Author’s response to reviews

Title: The effect of running task on muscle shear elastic modulus of posterior lower leg

Authors:
Shuhei Ohya (hpa14019@nuhw.ac.jp)
Masatoshi Nakamura (masatoshi-nakamura@nuhw.ac.jp)
Takafumi Aoki (hpa14001@nuhw.ac.jp)
Daichi Suzuki (hpa14050@nuhw.ac.jp)
Takanori Kikumoto (kikumoto@nuhw.ac.jp)
Emi Nakamura (emi-nakamura@nuhw.ac.jp)
Wataru Ito (wataru-ito@nuhw.ac.jp)
Ryo Hirabayashi (hirabayashi@nuhw.ac.jp)
Tomoya Takabayashi (takabayashi@nuhw.ac.jp)
Mutsuaki Edama (edama@nuhw.ac.jp)

Version: 1 Date: 28 Sep 2017

Author’s response to reviews:

Dr Alan Borthwick
Editor in Chief
Journal of Foot and Ankle Research
Sep. 29, 2017

Dear Dr. Alan Borthwick

Ref. No.: JFAR-D-17-00083
We are most grateful to you and your journal’s reviewers for the helpful comments on the original version of our manuscript entitled,


We have revised the manuscript in accordance with the reviewers’ suggestions and hope that the article is now suitable for publication in the Journal of Foot and Ankle Research.

Our point-by-point responses are set out below. For clarity, reviewer comments are italicized and the changes in the revised manuscript are highlighted in red.

Thank you for your time and we look forward to hearing from you at your earliest convenience.

Yours sincerely,

Masatoshi Nakamura

Institute for Human Movement and Medical Sciences, Niigata University of Health and Welfare, 1398 Shimami-cho, Kita-ku, Niigata City, Niigata, 950-3198, Japan

Telephone: +81-25-257-4451; Fax: +81-25-257-4451

E-mail: masatoshi-nakamura@nuhw.ac.jp

Reviewer #1: This study was mildly interesting, but I think there is a lot of concern before publishing it to this journal. My major concerns are study design and the results of the absolute values.

We thank the reviewer for the constructive comments and suggestions regarding our manuscript entitled “The effect of a running task on muscle shear elastic modulus of the posterior lower leg.” Below is a point-by-point reply to the reviewer’s comments. For clarity, the text is quoted in red, and the revisions are underlined.

#1

Was the subject selection appropriate for the aim of this study?
The author wants to know the changes in elastic moduli of the muscles after running task, since which could be a possible reason for MTSS occurrence. But, why the author excluded the person with history of musculoskeletal injury? The author indicated that the higher elastic moduli were found in subjects with MSST history and hypothesized that the elevation of shear elastic moduli of FHL and TP would occur after running task. I wonder whether the baseline values of elastic moduli would influence to the change in those values after tasks. Even if the results indicated the elevation of the elastic moduli after tasks, were the elastic moduli of normal subjects achieved to the substantial for inducing MTTS? I don't know whether there is the threshold of abnormal elastic moduli, but could the elevation of elastic moduli on this study explain enough elevation for occurrence of MTTS? Moreover, how do the authors think it possible to apply the results of the healthy subjects into the patients?

Thank you for your questions. In this study, we excluded subjects with a history of neuromuscular disease or musculoskeletal injury involving the lower extremities, including history of MTSS. According to your suggestion, we completely agree that the baseline values for shear elastic moduli would influence a change in these values after a running task. However, the purpose of this study was to investigate the effect of 30 min of running, which can cause MTSS, on the shear elastic modulus of the posterior lower leg; therefore, we excluded subjects with MTSS or who had a history of MTSS, considering that their baseline values for shear elastic moduli could have been affected after the running task.

Bouche et al (2007) reported that strain in the tibial fascia increased as tension on the PT, FDL, and SOL tendons increased. The results of this study showed that the shear elastic moduli of FDL and TP tendons increased after a 30-min running task. Because the shear elastic modulus can be used as an indirect index of tension applied to a muscle (Koo et al, 2013; Maisetti et al, 2012), our results suggested that passive tension applied to FDL and TP increased after the running task. Taken together, we assumed that the increases in passive tension applied to FDL and TP after the running task would lead to an increase in the strain on the tibial fascia, resulting in the development of MTSS. Therefore, we have revised the Discussion section as follows to clarify these points:

(PAGE 11, LINES 220–222)

Taken together, we assumed that the increases in passive tension applied to FDL and TP after the running task leads to an increase in the strain on the tibial fascia, resulting in the development of MTSS.

In addition, because the purpose of this study was to elucidate the mechanism of MTSS development by investigating the effect of running on the shear elastic modulus of the posterior
lower leg, we conducted the study with healthy adults and not with runners or MTSS patients. Because it is unclear whether the same change would occur in runners and MTSS patients, we have added the following explanation as a limitation of this study:

(Page 13, lines 247–253)

Second, in this study, we investigated only the acute effect of running on the shear elastic modulus of healthy subjects and not of runners and MTSS patients. Thus, further study is needed to investigate the retention time of changes in the shear elastic modulus as well as the effects of repeated running tasks on the shear elastic modulus of the posterior lower leg in runners and MTSS patients to elucidate the chronic mechanism underlying MTSS development.

#2

Please clearly indicate the unit in Table 1 and 2. It can be kPa.

If I accept it would be kPa, according to Ref. #15, the absolute values of shear elastic modulus in each muscle was 2–6 times smaller than those in previous report (Ref. #15). I guess it too small. Actually, subject of their work were collegiate runners, while this study investigated normal subjects. Is that the subject-difference? or methodological difference? Please explain why.

Thank you for your suggestions. We have added the unit kPa in Tables 1 and 2. In addition, as per your suggestion, the absolute values for shear elastic modulus in this study were 2–6 times lower than those in the previous study (Saeki et al, 2017), because the ankle joint positions differed between the two studies; the shear elastic modulus was measured at 0° dorsiflexion of the ankle joint in this study and at 20° dorsiflexion of the ankle joint in the previous study. It is well known that shear elastic modulus increases with muscle elongation (i.e., dorsiflexion), and we believe that the difference in the ankle joint position would have influenced the difference in absolute values between the two studies.

My specific comments are listed by order of appearance in the manuscript.

#3

In Background, Page 5 Line 62- and 72-

The topics of these paragraphs seem obscure. Please stick to one topic in one paragraph.

I conceive the implication of the author on these paragraphs, which would be "Higher shear elastic modulus of the posterior leg could be one of the reasons for MTSS occurrence. But the
previous studies investigated only the relationship between elastic modulus and the pain, or MTS history; it has never done if the changes of elastic modulus occur after prolonged running”. Is that correct? If so, please reorganize the paragraphs.

Thank you for your indications. In lines 62–71 of the original manuscript, we stated that the previous in vitro studies suggest that MTSS could be caused by the excessive elongational stress and muscle stiffness of the FDL and/or SOL. Also, in lines 72–91 of the original manuscript, we have stated facts from a previous study on shear elastic modulus. As per your suggestion, we have revised the manuscript text as follows to clarify these points:

(Page 5, lines 88–94)

Therefore, these previous studies suggested that higher shear elastic modulus of the posterior leg could be one of the reasons for the occurrence of MTSS. However, previous studies have investigated shear elastic modulus in only MTSS patients who experienced pain at the time of measurement or in those who had a history of MTSS; it remains unclear whether the changes in the shear elastic modulus occurred after prolonged running, which is believed to cause MTSS.

#4

Page 5 Line 80-81

I could not figure out the meanings on "the pain at the time of measurement could influence the shear elastic modulus". Pain and physical properties were a bit different concept. What influences elastic modulus, indeed? I guess it should not to be a pain itself. Please explain the detail.

Simons et al (1998) indicated that an increase in muscle stiffness can be caused by pain-induced spasms. Therefore, in a previous study by Akiyama et al (2016), the higher muscle stiffness in MTSS patients may have resulted from pain-induced spasms. We have therefore revised the manuscript text as follows to clarify this point:

(Page 5, lines 80–82)

However, because the increase in muscle stiffness can be caused by pain-induced spasms [15], the pain at the time of measurement may influence the shear elastic modulus.

#5
Please indicate the participants' daily physical activity level of fitness level, if possible.

As per your indication, we have added the participants’ daily physical activity level, as shown below:

None of the subjects were recreational or competitive runners; they were recreationally active but not involved in any ongoing strength training and stretching activities.

Thank you for your suggestions. There were individual differences in axial or mediolateral location, and we did not clearly define the measurement site of axial or mediolateral location. However, according to a previous study (Saeki et al, 2017), we confirmed the muscle by confirming the movement of muscle fibers using a B-mode ultrasound image during passive movement of the ankle or toes (lines 136–138 in the revised manuscript). In addition, the results of this previous study (Saeki et al, 2017) and the current study showed that the shear elastic moduli measurements were highly reliable. Therefore, we believe that we could reliably measure the shear elastic modulus of the target muscle.

Regarding the orientation of the ultrasound probe, we recorded measurements with longitudinal direction of the muscle. Moreover, we marked the measurement site with an oil pen and ensured that measurements were recorded from the same site before and after running. To clarify our measurement method, we have added Figure 2 for indicating the measurement site and revised the following sentences about probe direction and marking:
As shown in Figure 1, we measured the shear elastic moduli of the longitudinal axis of LG, MG, FDL, TP, PL, and peroneus brevis (PB) muscles. In addition, as shown in Figure 2, the measurement locations were determined based on a previous study [16].

In addition, we marked the measurement site with an oil pen and ensured that measurements were recorded from the same site before and after running task.

#6-2 Why the author did not collect the data of SOL and FHL, which were measured in Ref. #15?

SOL and FHL could not be measured due to machine performance and technical problems.

#6-3 Figure 1 would be cited at the wrong place, or the explanation of the figure legend would be different.

Thank you for your correction. Because Figure 1 was incorrectly cited, we have changed the position of this citation in the revised manuscript:

(Page 6, lines 126–127)

As shown in Figure 1, we measured the shear elastic moduli of the longitudinal axis of LG, MG, FDL, TP, PL, and peroneus brevis (PB) muscles.

#7

Page 11 Line 206-211

Why the author said "tension", in spite of the measurement was performed at resting state? Is that correct to change the word "tension" into "passive tension"? Please use appropriate word.

Why the elevation of the shear elastic moduli could be a risk factor? What makes passive tension? Does the passive tension cause the pain? The author seems to avoid the mechanism and only describe the phenomenon. If possible, please discuss the mechanism.
According to your suggestion, we have revised the word “tension” to “passive tension” in the revised manuscript. Also, we do not believe that passive torque directly causes pain. MTSS is the result of a lesion at the junction of the periosteum and fascia (Moen et al, 2009). In addition, because the strain in the tibial fascia increases with an increase in the tension on FDL and TP tendons [20], we assumed that the increase in passive tension applied to FDL and TP after the running task leads to an increase in the strain on the tibial fascia, resulting in the development of MTSS.

(Pager 11–12, lines 217–218)

Therefore, the passive tension applied to FDL and TP may have increased after the running task.

#8

Page 11 Line 212- Page 12 Line 223

Please write a topic sentence at the beginning of a paragraph, which apply throughout the manuscript. It makes me lost the meaning of the paragraph many many times.

By the way, this paragraph is written about the foot abnormality but I feel it does not fit to the flow of the discussion. Actually, the readers of this journal most interest the topic of foot and ankle; but please rewrite the paragraph in order to get in to the stream.

We agree that this paragraph did not fit the flow of the Discussion section. Therefore, we have deleted the paragraph in the revised manuscript.

#9

I am wondering if the elevation of elastic moduli disappears or sustains after prolonged resting. It may be beyond this manuscript, but if sooner the elastic moduli recover to the baseline, the results of this study do not a significant matter.

As you suggested, it is very important to ascertain the retention time of the changes in the shear elastic modulus after running. A previous study (Saeki et al, 2017) reported that the shear elastic moduli of FDL and TP were higher in subjects with MTSS history than in those without it; therefore, we believe that an increase in the shear elastic moduli of FDL and TP may be associated with MTSS development. Unfortunately, we did not measure the retention time of the changes in the shear elastic modulus after the running task. Therefore, we have added the
following description about the need of conducting future research for considering the retention time in the Limitations section as follows:

(Page 13, lines 249–253)

Thus, further study is needed to investigate the retention time of changes in the shear elastic modulus as well as the effects of repeated running tasks on the shear elastic modulus of the posterior lower leg in runners and MTSS patients to elucidate the chronic mechanism underlying MTSS development.

#10

Page 12 Line 230-233

The author discuss about the myofascial transmission. I wonder if the myofascial transmission occurs acutely, it seems less reasonable just 30 min running cause myofascial transmission.

We completely agree that myofascial transmission did not occur during the 30 min of running. Although TP is not attached to the margin of the tibia, which is commonly affected due to MTSS symptoms, it is a neighboring muscle of FDL; therefore, we assume that the increase in shear elastic modulus of TP after running may lead to an increase in the passive tension on FDL via myofascial force transmission, which may be associated with MTSS development. To clarify this point, we have revised the description as follows:

(Page 12, lines 231–235)

A previous study [16] found that a higher shear elastic modulus of TP could lead to myofascial force transmission to FDL, which is attached to a site commonly affected by MTSS [10]. Therefore, an increase in the shear elastic modulus of TP after running may lead to an increase in the passive tension on FDL via myofascial force transmission, which may be associated with MTSS development.

#11 Followings are the minor comments

Page 8 Line 166

0.710 or 0.709?
Thank you for your suggestion. We have revised “0.710” to “0.709.”

(Page 9, lines 174–177)
The ICC (1, 1) ranged from 0.709 to 0.985 for the shear elastic moduli of each muscle.

Page 11 Line 213-214
I could not figure out the meaning "which is commonly affected in MTSS at 95% in males and 100% in females".
Thank you for your suggestion. We have deleted this text in the revised manuscript.

References
Please indicate detailed information of Ref. #15.
As per your indication, we have added the details of Reference #16 in the revised manuscript as follows:

(Page 16, lines 327–329)

Reviewer #2:
I was a pleasure to review the article, 'The effect of a running task on muscle shear elastic modulus of posterior lower leg', for possible publication in the Foot and Ankle Journal.

The authors should be congratulated in how they conducted this research. I only have minor comments prior to publication.

We thank the reviewer for the constructive comments and suggestions regarding our manuscript entitled “The effect of a running task on muscle shear elastic modulus of posterior lower leg.” Below is a point-by-point reply to the reviewer’s comments. For clarity, the text is quoted in red, and the revisions are underlined.
- Page 4, line 54- Change 'long duration' to 'longer duration'
- Page 4, line 55- Change '1-10' to '10-point'
- Page 4, line 61- change 'method' to 'protocol'
- Page 4, line 62- change 'fully clarified' to 'clear'
- Page 5, line 73- change 'is drawing attention' to 'has emerged'

Thank you for your suggestions. Based on your comments, we have revised the descriptions as follows:

(Page 4, lines 53–56)

In addition, athletes with MTSS should stop participating in competition for up to 16 week [6], and a longer duration was necessary until the athletes with MTSS could run with a pain score of 4 or less on a 10-point scale [7].

(Page 4, lines 58–61)

Based on the injury prevention model proposed by Van Mechelen [8], it is necessary to identify the mechanism and factors of injury to prevent the injury, and this might be useful for constructing the injury prevention protocol.

(Page 4, lines 62–64)

Although the mechanisms and risk factors for MTSS are not clear, the symptoms of MTSS could be due to the stress response of the fascia and periosteum at the medial border of the tibia [9].

(Page 5, lines 72–73)

Recently, an ultrasound elastography technique, known as ultrasonic shear wave elastography (SWE), has emerged as a method for estimating shear elastic modulus [11].

- Page 6, line 99- Participants- were these individuals who were recreational runners or had were not undertaking any current running training?

The participants in this study were not recreational or competitive runners; however, they were recreationally active. We have added a description to clarify the participants’ activity level:
None of the subjects were recreational or competitive runners; they were recreationally active but not involved in any ongoing strength training and stretching activities.

Was the same person performing all the scanning? Was the same person analysing the shearwave scans? Was the person analysing blinded to the participant and when the scan was taken in relation to the scanning protocol?

In this study, one person performed all the scanning, while another person performed the shear wave analysis. Unfortunately, the researcher who analyzed the shear wave scans was not blinded to the participant information when the scans were recorded in relation to the measurement period. Therefore, we have added the following clarification as a study limitation:

First, the researcher who analyzed the elastographic images was not blinded to the subjects and measurement period.

Was the intra-class correlation performed for consistency or absolute agreement? Also and ICC (1,1) assumes that there are multiple raters. Was this the case?

Because one skilled individual (SO) conducted the measurements in this study, we examined the intersession reliability and reported the intraclass correlation coefficient (ICC; 1, 1) for relative reliability.

Can I suggest you calculate the minimum detectable difference based on your reliability data? This will strengthen the paper and allow you to state that any observed changes are not due to systematic error.

Thank you for your suggestion. ICC indicates relative reliability. Based on your suggestion, we have added the result of the minimum detectable difference at 95% confidence interval (MDD95%), which is an indicator of absolute reliability, in Table 1.
The minimal detectable difference at 95% confidence interval (MDD95%) was calculated as follows: \[ MDD95% = z \times SEM \times \sqrt{2}, \] where \( z = 1.96 \) and standard error of measurement (SEM) = \( SD\sqrt{(1 - ICC)} \) [18].

The ICC (1, 1) and MDD95% of intersession measurements are shown in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>ICC (1, 1)</th>
<th>reliability</th>
<th>MDD95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>LG</td>
<td>4.9 ± 1.4</td>
<td>4.8 ± 1.4</td>
<td>0.938</td>
</tr>
<tr>
<td>MG</td>
<td>11.3 ± 3.3</td>
<td>11.3 ± 3.3</td>
<td>0.916</td>
</tr>
<tr>
<td>FDL</td>
<td>4.3 ± 3.7</td>
<td>4.2 ± 3.7</td>
<td>0.985</td>
</tr>
<tr>
<td>TP</td>
<td>3.8 ± 1.0</td>
<td>3.7 ± 1.0</td>
<td>0.852</td>
</tr>
<tr>
<td>PL</td>
<td>6.5 ± 5.2</td>
<td>5.5 ± 4.7</td>
<td>0.709</td>
</tr>
<tr>
<td>PB</td>
<td>4.8 ± 3.0</td>
<td>4.4 ± 2.9</td>
<td>0.733</td>
</tr>
</tbody>
</table>

ICC: Intraclass correlation coefficients, MDD95%: minimal detectable difference at the 95% confidence interval, LG: lateral gastrocnemius, MG: medial gastrocnemius, FDL: flexor digitorum longus, TP: tibialis posterior, PL: peroneus longus, PB: peroneus brevis

Wasn't this paper performed in people without pain but history of MTSS? Please clarify

A previous study examined people without pain but with a history of MTSS. Therefore, we have revised the description in the manuscript as follows to clarify this point:
A previous study showed that there were no significant differences in the shear elastic moduli of these muscles between subjects with and without a history of MTSS and who did not have pain at the time of measurement [16].

-Page 12, line 242- 'were not mechanisms of' to 'may not be associated with'

Based on your comment, we have revised the description as follows:

(Pages13, lines 243–245)

Taken together, these results indicate that the elongation stress and hypertonicity of LG, MG, PL, and PB may not be associated with MTSS development.

-Page 12, line 246- Not so much a comment to act on, but I think it would be also interesting to look at the temporal nature of this response and when these changes in stiffness return to baseline. May add some understanding around periodisation of loading.

We agree that it would be very interesting to investigate the time course of changes in shear elastic modulus and the timing of return to baseline. In future, we propose investigating the time course of these changes and of return to baseline and the effects of a repeated running task on the lower leg.