Reviewer's report

Title: Skin-impedance in Fabry Disease: A prospective, controlled, non-randomized clinical study

Version: 2 Date: 26 February 2008

Reviewer: Gabor Egon E Linthorst

Reviewer's report:

Review report for Gupta et al.

The manuscript of Gupta et al reports on the outcome of sweat function in treated and untreated Fabry disease patients by means of skin impedance. The authors show that skin moisture levels as measured by skin impedance using the DDIM system differ significantly in Fabry disease patients as compared to normal controls. Whether patients were treated or untreated did not result in different skin impedance measurements.

This research was performed by a group that is well-known with studies on Fabry disease. Though this reviewer is not familiar with the method of skin impedance and as such cannot comment on its validity, the other methods in this study (such as patient selection) are sound.

The main part of the article is devoted to the method used. The authors demonstrate that all variables differ between Fabry disease patients and normal controls. Therefore, it is likely to assume that using the three proposed sites is only required. However, the authors are correct in their statement that this should be validated prospectively (page 13).

My main concern in this study is that the authors used a different method to capture sweat function than in their previous work. In these previous studies improvement in sweat function could be determined, but not with this method. The authors explain this difference by stating that the method used in the current study assesses basal level of skin moisture rather than induced sweating. Since patients with Fabry disease do complain of reduced sweat function, and not of dry skin, I wonder what the use of this DDIM method actually is in Fabry disease. My conclusion would be that although Fabry disease patients can be identified by demonstrating reduced skin moistur, there is no need to expand this method in Fabry disease patients. Moreover, it seems to me that the DDIM method is not a screening tool for Fabry disease, we have excellent other screening methods to diagnose Fabry disease (reduced aGal A activity or DNA mutation analysis).

On the other hand, it is useful to document the failing of the DDIM method in Fabry disease. As such I would recommend to thoroughly revise and shorten the article, which can be done without sacrificing the message.

Table 1, 2 and 3 can be omitted, as well as figure 2.
**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests'