PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>Feasibility and Tolerability of Bone Impact Microindentation Testing: a cross-sectional, population-based study in Australia</th>
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<tbody>
<tr>
<td>AUTHORS</td>
<td>Rufus, Pamela; Holloway, Kara; Diez-Perez, A; Kotowicz, Mark; Pasco, Julie</td>
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</table>

VERSION 1 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Oliver Richard Boughton</th>
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<tbody>
<tr>
<td>Imperial College London, UK</td>
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<tr>
<td>REVIEW RETURNED</td>
<td>11-May-2018</td>
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</tbody>
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<table>
<thead>
<tr>
<th>GENERAL COMMENTS</th>
<th>Overall, a well written paper answering an important question.</th>
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<tbody>
<tr>
<td></td>
<td>My concerns are that all the patients were male so does this apply to female patients?</td>
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<td>There should be a description of how the device works in the paper, such as one of the original descriptions by Dr Hansma. I know how it works but a general audience might find it too much to source other papers and the other papers may not be open access.</td>
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<td>It would have been much better if patients were involved in the research from the outset. See the UK NIHR's INVOLVE website for more details on how to do this.</td>
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<td>page 5, line 10 should be &quot;were&quot; rather than &quot;was&quot;</td>
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<td></td>
<td>Please add the ethics committee approval number.</td>
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<td></td>
<td>Page 6, line 29: a reference should be added for why you chose visual analogue scales</td>
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<td></td>
<td>page 7, line 24: all p and r letters should be italicised</td>
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<td></td>
<td>p=281 is surely a typographical error?</td>
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<tr>
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<td>table 1, p should be in italics</td>
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<td></td>
<td>table 2: do the results have a normal distribution? If not they should be reported as medians and interquartile ranges</td>
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<tr>
<td></td>
<td>In the discussion we bring to the authors' attention a potential concern that research group have with the Osteoprobe. The fact that it deliberately causes plastic deformation and microcracks in the bone, albeit on the microscale, is slightly concerning, particularly in a patient with low burn turnover and risk of microcrack accumulation (e.g. patients on long-term bisphosphonates). Would the authors be able to ask their patients</td>
</tr>
</tbody>
</table>
whether this was a concern for them? Here is our paper: https://www.ncbi.nlm.nih.gov/pubmed/28924020

The authors conclude that soft tissues were the main reason for non-participation. Is there any way to get around this problem? Also, how much did excessive soft tissue correlate with BMI?

In the discussion all p and r values should be in italics

Overall, I recommend it should be accepted, subject to the above changes being made.

REVIEWER
Simon Tang, Ph.D.
Washington University in St Louis, USA.
REVIEW RETURNED 22-Jun-2018

GENERAL COMMENTS
The authors Rufus et al present on their findings of willingness of participation in a microindentation study. The participants were surveyed for their willingness to undergo in vivo microindentation measurements, as well as subsequent pain and suffering surveys. This data is important for implementing this technology in the a clinical prospective study, and will critically advance the knowledge of the field.

This reviewer believes that there are few areas that would improve the manuscript:

- The title isn’t sufficiently descriptive of the scope of the study, Feasibility usually refers to the technical aspects of indentation and it is not immediately obvious that this is a study on participant willingness and subsequent reporting of pain/discomfort. I suggest that the title be revised accordingly.

- The authors should disclose the information provided to the participants relating to IMI as this plays a role in the individual decision to participate.

- Table 1, the p-values for Height and BMI were reported as 0.0 — is this a typographical error? In general the p-values should be reported out to at least 2 decimal places.

- One of the data exclusion criterion was skin infections, but it is not clear whether this is exist infections prior to indentation, or new infections developed as a result of the indentation.

- It may also be helpful if the authors could discuss strategies to improve recruitment of participants, as well as retention of participants, particularly those who report discomfort.

VERSION 1 – AUTHOR RESPONSE

REVIEWER 1 -Oliver Richard Boughton
My concerns are that all patients were male, so does this apply to female patients?
In this study, we have investigated men only and have acknowledged that the observations may not be generalisable to women or other populations—“In our study, we investigated men only, and recognise that the observations may not be generalisable to women or other populations” (Page 11,
Line 15). Future measurements for women are planned for women in their next assessment phase of the Geelong Osteoporosis Study (in a few years).

There should be a description of how the device works in the paper, such as one of the original descriptions by Dr Hansma. I know how it works but a general audience might find it too much to source other papers and the other papers may not be open access. This information has been included in the manuscript- “The Osteoprobe measures Bone Material Strength Index (BMSi). This parameter quantifies how well a bone resists microindentation. BMSi is defined as 100 times the ratio of the indentation distance from the impact to a calibration material, PMMA (poly methyl methacrylate), divided by the indentation distance from the impact into the bone. As the probe indents the bone, it induces microfractures. The more easily the bone is fractured, the deeper the probe indents and the lower the BMSi” (Page 3, Line 24)

It would have been much better if patients were involved in the research from the outset. See UK NHR’s INVOLVE website for more details on how to do this. Thank you for your comment. The Geelong Osteoporosis Study is an ongoing longitudinal cohort study; and micro indentation measurements were introduced at the 15-year follow up phase for men, which commenced recently (2016). Additionally, the OsteoProbe device was only first described in 2012. Hence, it was impossible to involve participants from the outset. The source population in this study is described on page 5. Page 5, line 10 should be “were” rather than “was” Thank you. This has been edited

A reference should be added for why you chose visual analogue scale. Page 7, line 24: all p and r letters should be italicised. P=281 is surely a typographical error? Thank you. These have been updated.

The results were normally distributed. The result section has been updated to reflect this. In the discussion, we bring to the authors’ attention a potential concern that research group have with the OsteoProbe. The fact that it deliberately causes plastic deformation and microcracks in the bone, albeit on a microscale, is slightly concerning, particularly with low bone turnover and risk of microcrack accumulation (e.g. would authors be able to ask patients whether this was a concern for them)? Thank you for your comment. It is impracticable to ask participants retrospectively and although there may be a potential concern for possible harm to the bone, all 252 participants who had a successful measurement indicated a willingness to undergo the measurement again-“while there may be a potential concern for possible harm to the bone, all participants who had a successful measurement indicated a willingness to undergo the measurement again” (Page 9, Line 4). Moreover, the published experience with the technique in different centers and by different investigators has not detected any harm to the bone whatsoever (Reference #15)

The authors conclude that soft tissues were the main reason for non-participation. Is there any way to get around this? The manufacturers of the OsteoProbe at ActiveLife acknowledge this limitation, and are currently working on several solutions for individuals with excessive soft tissue. It has been considered that longer probes be developed in order to reach the periosteum even in people with very thick soft tissue (morbid obesity for example). However, this would modify the mechanical conditions of the experiment and therefore significantly affect the results. How much did excessive soft tissue correlate with BMI

This has been updated in the results section- “The average BMI of participants excluded due to soft tissues was 33.4 ± 5.586” (Page 7, Line 17) In the discussion all p and r values should be italicised
Thank you. These have been updated.

REVIEWER 2- Simon Tang, Ph.D.
The title isn’t sufficiently descriptive of the scope of the study, Feasibility usually refers to the technical aspects of indentation and it is not immediately obvious this is a study on participant willingness and subsequent reporting of pain/discomfort. I suggest that the title be revised accordingly
Thank you. Title has been updated to “Feasibility and tolerability of impact microindentation testing in population-based research”
Table 1, the p-values for height and BMI were reported as 0.0- is this a typographical error? In general, the p-values should be reported out to at least two decimal places.
Thank you. These have been updated
The authors should disclose the information provided to the participants relating to IMI as this plays a role in the individual decision to participate.
This information has been added to the manuscript- “They were informed that the procedure is a new technique that might assess the resistance of bones to fractures by inducing micro fractures on a small area of the tibia. Furthermore, participants were told the procedure is minimally invasive and does not affect the ability of the individual to walk immediately after. They were then given the option to participate or not participate in the study” (Page 5, Line 16)

One of the data exclusion criteria was skin infections, but it is not clear whether this is existing infections prior to indentation, or new infections developed as a result of the indentation.
These participants were excluded due to existing skin conditions. The manuscript has been edited to reflect this- “Of 345 potential participants, exclusions were: needle phobia (n=8), existing skin infections (n=21), excessive soft tissues around mid-tibia region (n=56), due to discomfort (pressure, no pain) after the first indentation (n=5), unable to provide informed consent (n=2) (Page 7, Line 8)”. This is one of the contraindications of the technique as described by a methodology paper (Ref #15) It may also be helpful if the authors could disclose strategies to improve recruitment of participants, as well as retention of participants, particularly those who report discomfort
Thank you for your comment. However, we did not have any significant problems with recruitment and retention of participants in this study. The most common reason for exclusion was excessive soft tissues around the mid-tibia. Other reasons for exclusions were pre-existing skin infections, needle phobia, inability to provide informed consent and discomfort after the first indentation, but these affected only one-tenth of the study participants.
In general, most of the participants who were eligible for the microindentation test agreed to participate. Furthermore, all participants who had a successful measurement indicated a willingness to undergo the measurement again.

VERSION 2 – REVIEW

| REVIEWER | Oliver Richard Boughton
| Imperial College London |
| REVIEW RETURNED | 14-Aug-2018 |
| GENERAL COMMENTS | The authors have addressed my comments and it is now suitable for publication, providing the below very minor changes are made:
- The subtitle "Source population" needs to be on a new line.
- In the discussion section some r and p values needs to be put in italics still. |
One more minor comment is please put a space before and after the equals signs for all r and p values.

**REVIEWER**
Simon Tang  
Washington University in St Louis, USA

**REVIEW RETURNED**
13-Aug-2018

**GENERAL COMMENTS**
The authors did a nice job addressing this reviewer's concerns.

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**VERSION 2 – AUTHOR RESPONSE**

Reviewer 2
No comments

Reviewer 1
The subtitle "Source population" needs to be on a new line.

-In the discussion section some r and p values needs to be put in italics still.

-One more minor comment is please put a space before and after the equals signs for all r and p values.

Thank you. All of these changes have been made.