Force Characterization of Intracranial Endovascular Embolization: Coil Type, Microcatheter Placement, and Insertion Rate

Jonathan B. Lamano, MS*‡
Grace G. Bushnell, BS*
Hongyu Chen, BS*
Avanti Badrinathan, BS*
Najib E. El Tecle, MD*‡
Bernard R. Bendok, MD‡§¶
Matthew R. Glucksberg, PhD*

*Department of Biomedical Engineering, Northwestern University, Evanston, Illinois; Department of ‡Neurological Surgery, §Otolaryngology, and ¶Radiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois

Correspondence:
Bernard R. Bendok, MD, MSCI, FAANS, FACS, FAHA,
676 N Saint Clair,
NMH/Arkes Family Pavilion Suite 2210,
Chicago, IL 60611.
E-mail: bbendok@nmff.org

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BACKGROUND: Intraoperative rupture (IOR) is a rare, but potentially morbid complication of endovascular aneurysm coil embolization. Yet, IOR predictors have remained relatively uninvestigated in relation to coil design.

OBJECTIVE: To develop a novel in vitro aneurysm model to characterize forces exerted by coils of different design on the aneurysm during endovascular embolization that are hypothesized to contribute to IOR.

METHODS: A 3-mm saccular aneurysm model was developed with flat latex membrane at the dome apex. Membrane deflection was observed throughout simulated embolization and converted to force measurement. Simultaneous coil insertion and force measurement were accomplished with a compression strength-testing machine. Membrane and insertion forces across coil type, microcatheter tip placement, and insertion rate were evaluated.

RESULTS: Insertion force and force directly on the aneurysm wall exhibited a difference, with framing coils exerting greatest force, followed by filling and finishing coils. Regarding microcatheter placement, a similar graded response in membrane and insertion forces was observed with positioning in the top-third of the aneurysm generating the greatest force compared with central and bottom-third placement. Insertion rate was also a factor with the slowest rate (10 mm/min) exhibiting the greatest membrane force, followed by lower forces at 30 and 50 mm/min. A multiple linear regression model was created to assess the contributions of each factor toward aneurysm forces.

CONCLUSION: Increased force on the aneurysm is associated with framing coil use, microcatheter placement proximal to aneurysm dome, and slow insertion rate. Further characterization remains necessary to reduce IOR risk, especially concerning the contributions of insertion rate.

KEY WORDS: Coil embolization, Insertion force, Intracranial aneurysm, Intraprocedural rupture

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WHAT IS THIS BOX?
A QR Code is a matrix barcode readable by QR scanners, mobile phones with cameras, and smartphones. **The QR Code above links to Supplemental Digital Content from this article.**

Despite improvements in catheters, coils, and balloons, the complication rates of endovascular coil aneurysm occlusion remain significant. One important complication is intraoperative rupture (IOR). Although reports suggest low overall IOR risk, associated morbidity and mortality can be substantial and little is understood regarding the biomechanical forces involved.[1] IOR has been observed to occur as a consequence of aneurysm wall perforation by microcatheter, guidewire, or endovascular coil, in addition to increased intra-aneurysm pressure due to coil insertion and overpacking.[2,3] Compared with aneurysm clipping, IOR during coiling exhibits exaggerated adverse effects due to decreased ability to control bleeding, manage new subarachnoid hemorrhage, and prevent elevated intracranial pressures.[1] Documented factors that increase IOR risk include small

ABBREVIATIONS: ANCOVA, analysis of covariance; **ANOVA,** analysis of variance; **CI,** confidence interval; **CSTM,** compression strength-testing machine; **IOR,** intraoperative rupture; **VFC,** Versatile Range Fill Coil

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aneurysm size (≤3 mm diameter),[4] previous rupture,[5] and microcatheter tip placement against the aneurysm wall.[1]

Although coil manufacturers qualitatively describe implant stiffness, absolute forces exerted by coils during embolization have only recently been investigated.[6] Numerous variables exist that could modulate forces[7] during framing, filling, and finishing stages. Yet, characterization has revolved around insertion force, which, although intuitive to surgeons, may not indicate force directly on the aneurysm. With the use of insertion force as a surrogate of direct aneurysm force,[8] various coil types have been analyzed across simulated embolizations,[6] resulting in the proposal of mechanical coil insertion systems.[9] However, studies have not quantitatively related these insertion forces to those directly on the aneurysm or investigated the reliability of insertion force as a correlate of force on the aneurysm wall—a critical point, because aneurysm force, not insertion force, is ultimately responsible for IOR.

In an effort to quantify relationships between insertion and aneurysm force to better understand mechanical effects of coil embolization and, more importantly, characterize IOR relevant force properties of different coil types, a novel system was developed to characterize both insertion and direct forces in a model saccular aneurysm. Based on implant material properties and geometry, different coil types were hypothesized to exert distinct aneurysm forces during embolization.[6] Microcatheter placement was also expected to affect aneurysm force, because coil release closer to the dome could facilitate greater force transfer with less dissipation. Moreover, insertion rate was hypothesized to be correlated with direct aneurysm force, because faster insertion could facilitate a constant kinetic friction state requiring less insertion force than static friction states observed during slower insertion. Greater understanding of these variables may influence clinical technique and reduce IOR risk.

METHODS

Aneurysm Model

A 3-mm spherical aneurysm model with a 1.6-mm feeding artery was constructed of acrylic, in which the aneurysm dome was bisected to expose a 2.25-mm opening (Figure 1A). Latex membranes (0.150 mm) were affixed over exposed dome by using double-sided adhesive tape (McMaster Carr, Elmhurst, Illinois). Force-displacement calibration of membranes on the model was obtained via a compression strength-testing machine (CSTM) (MTS 6 Sintech 20/G, MTS Systems Corporation, Eden Prairie, Minnesota). With the use of the latex membrane elastic modulus (1.1 MPa), which is of the same order of magnitude as aneurysm wall (2 MPa),[10] finite-element analyses (Abaqus, Dassault Systemes, Velizy-Villacoublay France), and classical theory of plates and shells predicted similar force-displacement relationships following simulated coil insertion (see **Figure**, **Supplemental Digital Content 1**, http://links.lww.com/NEU/A681). Latex was selected to increase displacement detection sensitivity.

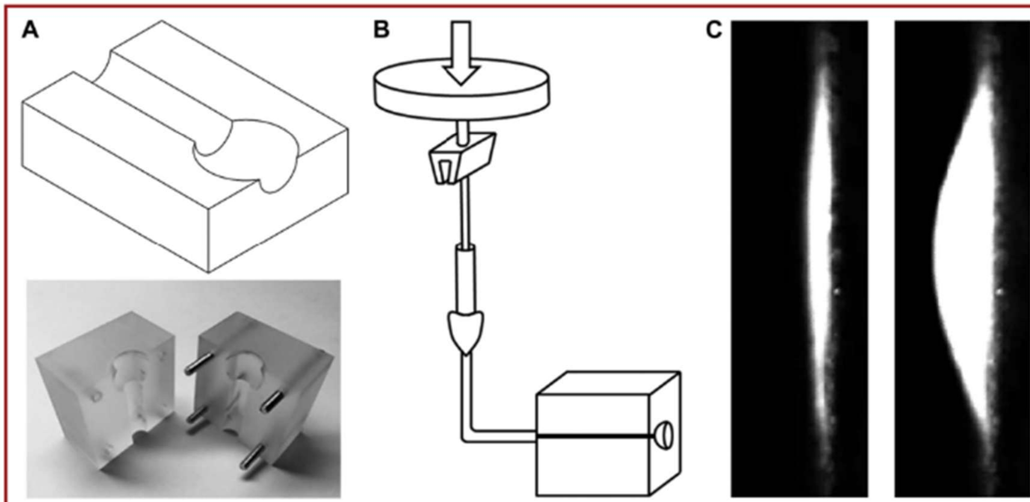

FIGURE 1. *In vitro aneurysm model.* **A**, *model consisted of 2 acrylic blocks into which a 3-mm saccular aneurysm was patterned. Dome bisection created an opening over which a latex membrane was affixed.* **B**, *a CSTM fed endovascular coils at a constant rate, while simultaneously measuring insertion force.* **C**, *latex membranes were visualized microscopically. Reference frames* (**Left**) *were subtracted from frames captured during embolization* (**Right**). *For each frame, maximum membrane displacement was calculated and converted to a force via calibration curve. CSTM, compression strength-testing machine.*

Membrane Force Measurement

The measurement of force exerted by an inserted coil was obtained through membrane displacement detection. A microscope (Zeiss OPMI 1-FC, Carl Zeiss AG, Oberkocken, Germany) was focused along the model face at the depth of the dome opening. Calibration of measured displacement was achieved through determination of length per pixel afforded by the microscope camera (AmScope MA1000-CK, AmScope, Irvine, California) when imaging an object of known width. Force resolution was 0.355 mN.

Simulated Embolization

Simulated embolization was accomplished via automated insertion. A stage for the model, hemostatic valve Y-connector, and side camera was constructed to fix component positions. Membrane force was measured with microcatheter tip in the top-third (near dome), center, or bottom-third (near neck) of the aneurysm. Insertion occurred until the implant length of a single coil was achieved.

Automated coil insertion was accomplished via CSTM (Figure 1B). A microcatheter was fixed proximally, and an insertion wire was advanced by CSTM load cell. Telescoping hypodermic tubing prevented insertion wire bend during embolization. Three feed rates—10, 30, and 50 mm/min—were implemented. In addition to controlling the feed rate and measuring coil insertion length, the system facilitated insertion force measurement. Other than a bend from vertical insertion through CSTM to horizontal stage on which the model was fixed, the microcatheter was positioned linearly to prevent variable friction from a tortuous path.

Coil Types

Three coil types were utilized to compare insertion and resulting aneurysm forces. As a representative framing coil, the MicroVention Cosmos (MicroVention Inc, Tustin, California; 3 mm diameter, 60 mm implant length) was implemented. Two filling coil types were represented by the MicroVention Versatile Range Fill Coil (VFC) (3-6 mm diameter, 60 mm length) and the MicroVention Hypersoft finishing coil (3 mm diameter, 60 mm length). Coil comparison was accomplished with central microcatheter placement and 30 mm/min insertion rate. Cosmos coil was utilized for analysis of the effects of microcatheter placement and insertion rate.

Analysis

Image analysis was accomplished in MATLAB (Mathworks Inc, Natick, Massachusetts). For each video frame, maximum membrane displacement in comparison with reference images was measured (Figure 1C and see **Video, Supplemental Digital Content 2**, http://links.lww.com/NEU/A682). With the use of the calibration, maximum displacement was converted into maximum membrane force for each frame. Trials with microcatheter kickback or coil parent artery prolapse were discarded.

Statistical analyses were performed by using SPSS (IBM, Armonk, New York) and MATLAB. Analyses of covariance (ANCOVAs) with coil length inserted as covariate were utilized to determine differences in insertion and membrane force across coil type, insertion rate, and microcatheter location. Kruskal-Wallis analysis of variance (ANOVA) was performed to determine the effects of coil type, insertion rate, and microcatheter location on maximum insertion and aneurysm force across 10-mm insertion length segments. Post hoc multiple comparisons tests utilized Bonferroni correction. The Fieller method was used to calculate 95% confidence intervals (CIs) for normalized insertion, and membrane force ratios were determined by estimated marginal means. Multiple linear regression was performed to model contributions of coil insertion length, insertion force, insertion rate, and microcatheter placement on aneurysm force during Cosmos coil embolization. Statistical significance was determined by $P < .05$.

RESULTS

Simulated Embolization Force Measurement

One hundred fifteen simulated embolizations were completed (Figure 2). Latex membranes were utilized for 6 consecutive trials before replacement as determined by calibration to ensure consistent membrane properties. Coil type, microcatheter placement, and insertion rate were randomized across membranes.

Effect of Coil Type

Analysis of coil type contribution to membrane and insertion forces was performed with central microcatheter placement and 30 mm/min insertion rate (Figure 3A). Embolizations with Cosmos (n = 13), VFC (n = 14), and Hypersoft (n = 14) coils were analyzed. ANCOVA indicated significant effect of Cosmos > VFC > Hypersoft on membrane force ($P < .001$). Membrane force ratio was 7.94:1.72:1 (Cosmos:VFC:Hypersoft). Regarding insertion force, ANCOVA similarly indicated Cosmos > VFC > Hypersoft ($P < .001$) with a ratio of 5.47:2.35:1. Comparisons

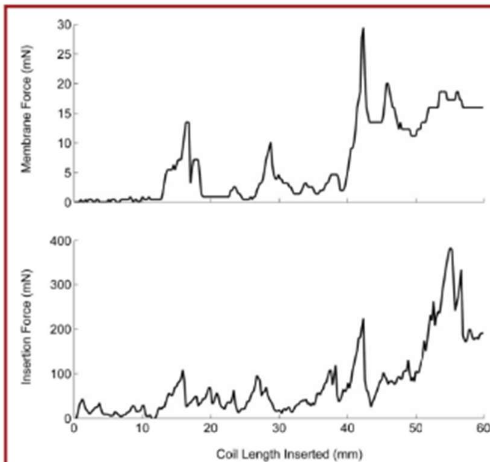

FIGURE 2. *Simulated embolization forces. Throughout simulated embolization with the Cosmos framing coil with central microcatheter placement and a constant insertion rate of 30 mm/min, coincident membrane and insertion force peaks were observed as a consequence of microcatheter "painting" motion (see* **Videos, Supplemental Digital Contents 2-3**, *http://links.lww.com/NEU/A683 and http://links.lww.com/NEU/A684).*

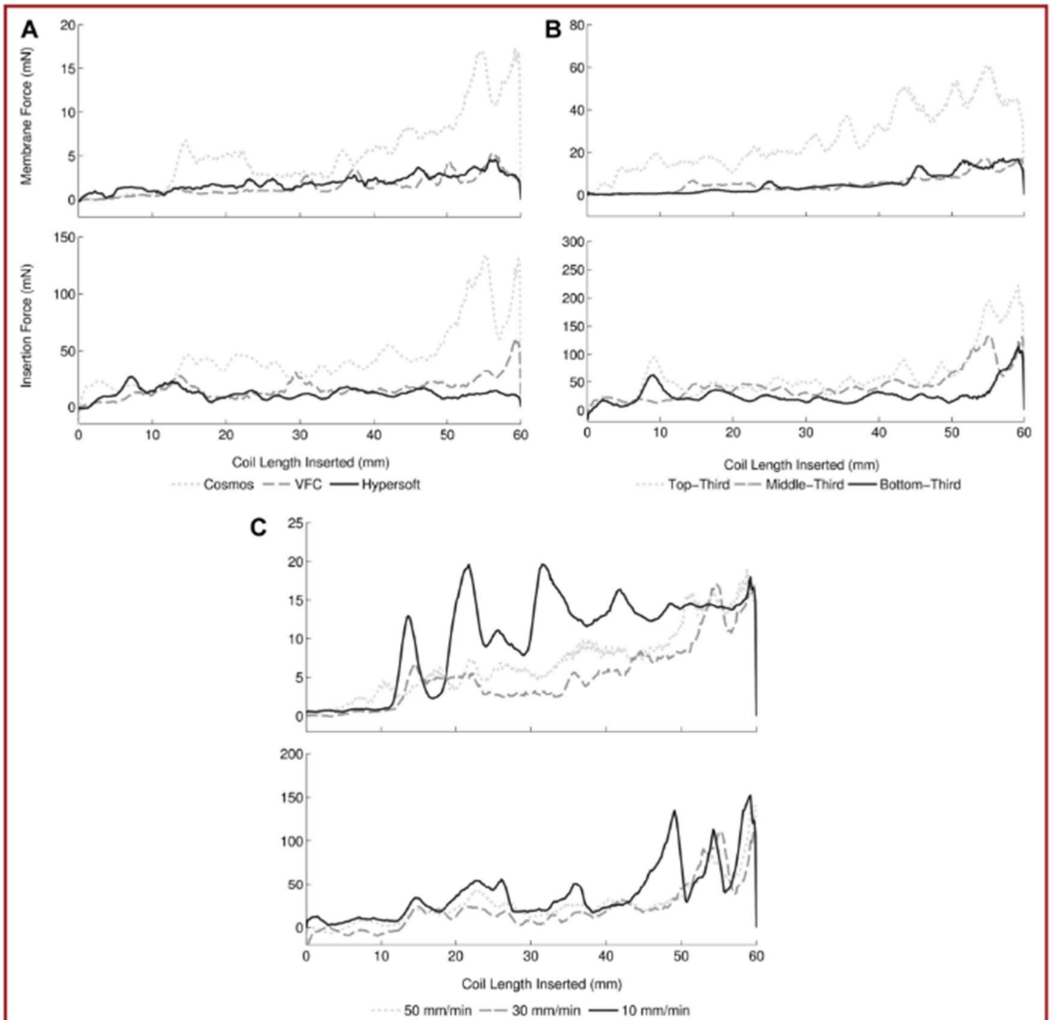

FIGURE 3. *Mean membrane and insertion forces.* **A**, *ANCOVA of forces across coil type indicated a significant effect of Cosmos > VFC > Hypersoft for membrane and insertion force (*P *< .001).* **B**, *analysis of microcatheter tip placement indicated a significant effect of top > middle > bottom (*P *< .001) for membrane and insertion forces.* **C**, *insertion rate exhibited a significant effect of 10 mm/min > 30 mm/min > 50 mm/min in membrane force (*P *< .001). Effect on insertion force was 10 mm/min = 30 mm/min > 50 mm/min (*P *< .001). ANCOVA, analysis of covariance; VFC, Versatile Range Fill Coil.*

of force ratios indicated nonoverlapping insertion and membrane force CIs for Cosmos data when normalized to Hypersoft data (Figure 4A). Further analysis of coil-type effects was performed by assessment of maximum aneurysm and insertion forces, which are theorized to be the most likely contributors to IOR (Figure 5A). Kruskal-Wallis ANOVA indicated Cosmos > VFC = Hypersoft on membrane force for all segments following the initial 10 mm of coil inserted ($P < .001$). Similar effects were

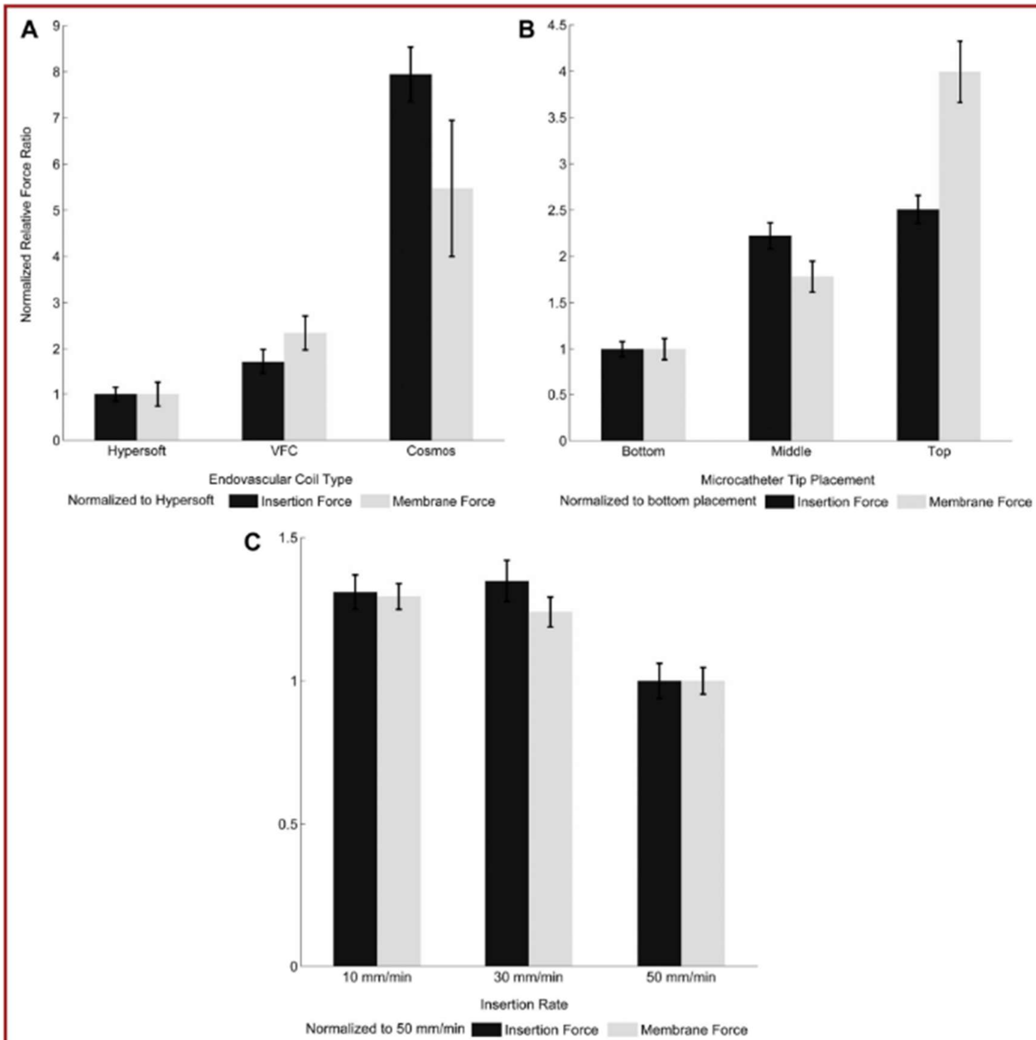

FIGURE 4. *Membrane and insertion force characterization.* **A**, *the Cosmos coil exerted approximately 8 times the force of the Hypersoft coil on the aneurysm and required 5 times the insertion force. The VFC required approximately double the insertion force of the Hypersoft and imparted double the force of the Hypersoft onto the aneurysm.* **B**, *microcatheter tip placement facilitated greater insertion and membrane forces in positions near the dome and decreased with placement further from the dome. Although membrane forces doubled with each placement closer to the dome, this was not reflected in insertion force.* **C**, *insertion rate analysis indicated a trend of increasing insertion rate leading to decreased force on the aneurysm. However, this trend was not exhibited by insertion force. VFC, Versatile Range Fill Coil.*

observed in insertion force measurements following 20 mm of inserted coil ($P < .001$).

Effect of Microcatheter Tip Placement

Microcatheter placement contribution to aneurysm and insertion forces was analyzed through simulated embolizations with the Cosmos coil and 30 mm/min insertion rate (Figure 3B). Microcatheter tip placement varied from top-third (n = 19), middle-third (n = 13), and bottom-third (n = 15) of the aneurysm. ANCOVA revealed significant effect of top > middle > bottom on membrane force ($P < .001$) with a ratio of 3.99:1.78:1 (top: middle:bottom). Insertion force ANCOVA indicated a similar significant effect of top > middle > bottom ($P < .001$) with a ratio of 2.51:2.22:1. Analysis of force ratios indicated non-overlapping insertion and membrane force CIs for top-third and bottom-third microcatheter placement when normalized to placement in the aneurysm bottom-third (Figure 4B). Analysis of maximum membrane force through Kruskal-Wallis ANOVA indicated an effect of top > middle > bottom on membrane force for a majority of segments, including the initial 10-mm insertion region ($P < .001$) (Figure 5B). Regarding insertion force, a similar effect was observed in the initial 10 mm of coil insertion; however, for the remainder of insertion, an effect of top = middle > bottom was observed ($P < .001$).

Effect of Insertion Rate

Analysis of the effect of insertion rate on aneurysm and insertion forces was performed with the Cosmos coil and fixed microcatheter placement in the aneurysm center (Figure 3C). Coil insertion occurred at constant rates of 10 mm/min (n = 20), 30 mm/min (n = 13), and 50 mm/min (n = 20). ANCOVA indicated significant effect of 10 > 30 > 50 mm/min on membrane force ($P < .001$) with force ratios of 1.29:1.24:1 (10:30:50 mm/min). Regarding insertion force, ANCOVA revealed a significant effect of 10 = 30 > 50 mm/min ($P < .001$) with a ratio of 1.31:1.35:1. Comparison of force ratios indicated completely overlapping insertion and membrane force CIs for both 10 and 30 mm/min insertion rates normalized to insertion at 50 mm/min (Figure 4C). Kruskal-Wallis ANOVA performed on maximum membrane force indicated no significant differences between insertion speeds (each segment $P > .05$) across all segments except between 40 and 50 mm where an effect of 30 > 50 = 10 mm/min on membrane force was observed ($P = .023$) (Figure 5C). Similarly, insertion force displayed no significant differences across insertion rates at a majority of segments (each segment $P > .05$), except between 10 and 20 mm where an effect of 10 = 30 > 50 mm/min was observed ($P = .013$) and between 40 and 50 mm/min where 30 > 50 mm/min was observed ($P = .010$).

Endovascular Embolization Force Model

Multiple linear regression was performed on Cosmos data to generate a model encompassing the contributions of inserted coil length, insertion force, insertion rate, and microcatheter placement on aneurysm force. All factors possessed a significant β-coefficient ($P < .001$) and $R^2 = 0.684$ (Table).

DISCUSSION

Although IOR during endovascular coil embolization possesses an incidence of only 2% to 5%, it can result in quadrupled risk of morbidity and mortality.[1] IOR has been observed due to coil overpacking, increased coil insertion pressure, and aneurysm wall perforation by microcatheter, guidewire, or coil.[2,3] Although insertion forces have been analyzed, they have not been related to forces directly on the aneurysm hypothesized to contribute to IOR.[6,8,9] This study presents a novel in vitro 3-mm-diameter spherical aneurysm model representing a high rupture scenario for determination of forces on a saccular aneurysm dome during simulated coil embolization for comparison with insertion force.

Simulated Embolization and Force Measurement

Maximum membrane deflections were observed during moments leading to microcatheter "painting" due to force buildup and subsequent relaxation (see **Videos, Supplemental Digital Contents 3-4**, http://links.lww.com/NEU/A683 and http://links.lww.com/NEU/A684). For each coil, consistent force peak values are related to tertiary coil properties. Thus, as force peaks occur immediately before and during "painting," the motion may indicate a procedural moment with increased IOR risk.

Coil Selection

Proper coil selection is vital for successful aneurysm obliteration while avoiding overpacking or recurrence. Analysis of Cosmos framing coils, VFCs, and Hypersoft finishing coils indicated an expected force hierarchy with framing coils exerting greater forces than versatile range filling and helical finishing coils. Mean insertion and membrane forces indicated similar

TABLE. Aneurysm Force Model for Cosmos Framing Coil[a,b]

Membrane Force Predictors	β (95% CI)
Independent variables	
Coil length inserted, mm	0.266 (0.261 to 0.270)
Insertion force, mN	0.074 (0.071 to 0.076)
Insertion rate, mm/min	−0.042 (−0.048 to −0.036)
Categorical variables	
Top placement	6.754 (6.482 to 7.025)
Center placement	0
Bottom placement	−4.027 (−4.313 to −3.741)

[a]CI, confidence interval.
[b]Multiple linear regression of Cosmos data revealed predictors of direct aneurysm force throughout embolization. Length of coil inserted and insertion force were positive predictors of membrane force, whereas insertion rate was a negative predictor. Microcatheter placement in the aneurysm top-third increased the basal force level, while placement in the aneurysm bottom-third decreased the basal force level, relative to placement in the aneurysm center.

effects; however, analysis of ratios of membrane and insertion forces suggested that insertion force was not a reliable predictor of membrane force. Normalizing to Hypersoft embolization forces, the VFC exhibited a 2-fold increase in membrane force, while the Cosmos displayed an 8-fold increase. Yet, this was not faithfully represented by Cosmos insertion force feedback, as only a 5-fold difference was recorded, indicating force feedback as a general reference, at best, of aneurysm force.

Regarding maximum forces, a consistent effect of Cosmos > VFC = Hypersoft was observed in membrane and insertion force, similar to results observed when analyzing mean forces. Together, these results indicate increased risk of framing coil insertion compared with filling and finishing coils. Previous research[9] has reported the incidence of lead coil complications, especially in aneurysms ≤10 mm in diameter. Current results indicate that increased forces generated by framing coils may contribute to these complications. Although several studies have characterized insertion forces as correlates of forces contributing to rupture,[6,8,9] the current findings indicate that they should be interpreted cautiously, because they may not reliably indicate aneurysm forces that appear more complex than simple correlations would predict. The factors hypothesized to contribute to this observation include variable friction between coil and microcatheter, geometrical and material coil properties, and microcatheter tortuosity. Thus, although insertion force serves as a general predictor, it may underestimate forces directly on the aneurysm and fail to scale in an intuitively appreciable manner.

Microcatheter Placement

Although microcatheter perforation[2,3] and kickback[11] have been associated with complications and unsuccessful obliteration, the difference in aneurysm force by coil delivery in different positions has remained uninvestigated. Microcatheter tip placement in top-third, center, and bottom-third of the aneurysm during simulated embolization resulted in membrane and insertion force gradients with placement near the dome generating the greatest forces and placement near the neck generating the lowest forces. As with coil comparisons, insertion force was indicated only as a general predictor of membrane force. Although membrane force exhibited a 2-fold increase for every position closer to the dome, this was not reflected in insertion force, which scaled in an underestimating manner.

This observation was reflected in the analysis of maximum insertion and membrane forces. Top placement was consistently greater than middle and bottom placement regarding membrane force. However, top and middle placements were indistinguishable regarding maximum insertion force. Thus, although microcatheter placement may be dictated by aneurysm specifics and kickback prevention,[11] the findings quantitatively confirm the intuition that placing the microcatheter tip closer to the aneurysm dome results in elevated aneurysm forces. Furthermore, top placement appeared to predispose greater microcatheter "painting" motions and resulted in more drastic movement compared with middle or bottom placement. As microcatheter movement within the aneurysm can contribute to IOR through wall perforation, the relationship between placement and microcatheter action may be an important consideration for IOR prevention.

Coil Insertion Rate

Clinically, insertion occurs in a "feed-pause-feed" manner as a result of manual insertion. Furthermore, rates are typically slow, except in the case of IOR when rapid embolization is required,[12,13] yet the insertion rate has not been evaluated for its effect on the aneurysm or insertion force. In the comparison of insertion at 10, 30, and 50 mm/min, a significant difference in membrane force was observed with the slowest insertion generating greater force than the fastest. Similar results were found in insertion force with the slowest and median insertion forces generating equivalent forces, both greater than forces observed during rapid embolization.

Analysis of maximum membrane and insertion forces across varying insertion rates found no significant differences. These results indicate that insertion rate exerts minimal effect on insertion and membrane force. Moreover, faster insertion rates may lower forces exerted on the aneurysm. Similar results have been previously reported,[14] indicating that constant kinetic friction states (requiring less force to overcome than static friction) account for reduced forces with rapid insertion, whereas static friction states occurring in slower insertions drive increased forces. While static friction states will inherently occur during manual insertion, minimizing these states can potentially reduce the force imparted on the aneurysm by approximately 30%. However, interpretation may be restricted to conditions prescribed by the model as discussed in "Limitations."

Multiple Linear Regression Model

Incorporating insertion rate and microcatheter placement data, a model for simulated embolization with the Cosmos coil was constructed to reveal contributions of insertion length, insertion force, insertion rate, and microcatheter placement to aneurysm force. Coil length inserted was a strong predictor of membrane force as a function of decreasing volume within the aneurysm, consistent with previous suggestions of an ideal lead coil length to avoid complications during initial coil placement.[15] Insertion force was a positive, but weaker predictor of aneurysm force, suggesting a general relationship between insertion and membrane force. Meanwhile, insertion rate exhibited a negative correlation with membrane force due to differences in static and kinetic friction states. Varying placement of microcatheter tip resulted in baseline elevation (top-third) or decrease (bottom-third) in predicted membrane force relative to central placement.

Limitations

Compared with the clinical scenario, nonspherical aneurysms or forces to regions other than the dome were not examined, nor were more frequently coiled larger aneurysms. While the results suggest insertion forces as weak IOR predictors, the model does not account for multiple coils, tortuous vasculature, calcification, or balloons and stents—although these factors arguably increase insertion force, further reducing correlations with aneurysm force. The constant catheter insertion rate utilized is unlike manual insertion characterized by push-pull motions and intermittent advancement. Moreover, coil interactions with pulsatile blood flow and pressure or differences in friction between model components and in vivo vascular intima with reduced coefficient of friction[16] remain unaccounted for in the model. Thus, the significance of insertion rate on force in vivo may be diminished, although this warrants further investigation, especially as increased insertion rates may be inadvertently accomplished with increased insertion forces clinically. Because aneurysm rupture thresholds remain poorly described, coiling force contributions remain difficult to place into clinical perspective.

CONCLUSION

Investigation of coil selection, microcatheter placement, and insertion rate resulted in quantitative evaluation of endovascular coiling with indications for increased IOR risk. Framing coil use, microcatheter placement proximal to dome, and slow insertion rate displayed associations with elevated aneurysm force. Although these findings shed light on coil selection, technical factors related to IOR, and nonlinear relationships between insertion and direct aneurysm force, continued characterization remains necessary to reduce IOR risk and associated morbidity and mortality, especially regarding the role of insertion rate.

Disclosure

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COMMENTS

The authors created a model of a cerebral aneurysm with a portion of that model rigid and another portion a flexible membrane. They then coiled these aneurysms and characterized the force generated by measuring displacement of the flexible portion of the model. They found that distal placement of the catheter and framing coils generated greater force on the membrane. Slower insertion rate was also associated with an increase in force, but this was significantly less relevant than coil and catheter placement. An important related finding is that the force generated at the proximal wire was a poor indicator of force on the aneurysm wall. These experiments are clearly described, and the statistical analysis is appropriate.

The clinical applicability of these results is limited by several factors. First, there is no control that quantifies the forces generated by an actual surgeon using their model. This is accounted for somewhat by reporting ratios. Second, they only used one size of aneurysm, and the small size used probably represents an uncommon clinical scenario, ie, we usually treat larger aneurysms. Finally, it would be interesting to quantify the effect of balloons or stents, which prevent prolapse into the parent artery. Is it correct to assume that more force is transferred to the wall? Perhaps this will be included in the authors' further investigations.