Author's response to reviews

Title: Assessment of a Novel Biomechanical Fracture Model for Distal Radius Fractures

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Author's response to reviews: see over
Dear editorial team, dear reviewers

On behalf of all coauthors, I would like to thank you for your time, effort and honest consideration of our paper. We were happy to address the reviewers’ comments and believe that this did raise the quality of the paper significantly. At the end of this cover letter you will find the request point-by-point response to the reviewers’ concerns. We hope we were able to sufficiently address all comments.

The authors are convinced that this paper will have an impact on further research as stated above and should consequently be accessible to a wide range of researchers. We believe BMC Musculoskeletal Disorders to be the only journal to meet those demands.

Competing interests:
Medartis Inc. provided the sawbones and osteosynthetic material. None of the authors is linked to Medartis (no conflict of interest) nor has Medartis Inc. been involved in the planning and execution of the study. The study was funded by a small research grand of the International Bone Research Association (IBRA, Basel, CH). The authors declare that they have no competing interests.

The paper has not been submitted to any other journal but has been accepted for oral presentation for this year’s European Congress of Trauma & Emergency Surgery (ECTES).

We would very much like to thank you for your time, effort and honest consideration of our paper. In case there are any question left, please feel free to contact us at any time.

We would be honored to publish in your journal and are looking forward to your feedback.

Kind regards,

Sebastian F. Baumbach, MD
## Reviewer #1

<table>
<thead>
<tr>
<th>Reviewers comment</th>
<th>Authors reply</th>
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<tr>
<td>Screw fixation angle in relation to the plate</td>
<td>We are sorry if we have not been clear on this point. We strongly agree with the reviewer, that the insertion angle of the screws in relation to the plate is an important factor. In order to standardize screw orientation, we used the manufacture’s drill guide block (A-2723.01; <a href="http://www.medartis.com/uploads/WRIST-0101001_02.pdf">http://www.medartis.com/uploads/WRIST-0101001_02.pdf</a>). This is also stated in the material and methods section.” The manufacture’s drill guide block (A-2723.01) was used to assure uniform placement of the distal two screw rows.” We hope this does clarify the reviewers concerns</td>
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<td>Fragment size and decreased total friction</td>
<td>Distal fragment size and subsequent friction differences might have an influence, but the authors believe friction to be of secondary importance, as the plate used herein is a locking plate (in this case a TriLock Locking Technology). You probably know better than we do, that locking plates work as internal fixators and subsequently do not rely on friction. The fixation mechanism relies on the internal contact between the screws and the bone. Consequently, the authors believe friction to play a secondary role in the measured mechanical properties of the construct.</td>
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<tr>
<td>Background, page 3, line 15, this sentence needs reference</td>
<td>The reference was listed at the end of the second sentence, but the authors agree that this might be confusing and replaced the Reference [19]</td>
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<td>Materials and Methods, page 6, line 12. The authors used t-test for comparison. Multiple comparison needs one-way ANOVA</td>
<td>Thank you very much for this comment. We conducted a statistician, who recalculated the stats. He said a ANOVA would also be the wrong model (and n would be too small to conduct an ANOVA). He used a linear mixed model and Wald test. A description of the statistics performed are following: To see whether significant differences exist between the old and new model of the osteotomy location, a linear mixed model is fitted. This model class is selected to take care for the special data situation, that data of the same specimen are expected to be more similar to each other than to data of other specimens. The model equation is</td>
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\[ b_{ij} \text{Load}_i + b_{ij} \text{Load}_j^2 + \varepsilon_{ij} \]

with \( b_{i1}, b_{i2}, \varepsilon_{ij} \) normally distributed,
i represents the specimens (bones, 1 - 20),
j represents the test cycle.

The Wald test is selected as test procedure. The Null Hypothesis, that the type of model has no important influence on the quality of the fitted mixed model, is:

\[ H_0: \beta_3 = \beta_4 = \beta_5 = 0. \]

<table>
<thead>
<tr>
<th>Appearance of Limitations</th>
<th>Thank you very much for this comment; the discussion was rearranged.</th>
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<tbody>
<tr>
<td>Stating the precise use of this model in biomechanical studies</td>
<td>We strongly agree with this comment, as the herein used model should now resemble the current gold standard and will consequently make inter-study comparison more meaningful. This in parts has been stated in the Discussion and has been further emphasized in the following sentence (page 10, line 02f).</td>
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<td>Limitation to the selection of plates for biomechanical studies using the novel fracture model due to the smaller distal bone fragment</td>
<td>Thank you very much for you comment on this issue. The authors believe that this is rather a strength than a limitation of the study. It emphasizes the need of polyaxial looking in order to achieve adequate reduction and retention of the fracture fragment. Moreover it is the first model mimicking the in vivo situation more closely, which will give the developers a better basis for their research. This information was added in the discussion (Discussion, page 10, line 09ff).</td>
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### Reviewer #2

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<th>Reviewers comment</th>
<th>Authors reply</th>
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<tr>
<td>1) Use of Sawbone #1027</td>
<td>The authors did choose the 1027 mainly for two reasons. First of all, it previously has been used successfully in our laboratory [1-3] and secondly, going through literature, it is one of the most frequently used bone surrogates for distal radius fractures [4-7].</td>
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<td>2) No plate/screw interface failures for the Sawbone model testing. Relevance?</td>
<td>The authors did report on screw/plate interface failures for the sawbone model. Although we do agree, that hardware failure in this context might not seem too relevant, the authors have included the results for the following reasons: 1) With the 1027 sawbone model, we did not see any difference between the fracture models for the biomechanical parameters assessed. But we did see a different hardware failure behavior, which made us move on to testing in fresh frozen radii.</td>
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2) As stated above, the 1027 model is a commonly used surrogate model for biomechanical studies. Nevertheless the herein reported results, when compared to in vitro testing on fresh frozen radii, do show a significant different behavior of the sawbone, where we did not see any difference for the biomechanical parameters assessed. This is “most probably due to the elastic properties of the sawbone” (Discussion, page 08, line 02f) model used.

3) Some clinicians suspected failure of the novel TriLock mechanism introduced by Medartis. The data herein proof, that polyaxial locking screws in general do work and if failure occurs, it occurs at loads outranging those expected in-vivo during postoperative rehabilitation.

3) How did the results, for the preliminary as well as the main experiment, match their predictions

Thank you very much for this comment.

_Preliminary setup:_ The first, part of this comment, i.e. the results of the sawbone experiment, has partially been addressed above (2.2). The authors believe, that the lack of statistical significance between the two fracture models is rather due to the material properties of the sawbone than due to insufficient statistical power (Discussion, page 08, line 02f). This is supported by the reported in-vitro results in fresh frozen radii.

_Main experiment:_ We have tried to include this comment in the discussion. In general the biomechanical results observed were as they were expected (see Discussion, page 07, line 20ff).

4) Wedge osteotomy

1) The authors did not use a jig or fixture
2) The osteotomy was marked on the radius using a permanent marker. The landmarks were chosen based on the authors previous study [8] as well as on their identifiably. The initial study was based on lateral x-rays. Therefore the authors chose the following landmarks for this study: Dorsal rimb of the radius, distal to the Tuberculum listerii. Volar rimb of the radius in extension of the radius shaft axis. An orthograd line to the shaft axis was drawn through those points and the whole wedge marked. A handsaw was used to assure straight cutting. Care was taken, that the volar cortex was fully separated (Material and Methods; Page 05; Line 07f).
3) The authors believe, that the combination of solid landmarks, fully marked osteotomy wedge, use of a handsaw and the sample size allows for a good comparability between the two groups

5) Was there a gap between the bone at the apex of the wedge in the model?

Thank you very much for the comment. The authors agree on the relevance of this information and added it in the Materials and Methods Section (Page 05; Line 07f). The separation of the cortex will most likely affect the stiffness of the construct. When both cortex are separated, the load is transmitted between the two fracture fragments only via the implant. The authors have decided for the separation of the volar cortex for many two reasons. First, separation has been performed in the majority of recent biomechanical studies on distal radius fractures [4,5,9-]. Secondly, the fracture model is supposed to mimic a dorsally displaced distal radius fracture (AO-23.A3). Displaced distal radius fractures almost always present with a lesion or complete disruption of the volar cortex.

6) Negative

A true size negative imprint of the articular surface of the distal radius was
| Imprint | created for each specimen separately. This way we were able to ensure sound contact between the mold and the distal radius. Each mold was created the same way with the help of a custom-made embedding jig: After embedding the proximal radius shaft, the distal radius was wrapped with plasticine leaving just the articular surface free. The specimen was then aligned in a way, that the articular surface was about horizontal. The actual embedding process was conducted in two steps. First, PMMA was poured into the cavity created by the articular surface and the plasticine. After hardening of the PMMA, the plasticine was carefully removed, the specimen rotated 180 degrees in the jig, the aluminum container mounted and finally the shaft of the negative imprint embedded. Care was taken, that there was enough space between the shaft of the negative imprint and the embedding material, so that the distal radius fragment could rotate. Although this process was time consuming, the authors were able to create a negative mold that ensured sound fitting of the mold to the distal articular surface as well as did not constrain the distal fracture fragment (Materials and Methods Section; Page 05; Line 16f). |
| 7) Loading protocol and forces during early rehabilitation | **A) Transition of the Wolfram loading protocol to our study:** The load protocol, previously used by Wolfram [13] to test the effect of damage on trabecular bone at the biopsy level, was adapted to get as much information as possible from the mechanical testing. In fact, with this protocol we could compute also the dissipated work for each load level (something that is not possible to compute from a simple monotonic test). As mentioned in the limitations, we did not apply long-term fatigue tests to not encounter problems due to dehydration of the samples. Moreover this did also allow us to test to failure, the most commonly used outcome parameter in previous biomechanical tests. Failure in this case was define as either failure of the construct or 3 mm displacement (as one can assume relevant damage to the callus and consequent impaired fracture healing). We consequently used a loading protocol, which would allow us to get an deeper inside into the biomechanical behavior of the construct and also test to failure, the current gold standard test. |
| **B) Loading of the wrist during rehabilitation.** We thank the reviewer for their comment but we do not totally agree. Distal radius fractures commonly occur in patients aged above 50 years and show a positive correlation to age [14]. With increasing age, we know that people suffer from muscle loss (sarcopenia). Moreover we know, that especially rising from sitting to standing requires a considerable amount of leg muscle strength, which older people often miss. Therefore they use their arms and hands to rise from bed or chair. Those theoretical thoughts match our clinical experience, where we often see older women using their hands (operated and non-operated wrist) to rise. They either push themselves up, which would mean about 400N resting on the wrist, or the pull themselves up. Few studies have investigated the relationship between forces at the
distal radius and power grip force of the hand. Putnam et al. [15] were able to show that in order to obtain 10N of grip force, 52N are transmitted through the wrist.
Taking those two thoughts into consideration, the authors do agree that forces in general will be smaller than 200N but one has to expect peak forces even during early rehabilitation, which might well exceed the 200N.

C) Relevance of the findings herein:
As discussed above, significant differences exceeding 600N seem on first sight a major limitation and might question the sense of this paper. But as stated in the Discussion (Page 08; Line 08f) “Not until the plate starts to bend, the lever arm, i.e. the osteotomy location, becomes an influential parameter”. This means that there are significant differences between the two loading protocols, but it highly depends on the material properties of the osteosynthetic device used, when they become relevant. This will play a decisive role when various plates are being tested against each other using the herein proposed novel fracture model.

<p>| 8) Actuator vs. fragment displacement. | Thank you very much for this comment. The limitation was added (Page 09; Line 09ff) |
| 9) Biomechanical setup and Statistics | Based on a comment by Reviewer #1 we conducted a statistician who redid our stats. Instead of paired t-test, a linear mixed model and Wald test was used. |
| | A) Level of significance: |
| | The requested information was added (Page 06; Line 16) |
| | B) Describe sample size estimation: |
| | No study has previously compared two different osteotomy locations. Therefore no data was available for a sufficient sample size calculation. The authors therefore geared the sample size to previous studies [16,17]. |
| 10) Materials: Subtraction of residual displacement | The authors tried to clarify what as been done (Page 06; Line 06) and changed Fig. 3 to visually outline it. |
| 11) Results: Were BMD values representative | With a mean age of 74 years, one in general can assume that the samples are highly osteoporotic. In course of this revision, the authors contacted the manufacture of the CT, asking for mean BMD and SD to calculate the T-score of the current sample. According to the manufacture, there is no standard data base for BMD values at the distal radius. The authors tried to address the representativeness of their values in the discussion, as “BMD and BMC were comparable to previous studies [17,18]” (Page 09; Line 21f). |
| 12. Results, paragraph 2: | The sentence was rephrased to make it more clear: “Ultimate load resulted in failure in 11 specimens (New model: n=5; Gold |</p>
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<td><strong>13. Results:</strong> Statement on failure mode.</td>
<td>The failure disruption is described in more detail, as listed above (12.). The exact cause of failure, in those specimens who did fail, was not determined, as this usually is not done in those type of studies. Failure in our tests also means failure of the osteosynthesis, the bone or displacement greater 3mm, which consequently means failure of the treatment. On a side note: Analyzing the actual failure mode, would mean either cutting the specimens or doing a CAT scan. Cutting the specimens, as done in a previous study [19], would mean that one had to remove the osteosynthesis material and possibly add more damage. CAT scans would be heavily altered due to the artifacts caused by the osteosynthesis material.</td>
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<td><strong>14. Discussion, paragraph 1:</strong> The model is described as “improved”... The statement should be supported or altered. (Major Compulsory Revision)</td>
<td>Thank you very much for your comment. We had a long discussion on whether to call the model new or improved, as these where the only two terms we though might be suitable. The authors believed that the model introduce herein is not a new, but an improved (Dictionary: “make or become better”) model, compared to what has been published previously in literature. The model has improved because it is the first model which is not only based on a thorough literature review but also on clinical data justifying the used osteotomy location. Furthermore the study is the first to not only show the relevance of the osteotomy location but also proposing a standardized model for further biomechanical studies, which again allows for actual inter-study comparison. Based on the before mentioned definition and following argumentation, we believe the word ‘improved’ to properly describe the herein introduced setup.</td>
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<td><strong>15. Discussion, paragraph 2:</strong> Discuss various loading protocols</td>
<td>Thank you very much for the comment. We agree with the comment and the manuscript was adapted accordingly (Page 09; Line 02f).</td>
</tr>
<tr>
<td><strong>16. Discussion, paragraph 4:</strong> Comaprability of new loading protocol in combination of novel biomechanical fracture model</td>
<td>Thank you very much for this interesting comment. Going through literature, one will see various fracture models as well as varying loading protocols. The aim of this study was to establish a fracture model, which should mimic the invivo situation and at least will make that variable consistent. We did not aim at generating a reference population for this precise setup (n would had to be greater and the sample-diversity greater). Loading protocols aiming at testing osteosynthetic devices are highly discussed in the field. There are two main opinions: 1) testing to failure, 2) fatigue testing. Fatigue testing always encounters the following two problems: dehydration (as addressed in point 7. and the Discussion) as well as the missing biofeedback on the stimulus, that usually tries to mimic load cycles representing 6 weeks of mobilization.</td>
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Although not the primary focus of this paper, we still do believe that the loading protocol used herein does add useful information as one does get longitudinal information next to ultimate failure. Further thoughts on the loading protocol used herein were discussed in point 7.

17. Discussion, paragraph 6: distal radius fractures can take on near infinite patterns

The authors agree with the reviewer on this point. We on purpose chose the phrase “more closely” to account for this fact but did not separately address it in the limitations. This fact now is accounted for in the limitation. Still one has to acknowledge the fact, that at least the distal fracture line in general seems to be pretty robust. Therefore we do believe that the phrase “more closely” is justified in this case.

18. The reviewers should modify their conclusions to focus on pointing out the sensitivity of the model until a more exhaustive study of fracture location frequency is completed

The authors have changed the wording of the conclusion, matching the focus set by the reviewer. We agree, that next to the implementation of the model, the sensitivity of the parameters assessed to the distal fracture fragment side is the main achievement of this study. Thank you for the comment!

19. Check spelling / Grammar

The paper was proofread by a native English speaker (s. Acknowledgements) following the corrections recommended by the reviewers.

References