Reviewer’s report

Title: Improved Healing Response in Delayed Unions of the Tibia with Low-Intensity Pulsed Ultrasound: Results of a Randomized Sham-Controlled Trial

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Reviewer: Peter Reynders

Reviewer’s report:

I reviewed this manuscript about a subject which is for many years controversial. The clinical relevance of this subject is without any doubt. Unfortunately I have some queries about this work.

1. Defining the delayed union at a cut-off point of four months from the incident is debatable. Six months, as a time frame would be more realistic;

2. Limiting this study to four months is a serious drawback, which makes conclusions about this study difficult.

3. I have the impression that, because of the missing data, an impressive arsenal of statistical methods were used to compensate for this. Missing data are are unavoidable but one should investigate the reasons for these missing data (maybe patients with bad results went to see another physician,). Where these missing data at random or not? Report details of the software used; Report the number of imputed datasets that were created. What variables were included in this imputation procedure; Were there non-normally distributed variables? The statistical interactions included in the final analyses, were they also included in the imputation models?

4. The chosen endpoints namely in first rank BMD and secondary, change in gap area are not really impressive for the clinicians. Hypertropic non-union have also an increase in bone formation around the fracture gap. So the statistical differences seen with this study corroborate this also with a significant clinical difference? For instance the differences in the transformed Hounsfield units, how important is this? Therefore it’s a pity that the local, ethical boards restricted the period of investigation to only four months.

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