Reviewer's report

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

**Version:** 4  **Date:** 13 March 2013

**Reviewer:** Georgios Tsivgoulis

**Reviewer's report:**

The authors attempted to introduce a novel lumped model to calculate the cerebral venous return, normalized to the arterial inflow, in the different segments of the IJV. However there are certain serious methodological shortcomings as outlined below

**Major Compulsory revision**

1. There is currently much controversy regarding the ultrasound criteria used for diagnosis of CCSVI and its potential association with Multiple Sclerosis. Therefore the authors should have described collateral outflow of cervical veins in patients with angiographically confirmed IJV thrombosis or stenosis. There have been previous reports indicating that ultrasound diagnosis of CCSVI does not correspond to abnormal cervical vein anatomy on DSA.
2. The authors do not report the inter-rater and intra-rater reliability of outflow measurements using their model
3. Sample size was limited to ten healthy controls and ten patients with CCSVI
4. Statistical comparisons were not adjusted for demographics and vascular risk factors
5. The Discussion is speculative and does not highlight the potential clinical implications of this study.
6. The authors do not cite recent studies rejecting CCSVI hypothesis in their Discussion and in particular MRI studies indicating that there is no impaired cerebral venous outflow in patients with MS

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

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