaging with and without dilute contrast injection demonstrated flow of blood outside the confines of the stent lattice. Comparison and correlation of these FPCT findings were made with post-treatment 3T-MRA thin-section MPR reconstructions, which consistently revealed that the site of ISA on FPCT corresponded to a characteristic 3T-MRA flow pattern of high signal intensity outside the stent struts (Fig 1C). This finding was dubbed CS on the basis of its unique crescent shape (Fig 2G and H).

Analysis of 3T-MRA in EN-treated aneurysms detected the presence of CS as an indicator of ISA in 19 of 39 patients (49%). Patient subsets with and without CS were statistically indistinguishable with respect to age (60.5 ± 8.0 years and 54.9 ± 10.6 years, respectively, P = .076) and sex (4 men/15 women; and 3 men/17 women, respectively, P = .622). Lengths of ENs (14, 22, 28, and 37 mm) used in the CS+ population (n = 0, 17, 1, and 1) were not statistically different (P = .122) than those in the CS− population (n = 1, 14, 5, and 0). Similarly, a jailing technique was used in 17 of 19 in patients with CS compared with 16 of 20 in those with CS− (P = .408). Of the 19 cases demonstrated to harbor CS, 18 were located in the intracranial ICA and 1, in the middle cerebral artery. Of the 20 cases without CS, 14 were located in the ICA, 3 in the anterior communicating artery, 2 in the basilar artery, and 1 in the middle cerebral artery.

**Internal Carotid Parent Vessel Characteristics Related to ISA**

To determine factors contributing to ISA, we analyzed shape features of the parent vessel with respect to the deployed stent (Fig 3). Figure 3B demonstrates 2 stent configurations used to treat the same aneurysm, in which 2 different stent-subtended arc angles are obtained for the same radius of vessel curvature. Statistical analysis of morphologic features was limited to the 32 cases with stents deployed in the ICA to avoid biasing of results by the uneven distribution of the deployment location among cases with and without CS, given the inherent variation of vessel size and anatomy in the cerebral circulation. Among the 32 ICA cases, 18 demonstrated the CS on 3T-MRA (56%). Univariate analysis (Tables 1 and 2) for correlation of the CS revealed the radius of curvature to be significantly lower (P = .002) in patients with the CS (signifying a tighter curve). Similarly, parent vessel diameter was greater in patients with the CS (P = .043), as was the angle α subtended by the deployed
EN (P < .001). Aneurysm size was also found to have no effect on this phenomenon (P = .546); endovascular technique (jailing versus sequential) was similarly not different (P = .427).

Multivariate analysis (Table 2) by using univariate significant factors (P < .05) for modeling ISA was performed by using the parent vessel diameter, the parent vessel radius of curvature, and the stent-subtended angle. Multivariate logistic regression yielded an area under curve of 0.9316 in the receiver-operating characteristic, with a sensitivity of 100% and a specificity of 85% with the highest significance for the vessel radius of curvature (OR, 253; P = .009), followed by the stent-subtended angle (OR, 225; P = .005) and vessel diameter (OR, 8.49; P = .044).

**Discussion**

ISA has been defined by Rathore et al as the “separation of one or more stent struts from the underlying vessel wall and observation of blood speckles between the stent struts and the vessel wall,” as demonstrated with the use of intravascular sonography for visualization of the stent-containing vessel. By confirming our findings by using FPCT imaging, which has been shown to be effective in the visualization of in vivo stents,13,14 we demonstrated the same blood flow phenomenon between the stent struts and the vessel wall by using the presence of the CS on 3T-MRA imaging. Univariate and multivariate results from this study demonstrate that following deployment of closed-cell design ENs in the intracranial ICA, ISA is more likely to be found in vessels with more tortuous anatomy.

Prior studies evaluating ISA in balloon-mounted stents deployed for coronary atherosclerosis have identified predictors of ISA to include atherosclerotic lesion length,15 use of drug-eluting stents, unstable angina, and the absence of diabetes.16 The significant differences in properties between balloon-mounted coronary stents and the low-radial-force self-expanding ENs make ISA etiology comparison between the 2 less compelling. EN consists of a self-expanding closed-cell design, which is significantly less stiff and has thinner struts than balloon-mounted variants.
The clinical impact of ISA in the coronary vasculature remains under debate. Onizuka et al demonstrated that no adverse clinical events occurred in 15 patients found to harbor ISA following carotid artery angioplasty and stent placement with a mean follow-up of 11 months. The RAVEL trial demonstrated no adverse events in patients found to harbor ISA with a follow-up of 12 months. Other studies evaluating the long-term consequences of ISA have highlighted a significant risk. Hoffmann et al described a higher incidence of myocardial infarction in patients with ISA after 4 years of follow-up compared with patients without ISA. Siqueira et al performed follow-up on patients for a mean of 29 months and observed an increased incidence of stent thrombosis in patients with ISA. Cook et al reported similar results, finding that patients presenting with stent thrombosis after a minimum of 12 months following stent deployment had a higher incidence of ISA. In their review of the coronary literature and the aforementioned studies, Rathore et al concluded that a definite relationship existed between ISA and stent thrombosis, though they conceded that longer follow-up is necessary to elucidate the true consequences of ISA. Because the coronary stents evaluated in these previous studies are balloon-mounted and constructed of thicker and stiffer stent struts, the results elucidated in these studies in patients with coronary atherosclerosis cannot be easily correlated to stent-mediated aneurysm coiling by using self-expanding flexible stents deployed in healthier nonstenosed vessel segments.

The finding of prevalent ISA in tightly curved vessels may be a direct result of the closed-cell design of the EN. Although the closed-cell design is advantageous at serving as a smooth interface at the aneurysm neck to act as scaffolding for coil deployment, our results point to this design as an inherent limitation in tortuous vessels having small curvature radius. In addition, the higher propensity for the EN to demonstrate ISA in larger diameter vessels suggests that the stent lacks outer radial force to sufficiently appose the wall near its deployment diameter. The EN may be better suited for use in smaller caliber vessels if significant curvature exists. If the vessel diameter is close to 4.0 mm, then the EN may be better limited to straight-vessel segments because its use in larger curved vessels

Fig 2. CS revealed in a 59-year-old woman with a wide-neck left carotid ophthalmic aneurysm. A—D, Lateral DSA (A), a 3D-RA reconstructed model (B), a postembolization lateral DSA (C), and an unsubtracted lateral digital angiogram show strut ends of the deployed 4.5 × 22 mm EN (D, arrows). E and F, Postembolization 3D-RA model (E) and FPCT reveal stent crimp at the siphon and an outer crescent region of ISA (F, arrow). G and H, Sagittal (G) and axial (H) 3T-MRA shows CS (arrow).
could be associated with ISA. The current EN is manufactured in varying lengths but at a single uniform maximum deployed diameter of 4.5 mm. The findings presented here suggest the need for a larger EN configuration for use in vessels of near 4-mm luminal diameter. The findings suggest that 1 way to decrease ISA likelihood in ICA EN coiling may be to select a
landing zone for the stent deployment that attempts to decrease the stent-subtended arc angle at any given aneurysm location as suggested in Fig 3B (left panel instead of right), provided that this is possible without compromising the ability of the stent to mechanically scaffold the coils properly.

The presence of poor stent apposition with the EN also has at least 2 technical ramifications for subsequent endovascular intervention. In the first, the presence of struts in the center of the vessel lumen may interfere with future microcatheter navigation or the addition of concentric stent placement; worse, it may lead to stent movement during microcatheter manipulation. In the second, the lack of stent apposition to the vessel wall harboring the aneurysm neck could potentially result in unintended partial coil herniation into the parent vessel or at least a higher exposure of the coil pack to intraluminal flow.

The EN has been linked by a number of case reports to a delayed migration phenomenon in the posterior circulation, which remains poorly explained.21-23 The poor stent apposition highlighted in curved-vessel segments adds another possible mechanism of stent migration, because the lack of stent strut contact to the vessel wall may make the already lubricious coated stent less anchored and more prone to sliding. Nonetheless, the current study is predominantly in the anterior circulation and may, therefore, be of limited relevance to the cases of migration, which were in the posterior circulation. Under such greater exposure would increase the hemodynamic drag on the stent, it is not likely to explain the reported cases of migration, which led to proximal, not distal, delayed movement of the deployed EN.

Etiologically, the crescent-shaped 3T time-of-flight MR imaging signal intensity in tightly curved vessels with ISA may be directly related to the curved nature of the artery and the less curved nature of the closed-cell design EN. Measurements of the volume of the CS by using summation of the 3T-MRA signal intensity as a potential proportional indicator of ISA severity did not demonstrate a linear relationship to the morphologic features reported in the study (data not shown). It is likely that the 3T-MRA CS is not linearly proportional to the degree of ISA and may be best used as a binary indicator. This is possibly the result of the relatively low spatial resolution of MR imaging and of metal artifact signal-intensity dropoff from the stent struts. Both could lead to the inability of 3T-MRA to sufficiently delineate the small margins of the CS area. A comparison of the crescentic area of ISA in Figs 1 and 2 between 3T-MRA CS and the corresponding FPCT images also confirms the lower spatial resolution of 3T-MRA. These limitations of MR imaging suggest that the true degree of less severe ISA may be underestimated and may be even higher than that reported in the current study. A more detailed quantitative analysis of the area and shape of the ISA would likely necessitate the use of FPCT for computation of the orphaned volume in the zone of ISA.

In light of the link between vessel anatomy, relative stent-deployment location, and development of ISA in the ICA, we recommend that use of closed-cell design ENs be reserved for vessels with narrower diameters and larger radii of curvature. Preferential selection of these vessels may promote a lower likelihood of stent malapposition and a more favorable deployed-stent architecture. Given the significant lack of stent-vessel wall apposition at vessel diameters close to 4.0 mm, stent-subtended arc angles >100°, and tight vessel curvature, procedures requiring stent deployment in tortuous intracranial locations such as the carotid siphon warrant careful analysis. The current findings may also be relevant to recent attempts to employ the EN for the treatment of intracranial atherosclerosis because these suggest that it may be better suited for straight rather than curved segments.24

Conclusions

The central finding of this study is that the closed-cell design EN is susceptible to malapposition to the vessel wall when deployed in vessels with tortuous anatomy. This phenomenon can be detected by the use of the CS on 3T-MRA. Careful preprocedural morphologic analysis is warranted to select vessels that will be less likely to induce incomplete stent apposition. Further work is needed to evaluate the long-term consequences of incomplete stent apposition of ENs in the cerebral vasculature.

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References


Table 1: Univariate analysis of the dependence of ISA as detected by the presence of CS on 3T-MRA in intracranial ICA lesions

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<th>CS+</th>
<th>CS−</th>
<th>P Value</th>
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<tr>
<td>Patient count with ICA lesions</td>
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<td>14</td>
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<tr>
<td>Vessel curvature radius (mm)</td>
<td>7.26±2.0</td>
<td>9.8±2.2</td>
<td>.002</td>
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<tr>
<td>Stent-subtended arc angle α</td>
<td>144±32°</td>
<td>95.2±42°</td>
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<td>Parent vessel diameter (mm)</td>
<td>4.06±0.32</td>
<td>3.74±0.54</td>
<td>.043</td>
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<td>Stent length (22, 28, 37 mm)</td>
<td>16:1:1</td>
<td>10:4:0</td>
<td>.125</td>
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<tr>
<td>Aneurysm size (mm)</td>
<td>6.99±5.2</td>
<td>7.99±3.6</td>
<td>.546</td>
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<td>Technique (jailing:sequential)</td>
<td>16.2</td>
<td>11.3</td>
<td>.427</td>
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Table 2: Multivariate analysis of the dependence of ISA on morphologic features in intracranial ICA lesions

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<th>x²</th>
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<td>Vessel curvature radius 6.842</td>
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<td>Stent-subtended arc angle α 8.046</td>
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<td>Parent vessel diameter 4.062</td>
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<td>Total model 21.323</td>
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