Author’s response to reviews

Title: Medical-grade polycaprolactone scaffolds made by melt electrospinning writing for oral bone regeneration – a pilot study in vitro

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Author’s response to reviews:

Dear Dr. Borzabadi-Farahani, dear reviewers,

first of all thank you for your valuable corrections on our submission!

Besides the requested changes, one mistake considering the name of one of the co-authors has been corrected. This was a simple spelling mistake. Instead of “Mr. Almoataz Youssef” the accidentally misspelt name was corrected to “Mr. Almoatazbellah Youssef”. The person itself (including his affiliation and contact data, etc.), as well as its position in authorship, are exactly the same. Furthermore the affiliation of Prof. Linz was supplemented by the "Interdisciplinary Center for Clinical Research". Again the person itself (including his affiliation and contact data, etc.), as well as his position in authorship is exactly the same.

Please find attached together with the revised submission “Medical-grade polycaprolactone scaffolds made by melt electrospinning writing for oral bone regeneration – a pilot study in
vitre” the requested point-by-point response letter. All changes in the manuscript have been highlighted as requested.

Editor comments:

The title has been revised (line 1-2). An annotation, that a pilot study with in vitro experiments was performed, was added.

In the abstract background section a list of disadvantages of currently available membrane systems was added (l 67-68).

The abstract background section has been revised (l 65-70); we hope you may find it more interesting as you requested.

The introduction has been revised as requested. The focus has been laid more on conventional membranes and their issues in clinical routine (l 97-110). In return the paragraph about soft tissue management has been dropped in order to build a case for our investigation.

In the abstract background section the number of samples was clarified with a remark, that it was a single set of membranes (l 73). Furthermore details according to the box-sizes were added (l 75-76). Further details can easily be added if desired, but I worry that this might go beyond the scope of an abstract.

The sentence “Our results reveal that MEW is an attractive approach to the fabrication of resorbable scaffolds for the regeneration of hard- and soft tissues in maxillofacial surgery.” at the end of the introduction has been removed. (formerly l 127)

Conclusions (at the end of the paper as well as in the introduction) have been revised. Sections that did not deal with our findings and clinical implications were deleted. A suggestion for further clinical trials was added (l 339-347)
Jimoh Olubanwo Agbaje:

The sentence “No definite trend towards a for osteoblast-like cells favored box size considering primary cell attachment could be found.” was replaced to enhance clarity of the statement (l 259-260; MG63 cells did not seem to favor any box size in particular but settled approximately equal on 225 μm, 300 μm, 375 μm, 450 μm and 500 μm scaffolds).

From line 272-276 it has been highlighted, that similar studies either in design or cell growth (bone regeneration by means of MEW scaffolds) can hardly be found, as literature has focused mostly on solution electrospinning in this context. Nevertheless rare studies have been mentioned.

Masako Fujioka-Kobayashi:

The term “maxillofacial surgery” has been replaced by “oral and maxillofacial surgery” wherever appropriate throughout the manuscript (l 65,84,92,264,331)

The focus of the manuscript was directed towards GBR rather than GTR. Sections dealing with soft tissues were removed due to a missing relation to GBR. (introduction, formerly l 59 and 89-95).

See the aforementioned point; the sentence “These well-defined 3D scaffolds consisting of medical-grade materials optimized for cell attachment and cell growth hold the key to a promising new approach in GBR and may enhance wound healing in certain maxillofacial issues.” has been modified towards to only bone- instead of soft tissue regeneration (l 92).

The section about MRONJ has been reconsidered and therefore was deleted (formerly l 89-95)

Pore sizes were chosen on the basis of current literature research. This was mentioned in the discussion section and has been further clarified (l 291).

As we performed a pilot study with only one set of samples the statement about average or median is not feasible. As mentioned before, the pilot study design and sample number (n=1 for each testing) was clarified (l 73). Subsequently no statistical analysis could be performed and all result values are actually shown in the figures.

For figures 9d and e, the wrong images (duplicates of fig. 9c) have accidentally been placed. Figures 9d and e have therefore been replaced with the right pictures. We apologize for this mistake.
Rohana de Silva:

A brief abstract about material properties of PCL was added in the discussion (l 279-281).

The caption of Fig 8b was modified as suggested (l 510).

All references have been formatted in a uniform manner according to the guidelines of BMC Oral Health. We apologize for this mistake.

Michael Edelmayer:

The respective sentence including the word “tissues” has been deleted (formerly l 77)

The pilot study design has been stated in the title as well as in the methods section (l 2,71,137).

Hydrolytic degradation of PCL actually happens very slowly. The small fiber diameter of the scaffolds used in this study should offer a bigger surface, on which hydrolytic degradation can take place. Degradation might therefore occur faster. Nevertheless, pH values were measured only to exclude any milieu change in initial settlement. A note to this can be found in the discussion (l 309).

Replicate samples would have been very desirable, especially in cytocompatibility testing. Unfortunately, this could not be realized due to a low quantity of samples. This issue was addressed in the “pilot-study design” as a first step of many more to come (l2,71,137,346).

Jamil Awad Shibli:

As suggested, melt electrospinning writing was spelled once more (l 112).

The objected sentence (formerly l 123) has been deleted.

Considering the pore sizes see above: Pore sizes were chosen on the basis of current literature research. This was mentioned in the discussion section and has been further clarified (l 291).

Microphotographies from all sizes of membranes have not been taken. Because of the macroscopical aspect, the same process parameters and the same amount of layers, no differences were reasonably expected. Hence an exemplary sample with the box size 225 μm was chosen. A note to this was added to further clarify that fact in the caption of Fig. 8 (l 510).

Considering statistical analysis and its illustration in the figures see above: As we performed a pilot study with only one set of samples the statement about average or median is not feasible.
The pilot study design and sample number (n=1 for each testing) was clarified (l 71). Subsequently no statistical analysis could be performed and/or discussed.

The conclusion section has been revised and in this context reduced (l 339-347).

References were revised. Publications which were prior only ahead of print and have been published in the meantime were updated. We apologize for this mistake.

We hope you may find the corrections sufficient and the research article now worth being published in BMC Oral Health.

With kind regards,

Andreas Fuchs