Reviewer’s report

Title: Variation in the circle of Willis in a Sri Lankan Population

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Reviewer: Peter B Canham

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MANUSCRIPT REVIEW – “Variations in the circle of Willis in a Sri Lankan Population”.

The authors have studied the external diameters of CW (circle of Willis) arteries, obtaining the circles from 225 autopsies. Their theme is that (i) the normal pattern for a circle [that has relative bilateral symmetry, with all segments complete and no severely undersize vessels] IS ACTUALLY NOT VERY COMMON (also discussed by Stehbens 1972, “Pathology of the Cerebral Blood Vessels”, page 25, where reference is made to about 4700 CWs reported by many authors), (ii) that racial and or ethnic variations among CWs can be significantly different from Caucasian-dominant data and (iii) that certain non-typical CW configurations may be associated with vascular pathologies, such as the incidence of aneurysm formation. The authors have already published a paper on intracranial aneurysms and variations in CWs in the same sub-population 2007.

1. The results are reported in a somewhat helpful way – including 6 columns of data from other researchers, 3 of which might be interpreted as from non-Caucasian populations (Japan, Morocco, Iran) in addition to their own data from Sri Lanka (225 autopsies). Three other studies are assumed to be Caucasian-dominated (Riggs and Rupp, USA, Fisher, 1965 USA, and Lazorthes et al. France 1979). However, only their own data are presented with percentages, leaving it to a reader to make essential calculations to see any obvious similarities or differences across their table. No statistical evaluations have been done on the data – a serious shortcoming to the manuscript in its present form.

2. The ABSTRACT is rather indigestible in the RESULTS component, with an exhaustive list of the alleged variations of CW in the Sri Lankan population that “appear” different from other populations. Perhaps only the more outstanding variations should be noted in the abstract. The CONCLUSIONS, both in the abstract and in the body of the manuscript are very sweeping and rather casual (e.g. “or a combination of any of the above”). A proper statistical assessment would provide a framework for drawing their conclusions, and would provide the evidence needed for the reader have confidence in the statements about population variations and ethnicity. [REQUIRED REVISION]

3. The METHODS are clear. A helpful and simple addition would be to include the diameter of the smallest detectable vessel, since some communicating
arteries can be quite tiny, and sometimes absent. This reviewer (Methods, p 8) is unsure if a limitation on acceptable normal vessel of > 1mm (outer diameter) might be too restrictive for communicating arteries. These vessels are generally smaller, and perhaps considered quite normal blood-carrying vessels at a size below 1 mm. The authors could clarify their definition of ‘normal’, in reference to the relatively small communicating arteries, confirming with definitions established in the field. [Possibly it is the uncertainty of ‘normal size’ that explains the high variation among classifications of normal CWs.] [SUGGESTED AS DISCRETIONARY REVISION]

4. This reviewer invites the authors to report on the compatibility of measurements among MR-angiography (possibly x-ray angiography), ultrasonography, and the cadaveric measurements used in their and many other studies (reports identified in their list of references – such as #5, 6, 7, 9 and 10. The reason is that data for the living patient are only accessible through angiography, methods which record luminal diameters of vessels distended by normal arterial blood pressure, versus the cadaveric studies which report on external diameters of collapsed vessels with zero luminal pressures. [STRONGLY SUGGESTED REVISION]

5. The DISCUSSION lacks authority because of the lacking statistical assessment. The table would be made much more reader-friendly by including the percentages in the incidences of each anomalous CW configuration, rather than just the absolute incidence (which the reader can readily calculate, of course, with a calculator, but shouldn’t need to). [ESSENTIAL MINOR REVISION] Upon consultation with statistical services at our medical school, this referee is suggesting a Chi-square test would be a basic test of value in this study, enabling a proper comparison among studies. The ethnicity (or racial relevance) of the individual studies is not noted, and possibly not available. One expects that the Iranian and Japanese studies are likely more homogeneous in their racial/ethnic status. The Moroccan study is uncertain, and one might expect that the two US studies, and the French study are Caucasian dominant. The Fisher study is from Harvard, and likely mainly a white population. However, the US studies may well have significant fractions of a negroid component in those studies. [ESSENTIAL STATISTICAL REVISION]

6. The conclusion that the “study reveals that there are marked variations in the circle of Willis” may be valid, but lacks authority, not only from the statistical perspective that needs to be explored, but also because of the lack of discussion of assumptions that are implicit in their table 1 of comparisons. Are the methods amongst the studies virtually the same, or are there differences that might affect the cataloguing of anomalies, are measurements to the nearest mm or 0.1 mm?, definitions of normal “circle”, etc. The references cited seem appropriate, and helpful. The inclusion of Stehbens’s book on Cerebral Blood Vessels might be of value, in part because of its comprehensiveness, but also because of its authority in the field of cerebral vascular pathology. [DISCRETIONARY REVISION]

The authors make the point in the covering letter that this is the first study of CW arteries in the Indian subcontinent. While the study represents a substantial
amount of work and care, the addition of 225 cadaveric measurements of CW arteries to a large body of similar cadaveric studies already published makes it a paper of modest scientific or medical impact in its present form.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare I have no competing interests.