Ruptured Status Discrimination Performance of Aspect Ratio, Height/Width, and Bottleneck Factor Is Highly Dependent on Aneurysm Sizing Methodology

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BACKGROUND: Numerous size and shape parameters have historically been used to describe cerebral aneurysms and to correlate rupture status. These parameters are often inconsistently defined.

OBJECTIVE: To evaluate the impact of definition variation on rupture status detection performance.

METHODS: Catheter rotational angiographic data sets of 134 consecutive aneurysms (60 ruptured) were automatically measured in 3 dimensions with a validated algorithm. According to the literature, aneurysm height was assessed as both maximal and orthogonal distances from dome to neck. Maximal and orthogonal widths were defined perpendicular to height definitions. Neck size was evaluated as minimum, maximum, and average diameter of the neck plane. Aspect ratio (AR; height/neck), height/width ratio (HW), and bottleneck factor (BNF; width/neck) were evaluated for alternative definitions of each size variable. Univariate statistics were used to identify significant features and to compute the area under the curve (AUC) of the receiver-operating characteristic.

RESULTS: The AR, HW, and BNF showed significant dependence on parameter definition. Statistical significance and performance varied widely, depending on alternative definitions: AR, AUC range of 0.59 to 0.75; HW, AUC range of 0.48 to 0.72; and BNF, AUC range of 0.57 to 0.72. Using maximal height, orthogonal width, and minimum neck resulted in the best AR, HW, and BNF performances. Compared with HW, AR and BNF were less sensitive to alternative definitions.

CONCLUSION: Alternative aneurysm size definitions have a significant impact on prediction performance and optimal threshold values. Adoption of standard methodology and sizing nomenclature appears critical to ensure rupture detection performance and reproducibility across studies.

KEY WORDS: Aneurysm shape, Aneurysm size, Aspect ratio, Height-width, Intracranial aneurysm, Morphology, Rupture risk

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ABBREVIATIONS: AR, aspect ratio; **AUC,** area under the curve; **BNF,** bottleneck factor; **Dmax,** aneurysm size; **Hdepth,** aneurysm maximal depth; **Hmax,** aneurysm maximal height; **Hortho,** aneurysm orthogonal height; **HW,** height/width ratio; **ICC,** intraclass correlation coefficient; **Navg,** average neck size; **Nmax,** neck maximal width; **Nmin,** neck minimal diameter; **Wmax,** aneurysm maximal width; **Wortho,** aneurysm orthogonal width

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Reportedly, between 2% and 6% of the general population harbors intracranial aneurysms,[1,2] the large majority of which are asymptomatic and remain undetected. Although the annual risk of rupture[3,4] of asymptomatic unruptured intracranial aneurysms has been variably estimated as high as 1% to 2% to as low as 0.1% to 0.2%, aneurysmal subarachnoid hemorrhage still carries high mortality and morbidity rates.[5,6] The increasing use of computed tomography and magnetic resonance angiography imaging in the outpatient setting has led to an

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increased detection of incidental, asymptomatic unruptured intracranial aneurysms.[7]

The ability to assess rupture likelihood of any given unruptured intracranial aneurysm is of great clinical value and represents the focus of many prospective and retrospective studies. In 2 analyses of the International Study of Unruptured Intracranial Aneurysms,[4,8] aneurysm size was identified as important, with a threshold of 7 to 10 mm proposed for considering aggressive therapy. However, although there is agreement that size plays a role in the rupture phenomenon, there seems to be no standard definition on measuring the size of an aneurysm (see Supplemental Digital Content 1, http://links.lww.com/NEU/A439, which details the use of alternative definitions in existing rupture analysis literature).

Although some studies measure size as the maximal dimension of the aneurysmal dome,[9,10] others consider the maximal projection from the aneurysm dome to the neck plane[11,12] or the maximal longitudinal diameter parallel to the neck plane.[13-15] Related to size, the height of the dome is another measure routinely evaluated for aneurysm rupture risk assessment. As with size, there is no unique definition of the aneurysm height, which is variably defined as the maximal dimension from the neck to the aneurysm dome,[9,16-18] the maximal projection from the aneurysm dome to the neck plane,[11-14] or the maximal orthogonal distance from the neck to aneurysm dome.[19,20] The definition of height influences the measurement of aneurysm width, a parameter defined as orthogonal to height. The size of the aneurysm neck, describing the attachment site where the aneurysmal sac pouched outward from the parent vessel, is also variably defined as either the maximum diameter[10,16,17] or the average diameter[11,12,14] of the neck region. In a chain reaction, the variable definitions of the aneurysm height, width, and neck affect the definition of complex parameters such as aspect ratio (AR; height-to-neck ratio), height/width ratio (HR), and bottleneck factor (BNF; width-to-neck ratio). In addition, more often than not, the exact definitions and protocols used for size measurements are not included in the methods description. This lack of detail and consistency of definition makes the interpretation of results across multiple studies difficult and unreliable and may explain the contradictory results reported in the literature regarding the performance of these parameters.

The actual measurement of aneurysm size parameters is still performed manually from 2-dimensional or 3-dimensional (3D) images.[17,18,20,21] Although established research groups use in-house tools for automatic measurements,[11,14] little work has been done toward an automated, validated measurement tool with documented reliability and robustness performance. With the availability of increasingly large data sets, the manual evaluation of aneurysm measurement—a time-consuming process requiring trained medical operators—can become more difficult and less consistent.

The objective of the present study is 2-fold. The first objective is to introduce a tool for automated measurement of size and shape parameters related to intracranial aneurysms having clear, unambiguous definitions for each measure. The second is to provide a retrospective statistical analysis for rupture status discrimination using automated measured parameters on a large patient-derived aneurysm data set to evaluate and discuss the statistical implications of using variable definitions (as encountered in the literature) for aneurysm size, height, width, and neck.

MATERIALS, PATIENTS, AND METHODS

Patient Selection and Demographics

Consecutive high-resolution 3D angiographic data of patients with intradural intracranial aneurysms diagnosed over a 4-year period were reviewed for this study. Fusiform, mycotic, and extradural aneurysms were excluded, the latter because of their known different natural history and low risk of subarachnoid hemorrhage.[22] Similar to other studies,[11] only cases in which the rotational angiographic images were of sufficient quality for accurate segmentation and reconstruction were included in this study by a process blinded to rupture status. A total of 134 aneurysms in 115 patients met the criteria. Aneurysm rupture status was labeled by the treating clinicians at the time of presentation, with a total of 60 aneurysms labeled as ruptured.

Cerebral Angiography and Data Processing

We obtained 3D catheter-based cerebral angiograms using a calibrated biplane system with volume reconstructions performed to yield a 3D volumetric data set (Figure 1A and 1B). Vessel segmentation was performed with a level-set algorithm based on the open-source Insight Segmentation and Registration Toolkit (version 3.20) libraries. The segmented volume was then analyzed in the Amira scientific visualization software (version 5.1; Visage Imaging, San Diego, California). For each set, the aneurysm dome was isolated from the surrounding vessels and represented as a 3D triangular mesh model (Figure 1C). A corresponding neck plane was defined for each aneurysm and was similarly represented as a 3D triangular mesh model. Similar to other studies in the field,[12,14] the aneurysm neck plane was selected to the best of our ability at the location where the aneurysmal sac protruded outward from the parent vessel.

Manual Morphological Feature Extraction

For validation, 30 of the 134 aneurysms (12 ruptured) were randomly selected to undergo manual measurement by 3 trained operators using the Amira 3D measurement tool. The operators were blinded to each other's results, the automated measurement values, and the aneurysm rupture status. The operators were provided with the following definitions of the measurements to be performed (Figure 2): Aneurysm size (Dmax) is the largest distance between any 2 points on the aneurysm surface that could be fitted inside the dome. Points that overflow the neck plane are to be ignored. Aneurysm maximal height (Hmax) is the largest distance between the neck center and aneurysm surface that could be fitted inside the dome. This distance is not necessarily orthogonal to the neck plane. The neck center is the centroid (geometric center) of the neck region. Aneurysm maximal depth (Hdepth) is the largest orthogonal distance from the neck to the aneurysm dome. Aneurysm maximal width (Wmax) is the largest distance orthogonal to the maximal height. This is the maximum diameter along all cross sections orthogonal on the aneurysm maximal height. Aneurysm orthogonal width (Wortho) is the largest orthogonal distance parallel to the neck plane. This is the maximum diameter along all orthogonal cross sections. Neck maximal width (Nmax) is the largest distance between any 2 points on the aneurysm neck plane. Finally,

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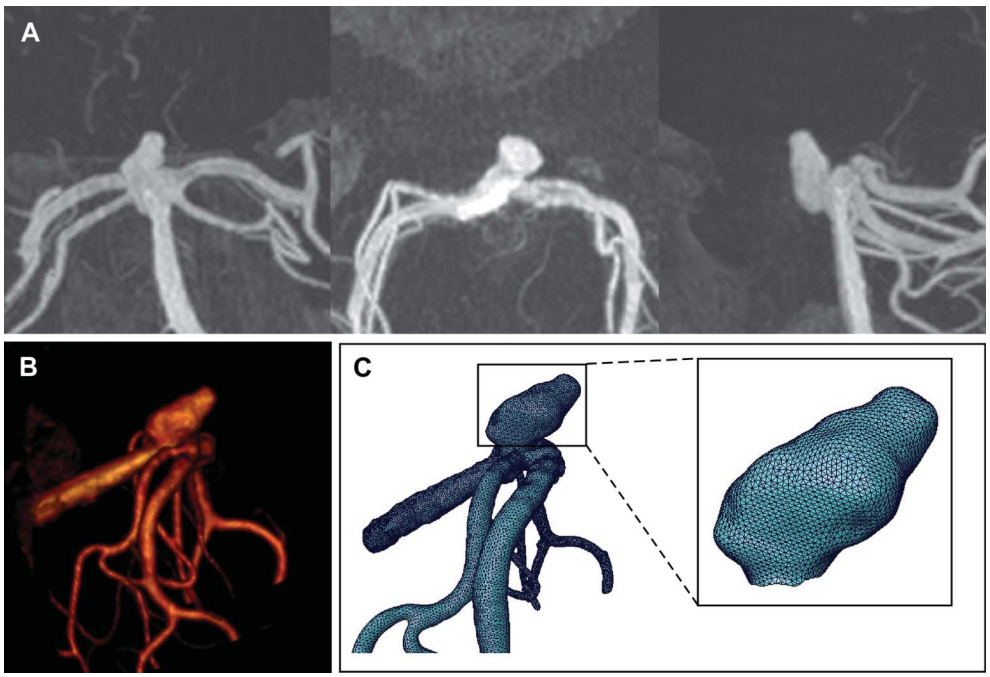


FIGURE 1. *Segmentation and isolation of aneurysms using catheter-based high-resolution 3-dimensional (3D) rotational angiography.* **A**, *maximal intensity projection of the reconstructed 3D volumetric data set in the axial, coronal, and sagittal projections showing a ruptured basilar artery aneurysm.* **B**, *3D volumetric rendering.* **C**, *segmentation of the vascular structure from surrounding tissue and representation of the surface as a triangular mesh.*

neck minimal diameter (Nmin) is the minimum diameter of the aneurysm (constrained to pass through the neck centroid).

Automatic Morphological Feature Extraction

The tool for automated size and shape measurements was coded in Matlab (version 7.10; MathWorks, Natick, Massachusetts). For each aneurysm, the tool requires as input two 3D triangulated surface files (in .STL file format) representing the dome and the corresponding neck plane. A third definition for height, the aneurysm orthogonal height (Hortho), is computed as the maximal projection of the dome to the neck plane (Figure 2). The average neck size (Navg) is computed as twice the average distance from the neck centroid to the neck border.[11] Hortho and Navg require automated measurement and cannot be evaluated manually.

To assess the effect of definition variation on more complex parameters, AR, HW, and BNF are described by 3 alternative definitions for aneurysm height (Hmax, Hortho, and Hdepth), 2 for aneurysm width (Wmax and Wortho), and 3 for aneurysm neck (Nmax, Nmin, and Navg). More specifically, this resulted in 3 HW alternative definitions (Hmax/Wmax, Hortho/Wortho, and Hdepth/Wortho) and 6 BNF definitions (Wmax/Nmax, Wmax/Nmin, Wmax/Navg, Wortho/Nmax, Wortho/Nmin, and Wortho/Navg). AR, described with 3 definitions for height and 3 definitions for neck size, resulted in 9 alternative definitions (Hmax/Nmax, Hmax/Nmin, Hmax/Navg, Hortho/Nmax, Hortho/Nmin, Hortho/Navg, Hdepth/Nmax, Hdepth/Nmin, and Hdepth/Navg).Note that the AR, BNF, and HW definitions evaluated in this study do not reflect all possible permutations but rather alternative definitions actually reported in the relevant literature (see Supplemental Digital Content 1). Although Nmax and Navg are alternatively used in the literature for defining AR and BNF, we also explore here the potential utility of using Nmin for the same purpose.

Statistical Analysis

The automated measurement tool was validated against 3 medical operators. The interobserver variability (3 observers, 30 measurements each) and the statistical correlation between automated and manual measurements (3 manual + 1 automated observer, 30 measurements each) were analyzed with the intraclass correlation coefficient (ICC)[23,24] for 7 size parameters (Dmax, Nmax, Nmin, Hmax, Hortho, Wmax, and Wortho). The ICC is a statistical measure used to estimate methodological reliability and reproducibility. The ICC takes values between 0 and 1; higher values mean higher agreement between sets of observations. More specifically, correlation values < 0.40 represent poor reliability, values from 0.40 to 0.75 represent fair to good reliability, and values > 0.75 represent excellent reliability.[25]

JMP statistical software (version 8.02; SAS Institute, Cary, North Carolina) was used to evaluate the performance of parameters in rupture status discrimination. Statistical significance was assumed for values of $P < .05$. All variables were tested independently with the Student t test.

RESULTS

Demographics and Presentation

A total of 134 aneurysms in 115 patients (83 women) with a mean age of 56 years (range, 24-89 years) were analyzed, with

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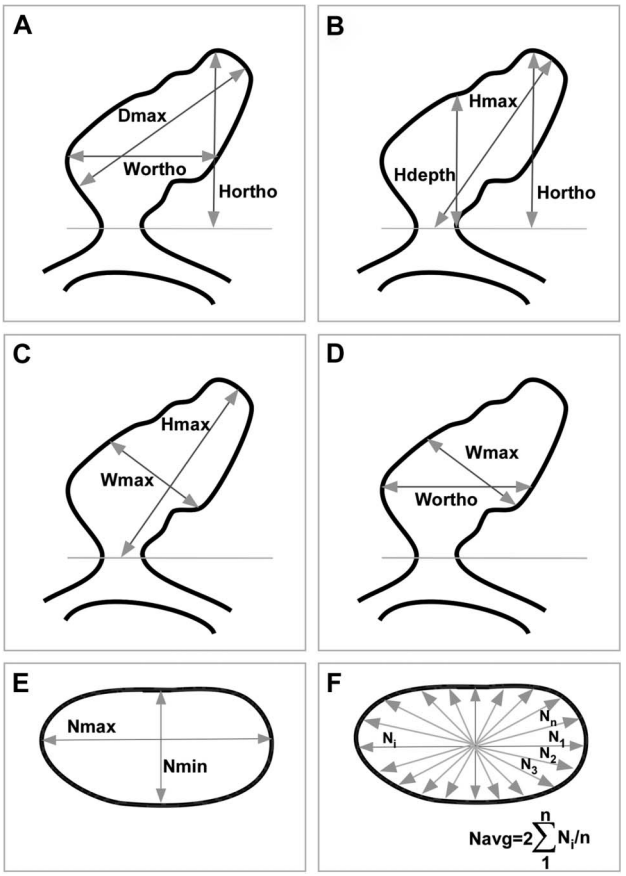


FIGURE 2. *Size and height measurement in 3-dimensional space. Neck plane is shown as a thin horizontal line.* **A**, *aneurysm size is variably defined as maximal diameter of the dome (Dmax), maximal orthogonal projection of the dome to the neck plane (Hortho), or maximal longitudinal diameter parallel with the neck plane (Wortho).* **B**, *aneurysm height is variably defined as maximal distance from the neck to aneurysm dome (Hmax), maximal orthogonal distance from aneurysm dome to the neck plane (Hortho), or maximal orthogonal distance from the neck to aneurysm dome (Hdepth).* **C**, *maximal width (Wmax) is measured orthogonal to maximal height (Hmax).* **D**, *maximal width (Wmax) and orthogonal width (Wortho) represent separate measurements.* **E**, *maximal neck width (Nmax) and minimal neck width (Nmin) are measured from the neck cross section.* **F**, *average neck size (Navg) is twice the average distance from the neck centroid to the neck border.*

60 classified as ruptured (44.7%). Aneurysm location was as follows: posterior communicating artery (31), anterior communicating artery (28), internal carotid artery (22), middle cerebral artery (22), ophthalmic artery (10), basilar artery (8), anterior choroidal artery (6), vertebral artery (3), superior cerebellar artery (2), posterior cerebral artery (1), and posterior inferior cerebellar artery (1).

Automated Measurement Validation

The validation analysis (Table 1) showed that manual interobserver ICC is comparable to manual-automated ICC for all parameters studied (average manual ICC, 0.94 ± 0.04 vs 0.93 ± 0.04 average manual-automated ICC). In both manual and manual-automatic cases, best ICC values are achieved for neck measurements (≈ 0.99), whereas lowest correlation (≈ 0.90) was seen for width measurements. This is expected because neck measurements are performed on a 2-dimensional plane, whereas width measurements are performed in 3D space and are further dependent on height measurement. All correlation values, including 95% confidence intervals, are > 0.75, consistent with excellent reliability and reproducibility.

TABLE 1. Automatic Measurement Validation Using Intraclass Correlation Coefficient[a]

	Interobserver ICC	Automated-Manual ICC
Dmax	0.97 (0.94-0.99)	0.97 (0.95-0.99)
Nmax	0.99 (0.98-0.99)	0.99 (0.98-0.99)
Nmin	0.99 (0.98-0.99)	0.99 (0.98-0.99)
Hmax	0.98 (0.94-0.99)	0.97 (0.96-0.99)
Hortho	0.92 (0.79-0.96)	0.90 (0.85-0.97)
Wmax	0.89 (0.80-0.96)	0.91 (0.83-0.97)
Wortho	0.90 (0.75-0.95)	0.88 (0.81-0.96)

[a]Dmax, maximal diameter of the dome; Hmax, maximal distance from the neck to aneurysm dome; Hortho, maximal orthogonal projection of the dome to the neck plane; ICC, intraclass coefficient; Nmax, maximal neck width; Nmin, minimal neck width; Wmax, maximal width; Wortho, maximal longitudinal diameter parallel with the neck plane. Comparison with interobserver correlation. Values are given as means (95% confidence interval).

Univariate Size Parameters Analysis

Results of the univariate statistical analysis using size parameters are shown (Table 2) for Dmax, Hmax, Hortho, Hdepth, Wmax,

TABLE 2. Univariate Analysis Results for the Size Parameters Examined (Size, Height, Width, Neck)[a]

Feature	Ruptured Mean	Unruptured Mean	*P*	AUC
Dmax	9.05 ± 4.00	6.90 ± 2.78	<.001[b]	0.67
Hmax	7.41 ± 3.55	5.36 ± 2.37	<.001[b]	0.68
Hortho	6.36 ± 3.22	4.90 ± 2.22	.002[b]	0.64
Hdepth	5.76 ± 2.88	4.72 ± 2.15	.02	0.60
Wmax	6.33 ± 2.93	5.55 ± 2.16	.07	0.57
Wortho	7.46 ± 3.38	6.05 ± 2.38	.005[b]	0.63
Nmax	4.60 ± 1.66	4.42 ± 1.68	.53	0.54
Nmin	3.37 ± 1.22	3.54 ± 1.35	.46	0.53
Navg	3.97 ± 1.38	3.96 ± 1.46	.98	0.50

[a]AUC, area under the curve; Dmax, maximal diameter of the dome; Hdepth, maximal orthogonal distance from the neck to aneurysm dome; Hmax, maximal distance from the neck to aneurysm dome; Hortho, maximal orthogonal projection of the dome to the neck plane; Navg, average neck size; Nmax, maximal neck width; Nmin, minimal neck width; Wmax, maximal width; Wortho, maximal longitudinal diameter parallel with the neck plane. Values are given as mean ± SD. Rupture status discrimination performance is quantified by the AUC measure.
[b]Significant.

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Wortho, Nmax, Nmin, and Navg. Dmax was statistically significant ($P < .001$; AUC = 0.67) in discriminating between ruptured (9.05 ± 4.0 mm) and unruptured aneurysms (6.90 ± 2.78 mm). Hmax was statistically significant ($P < .001$; AUC = 0.68) in discriminating rupture status (ruptured, 7.41 ± 3.55 mm vs unruptured, 5.36 ± 2.37 mm). Hortho ($P = .002$; AUC = 0.64) and Hdepth ($P = .02$; AUC = 0.60) were found to discriminate rupture status, although with lower performance compared with Hmax. Wmax was not statistically related to rupture status ($P = .07$; AUC = 0.57), in contrast to Wortho ($P = .005$; AUC = 0.63). Regardless of definition, the size of the neck was not found to be statistically significant for rupture status discrimination.

All AR definitions achieved statistical significance but with a wide performance range, as quantified by AUC values (Table 3). AR defined with maximal height and minimum neck (Hmax/Nmin) was the best performer ($P < .001$; AUC = 0.75) in discriminating between ruptured and unruptured aneurysms (2.24 ± 0.97 vs 1.58 ± 0.66). AR defined as Hdepth/Nmax had the worst performance ($P = .04$; AUC = 0.59). In general, AR definitions using Hmax performed better compared with using Hortho, which in turn performed better compared with using Hdepth. Similarly, using Nmin increased AR performance compared with using Nmax and Navg. The AR using Navg performed better than AR using Nmax. The receiver-operating characteristic plots illustrated in Figure 3A highlight the wide range of AR definition performance.

HW defined as Hmax/Wmax was statistically significant ($P < .001$; AUC = 0.72) in differentiating rupture status (1.19 ± 0.33 ruptured vs 0.97 ± 0.25 unruptured; Table 3). In contrast, both Hortho/Wortho ($P = .16$; AUC = 0.56) and Hdepth/Wortho ($P = .78$; AUC = 0.48) failed to achieve univariate statistical significance. The receiver-operating characteristic plots illustrated in Figure 3B show the difference in performance for the 3 HW definitions.

All BNF definitions except Wmax/Nmax ($P = .07$) achieved statistical significance in rupture status discrimination (Table 3). BNF defined as Wortho/Nmin ($P < .001$; AUC = 0.72) showed the best performance. In general, using Wortho resulted in a better BNF performance compared with using Wmax. Similarly, using Nmin increased BNF performance compared with using Nmax and Navg. BNF using Navg performed better than BNF using Nmax (Figure 3C).

DISCUSSION

Impact of Alternative Size Definitions on Rupture Analysis

Parameters describing the geometry and morphology of intracranial aneurysms have been used in prospective and retrospective studies and in clinical practice to describe the ruptured status of an aneurysm, to extrapolate the risk of rupture, and to determine the benefit of treatment vs observation. Given the clinical value of finding reliable risk predictors for aneurysm rupture, the historical

TABLE 3. Results From Univariate Analysis for Aspect Ratio, Height/Width, and Bottleneck Factor[a]

Feature	Definition	Ruptured Mean	Unruptured Mean	*P*	AUC
Aspect ratio	Hmax/Nmax	1.64 ± 0.71	1.25 ± 0.48	<.001[b]	0.69
	Hmax/Nmin	2.24 ± 0.97	1.58 ± 0.66	<.001[b]	0.75
	Hmax/Navg	1.89 ± 0.81	1.39 ± 0.54	<.001[b]	0.71
	Hortho/Nmax	1.41 ± 0.55	1.14 ± 0.45	.005[b]	0.64
	Hortho/Nmin	1.92 ± 0.89	1.45 ± 0.63	<.001[b]	0.69
	Hortho/Navg	1.62 ± 0.74	1.27 ± 0.51	.002[b]	0.66
	Hdepth/Nmax	1.27 ± 0.55	1.09 ± 0.41	.04[b]	0.59
	Hdepth/Nmin	1.72 ± 0.73	1.39 ± 0.58	.004[b]	0.66
	Hdepth/Navg	1.46 ± 0.62	1.22 ± 0.47	.01[b]	0.62
Height/width	Hmax/Wmax	1.19 ± 0.33	0.97 ± 0.25	<.001[b]	0.72
	Hortho/Wortho	0.87 ± 0.28	0.81 ± 0.21	.16	0.56
	Hdepth/Wortho	0.79 ± 0.26	0.78 ± 0.19	.78	0.48
Bottleneck factor	Wmax/Nmax	1.39 ± 0.45	1.27 ± 0.31	.07	0.57
	Wmax/Nmin	1.88 ± 0.59	1.60 ± 0.42	.002[b]	0.66
	Wmax/Navg	1.59 ± 0.48	1.41 ± 0.34	.01[b]	0.61
	Wortho/Nmax	1.64 ± 0.57	1.37 ± 0.32	.001[b]	0.64
	Wortho/Nmin	2.23 ± 0.76	1.72 ± 0.45	<.001[b]	0.72
	Wortho/Navg	1.88 ± 0.63	1.53 ± 0.36	<.001[b]	0.68

[a]AUC, area under the curve; Dmax, maximal diameter of the dome; Hdepth, maximal orthogonal distance from the neck to aneurysm dome; Hmax, maximal distance from the neck to aneurysm dome; Hortho, maximal orthogonal projection of the dome to the neck plane; Navg, average neck size; Nmax, maximal neck width; Nmin, minimal neck width; Wmax, maximal width; Wortho, maximal longitudinal diameter parallel with the neck plane. The alternative definitions used are shown in the second column. Values are given as mean ± SD. Rupture status discrimination performance is quantified by the AUC measure.
[b]Significant.

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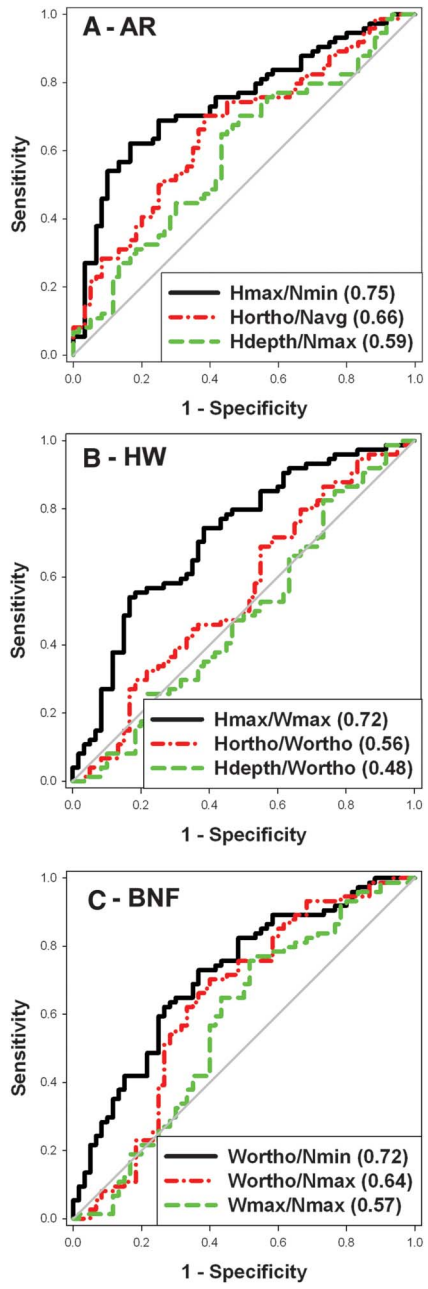


FIGURE 3. *Receiver-operating characteristic analysis. Area under the curve values are shown in parentheses. Alternative definitions for (A) aspect ratio (AR), (B) height/width (HW), and (C) bottleneck factor (BNF) are shown. Hdepth, maximal orthogonal distance from the neck to aneurysm dome; Hmax, maximal distance from the neck to aneurysm dome; Hortho, maximal orthogonal projection of the dome to the neck plane; Navg, average neck size; Nmax, maximal neck width; Nmin, minimal neck width; Wmax, maximal width; Wortho, maximal longitudinal diameter parallel with the neck plane.*

lack of consistency in definition of aneurysm size and shape parameters is surprising.

Indeed, there seems to be no standard definition even for the aneurysm size, the most ubiquitous parameter used in rupture risk assessment. Aneurysm size has been variably defined in the literature as Dmax, Wortho, or Hortho. The 3 alternative definitions for size are illustrated in Figure 2A. Although it is true that in our analysis (Table 1) all 3 parameters were statistically significant in discriminating rupture status, albeit with some differences in performance (Dmax being the best performer), these are not interchangeable definitions. Using Dmax definition resulted in a mean size for ruptured aneurysms of 9.05 ± 4.00 mm compared with 7.46 ± 3.38 mm using Wortho and 6.36 ± 3.22 mm with Hortho. This is consistent with the reports of Baharoglu et al[9] (mean Dmax size, 9.1 ± 3.7 mm), Joo et al[15] (mean Wortho size, 6.28 ± 5.08 mm), and Dhar et al[11] (mean Hortho size, 5.5 ± 1.9 mm). Although all these studies refer to aneurysm size, they each use a completely different geometric measure. Such inconsistent use under the same name makes it difficult to establish a reliable size threshold for rupture prediction across studies. In the present study, receiver-operating characteristic analysis identified optimal threshold values for rupture prediction as 7.33 mm using Dmax, 7.71 mm using Wortho, and 5.43 mm using Hortho. The optimal threshold values for Dmax and Wortho are similar to those proposed by the International Study of Unruptured Intracranial Aneurysms[4,8] (7-10 mm), in contrast to Hortho.

Similar to size, aneurysm height was described by 3 different definitions as Hmax, Hortho, or Hdepth (Figure 2B). This figure suggests that Hdepth and, to some extent, Hortho fail to describe the salient features of complex shaped and especially tilted aneurysms. In this study, all height definitions achieved statistical significance in discriminating rupture status, with Hmax outperforming Hortho and Hdepth (Table 2). Alternative definitions of height affect the definition of aneurysm width, constrained to be orthogonal to height and thus defined as either Wmax or Wortho (Figure 2C and 2D). Only Wortho achieved statistical significance, suggesting that the orientation of Wortho, orthogonal to the blood flow and parallel to the neck, is relevant for rupture status discrimination. The geometric relation between the aneurysm neck and the aneurysm width is reflected by BNF, and as expected, BNF defined using Wortho outperformed definitions using Wmax, regardless of the neck size used (Table 3).

It has been hypothesized[16,26] that intra-aneurysmal flow velocity can affect aneurysm evolution and rupture and is inversely related to rupture likelihood. AR inversely correlates with flow velocity because a deep dome with a narrow neck is characterized by slow intradome flow and low shear stress.[26] Figure 2B illustrates how, compared with Hortho and Hdepth, Hmax can better detect the presence of deeper distal dome regions characterized by lower shear stress and its associated greater risk of aneurysm wall degeneration. Indeed, AR defined as Hmax/Nmin outperformed all other AR definitions (Table 3)

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and was the best parameter evaluated in this study (AUC = 0.75). Although Nmax is often used to describe aneurysm neck size, it does not convey information about possible narrow neck regions, which would affect intradome flow velocity. Consequently, AR defined using Nmin and Navg outperformed AR using Nmax, regardless of height definition. These results delineate the importance of the neck measurement technique and are especially relevant when the latter is made from biplane angiography in which the value is highly dependent on the projection used. The utility of AR and its optimal threshold value for rupture prediction has been controversial.[16,27] In the present study, mean AR value for ruptured aneurysms varied between 1.27 $\pm$ 0.55 and 2.24 $\pm$ 0.97, depending on the definition used. This finding is consistent with the wide range for mean ruptured AR values reported in the literature by Prestigiacomo et al[20] (1.36 $\pm$ 0.66), Dhar et al[11] (1.5 $\pm$ 0.45), Yasuda et al[28] (1.8 $\pm$ 0.8), and Hoh et al[10] (2.39 $\pm$ 0.74). Our results suggest that the wide variability and potential disagreement regarding AR utility may be at least partly the result of the undocumented effect of its variable definition.

Regarding HW, we found that only HW defined using Hmax was statistically correlated to rupture status. This may explain why studies using Hortho and Hdepth do not evaluate HW or fail to report statistical significance. In contrast, in our analysis, HW defined as Hmax/Wmax was one of the best parameters evaluated (AUC = 0.72). Given the results of AR and HW analysis, Hmax definition emerges as the most useful method of describing aneurysm height. It should be noted that compared with HW, AR seems more robust to alternative height definitions; AR was statistically significant regardless of the height and neck definitions, whereas only HW using Hmax achieved statistical significance.

Given the large number of studies that omit accurate description of measurement parameters for the sake of brevity, there seems to be an implicit belief that the research community is using the same definitions and measurement methodology. The work presented here suggests this may not be the case and demonstrates that even small variations in definition affect performance significantly. The use of alternative definitions and their poor documentation affect the interpretation and reproducibility of the results of any given study. Explicit definition documentation and parameter standardization may be especially important when conducting literature reviews or performing multicenter studies and further highlights the additional variability present in measurements made from biplane compared with 3D rotational angiography.

Automated Measurement Tool

All measurements used in this study were measured in automated fashion with an in-house software package that was thoroughly validated against experienced medical operators. The use of a measurement robot eliminated operator bias but, most important, allowed the analysis of a large number of parameters. It also led to significant time savings because it takes an operator approximately 10 minutes per study to measure the 7 parameters used for tool validation; in contrast, the automated computation of $>$ 20 parameters requires only 48 seconds per aneurysm.

Study Limitations

Analysis of aneurysm shape to identify rupture status discriminants relies on the hypothesis that aneurysm shape does not change after rupture. Should aneurysm shape change significantly after rupture, the current class of analysis may not be helpful. Even though increasing evidence indicates that such a change does not occur,[21,29] conclusive data on this subject remain scant. The present analysis is retrospective in character and thus can only imply prediction of previously determined rupture status. The conclusions of this study require validation in prospective randomized studies before their performance can be validated and applied in risk assessment of the incidentally found unruptured aneurysm in clinical practice.

CONCLUSION

This study evaluated the impact of using alternative definitions to describe aneurysm geometry on rupture risk analysis. All parameters were measured in an automated fashion to eliminate operator bias while allowing the analysis of a large number of features and their competing definitions. The results revealed that small variations in aneurysm measurement definition (size, height, width, neck, AR, HW, and BHF) affect performance significantly and may explain the controversial findings across prior studies and the difficulty of establishing reliable size threshold values for rupture status prediction. Our analysis points to a strong need for better documentation of measurement methodology and for a standardization of parameter nomenclature to enable comparative analysis across studies.

Disclosures

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REFERENCES

1. Rinkel GJ, Djibuti M, Algra A, van Gijn J. Prevalence and risk of rupture of intracranial aneurysms: a systematic review. *Stroke*. 1998;29(1):251-256.
2. Wardlaw JM, White PM. The detection and management of unruptured intracranial aneurysms. *Brain*. 2000;123(pt 2):205-221.
3. Juvela S, Porras M, Poussa K. Natural history of unruptured intracranial aneurysms: probability of and risk factors for aneurysm rupture. *J Neurosurg* 2008;108(5):1052-1060.
4. Wiebers DO. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*. 2003;362 (9378):103-110.
5. Broderick JP, Brott TG, Duldner JE, Tomsick T, Leach A. Initial and recurrent bleeding are the major causes of death following subarachnoid hemorrhage. *Stroke*. 1994;25(7):1342-1347.
6. van Gijn J, Kerr RS, Rinkel GJ. Subarachnoid haemorrhage. *Lancet*. 2007;369 (9558):306-318.

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7. Wolfe SQ, Başkaya MK, Heros RC, Tummala RP. Cerebral aneurysms: learning from the past and looking toward the future. *Clin Neurosurg* 2006;53: 157-178.
8. Wiebers D, Whisnant J, Forbes G, et al. Unruptured intracranial aneurysms: risk of rupture and risk of surgical intervention. *N Engl J Med* 1998;339(24): 1725-1733.
9. Baharoglu MI, Schirmer CM, Hoit DA, Gao BL, Malek AM. Aneurysm inflow-angle as a discriminant for rupture in sidewall cerebral aneurysms: morphometric and computational fluid dynamic analysis. *Stroke*. 2010;41(7): 1423-1430.
10. Hoh BL, Sistrom CL, Firment CS, et al. Bottleneck factor and height-width ratio: association with ruptured aneurysms in patients with multiple cerebral aneurysms. *Neurosurgery*. 2007;61(4):716-722;; discussion 722-723.
11. Dhar S, Tremmel M, Mocco J, et al. Morphology parameters for intracranial aneurysm rupture risk assessment. *Neurosurgery*. 2008;63(2):185-196;; discussion 196-197.
12. Xiang J, Natarajan SK, Tremmel M, et al. Hemodynamic-morphologic discriminants for intracranial aneurysm rupture. *Stroke*. 2011;42(1):144-152.
13. Ma B, Harbaugh RE, Raghavan ML. Three-dimensional geometrical characterization of cerebral aneurysms. *Ann Biomed Eng* 2004;32(2):264-273.
14. Raghavan ML, Ma B, Harbaugh RE. Quantified aneurysm shape and rupture risk. *J Neurosurg* 2005;102(2):355-362.
15. Joo SW, Lee SI, Noh SJ, Jeong YG, Kim MS, Jeong YT. What is the significance of a large number of ruptured aneurysms smaller than 7 mm in diameter? *J Korean Neurosurg Soc* 2009;45(2):85-89.
16. Ujiie H, Tamano Y, Sasaki K, Hori T. Is the aspect ratio a reliable index for predicting the rupture of a saccular aneurysm? *Neurosurgery*. 2001;48(3):495-502; discussion 502-503.
17. Ryu CW, Kwon OK, Koh JS, Kim EJ. Analysis of aneurysm rupture in relation to the geometric indices: aspect ratio, volume, and volume-to-neck ratio. *Neuroradiology*. 2011;53(11):883-889.
18. Beck J, Rohde S, Berkefeld J, Seifert V, Raabe A. Size and location of ruptured and unruptured intracranial aneurysms measured by 3-dimensional rotational angiography. *Surg Neurol* 2006;65(1):18-25; discussion 25-27.
19. Parlea L, Fahrig R, Holdsworth DW, Lownie SP. An analysis of the geometry of saccular intracranial aneurysms. *AJNR Am J Neuroradiol* 1999;20(6): 1079-1089.
20. Prestigiacomo CJ, He W, Catrambone J, et al. Predicting aneurysm rupture probabilities through the application of a computed tomography angiography-derived binary logistic regression model. *J Neurosurg* 2009;110(1):1-6.
21. Rahman M, Ogilvy CS, Zipfel GJ, et al. Unruptured cerebral aneurysms do not shrink when they rupture: multicenter collaborative aneurysm study group. *Neurosurgery*. 2011;68(1):155-160; discussion 160-161.
22. Kupersmith MJ, Hurst R, Berenstein A, Choi IS, Jafar J, Ransohoff J. The benign course of cavernous carotid artery aneurysms. *J Neurosurg* 1992;77(5):690-693.
23. McGraw KO, Wong SP. Forming inferences about some intraclass correlation coefficients. *Psychol Methods* 1996;1(1):30-46.
24. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. *Psychol Bull* 1979;86(2):420-428.
25. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33(1):159-174.
26. Nader-Sepahi A, Casimiro M, Sen J, Kitchen ND. Is aspect ratio a reliable predictor of intracranial aneurysm rupture? *Neurosurgery*. 2004;54(6): 1343-1348.
27. Beck J, Rohde S, el Beltagy M, Zimmermann M, Berkefeld J, Seifert V. Difference in configuration of ruptured and unruptured intracranial aneurysms determined by biplanar digital subtraction angiography. *Acta Neurochir (Wien)* 2003;145(10): 861-865.
28. Yasuda R, Strother CM, Taki W, et al. Aneurysm volume-to-ostium area ratio: a parameter useful for discriminating the rupture status of intracranial aneurysms. *Neurosurgery*. 2011;68(2):310-318.
29. Asari S, Ohmoto T. Natural history and risk factors of unruptured cerebral aneurysms. *Clin Neurol Neurosurg* 1993;95(3):205-214.

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COMMENTS

This article sheds light on the variability inherent in defining and measuring morphological features of intracranial aneurysms. The authors are commended for addressing this important issue because variability in definition and measurement adversely affect the ability to interpret and compare results from multiple studies evaluating the morphological features of intracranial aneurysms. This is a significant problem from both a clinical and research perspective.

We first consider the issue as it applies to research protocols. Within a given study, the use of consistent definitions and measurements of morphometric indexes is essential. Computational approaches that allow consistent measurement of aneurysm size and shape indexes must be developed and clearly stated. It would be ideal if all investigational reports could agree on standard definitions of morphometric features and a standard methodology of measurement; unfortunately, this is not the case. It is also important to recognize that the biggest source of uncertainty in the morphological description of intracranial aneurysms may lie in the steps undertaken before we begin to calculate indexes like aspect ratio and bottleneck factor. The segmentation of the aneurysm surface from clinical images needs to be rigorously defined and measured, which can be very difficult. For instance, even determining where the normal vessel ends and the aneurysm begins can be fraught with difficulty and can significantly affect our measurements. Recent advances in computational image analysis such as the Vascular Modeling ToolKit (www.VMTK.org) and ongoing studies by many research groups are likely to help resolve these issues and lead to more generally accepted definitions and methods of measurement.

In the clinical setting, definitions and measurement of aneurysm size and shape are far less rigorously determined than they are in a research study. This variability has significant clinical implications in that there is a growing body of evidence that morphological features affect the likelihood of aneurysm rupture and that these features are routinely used to decide whether to recommend treatment for unruptured aneurysms. Variability in definition and measurement of size and shape indexes may also be affected by the clinician's desire to reinforce a treatment recommendation on the basis of other factors.

Our work in this area has demonstrated that aneurysm shape is an important feature differentiating ruptured and unruptured aneurysms and that the morphology of the aneurysm and adjacent vessels determines the wall stress, shear stress, and other hemodynamically important forces acting on the aneurysm wall.[1-4] We believe that this area of inquiry will be important for our understanding of aneurysm growth and rupture. Such understanding will allow us to refine our treatment indications for patients with unruptured aneurysms. The use of consistent definitions and measurements of aneurysm size and shape will facilitate this area of inquiry.

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1. Ma B, Harbaugh RE, Raghavan ML. Three-dimensional geometrical characterization of cerebral aneurysms. *Ann Biomed Eng* 2004;32(2):264-273.
2. Ma B, Lu J, Harbaugh RE, Raghavan ML. Nonlinear, anisotropic stress analysis of anatomically realistic cerebral aneurysms. *J Biomech Eng* 2007;129(1):88-96.
3. Raghavan M, Ma B, Harbaugh RE. Quantified aneurysm shape and rupture risk. *J Neurosurg* 2005;102(2):355-362.

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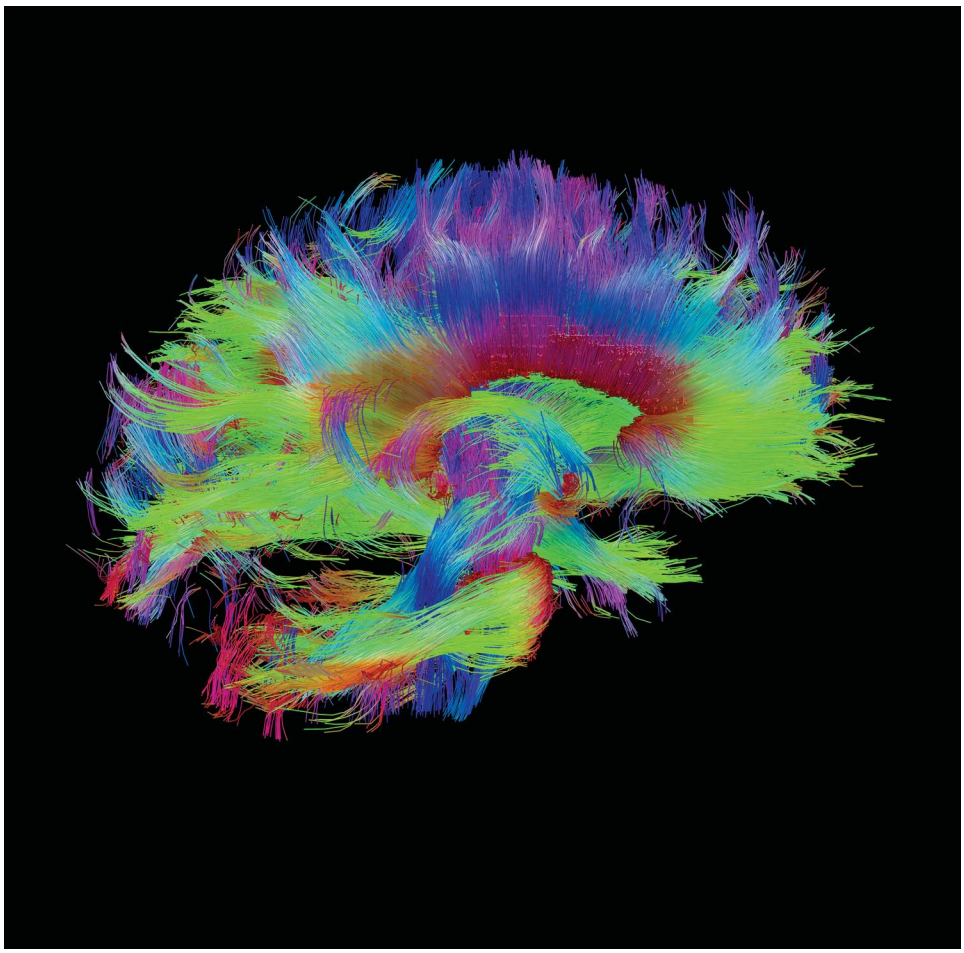
4. Zhou X, Raghavan ML, Harbaugh RE, Lu J. Patient-specific wall stress analysis in cerebral aneurysms using inverse shell model. *Ann Biomed Eng* 2010;38(2):478-489.

The authors present a well-designed study concerning the variability in defining intracranial aneurysm measurements described in the literature to discriminate rupture risk. They evaluate the reliability of automated tools to measure intracranial aneurysm size and morphology and to determine the statistical validity of various aneurysm measurement definitions in discriminating rupture status. Interestingly, the interobserver correlation of all measurements was high with either the manual measurements or automated parameters. Inaccuracy in determining rupture risk may result from confusion in how to actually measure the aneurysm size or morphologic characteristics that have been described in the literature. The authors are able to describe the most accurate method for each measurement parameter to be able to predict rupture risk. This work is critical in being able to accurately counsel patients in treatment decisions.

Our group has previously demonstrated that size ratio,[1] bottleneck factor,[2] and height-width ratio[2] are predictive of aneurysm rupture risk. As parameters that take into account aneurysm morphology and relationship to the parent vessel such as aspect ratio, bottleneck factor, and size ratio become more important, the definition of these measurements must be consistent among research studies and clinical practice.

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1. Rahman M, Smietana J, Hauck E, et al. Size ratio correlates with intracranial aneurysm rupture status: a prospective study. *Stroke*. 2010;41(5):916-920.
2. Hoh BL, Sistrom CL, Firment CS, et al. Bottleneck factor and height-width ratio: association with ruptured aneurysms in patients with multiple cerebral aneurysms. *Neurosurgery*. 2007;61(4):716-722.



White Matter Fibers, HCP Dataset Red Corpus Callosum

White matter fiber architecture from the Connectome Scanner dataset. The fibers are color-coded by direction: red = left-right, green = anterior-posterior, blue = ascending-descending (RGB = XYZ). Laboratory of Neuro Imaging, Jack Van Horn, PhD and Vaughan Greer.

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