Reviewer’s report

Title: Trial to Re-evaluate Ultrasound in the Treatment of Tibial Fractures (T.R.U.S.T.): A Multicentre Randomized Pilot Study

Version: 1 Date: 28 August 2013

Reviewer: Xavier Griffin

Reviewer’s report:

I have used the CONSORT checklist for non-pharmacological interventions to structure this review.

In summary I find this manuscript to be well written, concise and a useful contribution to our knowledge. I have raised some relatively minor points below but would recommend that the Editor publish this manuscript following minor amendments.

Item 1

Random allocation is described in the title.

I recommend that the abstract include brief details of the countries involved in the study and the specialism of the treating clinicians and committee of outcome assessors.

Item 2

Adequately described.

Item 3

The description of the participant eligibility criteria is sufficient. Some description / defining characteristics of the selection of the six centres is required. A brief description of the specialism / seniority of the supervising clinicians or teams for this complex intervention is required.

It is not clear to me whether patients in whom a fracture gap was apparent were eligible for inclusion. Descriptions in the eligibility criteria, peri-operative treatment and statistical analyses paragraphs do not seem consistent. Please clarify.

Item 4

Adequately described.

Item 5

A formal hypothesis, or perhaps better, a formal research question should be stated – ideally at the conclusion of the introduction. The current concluding sentence of the introduction is inadequate.
Item 6
Primary outcome is clearly described. Further detail is required concerning:

How mal-union was defined.
When non-union was determined to have occurred.
Why 2 or 3 was used as a cut off on the RUST score (please provide reference or justification).

Item 7
Please clarify in this section that statistical significance was determined at 0.05. Please clarify that the sample size calculation was based upon a standard two-way superiority comparison between the two groups. Stratification strategy is clearly explained.

Item 8
Adequately described.

Item 9
Adequately described.

Item 10
Although implied in the text this should be made more explicit – who administered the sequence generation and allocation assignment and how this was implemented to a specific machine.

Item 11
This is appropriately described. However, please specify that the treating clinicians administering the co-intervention of fixation were also blinded if that was indeed the case.

Please provide some description of how the machines were known to be similar other than the transmission of LIPUS. There has been some speculation in past literature that blinding with similar machines has not been as successful as investigators may have liked.

Item 12
I am not a medical statistician and my comments here should be interpreted in that light. Additional opinions from more appropriate reviewers should be sought.

Overall, these seem reasonable. However, I am concerned that the primary analysis was a complete case analysis. Perhaps this was selected since this was a pilot study and a more usual ITT analysis may not have proven terribly helpful to inform a future study. Could the authors justify this decision? Perhaps consider presenting both CC and ITT analysis?

Do the authors think that an adjustment for centre might be appropriate. Whilst the allocation was stratified by centre it might be reasonable to check that centre
was not an important independent predictor of outcome.

Item 13
The diagram is clear and helpful. Please make the single protocol violation more apparent in the diagram.
Please report your loss to follow-up in the text.

There is no description of the number of participants who were recruited within each centre for each treatment arm – this is important information and should be made clear in the text. I think that this information should also be extended to the surgeons providing the co-intervention of IM nailing.

Additional item ‘a’
Reasons for reduced patient compliance are clearly reported. However, for this information to be as useful as possible it would be helpful to know what the compliance was like in each group – perhaps a summary statistic (median time administered) might be appropriate to summarise the duration of the intervention in both groups. Whilst clearly there was no ‘active’ treatment from the sham unit it is possible that a non-compliant participant may not have experienced the same placebo effect as another participant who wore the sham unit throughout the treatment period.

Item 14
Adequately described.

Item 15
Table 1 is clearly presented.

There is no description of the expertise of the treating clinicians with regard to the intervention or co-intervention of IM nailing. Information is required for both.

Item 16
Denominators are clearly reported. Why did the authors choose to only report a CC analysis. I would expect to see an ITT analysis too.

Item 17
I have not been able to access the appendices. I would expect to see mean differences, CIs and ORs with p values as appropriate. I would think that such data might easily be contained within the manuscript in tabular format. Please consider this addition.

Item 18
Adequately described but see item 17.

Item 19
Please clarify in which group these events occurred. Consider tabular format.
Item 20
Loss to follow-up was 8/51. In my experience this is the absolute upper limit of what is acceptable in a surgical trial where recruitment number is relatively small. Please reconsider your statement that follow-up was ‘high’. Only 39/51 participants registered full compliance – again please reconsider the phrasing ‘excellent’. The authors comment that the recruitment rate between centres was highly variable. These data are not reported – see Item 13.

Can the authors ‘re-run’ their sample size analysis substituting their initial assumptions with the data from this feasibility study to refine their required sample size?

Item 21
Not appropriate here.

22
Appropriate discussion of the changes made to the design of the TRUST study.

**Level of interest:** An article of outstanding merit and interest in its field

**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