Reviewer's report

Title: A lumped model to calculate non invasively in clinical practice the brain outflow through collateral vessels

Version: 4 Date: 22 December 2012

Reviewer: Marcello Mancini

Reviewer's report:

In the present study, the author investigates the potential value of a novel lumped model which permits a detailed ECD quantification of the cerebral venous return, including an estimation of the amount of blood flowing from the collaterals. They observe that in CCSVI patients the collateral flow significantly increases as compared to healthy controls. This topic and the obtained results are highly interesting for a better understanding of the pathophysiology of cerebral venous outflow.

Minor Essential Revisions

Evaluation of Doppler venous haemodynamics
The authors should report the duration of the Doppler spectrum on which it was carried out the measurement of the TAV. In the artery the duration of Doppler spectrum should be at least three complete cardiac cycles, in the case of the veins over a period of at least one complete respiratory cycle.

To perform venous flow measurements with an uniform insonation technique could be better to use a sample volume of magnitude of at least half the diameter of the vessel and positioned in the center of the vessel in order to avoid the vessel wall artifacts

it is unclear which measurement of CSA was used for the calculation of venous flow, the minimum or maximum? I think that the most useful measure may be the mean value of CSA during a complete respiratory cycle. In addition, the CSA vein was measured with manual tracing or by other method? Please specify in the text

Refinement of Doppler haemodynamics assessment
Is not very clear the formula used to evaluate the uncertainty of measurement of TAV. The authors delta TAV means the difference between the measured velocity and actual one. However, in this case, the reported formula seems to be wrong, (as, in the limit of vanishing epsilon, according to the formula, delta TAV = TAV instead of 0, as expected). Instead, what can be said is that TAV_actual= TAV_measured * cos(theta)/cos(theta+epsilon).

Neck veins lumped model
The authors in the text and in the figures insert the resistances that are not calculated. This make more difficult the interpretation of the figures and that does
not add anything to the results of the work. In the lumped model that authors used I suggest to remove the resistance and the corresponding boxes. The figures thus becomes more simple and easy to understand.

In the section Calculated indexes the DJDI should be renamed Distal Cerebral Venous Outflow as it includes the blood flow of the vertebral veins.

For the calculation of the inflow would be better to use the velocity integrated in time of cardiac cycle and the velocity integrated in the respiratory cycle time for the calculation of the venous outflow.

CC=cardiac cycle
RC = respiratory cycle
= speed averaged over the cross section (spatial average)

The calculation of Cerebral collateral draining index could be better described by the formula:

The references 14-15 do not correspond to the text
The neck veins lumped model section
“and in collateral segments C2-C3” add C1-2. Change: “and in collateral segments C1-C2 and C2-C3”

In formulas the definition of parameters the subscript “s” is not define

First phase of the study. Arterial inflow
The total flow measured at the level of the common carotid artery both in patients than in controls, does not correspond to the sum of the flow in the internal carotid artery and external carotid artery. In addition the authors also included the flow of the vertebral arteries that should be considered separately. Can the authors discuss this topic?

Venous outflow in supine posture
“In our sample the rate of HBinF drained by the IJVs is 37% in J3, 55% in J2 and more than 90% in J1, respectively, and thus suggesting a re-entry of significant volume of blood along the course of the jugular vein through the collaterals. “
This is different from the values showed in the table where in the normal subjects the trend looks completely different and the blood flow is reduced from J3 to J1 (167ml/min J1 293 ml/min J2 607 ml/mi J3).

Figure 2
in Figures 2a and 2b the right part of the writing circuit is incorrect:
QJ3 200, QJ3 410, QJ3 310 must be modified: QJ3 200, QJ2 410, QJ1 310; in the same way fig. 2b
Moreover it would be better to place the Q at level of the segments and not at
level of the joints of circuit.

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.