Reviewer's report

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

Version: 6 Date: 22 October 2009

Reviewer: Peter B Canham

Reviewer's report:

General comment: significant revisions have been made to the manuscript that provide a much better scientific basis for the conclusions. The key addition is the statistical analysis. There are a number of suggested further changes – mostly related to clarity, and others as minor errors. The inclusion of two photographed circles is a good concept, but not well done. The photos are of poor quality. The discussion of postulates such as neck movement and hemodynamics adds little to the value (mainly because the causes of death are not part of the data presented, or analysed). A brief discussion of the criteria for obtaining diameters from the several studies might provide a valid explanation of why some of the various studies have different results. The authors might remark (if it is true) that to the best of their knowledge all of the several studies appear to have the same methods of measurement, and definitions of hypoplastic, normal size, etc.

i) Abstract, line 2 uses the word “efficient” to describe collateral circulations. (also used in the text). Strong preference would be the word “effective”. Efficient implies some sort of energy saving feature. While energy related to hemodynamics may be involved it is unlikely that the authors wish to imply that it is a causative factor in ‘circle’ design.

ii) Abstract line 6: grammar: “as a whole HAVE has not been studied.

iii) Abstract (methods) “ . . . occurrence of variations in the CW” (this addition is consistent with similar language elsewhere)

iv) Racial and ethnic population groups are challenging to define. In the abstract, but not in the text, the inference is that the Japanese study was not included as “Asian” whereas the Iranian data and Sri Lankan data are Asian. If one is dividing up the world we might use America (north and south), Europe, Australia, Africa and Asia, but that isn’t useful for racial or ethnic boundaries. In this reviewer’s mind the main Asian population groups would be Japan, China, Korea etc. STRONG suggestion to define racial groupings, and preferentially using a common standard (if there is one). This reviewer doesn’t know the proper approach.

v) Abstract conclusions are confusing: “marked variations in the CW . . . . (p<0.5 among Caucasian dominant . . .) Possibly this is a typographical error, but such a high p range is not significant -- maybe p<0.05?? The sentence reads awkwardly, as well.

vi) Background (page 5 top). The sentence is long, and the referencing seems a bit out of place: suggesting: “Based on anatomical [1-4] and radiological studies,
it has been shown that more than 50% of healthy control subjects have anatomical variations in the circle of Willis (CW). Comparisons based on radiological studies [5-8] in living patients and anatomical autopsy studies [1-4] are not possible as in-vivo data from angiography record luminal . . .”

vii) Word choice and grammar: page 5, line 8: “as a collateral anastomotic network; patients with effective collateral circulations . . .”

viii) The sentence beginning “Autopsy studies have . . .” is very confusing to this reviewer.

ix) Methods: line 8: suggesting 2 sentences: Blood was carefully washed out from the CW with isotonic saline. Line diagrams of all 225 circles were obtained, including photographic records in some cases.

x) Methods paragraph 2, line 2: internal internal

xi) Method (top of page 8) unclear as to the random “section” or whether several diameters were obtained for each vessel segment, and then averaged. How many readings per segment. (issue raised by another reviewer) This is a strongly requested clarification.

xii) Page 9 top: “. . . variations of the CW and their classification into a few clearly arranged groups is hardly possible. We classified variations of CW using 28 Types . . . .”

xiii) Perhaps here, page 9, the authors could clarify their use of the “Asian” labelling.

xiv) RESULTS: line 3 “present study is are

xv) Table 1: there seems to be a few minor errors in the table, perhaps one more serious error, needing explanation: The Sri Lankan study is claimed to have 225 autopsies, while this reviewer adds up the numbers in the Sri L. Column and gets a total of 216. Are there undecided autopsies, that are omitted? Riggs and Rupp column (#10) 33 is stated as 0.1% (why not 3.3%?) The Ozaki study is said to have 134, but the column only adds up to 108. Is row “23” an undecided row? For some of the columns there are “0” entries, and others are left blank. What are the criteria? Line 18 in the table has 58 entries as 3.8%, why not 5.8%. There are many entries in the Sri Lankan study, and the Japanese study that have zero or “1” entry in a category. This reviewer wonders if this large number of insignificant categories has any impact on the conclusions. A MUST FIX CATEGORY IS THE DOUBLE CHECKING ON THE COLUMN ENTRIES FOR THE ENTIRE TABLE, AND THE VERIFICATION THAT SIMILAR CONCLUSIONS COULD BE MADE AFTER THE STATISTICS ARE RERUN. There needs to be clarification of the difference between a blank entry, and a zero entry.

xvi) Discussion, para 2: the first sentence is confusing regarding the numbers: e.g. “in Chandigarh, India [4]” what percentage? What are the sizes of the Indian subcontinent studies, and is the claim that these must be ethnic/cultural differences since there is racial similarity??

xvii) If the Indian sub population studies appear as very similar racially, are the authors confident that the variations among the data could not be due to differences in data assessment?
xviii) The discussion on pages 11 and 12 is rather peripheral – since there were no matching data between cause of death in the Sri Lankan study and the anatomical configurations of the CWs. This reviewer suggests that the discussion SHOULD focus mainly on the circle variations rather than the speculations of stroke incidence at various hospitals.

xix) REFERENCES: it is noted that some of the titles of papers include capitalized nouns, where most do not (the more common convention) e.g. #10,21,22.

xx) The two new figures – photographs of circles, have very unclear lettering (fig. 1 or 2) and from this reviewer’s printout were of quite poor resolution. No scales were presented, and no features noted regarding either circle. While one of the other reviewers did suggest including photographs of example circles, it would be assumed that high quality, informative photos were to be expected.