Author's response to reviews

Title: Revascularization of onlay autogenous iliac grafts for lateral alveolar ridge augmentation.

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Version: 2 Date: 3 September 2013

Author's response to reviews: see over
We would like to thank the editor and the reviewers for their thoughtful comments to improve the quality of our manuscript. We addressed all comments as outlined below. Text boxes have been added to the annotated manuscript indicating reviewer (R1, R2) with comment number (C1 to C5). Also revised sections of the manuscript have been changed using the track changes mode in MS word to facilitate review of the revision.

Reply to reviewer # 1

1. Concern of the reviewer:

   The control experiment. It is not clear to me that experiment 3 (the graft was covered with a Silicone sheet, presumably to prevent vascular ingrowth from the recipient bed) is an acceptable control. I would favor experiment 1 as the control. The authors must discuss their choice of a non-physiologic control.

   Our response:

   Originally, we chose experiment n°3 using a non-porous membrane between the graft and the host site as a negative control group where no vascularization of the graft from the host site could take place to study the influence of GBR and DBBM. Because of it’s clinical irrelevance we excluded experiment n°3 from statistical analysis. Therefore we only have insufficient data. After extensive discussions, the authors decided to exclude experiment n°3 from this study.

   Revised text: Experiment n°3 was excluded from the manuscript.

2. Concern of the reviewer:

   Results from experiment 3. Even if experiment 3 is determined to be an acceptable control, the authors have omitted all results in the current manuscript.

   Our response:

   See comment above.

   Revised text: not applicable.
3. Concern of the reviewer:

*The experimental groups. I do not understand why the authors did not study guided bone regeneration alone (the graft covered by a collagen membrane). This is purported to be a study of bone graft revascularization, not a study of guided bone regeneration in combination with Bio-Oss granules.*

**Our response:**

The histological immunohistochemical analysis of the bone grafts using GBR and DBBM as described in this manuscript is only part of the project: Bone grafts using collagen membranes only were described by Adeyemo et al. from our study group previously in the same experimental setting:


Revised text: not applicable.

4. Concern of the reviewer:

*Infections in experiment 2. Experiment 2 became infected in 2/12 animals. This is a high percentage in light of the absence of infections in the other groups. The authors should discuss this.*

**Our response:**

All changes were incorporated as requested.

Revised text:

The biocompatibility of DBBM such as Bio-Oss® has been shown in previous studies [38]. However, the two cases of infection in this study occurred in Experiment 2 using a DBBM coverage. DBBM is a xenograft material and foreign to the body. Even though it is deproteinized, others report about low levels of osteoinductive or immunogenic proteins within the spongiosa granules [39, 40]. In this context an intense and prolonged immune response seems to be possible. As DBBM are resorbed slowly, the potential chance of being infected should not be underestimated. These effects have to be studied in long-term follow-up clinical trials.
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5. Concern of the reviewer:

_Von Willebrand factor. Use of vWF as an endothelial cell marker is not widely appreciated. The authors should discuss this._

Our response:

All changes were incorporated as requested.

Revised text:

In the current study vWF as a marker protein of the endothelium was used to study angiogenesis using immunohistochemistry. VWF (factor VIII-related antigen) is a glycoprotein that mediates platelet adhesion and stabilizes factor VIII at sites of vascular injury [38]. Although it is commonly used as an immunohistochemical marker for endothelial cells, stainings on other specific endothelial markers such as CD31, CD34, and Fli-1 could be done in future studies [39].


Reply to Reviewer # 2

1. Concern of the reviewer:

   The author stated in the second sentence of paragraph 3 in the discussion section that "Moreover, they illustrated that recipient bed perforation and excision of the host overlying periosteum did not result in any advantages regarding healing and integration of the bone graft". The author should change this sentence to "They illustrated that recipient bed perforation did not result in any advantage over non-perforation, however, they reported that retention of overlying periosteum resulted in better volume maintainance of the bone graft"

   Our response: All changes were incorporated as requested.

   Revised text:

   Adeyemo et al. were able to show in previous studies the clinical advantages of the use of DBBM in combination with GBR [4]. They illustrated that recipient bed perforation did not result in any advantage over non-perforation, however, they reported that retention of overlying periosteum resulted in better volume maintainance of the bone graft [3].

2. Concern of the reviewer:

   Authors should avoid the use of "we" in the manuscript. Rather, a statement like "It was found", "This study shows" rather than "We found".

   Our response: All changes were incorporated as requested.

   Revised text:

   Changes were highlighted using the MS word track changes mode.

3. Concern of the reviewer:

   Minor grammar corrections need to be effected.

   Our response: All changes were incorporated as requested.
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Revised text: All changes were highlighted using the MS word track changes mode.