

## ORIGINAL RESEARCH

# Variability in Intracranial Vessel Diameters and Considerations for Neurovascular Models: A Systematic Review and Meta-Analysis

Mahmood Mirza, MD ; Katie Kummer, PhD; Jillienne Touchette, PhD; Ray McCarthy, PhD; Ansaar Rai, MD; Patrick Brouwer, MD; Michael Gilvarry, MEng

**BACKGROUND:** In vitro experiments are critical for understanding the impact of medical devices and techniques on blood vessels and blood flow. However, their interpretation is often limited by anatomical models' inability to capture the wide range of vessel sizes observed in real-world practice. The current study aims to address this limitation by describing the distribution of vessel diameters in a real-world population.

**METHODS:** This systematic literature review using the PubMed database analyzed cerebral vessel diameters in patients from 2000 to 2022. The diameter measurements of various vessels within the neurovasculature were extracted. Random-effects meta-analyses were performed to synthesize vessel diameters across studies. Predicted distributions were generated from the meta-analytical results.

**RESULTS:** Seventy-six studies were included in the analysis. The M1 segment, internal carotid artery (cervical and communicating segments), A1 segment, V2 segment, V4 segment, and basilar artery had sufficient data for generating predicted distributions of vessel diameters. Predicted mean diameters were as follows: M1 segment,  $2.55 \pm 0.42$  mm (95th interpercentile range [IPR]: 1.71–3.38); internal carotid artery-cervical segment,  $4.74 \pm 0.64$  mm (95th IPR: 3.49–5.99); internal carotid artery-communicating segment,  $3.40 \pm 0.64$  mm (95th IPR: 2.15–4.66); A1 segment,  $1.89 \pm 0.34$  mm (95th IPR: 1.23–2.55); V2 segment,  $3.36 \pm 0.67$  mm (95th IPR: 2.05–4.67); V4 segment,  $2.42 \pm 0.74$  mm (95th IPR: 0.98–3.86); and basilar artery,  $2.96 \pm 0.52$  mm (95th IPR: 1.94–3.97).

**CONCLUSION:** Cerebral vessel diameter measurements can vary substantially due to patient-specific factors and imaging techniques. This literature review highlights the diverse range of vessel sizes observed in different patient populations, emphasizing the need for anatomical models that accurately represent clinical observations.

**Key Words:** cerebral vasculature ■ hemodynamics ■ imaging techniques ■ meta-analysis ■ morphometry

In the field of neurovascular research, in vitro experiments are crucial for demonstrating the impact of techniques and technologies on procedural outcomes,<sup>1,2</sup> understanding pathophysio-

logical mechanisms,<sup>3</sup> and unraveling the complex interactions between devices, blood vessels, and blood flow patterns.<sup>4,5</sup> However, these experiments often rely on anatomical models developed to

Correspondence to: Mahmood Mirza, MD, Medical Affairs, Cerenovus, Galway, Ireland, Block 3, Corporate House, Ballybrit Business Park, Galway H91 K57D, Ireland. E-mail: mmirza8@its.jnj.com

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### Nonstandard Abbreviations and Acronyms

<b>A1</b>	A1 segment of the anterior cerebral artery
<b>BA</b>	basilar artery
<b>C1</b>	cervical segment of the internal carotid artery
<b>C7</b>	communicating segment of the internal carotid artery
<b>CTA</b>	computed tomography angiography
<b>DSA</b>	digital subtraction angiography
<b>ICA</b>	internal carotid artery
<b>IPR</b>	interpercentile range
<b>M1</b>	M1 segment of the MCA
<b>MCA</b>	middle cerebral artery
<b>MRA</b>	magnetic resonance angiography
<b>V2</b>	V2 segment of the VA
<b>V4</b>	V4 segment of the VA
<b>VA</b>	vertebral artery

resemble average patient anatomies,<sup>6</sup> which may be too simplistic as discussed by Johnson et al in a recent review of in vitro model advancements.<sup>7</sup> Depending on the experiment, some models are designed with various lengths, number and location of branches, and tortuosity in the aortic arch, supra-aortic vessels, or intracranial vessels to differentiate various techniques or technologies in a preclinical environment.<sup>8–12</sup> However, they often use average vascular diameters, which can limit their interpretation and translation to clinical practice, particularly when device size or fluid flow is an important parameter.

For example, a recent study examined the impact of a super bore aspiration catheter on flow reversal and aspiration ability in the middle cerebral artery (MCA) M1 segment (M1).<sup>13</sup> The internal diameter of the in vitro model was selected to match the mean M1 size reported in 1 article, which indicated an M1 diameter of  $3.1 \pm 0.4$  mm. However, another study reported a different mean M1 diameter of  $2.15 \pm 0.36$  mm.<sup>14</sup> The outer diameter of the catheter was 2.65 mm, close to the 3.1 mm diameter in the in vitro model. Considering the variations in M1 diameter, if the M1 measured 2.7 mm (1 SD below the mean) or 2.15 mm (mean diameter from the other article), the catheter may have struggled to fit appropriately within the vessel. However, if the M1 diameter was 3.5 mm (1 SD above the mean), it may fit easily but could significantly alter the flow pattern. Hence, it is important to characterize the entire range of vessel diameters reported in the literature to develop neurovascular models that accurately represent clinical variations.

### CLINICAL PERSPECTIVE

#### What Is Known?

- The development of endovascular medical devices and techniques relies on anatomical models of vessel sizes; however, they do not represent the wide range observed in real-world clinical settings. A description of the distribution of intracranial vessel sizes in a real-world population would guide the development of more comprehensive and representative anatomical models.

#### What New Information Does this Article Contribute?

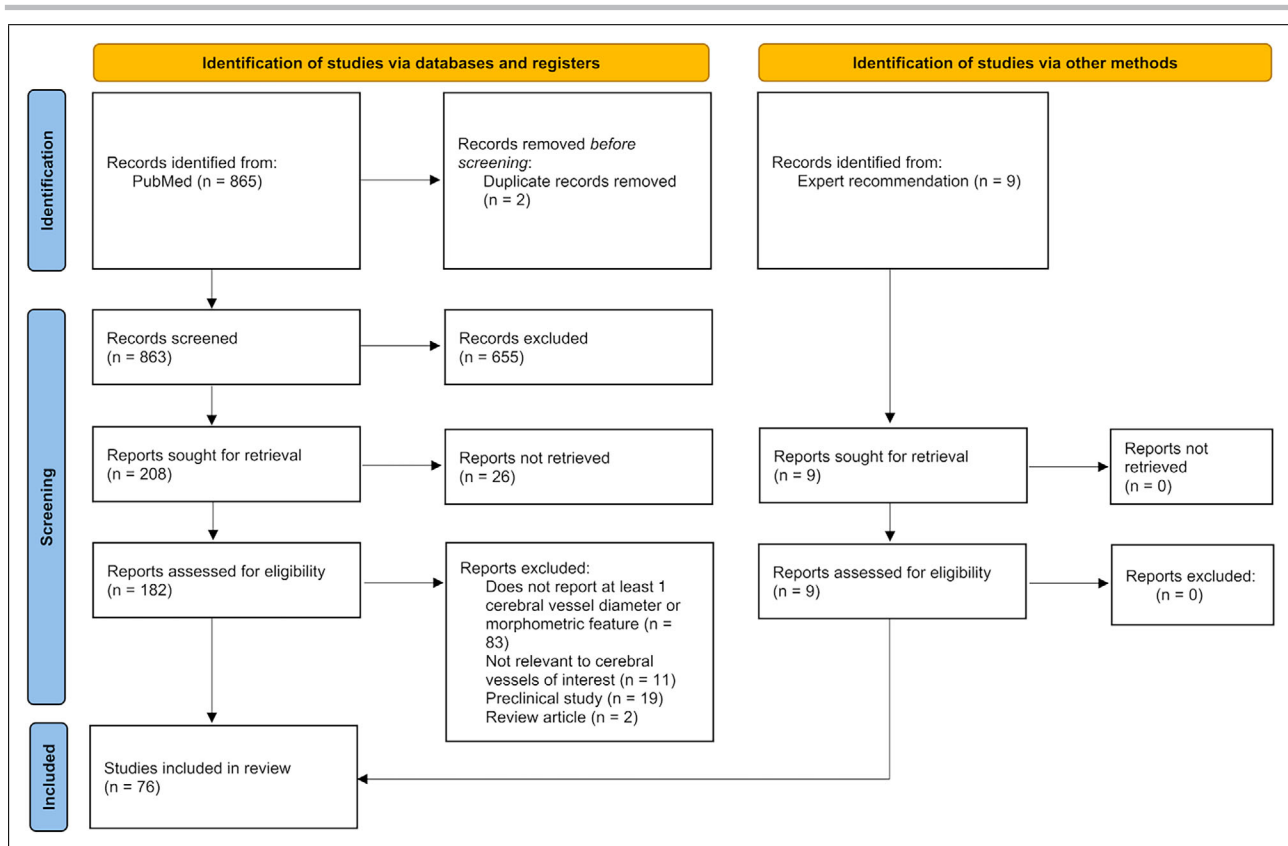
- Our observations from 76 studies using valid, reliable, and modern imaging technologies in a wide patient population found different distributions in intracranial vessel diameters compared with previously reported sizes.
- Intracranial vessel diameters exhibit a considerable degree of variability, and existing neurovascular models may not fully capture the range of sizes observed in patients.

Additionally, the morphometric characteristics of the cerebral vasculature significantly affect the navigability of devices. Factors like tortuosity, torsion, curvature, and branching angles can influence neurointerventionalists' ability to successfully navigate catheters and stents along vascular paths to treatment sites. Because demographic factors and disease states influence vessel diameters, comprehending the diverse range of vessel calibers in patient populations is challenging. Therefore, it is prudent to compile all available vessel diameter data to enhance the design of neurovascular devices and optimize treatment strategies.

This review aims to characterize the diversity of intracranial vessel diameters and highlight discrepancies in measurements related to demographics and disease states.

### METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request. This study did not require institutional review board or ethics committee approval.



**Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram of search records and included studies.**

## Search Strategy

A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) compliant systematic review of the literature was done using the Nested Knowledge platform. The initial literature search was performed on the PubMed database using the AutoLit platform in Nested Knowledge. We searched for all relevant articles reporting on intracranial vessel diameters except case reports or systematic reviews. The search string included keywords such as “diameter,” “flow rates,” “morphometr\*,” and “cerebral.” The full search string can be found in Table S1.

Studies were initially screened by one reviewer and were checked for accuracy by a second reviewer. Any disagreements were resolved by consensus. Additional records not captured in the initial search have been added based on expert recommendation. The last search ran on December 20, 2022 and returned 865 total results (Figure 1).

## Population

The study population included patients who had undergone a validated imaging procedure for assess-

ing intracranial vessel diameter. Vessels of interest included anterior cerebral artery, anterior communicating artery, basilar artery (BA), internal carotid artery (ICA), mMCA, posterior cerebral artery, posterior communicating artery, and vertebral artery (VA). Studies were considered for inclusion if they (1) included living human data, (2) included original data (not duplicated or referenced from other studies), (3) included at least 1 cerebral vessel diameter of interest, and (4) used a valid and reliable imaging procedure, determined at the discretion of the study team.

The following study exclusion criteria were applied: case report, did not report at least 1 cerebral vessel diameter or morphometric feature, published before January 1, 2000 to ensure modern and accurate technologies were used, preclinical study (in vitro, in vivo, in silico, animal, cadaveric – to ensure models replicate living patients), pediatric study, not relevant to cerebral vessels of interest, and review article. Although review articles were excluded from the review, references of these studies were screened to determine whether other original studies were relevant.

## Data Extraction

Data extraction was performed by 2 reviewers and discrepancies were resolved by consensus. Along with the intracranial vessel diameters measured in millimeters (mm), data shown were collected as available. Patient baseline characteristics included gender, age, comorbidities, and height. Study characteristics included the publication date of the study. Imaging modalities as procedure characteristics were important in strengthening the methodology of each study. These modalities included computed tomography angiography (CTA), Doppler/duplex ultrasound, digital subtraction angiography (DSA), magnetic resonance angiography (MRA), magnetic resonance imaging, and noncontrast computed tomography.

## Statistical Analysis

Original data from each study are described. Mean values were recorded together with the SE, SD, or CI. Median values were recorded together with the interquartile range or simple range.

To be eligible for quantitative synthesis, study-level vessel diameter data needed to include at least (1) the mean, SD, and sample size; or (2) the median, interquartile range, and sample size for a specific vessel of interest. When necessary, we combined within-study morphological measurements using simple weighted averages and variances. These included combining within-study groups based on laterality of measurements, specific segments within vessels (proximal, distal, etc), and if multiple measurements were made for a single vessel (eg, multiple rater cases). If diseased vessels were encountered (aneurysm cases, stenotic side, etc) the contralateral/healthy side was used. If healthy vessels were unavailable, data were omitted. If different procedures, medications, or study conditions were used and known to affect the vessel diameter (eg, glyceryl trinitrate administration), baseline measurements were used. Due to the heterogeneity of reporting and scarcity of data, various comorbidity and patient age groups were combined within studies when possible and were not considered as covariates.

Most studies reported continuous data as means and SDs; however, in cases where medians and interquartile ranges were reported, we used methods described by Luo et al<sup>15</sup> and Wan et al<sup>16</sup> to estimate means and SDs, respectively. For each study that used this data transformation procedure, the assumption of normal approximation was assessed using methods described by Shi et al before transformation.<sup>17</sup> In all cases, there was no significant evidence to show that the data were skewed, and they were deemed to have a roughly normal underlying distribution. Subsequently,

random-effects meta-analyses were performed on a homogenous set of summary measures.

For comparative meta-analyses, effect sizes were first calculated as log-transformed mean differences. Effect sizes were pooled using inverse-variance weighted, random-effects meta-analyses, with random effects on the study and intracranial artery nested within study. Similarly, for calculation of an overall mean from studies reporting a single mean, studies were pooled using the random effects, inverse variance weighting from log-transformed means. Meta-analyses by vessel type were performed if there were at least 5 studies with sufficient data reporting on a specific vessel of interest. The between-study variance component,  $\tau^2$ , was estimated using restricted maximum likelihood estimation with corresponding 95% CIs computed using the Q-profile method.<sup>18</sup> To aid in interpretation, log-transformed results were back transformed to their original scale after pooling.

Predefined subgrouping variables (including sex and imaging modality) were assumed to vary across studies and were considered random effects with a separate estimator of  $\tau^2$  assumed on each distinct subgroup. There were insufficient data for direct within-study comparisons of vessel diameter by imaging modality, so imaging modality was instead used as a study-level subgrouping variable. Some studies reported vessel diameter for both sexes, which enabled direct comparative meta-analyses that better account for study-level sources of heterogeneity. Statistical comparisons of subgroup differences by imaging modality are based on Q-tests for subgroup differences and direct comparisons by gender are based on z-tests of overall effects. *P* values <0.05 were considered statistically significant.

$I^2$  statistics were used to measure the percentage of the total variability in effect estimates that could be attributed to heterogeneity rather than sampling error.<sup>12</sup> Prediction intervals (95%) based on t-distributions were calculated around pooled effect sizes using methods described by Higgins et al.<sup>19</sup> In brief, a 95% prediction interval estimates where the true effects are to be expected for 95% of similar studies that might be conducted in the future.

After meta-analyses were performed, predicted distributions of vessel diameters were generated for each vessel type based on the assumption that the underlying distribution of diameters is roughly normally distributed. In all cases, there was no significant evidence of a departure from normality. Normal distribution plots show data as a density curve, highlighting the mean,  $\pm 1$  SD from the mean, and the 2.5th, 5th, 95th, and 97.5th percentiles. For in-text summary statistics, we reported the mean and the 95th interpercentile range (IPR).

Mahmood Mirza had full access to all data in the study and takes responsibility for their integrity and the data analysis. Analyses were performed in RStudio (2022.12.0 Build 353) using the “meta”<sup>20</sup> and “metafor” packages.<sup>21</sup>

## RESULTS

### Search Results

The search returned a total of 865 studies. After searching by title and abstract, the following exclusions were applied: duplicate study ( $n = 2$ ), published before January 1, 2000 ( $n = 224$ ), case report ( $n = 15$ ), review article ( $n = 13$ ), pediatric study ( $n = 2$ ), preclinical study (in vitro, in vivo, in silico, animal, cadaveric) ( $n = 63$ ), does not report at least 1 cerebral vessel diameter or morphometric feature ( $n = 294$ ), and not relevant to cerebral vessels of interest ( $n = 44$ ).

Full text review was completed on 208 studies. Additional exclusions were made based on the following: full text not available ( $n = 26$ ), does not report at least 1 cerebral vessel diameter or morphometric feature ( $n = 83$ ), not relevant to cerebral vessels of interest ( $n = 11$ ), preclinical study ( $n = 19$ ), and review article ( $n = 2$ ). Nine studies were added based on expert recommendation.

Only vessels that had at least 5 articles with quantitative information were included for quantitative synthesis. The arteries included the MCA-M1, ICA (cervical segment of the internal carotid artery [C1] and communicating segment of the internal carotid artery [C7]), anterior cerebral artery-A1 segment (A1), VA-V2 segment (V2) and V4 segment (V4), and BA. Predicted distributions of all vessel diameters are summarized in Table. The full list of included studies and relevant patient demographic information can be found in Table S2.

### Middle Cerebral Artery

After excluding 2 extreme outlier studies,<sup>22,23</sup> 19 studies had sufficient information for quantitative synthesis of M1 vessel diameters<sup>14,25,29–31,39,44,45,47,49,58,70,76–78,85,87,88,95</sup> and used advanced imaging modalities (CTA, MRA, DSA). From the global meta-analytical results (Figure S1), a predicted distribution of M1 diameters was generated (Figure 2A). The pooled mean diameter of the underlying population was  $2.55 \pm 0.42$  mm (95th IPR: 1.71–3.38).

In an exploratory subgroup analysis, 4 studies had sufficient information for direct comparisons of M1 vessel diameters between male and female patients.<sup>25,30,77,85</sup> The pooled mean diameter for males was 2.56 mm (95% CI: 2.25–2.92) and for females was 2.43 mm (95% CI: 2.07–2.84). This difference was statistically significant, with a pooled mean difference

of 0.13 mm (95% CI:  $<0.01$ –0.27;  $P = 0.049$ ; Figure S2). The estimated statistical heterogeneity among the studies ranged from low to high ( $I^2 = 64.0\%$  [95% CI: 0.0–87.9%]).

### Internal Carotid Artery

Twenty-five studies had sufficient information for quantitative synthesis of ICA vessel diameters. Of these studies, 13 used advanced imaging<sup>14,25,30,31,39,45,46,53,55,79,83,85,95</sup> and 12 used ultrasound-based imaging.<sup>33,34,41,43,62–64,66,69,82,98,99</sup> From the global meta-analytical results (Figure S3), a predicted distribution of ICA diameters was generated. The pooled mean diameter of the underlying population was  $4.45 \pm 0.72$  mm (95th IPR: 3.03–5.97).

In an exploratory subgroup analysis, 3 studies had sufficient information for direct comparisons of ICA vessel diameters between male and female patients.<sup>30,41,85</sup> Two studies used advanced imaging and 1 used ultrasound for measuring vessel diameter. The pooled mean diameter for males was 3.73 mm (95% CI: 2.72–5.10) and for females was 3.45 mm (95% CI: 2.56–4.63). This difference was statistically significant, with a pooled mean difference of 0.32 mm (95% CI: 0.14–0.51; Figure S4). The estimated statistical heterogeneity among the studies ranged from low to high ( $I^2 = 30.0\%$  [95% CI: 0.0%–92.7%]).

When stratifying ICA measurements by specific segment (C1–C7), only the C1 (cervical) and the C7 (terminal) segments had sufficient data for quantitative synthesis. The C1 segment had 13 studies with sufficient information, including 3 studies using advanced imaging<sup>39,55,83</sup> and 10 studies using ultrasound-based imaging<sup>33,34,41,43,62–64,66,94,98</sup> (Figure S5); the pooled mean diameter was  $4.74 \pm 0.64$  mm (95th IPR: 3.49–5.99; Figure 2B). After excluding 1 extreme outlier study,<sup>22</sup> the C7 segment had 6 studies with sufficient information, all of which used advanced imaging<sup>14,25,30,39,85,95</sup> (Figure S6); the pooled mean diameter was  $3.40 \pm 0.64$  mm (95th IPR: 2.15–4.66; Figure 2C).

### Anterior Cerebral Artery

Six studies had sufficient information for quantitative synthesis of A1 vessel diameters.<sup>31,47,68,72,83,96</sup> All of these studies used advanced imaging modalities. From the global meta-analytical results (Figure S7), a predicted distribution of A1 diameters was generated (Figure 2D). The pooled mean diameter of the underlying population was  $1.89 \pm 0.34$  mm (95th IPR: 1.23–2.55).

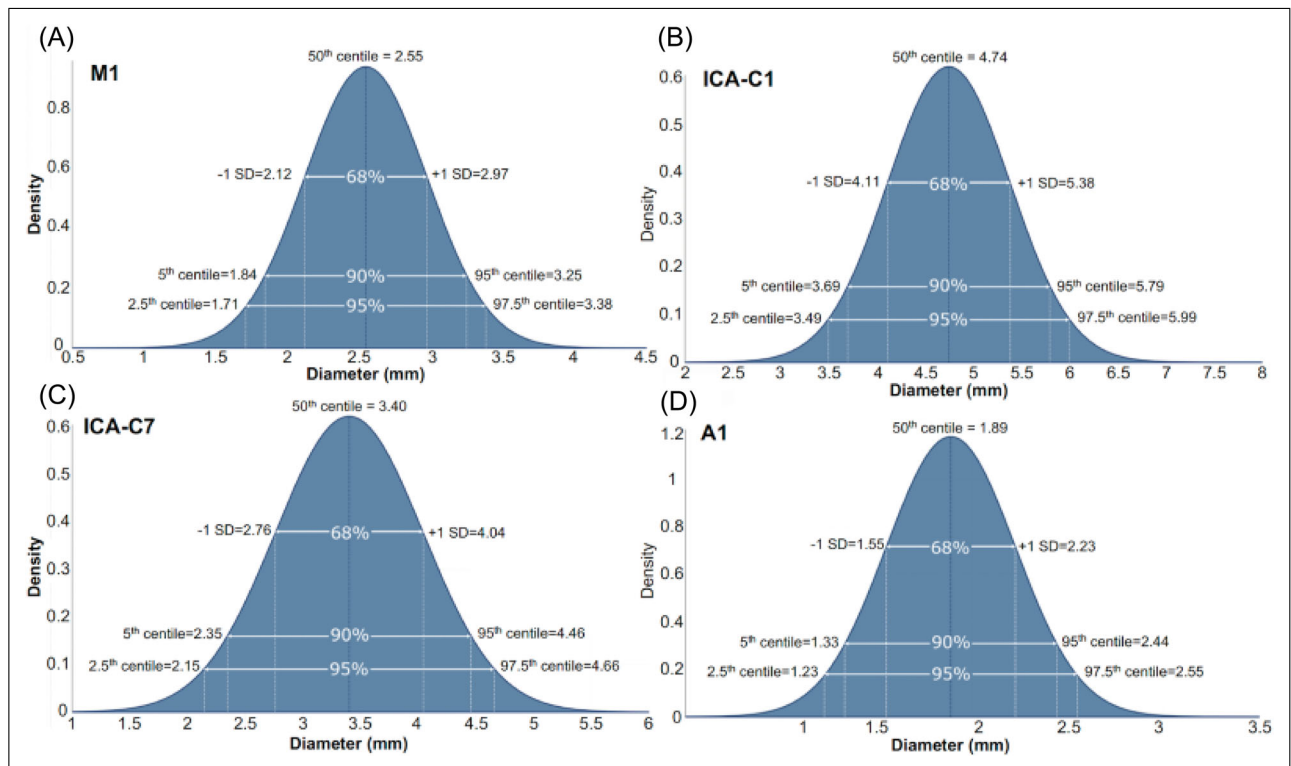
### Vertebral Artery (V2 and V4)

Five studies had sufficient information for quantitative synthesis of V2 vessel diameters. Of these studies, 2

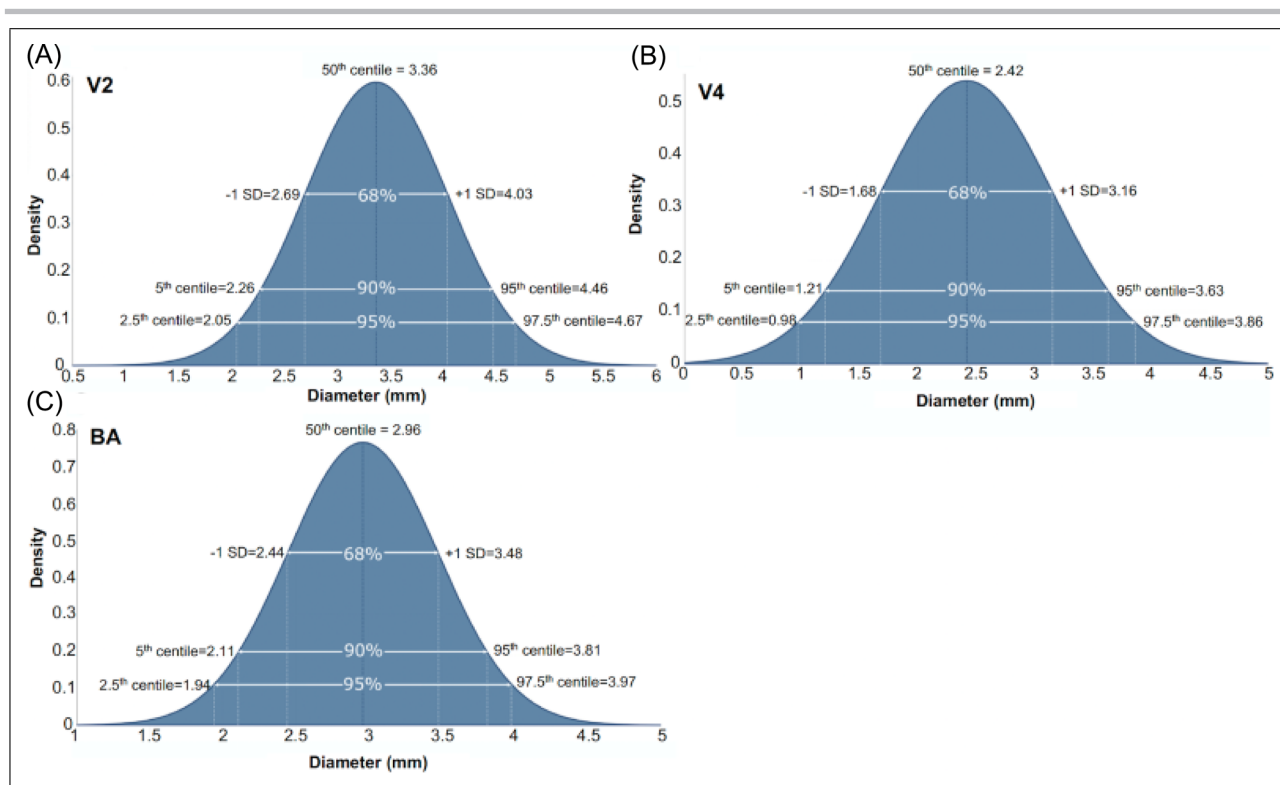
**Table. Vessel Diameters**

Vessel	Imaging modality	No. (studies)	No. (vessels)	No. (patients)	Diameter mean±SD (mm)	90th IPR (5th to 95th centile)	95th IPR (2.5th to 97.5th centile)
M1	Overall (advanced imaging only)	19	2292	2290	2.55 ± 0.42	1.84–3.25	1.71–3.38
ICA	Overall	25	1880	1883	4.45 ± 0.72	3.26–5.65	3.03–5.97
	Advanced imaging	13	1330	1336	3.93 ± 0.79	2.64–5.22	2.39–5.47
	Ultrasound	12	550	547	5.06 ± 0.66	3.97–6.15	3.77–6.35
ICA C1	Overall	13	370	364	4.74 ± 0.64	3.69–5.79	3.49–5.99
	Advanced imaging	3	77	77	3.77 ± 0.75	2.53–5.01	2.29–5.25
	Ultrasound	10	293	287	5.00 ± 0.61	4.00–6.00	3.81–6.19
ICA C7	Overall (advanced imaging only)	6	700	700	3.40 ± 0.64	2.35–4.46	2.15–4.66
A1	Overall (advanced imaging only)	6	721	965	1.89 ± 0.34	1.33–2.44	1.23–2.55
V2	Overall	5	1124	1124	3.36 ± 0.67	2.26–4.46	2.05–4.67
	Advanced imaging	2	110	110	3.54 ± 0.67	2.44–4.64	2.23–4.85
	Ultrasound	3	1014	1014	3.26 ± 0.67	2.16–4.36	1.95–4.57
V4	Overall (advanced imaging only)	6	717	717	2.42 ± 0.74	1.21–3.63	0.98–3.86
BA	Overall (advanced imaging only)	14	1714	1135	2.96 ± 0.52	2.11–3.81	1.94–3.97

Advanced imaging = CTA, MRA, DSA. A1 indicates A1 segment of the anterior cerebral artery; BA, basilar artery; CTA, computed tomography angiography; DSA, digital subtraction angiography; ICA, internal carotid artery; ICA C1, ICA cervical segment of the internal carotid artery; ICA C7, ICA communicating segment of the internal carotid artery; IPR, interpercentile range; M1, M1 segment; MRA, magnetic resonance angiography; V2, V2 segment; and V4, V4 segment.



**Figure 2. Predicted distributions of artery diameters in the anterior circulation. A,** M1 artery diameters; **(B)** ICA-C1 artery diameters; **(C)** ICA-C7 artery diameters; **(D)** A1 artery diameters. A1 indicates A1 segment of the anterior cerebral artery; C1, cervical segment of the internal carotid artery; C7, communicating segment of the internal carotid artery; ICA, internal carotid artery; and M1, M1 segment of the middle cerebral artery.



**Figure 3. Predicted distributions of artery diameters in the posterior circulation. A,** V2 artery diameters; **(B)** V4 artery diameters; **(C)** basilar artery diameters. BA indicates basilar artery; V2, V2 segment; and V4, V4 segment.

used advanced imaging<sup>39,60</sup> and 3 used ultrasound-based imaging.<sup>48,81,99</sup> From the global meta-analytical results (Figure S8), a predicted distribution of V2 diameters was generated (Figure 3A). The pooled mean diameter of the underlying population was  $3.36 \pm 0.67$  mm (95th IPR: 2.05–4.67).

Six studies had sufficient information for quantitative synthesis of V4 vessel diameters.<sup>39,42,56,83,86,95</sup> All used advanced imaging modalities. From the global meta-analytical results (Figure S9), a predicted distribution of V4 diameters was generated (Figure 3B). The pooled mean diameter of the underlying population was  $2.42 \pm 0.74$  mm (95th IPR: 0.98–3.86).

### Basilar Artery

After excluding 1 extreme outlier study,<sup>24</sup> 14 studies had sufficient information for quantitative synthesis of BA vessel diameters.<sup>31,39,42,45,47,54,59–61,65,67,86,88,95</sup> From the global meta-analytical results (Figure S10), a predicted distribution of BA diameters was generated (Figure 3C). The pooled mean diameter of the underlying population was  $2.96 \pm 0.52$  mm (95th IPR: 1.94–3.97).

## DISCUSSION

In this systematic review and meta-analysis, we assessed the distributions of intracranial vessel diameters, specifically the ICA-C1, ICA-C7, MCA-M1, anterior cerebral artery-A1, VA-V2, VA-V4, and BA. The data demonstrate significant variability in these vessel diameters. Various patient-specific factors such as age, pregnancy, disease state, and the imaging modality used contribute to the wide range of vessel diameters observed. Furthermore, we compared our findings to a foundational publication in the field, revealing additional variability in reported vessel diameters.

A commonly referenced study on MCA and ICA vessel size is Rai et al.<sup>25</sup> According to their findings, the mean M1 vessel diameter is  $3.1 \pm 0.4$  mm (SD) based on CTA data from 100 patients without underlying vascular disease. In contrast, our systematic review yielded different results, observing a mean M1 vessel diameter of  $2.55 \pm 0.42$  mm (SD) with a range of 1.84–3.25 mm (5th–95th centile) using various imaging modalities. Notably, there is a difference of 0.55 mm in mean vessel diameter between these studies.

Nogueira et al recently published a study using an in vitro thrombectomy model to evaluate the effect of

catheter-to-vessel size on the success of aspiration thrombectomy.<sup>13</sup> Although the MCA-M1 diameter used to design the in vitro model was based upon the Rai et al study described previously,<sup>25</sup> the authors gave other model vessel diameters that were notably larger than those found in this review. The proximal ICA diameter was 5.1 mm, whereas the mean value found in our study was 4.74 mm for the C1 segment. Likewise, the mean distal ICA was 4.3 mm compared with a predicted value 3.40 mm found in our study. The A1 artery was also reported to be 2.5 mm compared with our mean value of 1.89 mm. In studies using cerebrovascular modeling to assess thrombectomy devices, the diameter of cerebral vessels may affect conclusions about device efficacy and optimal treatment methods for real-world thrombectomy scenarios.

Sex is known to affect intracranial vessel diameters, with males generally having larger vessel diameters than females. Though our analysis of sex-dependence was limited by a lack of studies, our finding that M1 diameter varies by a mean of 0.13 mm between males and females (Figure S2) supports considering sex differences when creating cerebrovascular models.

Correlations between age and vessel diameter have been previously observed. El-Barhoun et al used MRA and magnetic resonance imaging to assess BA diameters in 171 patients,<sup>26</sup> and their results indicated a significant association between BA diameter and age of the patient. We did not analyze the effect of age on vessel diameter due to insufficient data, but the patients in our systematic review had a wide range of ages from a mean of 16.92 to 77.3 years (Table S1). Further studies comparing vessel diameters between age groups will be essential to better understand its impact on cerebral vasculature.

There is debate on the use of the various advanced imaging techniques such as CTA, MRA, and DSA (using catheter angiography) to capture vessel diameters,<sup>27,28</sup> each having advantages and disadvantages. Although there were insufficient data to systematically analyze the impact of different imaging modalities, variability across all imaging modalities was observed without any obvious discrepancies. Some studies using different imaging modalities found very similar results, such as Han et al<sup>29</sup> who used MRA to find M1 vessel diameters of nearly  $3.0 \pm 0.3$  mm, and Rai et al<sup>25</sup> who used CTA to find M1 vessel diameters of  $3.1 \pm 0.4$  mm, whereas others were different. Some of the articles measured with multiple methods to show very similar results, such as Tarasów et al<sup>30</sup> who found similar diameters when comparing the use of MRA and DSA. Moreover, we conducted informal comparisons between advanced imaging techniques and ultrasound measurements of the ICA C1 and VA V2s. Our observations, depicted in Figures S5 and S8, indicate that ultrasound mea-

surements tend to yield larger diameters for the C1 segment, but smaller diameters for the V2 compared with measurements obtained through advanced imaging methods such as MRA, CTA, and DSA. Notably, for the C1 segment, the choice of imaging modality led to a mean diameter difference of more than a millimeter, underscoring the importance of considering the imaging method when evaluating vessel diameters.

The variable patient conditions included in this review allowed us to informally appreciate the effects of hypoxia,<sup>31,71,80</sup> anesthesia,<sup>32</sup> hypercapnia,<sup>33,73</sup> and insulin levels<sup>34</sup> on intracranial vessel diameters. Our observations indicate that pathological variations from disease states or medications may contract or dilate cerebral vessels by multiple tenths of a millimeter. This may have consequences if neurovascular treatment is needed.

Future analyses should include pregnant patients, as cerebral vasculature is altered during pregnancy. Johnson and Cipolla<sup>35</sup> noted that intravascular pressure was altered and structural changes were present in pregnant rats. Further, Nevo et al<sup>36</sup> studied 210 low-risk pregnant women with doppler imaging and found increased ICA diameter size and decreased cerebral vascular resistance from the first trimester to third trimester. Cerebral blood flow and alterations throughout pregnancy dramatically alter intracranial vasculature. The impact of these changes is an underdeveloped research area.

Although many factors influence intracranial vessel diameters, including disease states such as Fabry disease,<sup>37</sup> hypertension,<sup>38</sup> and Pompe disease,<sup>39</sup> along with natural variability in vessel diameter, our data do not reveal the specific sources of size differences. However, our data do offer a quantifiable way to include the range of vessel size variability in models. Further studies are needed to evaluate the effects of age, patient populations such as pregnant women, and disease states on intracranial vessel diameter.

## Limitations

Important patient differences that may affect vessel diameters such as body size and body mass index were not individually analyzed in the current study. Our analyses provide a general distribution of intracranial vessel diameters that may be generalizable to a large proportion of patients but may not be applicable for those with characteristics that place patients at a higher risk for large vessel strokes. Additionally, it is important to consider that some vessel diameters included in this review may be associated with pathology and therefore not representative of a healthy patient population. This further reflects the need for more models to capture the true variation observed in a patient population. Each meta-analysis must be considered separately, as

they do not characterize the same patient populations. Additionally, all meta-analytical comparisons have considerable statistical heterogeneity. Large differences in vessel morphologies are attributable to within-study differences in patient characteristics and therefore may not represent an adequate match to a specific population of interest.

There is also considerable variability in measurement techniques, imaging modality, and image quality, which may affect vessel diameter measurements. For example, though MRA is commonly used to evaluate vasculature, there is debate regarding its accuracy in measuring communicating vessels.<sup>40</sup> Additionally, differences in resolution, contrast, and factors such as artifacts can hinder visualization and lead to variability in measurement. Further, the current review did not include a standardized method to measure vessel diameter, potentially contributing a level of variability from human error. Although advanced imaging methods were included in this review, it is important to consider the imaging method and potential variability in measurement techniques when evaluating the results.

Furthermore, this study considers only literature published on PubMed and used title and abstract filters in the search strings, which may overly restrict the systematic review. A comprehensive search of all studies reporting vessel diameter in large vessel occlusion patients is beyond the scope of this review. Although this study helps characterize the general variation in intracranial vessel diameters, meta-analyses of individual patient data are required to generate predicted distributions of intracranial vessel diameters for specific patient populations. The current review provides a wide view of full vessel variation currently seen in the literature. Future work would benefit from multicenter randomized controlled trials with standardized measurement protocols to characterize specific patient populations.

Finally, additional characteristics of vessel sizes such as segment lengths and radii of curvature may affect how medical devices and techniques influence blood flow. Future research should evaluate these features to better capture the wide range of vessel morphometry observed in real-world clinical scenarios.

## CONCLUSIONS

Intracranial vessel diameters exhibit a considerable degree of variability, and existing neurovascular models may not fully capture the range of sizes observed in patients. This comprehensive meta-analysis represents the first systematic examination of cerebral vessel sizes, enabling researchers to develop neurovascular mod-

els that accurately represent the spectrum of clinically observed cerebral vessels.

## ARTICLE INFORMATION

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### Affiliations

Medical Affairs, Cerenovus, Galway, Ireland (M.M.); Superior Medical Experts, Inc., St. Paul, MN (K.K., J.T.); Cerenovus, Ballybrit, Galway, Ireland (R.M., M.G.); Department of Radiology and Neurosurgery and Neurology, West Virginia University Healthcare, Morgantown, WV (A.R.); Cardiovascular & Specialty Solutions Group, Cerenovus, Irvine, CA (P.B.)

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### Author Contributions

Concept and design: M.M., R.M., A.R., P.B.; Acquisition of data: K.K., J.T.; Analysis and interpretation of data: M.M., R.M., A.R., P.B., J.T.; Drafting of the manuscript: M.M., K.K., J.T.; Critical revision of the manuscript for important intellectual content and Final approval of the manuscript version to be published: All authors.

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M.M., R.M., P.B., and M.G. are employees of Cerenovus. K.K. and J.T. are employed by Superior Medical Experts. J.T. has ownership interest in Superior Medical Experts. A.R. has nothing to disclose.

### Supplemental Materials

Tables S1–S2  
Figures S1–S10

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