

Dear Editor,

Please find enclosed the edited manuscript in Word format (17951 Review.doc)

Title: Invited Editorial: Aetiology and mechanisms of injury in Medial Tibial Stress Syndrome: Current and future developments

Authors: Melanie Franklyn and Barry Oakes

Name of Journal: *World Journal of Orthopaedics*

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Response to reviewers by authors

We would like to thank both reviewers for spending the time to read and comment on our manuscript. We believe the paper will be significantly improved by their suggestions. Please find our responses to individual issues below. We have marked-up all the changes in the text so the reviewers can easily identify the changes which have been made.

Response to Reviewer 1 (Number 02699758)

Thanks kindly for your positive comments, and we are glad you think the paper is readable to a wider audience than just sports medicine researchers. We hope it will appeal to most readers of the *WJO*. We understand that many individuals believe that MTSS is just periostitis, and besides a few earlier papers such as the work by Johnell and colleagues, it is only more recently that research has shown the cortical bone involvement in MTSS. However, we believe that the recent work on bone geometry and BMD is just the start of understanding the relationship between these factors and MTSS, and more work is clearly needed.

With regards to the issues you raised:

1. Page 8, lines 12 and 22: Is “cadavera” correct? Is “cadavers” correct instead of “cadavera”?
Both ‘cadavers’ and ‘cadavera’ are correct for the plural form of cadavers. ‘Cadavers’ is used by the US, whereas ‘cadavera’ is used in the UK (and thus also used in Australia). This is similar to tibiae (US) and tibiae (UK/Australia).
2. Page 12, line 5 from the bottom: The word “early” probably does not have to be underlined.
We have removed the line under the word ‘early.’ It was initially included to emphasise the point; however, we agree with you it is not really needed, so we have removed it.

Thank-you kindly for reading our manuscript and we greatly appreciate your time and comments.

Response to Reviewer 2 (Number 03065340)

Thank-you very much for your very helpful comments and suggestions. We are glad you think we have presented valuable information and hope this paper will be a good reference for clinicians and researchers in the sports medicine field as well as of interest to individuals in orthopaedics.

We have addressed some of your individual comments below:

1. However, for my opinion the main text as well as the conclusion part lacks of some sentences about the clinical relevance and some instructions for sports orthopaedics and military medicine treating athletes or military recruits with MTSS or TSF. What evaluation method should be used in which situation? Does the current data give any information about treatment methods??

We agree with your comment and on review, we see that this information is lacking in our paper. We have now added in some text to address this issue. Firstly, we have added a new section in the text 'Advice for the treating physician' (Section 9) which has detailed information on diagnosis and differential diagnosis for the clinician. We have also added a summary of this information in both the Abstract and the Conclusion sections. In both Section 9 and the Conclusion, we have also included some information on treatment; however, this is not extensive as we felt it is too complex to do it justice in a review on aetiology and mechanisms of injury.

2. Correction of the chapter-numbering is necessary. (3. is used several times)

Thank-you for pointing this out, as we obviously missed this when we re-ordered some of the chapters. The chapter numbering has now been amended.

3. References: However, only three papers out of 60 are published 2012 or later. There is a big request to conduct further studies in this topic. At present, no definite results are available and it seems that new findings with current evaluation methods can't be expected in the near future.

We are not sure if the reviewer would like us to add some additional references from 2012 and later or to address their question. We have addressed the question here.

One of the main issues is that more recently, most papers have focused on risk factors, interventions or treatment options, but not on the actual mechanisms (the focus of our paper). We mentioned this in the text in the first paragraph in the Strain Gauge Analysis and Computer Modelling section, and also in the first paragraph of the Conclusion section.

A search on Google Scholar for MTSS papers published from 2012-2015, for example, shows there is a thesis on rehabilitation exercises for MTSS, four papers on risk factors, two papers on treatment options (one of which is also a review paper), one paper on the incidence of MTSS in

runners, and one paper on clinical testing. In some of these papers, risk factors or treatment options which have previously been identified are 'rediscovered', and there are no papers on specific mechanisms. We believe that future research needs to focus on longitudinal studies examining these mechanisms (which we discussed in the paper e.g. in the Conclusion section) in order to develop appropriate clinical tests and specific treatment protocols.

However, studies on specific injury mechanisms require significant effort: potentially large cohorts of subjects, medical imaging studies and detailed analyses. As many organisations or funding bodies currently want 'quick-fix' solutions such as simple clinical tests or easy treatment options, researchers are forced to focus on these topics for their studies, particularly if they want to gain research funding.

Thus, although we did not wish to quote a lot of our own work in the paper, there are only a few groups of researchers we know of investigating bio-mechanisms involved in MTSS. While we have mainly focused on cortical bone geometry, the Magnusson researchers are the main groups who have examined BMD in MTSS patients.

4. The paper is an invited Editorial paper and should be stated as one in the title.

We have now changed the title to 'Invited Editorial: Aetiology and mechanisms of injury in Medial Tibial Stress Syndrome: Current and future developments.' We hope this is clearer or if not, if you have an alternative suggestion, please let us know.

Final comment: We have changed 'scintigraphy' to 'nuclear bone scan' throughout the paper: the former is usually used by nuclear medicine experts, while the latter is usually used by clinicians. As this paper will be mainly read by clinicians (and scientists), we changed it to 'nuclear bone scan'.

Thank-you kindly for all your comments and we think our paper has greatly improved as a result.

Yours sincerely,

Melanie Franklyn

Department of Mechanical Engineering
Engineering Block E Building Level 4
The University of Melbourne
Parkville, Victoria, 3010
Australia
Email: melanief@unimelb.edu.au
Phone: +61 3 9626 7171
Fax: +61 3 9626 7830