Reviewer's report

**Title:** Prospective Study on the mismatch concept in acute stroke patients within the first 24h after symptom onset - 1000Plus study

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**Reviewer:** julien bogousslavsky

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In ischemic stroke, identifying viable tissue susceptible to recovery with thrombolytic reperfusion would be a major advance in selecting patients for this treatment. Thus, the mismatch (surrogate of viable penumbral tissue) concept applied to acute stroke therapy is an attractive hypothesis, grafted into clinical studies from animal experiments. However, probably because of the failure of convincingly significant demonstrations of its usefulness in selecting candidates for thrombolytic therapy and in assessing treatment results, it already seems to belong to old-fashioned methods. Perfusion CT and MR techniques have been proposed, but with variable prediction accuracy of lesion growth and final volume. In the ongoing observational 1000plus study, a 3T MR program is used with an extended time window (24h), which is indeed a critical prolongation of the generally accepted limit of 3-4.5 hours after stroke onset for theombolytic therapy. One should not forget that there is only one randomized trial, which has shown a significant benefit of therombolysis, i.e. the 13-year-old NINDS, where the treatment window was 3 hours. However, since there is no reason that certain patients have no more viable tissue several hours later, a prospective study such as 1000plus is certainly welcome. It may stimulate a new interest in the unfortunately decaying implementation of the mismatch concept into patients management, or on the other hand it may clearly demonstrate its lack of routine practical interest. At the moment, the weakness of the presented protocol is the absence of analysis of stroke type and etiology, which can however strongly influence clinical severity, lesion volume risk of recurrence, availability of collateral circulation, and potential for reperfusion and neurological improvement (minor essential revisions)

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests