Validation and Initial Application of a Semiautomatic Aneurysm Measurement Software: A Tool for Assessing Volumetric Packing Attenuation

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ABSTRACT

BACKGROUND AND PURPOSE: Precise aneurysm measurements and volume embolization ratios are essential for long-term durability of endovascular coil embolization. We evaluated the accuracy of newly developed semiautomatic cerebral aneurysm measurement software, NeuroVision, and explored the value of volume embolization ratio in the prediction of re-treatment.

MATERIALS AND METHODS: We compared software-derived volume measurements of 4 silicone aneurysm models with those calculated with an approximation formula and ground truth values (validation study). We used NeuroVision to retrospectively evaluate outcomes of 100 unruptured aneurysms (97 patients) treated with embolization (clinical study). Aneurysm size (height, width, and neck), volume, and volume embolization ratios were calculated for 3 groups (stable, recanalization, and re-treatment) and were compared.

RESULTS: This validation study illustrated higher accuracy of NeuroVision in computing aneurysm volume compared with an approximation formula: percentage absolute errors were 4.50% and 3.18% and 23.07% and 17.60%, with maximal percentage absolute errors of 8.99% and 45.63%, respectively. Of 100 unruptured aneurysms, 20 recanalized and 12 were re-treated. Average volume embolization ratios of stable and re-treated aneurysms were 24.88% ± 5.91% and 20.50% ± 4.06%, respectively (P = 0.01). The optimal volume embolization ratio cutoff point for re-treatment was < 19.15%, at which the Youden index was 0.50 (sensitivity, 58.33%; specificity, 87.50%; area under the receiver operating characteristic curve, 0.74).

CONCLUSIONS: The NeuroVision software provided accurate aneurysm volume measurements and may be a useful standardized tool to measure aneurysm size and volume, especially for multicenter clinical studies. Volume embolization ratio may be a valuable predictor of aneurysm occlusion changes.

ABBREVIATIONS: AF = approximation formula; GDC = Guglielmi detachable coils; NV = NeuroVision; ROC = receiver operating characteristic; VER = volume embolization ratio

Endovascular coil embolization of cerebral aneurysms is now considered a valuable method to safely and effectively prevent aneurysm rupture.1-4 However, immediate postembolization angiographic evidence of complete aneurysm occlusion does not guarantee a good long-term outcome.5 Volume embolization ratio (VER), the percentage of aneurysm sac volume occupied by coils, is considered a valuable predictor of aneurysm recanalization,6-11 in addition to large size, wide neck, ruptured status, and suboptimal immediate angiographic result.

However, the accuracy of the methods used to measure aneurysm volume, and thus assess these predictors of recanalization, has not been well evaluated. A standardized aneurysm measurement methodology is necessary to enable multiple institutions to conduct collaborative investigations and compare their results.

A new analytic measurement software was developed for the measurement of cerebral aneurysms (NeuroVision [NV]; Cybernet Systems, Tokyo, Japan). We evaluated the accuracy of this software by using phantom aneurysm models. In addition, we used the software to retrospectively analyze the long-term outcome of a series of embolized aneurysms and investigate the value of VER, as semiautomatically computed by NV, in the prediction of aneurysm recurrence and re-treatment.

MATERIALS AND METHODS

Software Description and In Vitro Validation

NV Software. The NV software measurement process was initiated by a few discrete steps (Fig 1). Through a simple user interface, the image region containing the aneurysm was separated...
manually, and an image threshold was subsequently applied to extract the aneurysm and blood vessels from the surrounding background image. The threshold was semiautomatically set by use of the discriminant analysis method, which guaranteed that the selected threshold optimally separated the image intensities belonging to blood vessels from those that belonged to the background. The optimal threshold was that which corresponded to the maximal value of the Fisher linear discriminant, defined as the ratio of variance between the image intensities of the 2 classes (vessel and background) to the within-class variance. Use of discriminant analysis to determine the image segmentation threshold avoided the problems associated with varying measurements because of the arbitrary choice of window center and with the varying image quality of different imaging systems.

Aneurysm Size Measurements. Neck length, height, and width were measured by NV. Aneurysm neck length was defined as the largest diameter at the orifice plane of the aneurysm. Aneurysm height was defined as the longest distance from the midpoint of the aneurysm neck length line to the aneurysm wall. Aneurysm width was defined as the largest aneurysm diameter perpendicular to the height line.

Aneurysm Volume Measurement. NV virtually reconstructed the parent artery after semiautomatic aneurysm removal. The aneurysm neck plane was manually adjusted for complex aneurysm neck shapes through the manipulation of 3 points on the plane. The aneurysm volume was calculated semiautomatically based on the aneurysm neck plane.

Validation Study. We prepared 4 silicone aneurysm models with known sizes and volumes. The aneurysm models had different shapes: round, with a bleb; conjoined aneurysms (heart-shaped); aneurysm with a daughter sac; and round without bleb (Fig 2).

We compared the ground truth aneurysm volumes with the NV volume measurements and the estimated volumes based on a commonly used approximation formula (AF): \[\text{aneurysm volume} = \frac{4}{3}\pi \times (d_1/2) \times (d_2/2) \times (d_3/2)\], where \(d_1\), \(d_2\), and \(d_3\) are 3 orthogonal measurements denoting aneurysm height, width, and breadth. We calculated the errors of each approach.

Calculation of VER with Use of NV. Coil volume was easily calculated based on the Guglielmi detachable coil (GDC) diameter and length data provided by the manufacturer (Boston Scientific, Natick, Massachusetts), which were preloaded into the NV software. VER was semiautomatically calculated based on the aneurysm volume and the volume of coils used during embolization.

Initial Testing of NV Software in a Clinical Cohort

Patient Population. To assess the value of the measurement parameters provided by the software, we used NV to retrospectively measure aneurysm volume and VER on 3D DSA images from a cohort selected from our institutional data base of patients with cerebral aneurysms who were treated with coil embolization. A total of 295 patients with 308 cerebral saccular aneurysms underwent endovascular embolization with detachable platinum coils at our institution between January 2006 and August 2008. They included 115 patients with 121 unruptured cerebral aneurysms...
treated only with GDC; only patients treated with GDC\ref{3,11} were included in this study because only volume information for this coil was available from the manufacturer. Eighteen of the 115 patients were excluded for either refusing to undergo follow-up angiography or only undergoing MRA follow-up (follow-up rate, 84.35%). Thus, our study cohort included 97 patients with 100 aneurysms treated with GDC who underwent follow-up angiography approximately 1 year after the procedure. There were 72 women and 25 men. The mean age of the patients at the time of treatment was 58.85 ± 11.57 years (age range, 31–83 years). Seventy-eight (78.0%) aneurysms were located in the anterior circulation and 12 (12.0%) in the posterior circulation (Table 1).

### Embolization of Aneurysms

Before embolization, patients underwent 3D DSA by use of a biplane flat detector C-arm angiographic system (Axiom Artis dBA; Siemens, Erlangen, Germany). 3D DSA images were reconstructed on a clinical workstation (syngo XWP VB15B; Siemens) at 256 × 256 image matrix size.

The embolization procedure was performed with the patient under general anesthesia. Systemic heparinization was administered as an initial 3000-U bolus, followed by 1000 U/hour under whole-blood activated clotting time monitoring throughout the procedure. In all patients, systemic heparinization was continued for 24 hours after embolization.

Aneurysms were embolized with GDC coils by packing as densely as possible. The percentage of occlusion at the end of the procedure was evaluated by embolized volume. VER was calculated by use of the following formula: \( \text{VER} = \frac{\text{(volume of the embolization coils)}}{\text{(volume of the aneurysm)}} \times 100 \).

Using the classification schema reported by Raymond et al\ref{15,16} and Roy et al,\ref{16} we categorized the rate of occlusion immediately after initial treatment as measured on angiographic images as: complete occlusion, when the sac and neck were densely packed in any projection; subtotal occlusion (residual neck), when the sac was occluded but there was suspicion of a neck remnant or there was an obvious tiny neck remnant; and partial occlusion (residual aneurysm), when there was loose packing and/or persistent opacification of the sac or neck remnant.

### Table 1: Location of 100 unruptured aneurysms treated with GDC

| Location           | Number |
|--------------------|--------|
| ACA                | 19     |
| AcomA              | 19     |
| Others             | 3      |
| ICA                |        |
| Top                | 6      |
| Anterior choroidal | 5      |
| PcomA              | 23     |
| Paracolmnooid      | 11     |
| Ophthalmic         | 6      |
| Cavernous          | 3      |
| MCA                | 12     |
| Vertebrobasilar system | 5 |
| Tip                | 5      |
| SCA                | 5      |
| Trunk              | 1      |
| PICA               | 1      |
| Total              | 100    |

Note:—ACA indicates anterior cerebral artery; AcomA, anterior communicating artery; PcomA, posterior communicating artery; SCA, superior cerebellar artery.

### Results

#### Validation Study: Silicone Aneurysm Models (AF, NV)

When we compared the accuracy of an AF with that of NV at measuring volume in the 4 silicone aneurysm models, the per-

**Statistical Analysis.** All values were expressed as mean ± standard deviation. The statistical significance of differences in mean value between 2 populations was assessed by use of the Student \( t \) test if variances were equal, as determined by \( F \) value; otherwise, the Welch \( t \) test was used. If population distribution was not a “normal” distribution, we analyzed it by using the nonparametric Mann-Whitney \( U \) test.

A receiver operating characteristic (ROC) curve was used to analyze the effect of varying VER, as a discriminating variable, on embolization outcome (eg, re-treatment vs no re-treatment). The ROC area under the curve (and its 95% CI) was calculated to determine the discriminating level of VER.

The Youden index\ref{17,18} (\( J \)) was defined as the difference between the true-positive rate and the false-positive rate in the outcome variable. Maximizing this index allowed us to find, from the ROC curve, an optimal cutoff point, independently from the prevalence. \( J \) was defined as the maximal vertical distance between the ROC curve and the diagonal or chance line, and it was calculated as \( J = \max(\text{specificity} + \text{sensitivity} - 1) \). With use of this measure, the cutoff point on the ROC curve was selected so that it corresponded to the maximal \( J \).
percentage absolute error for an AF was $23.07\% \pm 17.60\%$ and for NV $4.50\% \pm 3.18\%$, with a maximal percentage absolute error of $45.63\%$ and $8.99\%$, respectively (Table 2; Table 3).

**Clinical Study (NV)**
Using NV, we calculated size and volume measurements for all aneurysms within 1 minute after data input. Mean aneurysm size measurements were height, $6.93 \pm 3.35$ mm; width, $6.07 \pm 2.90$ mm; and neck length, $5.48 \pm 2.27$ mm. Mean aneurysm volume was $280.7 \pm 530.6$ mm$^3$, and mean VER was $24.13\% \pm 5.75\%$.

The VERs by aneurysm location were ICA ($23.34\%$), residual aneurysm in $5$ aneurysms ($5\%$), VER in cases by use of a simple technique ($24.08\%$), and VER in residual aneurysms ($25.20\%$). VER in cases by use of an adjunctive technique was $23.84\%$ and $4.28\%$, respectively (Table 2; Table 3).

**Relationship between Immediate Angiographic Occlusion and VER**
Immediate anatomic outcome on 3D angiography was complete occlusion in $17$ aneurysms ($17\%$), residual neck in $78$ aneurysms ($78\%$), and residual aneurysm in $5$ aneurysms ($5\%$). VER in completely occluded aneurysms (large-volume group, $n = 1$; small-volume group, $n = 16$) was $26.04\% \pm 3.63\%$. VER in aneurysms with residual neck (large-volume group, $n = 25$; small-volume group, $n = 53$) was $24.08\% \pm 5.97\%$. VER in residual aneurysms (large-volume group, $n = 5$) was $18.36\% \pm 4.60\%$.

**Relationship between Use of Simple or Adjunctive Technique and VER**
Coiling by use of an adjunctive technique was performed in $54$ aneurysms (balloon-assisted technique in $46$ aneurysms, double-catheter technique in $8$ aneurysms, and both combined in $3$ aneurysms). VER in cases by use of an adjunctive technique was $24.79\% \pm 6.60\%$, and VER in cases by use of a simple technique was $23.34\% \pm 4.49\%$. There was no statistically significant difference in VER between cases by use of an adjunctive or a simple technique ($P = .41$, Mann-Whitney test).

**Relationship between Aneurysm Volume and VER and Its Impact on Outcome**
There were $31$ aneurysms in the large-volume group, with a VER of $22.76\% \pm 4.38\%$. There were $69$ aneurysms in the small-volume group, with a VER of $22.76\% \pm 4.38\%$. There was no statistically significant difference in VER between the large- and small-volume groups ($P = .12$, Mann-Whitney $U$ test).

In the large-volume group, $19$ aneurysms were stable and had a VER of $23.84\% \pm 4.28\%$, and $12$ aneurysms with recanalization had a VER of $21.05\% \pm 4.13\%$. There was no statistically significant difference in VER between stable and recanalized aneurysms in the large-volume group ($P = .11$ at $t$ test).

Conversely, in the small-volume group, $61$ aneurysms were stable and had a VER of $25.20\% \pm 6.33\%$, and $8$ aneurysms with recanalization had a VER of $21.18\% \pm 3.64\%$. There was a statistically significant difference in VER between stable and recanalized lesions in the small-volume group ($P \leq .01$, Mann-Whitney $U$ test).

**Relationship between Anatomic Follow-Up Results and VER**
Evaluation of anatomic outcomes at 1-year follow-up angiography showed the following: The stable group included $80$ aneurysms, $55$ unchanged and $25$ with further thrombosis ($n = 25$); VER in the stable group was $24.88\% \pm 5.91\%$. The recanalization group (recanalization seen on follow-up angiography before re-treatment decision) included $20$ aneurysms with an overall VER of $21.10\% \pm 3.85\%$. Eight aneurysms in the recanalization group were only observed, as they had minor recurrences that were considered at low risk for rupture (and with a residual space too small to re-treat), and had a VER of $22.00\% \pm 3.57\%$. The re-treatment group included $12$ aneurysms with a VER of $20.50\% \pm 4.06\%$ (Table 4).
The optimal VER cutoff point for recanalization was 25.40% at a VER of 20%. Recanalization alone does not imply the need for re-treatment. However, the cutoff point for re-treatment has not been previously reported in the literature. Our results showed an optimal VER cutoff point for re-treatment of <25% (P = .005). The VER for recanalized aneurysms (recanalization, n = 20) in the same 2 groups were 20.36% ± 4.03% (13 aneurysms) and 22.47% ± 3.31% (7 aneurysms), respectively. In some cases, the use of an adjunctive technique did not influence VER; in the stable group, the 41 aneurysms that were embolized by use of an adjunctive technique had a VER of 26.20% ± 6.67%, and the 39 aneurysms that were embolized with the simple technique had a VER of 23.50% ± 4.70% (P = .08, Mann-Whitney U test).

Although VER is considered a valuable predictor of aneurysm recanalization, this has yet to be verified in a controlled, prospective, multicenter study. The NV volume measurement software may be useful in such a study.
Possibility of Use of Bioactive Coils and Hydrogel-Coated Coils

The development of bioactive coils promises further improvement in the long-term outcome of patients with aneurysms. With these coils, aneurysm occlusion stability may be achievable even at VER of < 25%, and even large aneurysms may become candidates for successful embolization. Watanabe et al have reported the hydrogel-coated coil as being a safe and feasible device for improving the packing efficacy in endovascular coil embolization.

Study Limitations

The major limitation of our study was that it summarized data from a single center with a small number of patients treated and limited validation data from silicone phantom models. We need a multicenter, prospective cohort study with a large number of patients in which to conduct an evaluation of other detachable coils. A multicenter collaborative investigation of the NV software for the evaluation of recanalization of cerebral aneurysms after coil- ing is ongoing in Japan. As a next stage, we are considering the possibility of launching an international cooperative study.

CONCLUSIONS

The NV software provided accurate aneurysm volume measurements, which suggests that NV may be useful as a standardized tool to measure aneurysm size and volume, especially for conducting multicenter clinical studies. In addition to angiographic assessment, measurement of VER may be useful to predict future angiographic changes of aneurysm occlusion.

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