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ANEURYSM SHAPE RECONSTRUCTION FROM BIPLANE ANGIOGRAMS IN THE ISUIA COLLECTION

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Abstract

Background and purpose—The International Study of Unruptured Intracranial Aneurysms (ISUIA) is an epidemiologic international study of the natural history of unruptured intracranial aneurysms that enrolled 4060 subjects. A conventional biplane cerebral angiogram available for central review was required for enrollment resulting in a large database. Data on aneurysms that ruptured during followup of the 1692 untreated subjects provides an opportunity to investigate the anatomic features that may be predictive of future rupture. The objective of the study is to develop

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COMPLIANCE WITH ETHICS REQUIREMENTS

Conflict of interest

- Madhavan Raghavan declares that he has no conflict of interest
- Gaurav Sharda declares that he has no conflict of interest
- John I. Huston III declares that he has no conflict of interest
- J Mocco declares that he has no conflict of interest
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- James C. Torner declares that he has no conflict of interest
- Punam K. Saha declares that he has no conflict of interest
- Irene Meissner declares that she has no conflict of interest
- Robert D. Brown Jr. declares that he has no conflict of interest

Human subjects research

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study.

and test a method for 3D shape reconstruction of aneurysms using biplane angiographic data in the ISUIA for retrospective morphometric assessment.

Materials and methods—Beginning with the two boundaries of the biplane views, curve morphing techniques were employed to estimate a number of intermediate boundaries around the aneurysm sac resulting in the creation of a 3D sac surface. The method was tested using simulated biplane ‘angiograms’ of pre-reconstructed 3D models of patient-specific aneurysms. An algorithm to perform the image analysis was developed and the morphometric indices of 150 intracranial aneurysms in the ISUIA database were estimated. Simultaneously, experienced neuroradiologists made manual measurements of key dimensions in the sac from the biplane angiograms for all cases.

Results—3D reconstructions using our proposed method matched well with the original pre-reconstructed 3D geometries and were consistent with manual measurements of the neuroradiologists for the ISUIA aneurysms.

Conclusion—A method for reconstructing the 3D geometry of the intracranial aneurysm sac from biplane angiograms in the ISUIA database with reasonable fidelity has been developed.

INTRODUCTION

Morphological characteristics of unruptured intracranial aneurysms may be predictive of their risk of growth and/or rupture. Studies that test the correlation between aneurysm morphology and natural history outcome on large longitudinal cohorts are needed. Such studies can also help ascertain which specific morphological characteristics best serve as prognostic indicators. The International Study of Unruptured Intracranial Aneurysms (ISUIA) is an epidemiologic international study of the natural history of unruptured intracranial aneurysms that enrolled 4060 subjects. In ISUIA, bi-plane cerebral angiograms were required for enrollment and forwarded for central review.¹ The study included followup of the 1692 subjects that did not have treatment of their unruptured aneurysm and reported that the size and location of the aneurysms are factors in their rupture risk.² They did not assess what role if any, that aneurysm sac shape characteristics may play in their outcome. The bi-plane angiograms of the aneurysms of this large cohort of study subjects form a valuable resource to further test the potential for shape characteristics to serve as prognostic indicators. The goal of this study was to develop and determine the efficacy of a novel methodology to calculate morphometric characteristics of aneurysms utilizing bi-plane angiographic data collected in the ISUIA. The morphometric characteristics of an intracranial aneurysm are best estimated from its three-dimensional (3D) geometry. Many recent reports have proposed quantitative indices of the 3D aneurysm sac shape that may be estimated by first building 3D models of the aneurysm using image data from volumetric scans such as computed tomography angiography (CTA), magnetic resonance angiography (MRA) or 3D rotational angiography (3DRA).^{3–8} But bi-plane angiograms do not provide all of the information necessary for 3D reconstruction of the aneurysm sac geometry. Nevertheless, it is important not to forsake this important legacy data in ISUIA because they have documented natural history outcomes for very large study populations. While imperfect, bi-plane angiograms do provide information on the essence of the 3D morphology including surface characteristics, shape such as spherical or elliptical and

identify those with daughter sacs or multiple lobulations. If bi-plane information may be used to reconstruct a reasonable three-dimensional geometry of the aneurysm, then additional morphometric characteristics may be calculated and studied in an objective manner.

Methods to reconstruct the 3D surface shape of vascular structures from just cerebral biplane angiograms have been sparsely reported. Coste et al.⁹ and Foroni et al.¹⁰ reported on the reconstruction of the 3D shape of arteriovenous malformations while Bescos et al.¹¹ reported on the 3D reconstruction of cerebral aneurysms from biplane angiograms. The biplane angiograms were presumed to represent two orthogonal silhouettes that are registered in 3D space within an epipolar space. Elliptical cross-sections are interpolated between the two silhouettes at numerous incremented slices along the centerline creating the 3D skeleton of the arteriovenous malformation or aneurysm sac and subsequently, the 3D surface shape. Assumptions in their approach are that the two biplane images are near orthogonal (not always the case in clinical biplane angiograms for aneurysm diagnosis), that they have elliptical cross-sections and that there exists only one closed curve within a cross sectional slice (not true for aneurysms with surface bifurcations such as with daughter sacs or multiple lobulations). These were reasonable assumptions for estimating sac volume in non-undulated shapes, which was the objective for these reported studies. However, these assumptions render this approach unusable for many aneurysms in the ISUIA database including those with irregular shapes or image pairs with more arbitrary relative orientations, and those where the neck is visible along only one of two bi-plane views, which are precisely of interest here. And finally, the ISUIA collection is a set of hard copies of angiograms from 61 clinical centers in the USA, Canada and Europe acquired in the 1990s that lacked the sort of image acquisition information necessary for epipolar registrations and scaling used in these studies. It was therefore necessary to develop an image analysis protocol that accommodated these practical limitations.

We present advances in computational geometric techniques that may be leveraged to reconstruct the 3D surface shape of the aneurysm sac with reasonable fidelity while accommodating considerable variability of shapes and non-orthogonal biplane views that may be expected during biplane angiography. The objective of the study was to (1) develop and test a protocol for the 3D reconstruction of brain aneurysm sac geometry from biplane angiograms; and (2) adopt the approach to suit the demands of the angiographic data collected in ISUIA and compare with manual measurements performed by neuroradiologists.

METHODS

A method was first developed to approximate the 3D surface geometry of an aneurysm sac from the boundaries of the aneurysm sac (the ‘silhouettes’) whose relative orientation in 3D space (epipolar geometric information) is known *a priori*. Subsequently, the method was modified to suit the unique demands of the ISUIA database of biplane angiograms. Modern biplane angiographic data provide the image acquisition parameters necessary for scaling and epipolar registration of the biplane silhouettes. Assuming the epipolar registration of the silhouettes in 3D space is possible, the underlying principle of approach is that the gradual

and smooth evolution of one silhouette to the other must define the 3D surface geometry of the aneurysm sac. The silhouette evolution process is accomplished using a technique called 'curve morphing interpolation' proposed by Sederberg and Greenwood¹² in the computer graphics literature. In brief, Sederberg and Greenwood proposed to find the point-to-point correspondence between any two curves such that the energy required to bend and stretch one into the other is minimized. Their approach is grounded in the mechanics of wire deformation that naturally links corresponding points with similarities in shape features such as the sharp corners at the boundaries of the neck-lines and inflections at daughter sacs. Once the correspondences have been established, any number of intermediate curves may be generated by linear interpolation. A detailed mathematical description of the curve morphing used here may be found in Sederberg and Greenwood¹². The evolved curves may then be placed on a rotational coordinate system about an axis common to the two silhouettes in order to form the skeleton of the aneurysm surface.

The method for image processing and surface development from biplane angiographic data is illustrated in Figure 1. In brief, the digitization of the near-AP and near-LAT silhouettes (Figure 1-A) is followed by registration of these images in 3D space assuming that the silhouettes form the sectional slices at those locations (Figure 1-B). The two curves are divided into four individual half-curves divided at the common axis between the two silhouettes. The transition between the four half-curves modeled with intermediate curves are estimated using a curve evolution algorithm developed by Sederberg and Greenwood.¹² In total, about 90 intermediate curves are generated between the near-AP and near-LAT silhouettes (Figure 1-C). The intermediate curves are placed in 3D space rotated about the common axis between the near-LAT and near-AP silhouettes based on a nonlinear function approximating a sinusoid between the curve increment fraction and the rotational angle increment to form the surface skeleton (Figure 1-D). The aneurysm sac surface is then created by triangulation of the skeleton resulting in a 3D finite element mesh. Noisy sharp corners in the surface are assumed to be artifacts in the reconstruction and these are smoothed using a Taubin non-shrinking smoothing method. The neck plane of the aneurysm sac is then created by slicing this surface with the plane defined by the intersection of the necklines of LAT and AP silhouettes. Where the neck line is visible from only one silhouette, the plane is defined to be orthogonal to that view and defined by only that neck line. If neck plane is invisible or untraceable from both bi-plane views, the aneurysm is excluded from analysis. Although biplane images in the representative example shown are orthogonal (true LAT and AP), the method works as well even if they are not. When non-orthogonal, the LAT and AP lines on the top view (in Figure 1-D) will appear non-orthogonal, but the intermediate curves will permit their reconstruction just as well.

The underlying premise of the proposed protocol is that biplane silhouettes alone may be used to reconstruct the aneurysm geometry with reasonable fidelity. To test this premise, ten patient-specific 3D surface models that had already been reconstructed from traditional volumetric imaging modality data (CTA, MRA) as part of an independent study¹³ were subjected to the proposed protocol. The aneurysms in the test population spanned the typical range of sizes (min, median and max: 1.5, 4, and 15 mm) and shape features (regular, multi-lobed, short neck, long neck) found in the unruptured follow-up cohort. From each 3D surface model, two snap shots were taken from two convenient views to simulate clinical

biplane angiography. They were accurately registered in 3D space because their view angles were known *a priori*. The aneurysm was then reconstructed using just these two silhouettes utilizing the developed protocol. The volume and surface area of the aneurysm surface reconstructed from biplane images were compared with that from the original 3D model reconstructed using volumetric imaging data employing traditional approaches.

The developed protocol was modified in order to use the legacy biplane conventional angiogram image data available in the ISUIA database². While being a unique resource, two key pieces of information were not available on most of the angiograms – the scaling factor and relative positions of the two biplane views. These parameters are required to register the two views in the proposed protocol. Therefore additional steps were incorporated in the protocol. First the neuroradiologist investigators identified and recorded the location of matching landmarks and the relative angle between the biplane views based on cues from the angiographic images such as the center of the neck line and skull landmarks. Next angiographic traces were scaled to dimensions based on the average size of the human adult skull from the lateral and AP views based on the methodology developed for angiographic measurements of the ISUIA aneurysms.¹ Once the two silhouettes were registered in 3D space, the protocol outlined in Figure 1 was followed.

A matlab program was developed to automate the entire process of 3D aneurysm surface shape reconstruction starting with visual digitization of the biplane silhouettes and the identification of the necessary landmarks provided by neuroradiologist investigators. Subsequently, the calculation of metrics of the size and shape of the aneurysm sac were accomplished by methods developed and reported in earlier publications by members of our group^{3,14}. The ISUIA-specific biplane 3D reconstruction protocol was used to reconstruct the 3D geometry of a representative sample of 150 study aneurysms chosen randomly from the ISUIA database. Aneurysm locations included the internal carotid (57), middle cerebral (32), posterior communicating distinct from carotid junction (18), basilar terminal (16), anterior communicating (9), superior cerebellar (4), anterior cerebral (3), posterior inferior cerebellar (3), anterior inferior cerebellar (1), posterior communicating (1) and basilar trunk (1). Five others were excluded because they were regarded as infundibulum (3) or not an aneurysm (2). The aneurysm sizes ranged from 1 to 40 mm with a median of 7mm. In 23 of the 150 aneurysms, the neck of the aneurysm was not identifiable in either of the biplane angiogram views and hence not analyzed. The 3D aneurysm surface was reconstructed for the remaining cases. Morphometric quantities including sac diameter, sac height, volume, surface area, neck diameter and non-sphericity index were calculated³. Independently, two experienced neuroradiologists manually measured the aneurysm sac dimensions from the biplane images along roughly the antero-posterior (*ap*), medial-lateral (*ml*) and cephalo-caudal (*cc*) orientations. In addition, the aneurysm neck size was also measured. The purpose of comparing the 3D model to the Neuroradiologist estimates is not for validation of the 3D model, but rather to assess how consistent the 3D model estimates are with established traditional approaches and identify any major shortcomings in the process. Four size estimates – maximum sac dimension, sac height, neck dimension, and sac volume – were compared between the bi-plane 3D model algorithm and neuroradiologists' measurements (see Figure 4). An earlier report detailed our protocol for estimating sac

diameter (Dmax), height (H) and neck diameter (Dn) using a 3D computer model of the aneurysm sac.³ Maximum sac dimension was defined as the maximum of Dmax and H for the biplane-3D model and maximum of antero-posterior, medial-lateral and cephalo-caudal dimensions for the neuroradiologist measurement. Neck dimension was defined as the average neck diameter for the 3D bi-plane model³ and the neck length measured directly on angiograms to get the neuroradiologist estimate. Volume calculation was by numerical integration for the biplane-3D model³. The neuroradiologist volume estimate was calculated assuming that the sac is a closed ellipsoid defined by the three measured sac dimensions as its axis lengths ($V = \frac{1}{6} \pi [ap][ml][cc]$). In about 10 cases, where only one angiogram was available, the missing third dimension was assumed to be equal to the average of the other two.

RESULTS

The application of the developed protocol on the virtual biplane angiograms from each of the ten pre-reconstructed 3D model aneurysms yielded fairly reasonable 3D reconstructions (see Figure 2). Bi-plane based models retained most all of the key shape characteristics of the aneurysms. The sac volume and surface area of biplane-reconstructed models were consistent with the original models (see Figure 3).

Three-dimensional reconstruction from biplane images from the ISUIA database was completed in all cases analyzed. Four size estimates were compared between the biplane 3D model and neuroradiologist measurements (see Figures 4 and 5). Because the size metrics were all skewed toward lower values, Spearman's rank (ρ) correlation coefficient was used for all comparisons. There was broad agreement in the metrics with high Spearman's rank (ρ) correlations for maximum sac dimension ($\rho=0.90$), sac height ($\rho=0.93$) and neck dimension ($\rho=0.70$). The relatively low correlation for neck dimension was expected given the known difficulty in the 3D reconstruction process to recreate the neck accurately (as illustrated in Figure 2). Distribution of volumes was particularly skewed towards lower values, so aneurysms with less than 500 cubic mm volume (77% of cases) were visualized and also compared in log for all aneurysms ($r=0.86$; $\rho=0.85$) as shown in Figure 5. Although the correlations are high, many cases of significant disagreement do exist. This can be attributed to the fact that the ellipsoidal approximation may not be a reliable method for volume calculations from neuroradiologist measurement of three aneurysm dimensions as pointed out by Pötter et al.¹⁵ and not necessarily to the ability of the biplane 3D model to estimate sac volume accurately.

DISCUSSION

While three-dimensional imaging such as CTA, MRA or 3DRA are becoming the imaging methods of choice, biplane cerebral angiography was historically the only method for the diagnosis and evaluation of intracranial aneurysms and continues to be widely used. Physicians integrate the 3D morphology of the aneurysm sac based on these biplane angiograms and infer the geometry of the aneurysm. Reported methods^{9–11} for quantitatively reconstructing the 3D geometry of the vascular sac from biplane angiograms have been constrained by restrictions that make them difficult for reliable morphometric

estimations in the ISUIA angiographic database. The novel approach presented here leverages advances in computer graphics literature in order to reconstruct an approximation of the 3D morphology while accommodating many of the inherent arbitrariness in aneurysm sac shape and image acquisition.

In principle, the reconstruction is framed as a problem of ascertaining the transition in shape between the near-lateral and the near-AP sections of the surface without major restrictions on their relative orientations, cross-sectional slice shape, presence of multiple lobulations or appearance of the neck. We submit that the optimal transition will be the one that is smooth and accommodates similarities in shape features. The Sederberg-Greenwood method¹² of curve evolution minimizes the energy for stretching and bending of one curve on to the other based on wire deformation mechanics. Theirs was a convenient approach to attain our objective of identifying the intermediate curves that smoothly transition from one biplane silhouette to the other. The proposed method of reconstruction accommodates irregular shape characteristics, non-elliptical cross-sections, non-orthogonal biplane views and can even seamlessly incorporate and improve with multiple additional views as well. Our approach may be framed as an attempt to ascertain, however approximately, the silhouettes of the aneurysm sac that one may expect to see during sequential frames obtained during rotational angiography. Only here, we seek to estimate these silhouettes with just biplane images. The results of the validation study with pre-reconstructed 3D models comparing known to newly computed volumes and surface areas suggest that the developed protocol does indeed result in a fairly accurate approximation of the original surface shape. This is consistent with the fact that physicians have long used just biplane views to infer the geometry of the aneurysm, save some rare irregular cases. Still, we acknowledge that we have stopped short of true validation. Validating our methodology against 3DRA-based reconstructions is certainly better, but even that would not account for the sources of error from the use of hard-copy angiograms and assumptions on scaling and orientation. In essence, this represents a systemic challenge in any study that attempts to look back retrospectively to analyze legacy data from decades past. That aside, we have further demonstrated that this method may be used to analyze a large cohort of angiograms from the ISUIA database and in the process, refine our algorithms and approaches for consistency and accuracy to the extent possible. The comparisons of the reconstructed and the neuroradiologists' measurements for this large cohort of study subjects suggest that the proposed method while sophisticated, is consistent with traditional measurement techniques as well.

The application of this protocol to the ISUIA biplane angiograms allow us to test important hypotheses on the potential relationship between morphological characteristics and rupture or growth risk for these aneurysms beyond maximum diameter and location. However, the ISUIA data does require additional assumptions including those on scaling and view orientations. For these features, tracing of the aneurysm boundary and the identification of landmarks on the angiograms for registration of the biplane views with adjudication where necessary was required. Incorporating these features allowed an automated algorithm to calculate the morphometric indices on a large population of aneurysms in the ISUIA database.

Despite many of the advances proposed, it is important to recognize the pitfalls of the proposed method. Although biplane angiograms capture the essence of the aneurysm surface shape, they do not capture all of it. Therefore, the reconstructed surface is always only an approximation. A truly orthogonal biplane angiogram taken in such a manner that at least one view captures the most irregular shape feature – if any – of the aneurysm sac is likely to result in an optimal approximation of the true 3D geometry. Accuracy of reconstruction drops as the biplane angiograms deviate from this. Often neuroradiologists perform multiple views during biplane angiograms because it offers better documentation of the sac morphology. One unstated assumption in the proposed protocol is that the biplane silhouettes are the sectional views at their locations. This may not be the case in highly irregular aneurysms and may cause some error. Visual comparisons between the biplane-based models with the original pre-reconstructed 3D models reveal that the former sharpens the shape of daughter sacs. This is likely a result of the silhouette-as-sectional view assumption. Poor formation of neck plane profile was also noted in some cases, but comparison of neck diameter with neuroradiologists' measurements (Figure 4) suggests this may not be widespread. Nevertheless, this should be of concern given that neck dimension is a determinant of metrics such as aspect ratio^{16,17} and bottleneck factor^{3,18} that may be of interest as a risk factor for rupture. The scope for error increases to some extent in the adoption of this proposed method to ISUIA database owing to inevitable additional assumptions on scaling and orientation. Errors in scaling may affect the size metrics of the morphology, but are unlikely to have a major impact on the shape metrics. For orientation and picking of landmarks, the role of experienced neuroradiologists likely mitigates the scope of this error. Nevertheless, these remain causes for some concern. It is therefore possible, in some cases, for surface reconstructions using our method to not do justice to the true aneurysm geometry in a subject because either the biplane views do not capture the essential geometric features in the aneurysm or errors in visual registration and scaling combine to misrepresent the shape. And finally, we did not attempt to reconstruct parent vessels given the focus on the sac in this effort although neuroradiologist measurements of their dimensions have been documented. As a result, estimates of metrics such as size ratio (ratio of aneurysm dimension to parent vessel dimension^{4,18–20}) are performed independent of this proposed methodology.

CONCLUSION

A methodology for rapidly generating 3D models of brain aneurysms starting with visual tracings of hard copy biplane angiograms documented in the ISUIA database has been developed and demonstrated. In developing this methodology, we believe that we have made reasonable compromises within the constraints of the data collected. It is important to realize in this context that the ISUIA database provides us some unique and highly valuable data – both on morphology and on longitudinal clinical outcome. The size of the study population has already made the ISUIA findings the primary driver of clinical practice in the management of patients with aneurysms around the world. The proposed protocol that we have developed and demonstrated may help us leverage this key data for performing retrospective assessment with a reasonable fidelity of the role of morphology in the natural history of unruptured intracranial aneurysms.

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Figure 1.
Illustration of image analysis protocol for reconstruction of the 3D surface shape of intracranial aneurysm sac from biplane angiographic data.

Figure 2.

Comparisons of aneurysm surfaces reconstructed from a pair of biplane silhouettes and the original models from which the silhouettes were obtained. The biplane-based models retained key shape characteristics of the multilobular PCOM and ACA aneurysms. Note however that the daughter sacs are less round in the biplane-based models (view 2). Further, the neck plane reconstructions are not as rounded and appear underestimated compared to the original surfaces (view 4).

Figure 3.

Comparison of aneurysm sac volume and surface area between original 3D models and the models reconstructed using just the biplane views based on proposed protocol.

Figure 4.

Comparison of sac maximum dimension, sac height and neck dimensions estimated from the biplane 3D reconstruction algorithm with those measured by neuroradiologist investigators.

Figure 5.

Comparison of sac volume estimated from biplane 3D reconstruction algorithm with that calculated based on an ellipsoid approximation using antero-posterior, medial-lateral and cephalo-caudal dimensions measured by neuroradiologists. Since volumes are skewed toward lower values, they are shown for the bottom three quartiles and in log.