Reviewer's report

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

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Reviewer: stefano bastianello

Reviewer's report:

The novelty in this article is represented by the introduction of a new model that permits to study the haemodynamics of cerebral venous return normalized to the head blood in-flow calculating the amount of blood flowing from the collaterals to the Caval System or to the Internal Jugular Vein.

The methods applied are clearly described and the data provided could permit to replicate this work but the method applied is not so easy to understand and has to be widely validated before considering it for clinical trial.

The strengths of the method is represented by mathematical methodology with which they extrapolate the collateral flow but at the same time the weakness is represented by the lack of objective measurement of the same flow!

The use of a constant volume sample size ensures the repeatability of the measure and so far so good but a small sample volume (adjusted for artery) does not seem ideal in a vein where the trend of the flow may not be parallel to the direction of the vessel (helical, etc.)! We read the letter to the editor in which the bibliographic reference but we can not understand how one can, in the proposed manner, to minimize the parameter epsilon (angle error induced by the operator). Some concerns regarding the feedback of physics / fluid dynamics, in my opinion, deserve a review by a professional matter.

Furthermore, the authors provide tables and diagrams to try to help with the interpretation. However they aren't entirely clear and the scheme which shows this new model can be improved by specifying more clarity the entity of collateral and Jugular flow, the flow direction in the distal portion of the Jugular in CCSVI patients, which collateral vessels are involved and finally why the right Jugular drains more than the left Jugular.

Considering the population studied, controls were screened for CCSVI absence by means of established ECD criteria whereas cases are patients affected by CCSVI, screened by the same ECD criteria among patients affected by multiple sclerosis.

The results are not totally conclusive and leave room for new interpretations. The authors provide references to other work to confirm some but not all the data obtained. However, some references are overly cited throughout the text. For
example, reference number 5 is cited six times.

The text is for the most part clearly written but could use some revision by someone with better English.

For example:
1. "... which could potentially compress the neck veins and consequently affecting measurements."
2. ".blood can flow throw all such pathways."
3. "This quota is dramatically increased because does not include only the..."
4. "As an example, we apply the proposed model to compare HC subjects with a CCSVI ones having same age and gender."

In addition, abbreviations are not kept consistent throughout the manuscript. For example:
1. CSA is defined as “cross sectional area” as well as “cross section area”
2. EC/ECA are both used to define “external carotid artery”

The title and abstract sum up adequately the subject matter below, but the term “lumped” is not straightforward to understand.

In conclusion, the rational part of Doppler venous haemodynamics assessment seems to me very important, but I am not competent enough compared to the complexity of the physical explanation of the proposal and, I think, with me 99% of potential readers. A review by an expert in fluid dynamics and, probably, the publication of a magazine like UMB at least part of the specification, make the work unassailable!

Specific comments that need to be addressed:

1. Methods
   1. Off-line assessment of Doppler inflow and outflow haemodynamics

"The acquisition phase was performed by two operators (FS and EM)"

What was the inter and intra rater reproducibility?

2. Methods - Calculated indexes

While the formulae are given, besides CFI, what these values actually represent are not clearly described in the text. The manuscript needs to be updated to better explain them.

2. Results
   1. First phase of the study

"As shown in Table 1, this is a consistent amount of blood never measured before: up to 350 ml/min for C2-3 and more than 500 ml/min for C1-2"

I am unable to follow this statement this based on the data presented in the table.
2. For DJDI/CCDI/DCVO data presented, are these the mean values for all ten controls/patients? This should be more clearly described, as well as presenting the standard deviations.

3. Discussion

1. First phase of the study

"Moreover, we estimated an uncertainty of about 5 degrees in theta when the operator places the sample volume into the J1 lumen."

How was the degree of uncertainty estimated?

2. Several of the proposed indicies and subsequent results aren't even mentioned in the discussion! (CCDI, DJDI, DCVO). Why is this?

4. Table

1. “right”/“left” should be used in favor of “dx”/“sx”

2. “supine”/“upright” should be used in favor of “clino”/“orto”

3. “mean” should be used in favor of “values”

5. Figures

1. It is not clear why the resistance boxes are not labeled in the "IJV-sx" and VV-sx" columns in Figure 1a.

2. In Figure 1b, why are there no flow arrows in the "IJV-sx" and VV-sx” columns? Neither of these questions are explained in the manuscript nor in the text of the figures themselves.

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

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

**Declaration of competing interests:**

NOT TO ALL