Author’s response to reviews

Title: Autotransplantation of mature impacted tooth to a fresh molar socket using a 3D replica and guided bone regeneration: two years retrospective case series

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Author’s response to reviews:

Answers to the Questions and Suggestions of the Reviewers
The revised words and sentences had been marked by red colour in the manuscript.

Reviewer reports:
Meenakshi Vishwanath (Reviewer 1): OHEA-D-19-00465
Autotransplantation of mature impacted tooth to a fresh molar socket using a 3D replica and guided bone regeneration: a one year retrospective study
The authors of the manuscript are evaluating the survival and accuracy of autotransplanted mature third molar teeth to a fresh molar extraction socket using a 3D replica and GBR where necessary.
Though it is a retrospective study, the technique of autotransplantation needs to be recognized as an evidence-based alternative for the replacement of missing teeth. Therefore, I consider the topic is pertinent and current. However, I think there are some major issues in the overall rationale and objective of the study, which extends into the material and methods section. Though normally I would consider grammatical and typographical errors minor issues, they are so many in this particular manuscript that it is hard to infer the meaning of certain sentences. I urge the authors to thoroughly proof read the manuscript before resubmission.

Major issues:
1. Objective of the study: The author's main objective was to evaluate the performance of a fully mature third molar tooth that was autotransplanted to a fresh extraction socket of another molar tooth and do it with the aid of a 3D replica. I infer from the objective, that the main emphasis here is the use of the 3D replica to reduce the extra-oral time and obtain a better fit of the donor tooth.
Though, the protocol followed for the entire procedure is good and the follow-up assessments are also well done, considering the authors’ main objective, I would have expected more information in the material and methods about:

a. What were the measurements made on the CBCT to determine the best candidate for the donor tooth? Image with the measurements.
Answer: Thank you for the suggestion. The mesio-distal and bucco-lingual dimension and height of the donor tooth and the recipient site was made on the CBCT. And we add the detail measurements of the donor tooth and the recipient site where the tooth need to be extraction in the Preoperative work-up part. The image with the measurements had been provided in the manuscript as Fig.1.

b. Did they know beforehand the cases that might need GBR based on these measurements?
Answer: Thank you for the suggestion. We know whether the case need GBR or the extraction socket need to be re-prepared according to the measurements of the CBCT. If the mesio-distal or bucco-lingual dimension of the recipient socket were larger than the donor tooth, or there was bone defect around the extraction socket, the GBR is needed.

c. How was the CBCT sectioned in order to obtain the data to create the replica?
Answer: Thank you for your suggestion. The CBCT data was imported into Materialize Proplan software, this allowed the segmentation of the donor tooth as it show in the following figure. And we also add this to the manuscript.

• 2. Guided Bone regeneration: The authors have mentioned evaluating GBR-specifically grafting with autogenous bone to fill the gap between the tooth and the prepared socket in the purpose of this study and have mentioned the procedure in the title. They have also stated in the introduction that ‘investigations of the clinical advantages and the success rate of this autotransplantation technique in association with association with GBR are still lacking’. This would indicate to the reader that they are performing this procedure to highlight the clinical advantages and improvement of the success rate due to this technique along with the use of a 3D replica. Since they did not have control patients, they have been unable to highlight how this combination helped with the success rate. However, as the procedure was performed in 8 out of 10 patients, advantages and/or other clinical factors of using GBR could have been elaborated in the discussion section. In fact, in the discussion they have referenced an article suggesting that the success rate of using GBR in autotransplantation is consistent with the non GBR one. Hence, what was the rationale or even advantages of GBR in this particular study that might help the readers in clinical practice?
Answer: Thank you for your suggestion. We could not prove that tooth autotransplantation using a 3D replica combined with GBR can help with the success rate as the reviewer said. But as a retrospective observation study, we can demonstrate that no matter combined with GBR or not, tooth autotransplantation using a 3D replica can improve the success rate of the short-term
through shorten the extra-oral time and facilitated the surgery. From the results of our study, the success rate of the tooth autotransplantation was the same no matter combined with GBR or not as the reference said. Also we added how and why we need to do GBR in the discussion section.

Based on points 1 and 2 - The authors need to highlight the uniqueness of the article. Either based on the 3D replica technique or the addition of the GBR as there are other similar studies with follow-up periods that are longer in duration and or studies with a higher sample size:
https://www.joms.org/article/S0278-2391(19)31003-1/fulltext
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6252245/
https://bmcoralhealth.biomedcentral.com/articles/10.1186/s12903-017-0468-0
Answer: Thank you for your suggestion. As we known that there are some studies talking about the tooth autotransplantation by the 3D replica or using GBR, but most of them were done in a healed alveolar ridge. The uniqueness of the article is that the tooth was autotransplanted to a fresh extraction socket, not a traditional healed alveolar ridge. Using a 3D replica of donor can facilitated the surgery procedure of the preparation of the fresh socket. And the grafting material is autogenous bone combined with concentrated growth factors, which may benefit for the regeneration.

3. The entire manuscript needs to be thoroughly proofread. Use of words such as 'expect' instead of 'except' and several other such typographical and grammatical errors make the article incomprehensible in certain areas.
Answer: Thank you for your suggestion. The entire manuscript had been thoroughly proofread and rewritten, also the typographical and grammatical errors had been eliminated.

M. EzEldeen (Reviewer 2): I would like to thank the authors on their effort to write this paper. However, the paper is not ready for publication in its current form. I will elaborate in the next lines.

Title: Does not describe what is in the paper and should be changed to: One year retrospective case series describing the autotransplantation of 10 mature third molars
Answer: Thank you for the suggestion of the title. Our study are case series definitely, but the current title contained some special issues like 3D replica and guided bone regeneration, which can make the reader know what methods were used in the study. So the title was modified to “Autotransplantation of mature impacted tooth to a fresh molar socket using a 3D replica and guided bone regeneration: a one year retrospective case series”

Abstract:
Aim: the aim is not to evaluate one tooth transplantation is to report the outcome for a case series
Answer: Thank you for your suggestion. The aim of the study was definitely not to evaluate one case of the tooth transplantation, the usage of word “a” was misunderstood by us. And we evaluated the clinical outcome of the case series. So the objective was modified to “The aim of this study was to evaluate the clinical outcome of autotransplantation of mature third molars to fresh molar extraction sockets using 3D replicas”.

Answer: Thank you for your suggestion. As we known that there are some studies talking about the tooth autotransplantation by the 3D replica or using GBR, but most of them were done in a healed alveolar ridge. The uniqueness of the article is that the tooth was autotransplanted to a fresh extraction socket, not a traditional healed alveolar ridge. Using a 3D replica of donor can facilitated the surgery procedure of the preparation of the fresh socket. And the grafting material is autogenous bone combined with concentrated growth factors, which may benefit for the regeneration.

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3. The entire manuscript needs to be thoroughly proofread. Use of words such as 'expect' instead of 'except' and several other such typographical and grammatical errors make the article incomprehensible in certain areas.
Answer: Thank you for your suggestion. The entire manuscript had been thoroughly proofread and rewritten, also the typographical and grammatical errors had been eliminated.
Results: poorly reported please refer to Shahbazian et al., 2013 (DOI 10.1016/j.oooo.2013.01.025) for the appropriate method of reporting
Answer: Thank you for offering a reference. And the results were modified to “The average extra-oral time of donor tooth had been shortened to 1.65 min when used the 3D replica. Some probing depth of the transplanted tooth were deeper than 3 mm at 4 or 5 weeks temporarily. And one patient felt slight sensitive when chewing with soft food at 4 weeks, then disappeared. The clinical examination of the teeth autotransplantation during two years follow-up showed no sign of failure.”

Conclusion: not in line with what is reported please revise
Answer: Thank you for your suggestion. The statement of “reduce the demand of the experience of the surgeon” could not be derived from the results. So we modified the conclusion part to “The tooth autotransplantation using 3D replica is an effective method which can reduce the extra-oral time of the donor teeth and may result in less failure.”

Introduction:
In general poor english and needs to be rewritten
Answer: Thank you for your suggestion. The entire manuscript needs to be thoroughly proofread and rewritten, and it had been revised by professional institute of translation services.

Page 2: line 33: rewrite to &gt; Tooth autotransplantation instead of Autotransplantation of a tooth
Answer: Thank you for your suggestion. We had change “Autotransplantation of a tooth” to “Tooth autotransplantation” in the entire manuscript.

First paragraph needs to be rewritten:
Answer: Thank you for your suggestion. We had rewritten the first paragraph of the introduction part.

The authors are missing or ignoring key references for tooth autotransplantation in general mainly from the Jens Andreasen
1- (http://www.ncbi.nlm.nih.gov/pubmed/2318261)
2- (http://www.ncbi.nlm.nih.gov/pubmed/2318262)
3- (http://www.ncbi.nlm.nih.gov/pubmed/2318259)
Answer: Thank you for your suggestion. 1- “A long-term study of 370 autotransplanted premolars. Part I. Surgical procedures and standardized techniques for monitoring healing”. The research is talking about using electrometric pulp sensibility testing and radiographic examination to monitor the healing of the immature premolar. In our study we autotransplanted mature third molar, so we used radiographic examination and not used electrometric pulp sensibility testing. 2- “A long-term study of 370 autotransplanted premolars. Part IV. Root development subsequent to transplantation”. The research is talking about the root development of the transplanted immature tooth after autotransplantation. The reference is classic and significance. But the reference may be not the key one to our study which is autotransplantion of mature tooth. 3- “A long-term study of 370 autotransplanted premolars. Part II. Tooth survival and pulp healing subsequent to transplantation.” The study indicates that the size of the apical foramen and possibly the avoidance of bacterial contamination during the surgical procedure are
explanatory factors for pulpal healing. And the Teeth transplanted with incomplete and complete root formation showed 96 per cent and 15 per cent pulp healing respectively. So we did the root canal treatment of the mature donor tooth. These three references are classic and significant to our study, so we add the references to our manuscript in the introduce and discussion section.

Moreover, key reference for CBCT-guided tooth autotransplantation (PMID: 30786806) where a CBCT guided is compared to conventional transplantation in a clinical trial.

Answer: Thank you for your suggestion. The references (EzEldeen M 2019) are the latest research talk about the CBCT-guided tooth autotransplantation, which had very high reference values to our study. So we add the references.

Page 3: line 9: change to stage of root development
Answer: Thank you for your suggestion. We had change “the root development stage” to “the stage of root development”.

Page 3: line 11: and so on !! -&gt; not scientific writing
Answer: Thank you for your suggestion. We had removed the phrase.

Page 3 line 22: please add references Shahbazian 2013 (DOI 10.1016/j.oooo.2013.01.025) and EzEldeen M 2019 (PMID: 30786806) for clinical trial CBCT guided TAT
Answer: Thank you for your suggestion. The two references especially the EzEldeen M 2019 are the latest research talk about the CBCT-guided tooth autotransplantation, which had very high reference values to our study. So we add the two references.

Materials & Methods:
Page 4: what is concentrated growth factor, which growth factor it is?
Answer: Thank you for your suggestion. Concentrated growth factors (CGFs) developed by Sacco in 2006 are produced by a centrifuge device (Medifuge Silgradent srl, Italy) in a similar manner to PRF but with different speeds. Compared with PRF, the fibrin matrix of CGFs is larger, denser and richer in growth factors. It contained many growth factors like TGF -1, PDGFs, IGFs, VEGF.

Pre operative procedure:
- What is the CBCT scan protocol?
Answer: Thank you for your suggestion. The CBCT scan protocol is that a low-dose CBCT imaging was done by the NewTom GiANO (NewTom, Italy) with voxel size 0.150 mm, tube voltage of 90 kV, current of 7.00 mA, and exposure time of 9 s.

- What is the segmentation method?
Answer: Thank you for your suggestion. The CBCT data was imported into Materialize Proplan software, this allowed the segmentation of the donor tooth as it show in the following figure.

- Which software used for 3D planning is any was used?
Answer: Thank you for your suggestion. We used the Materialize Proplan software to mimic the tooth transplantation.

- Did you validate the printer for accuracy?
Answer: Thank you for your suggestion. The accuracy of the printer was validated by the company who owned the 3D printer each week.

Surgical procedure:
- Poor English example line 30: we put.. should be the donor tooth was transplanted
Answer: Thank you for your suggestion. We had rewritten the surgical procedure part. Example: We put the donor teeth into the recipient socket and checked whether it achieve an optimal fit. If there were bone defect around the donor tooth, we grafted the autogenous bone which was collected during the socket preparation process, mixed with concentrated growth factors (CGFs) which was done immediately before surgery. Whole blood drew from the patient was centrifuged using a tabletop centrifuge (Medifuge, Silfradenstr, S. Sofia, Italy) and it was divided into four layers as described by Bozkurt et al. The CGF layer, which was the second growth factor and stem cell layer of the four layers, was separated using sterile scissors.

- CGF do you mean L-PRF membrane?
Answer: Thank you for your suggestion. Concentrated growth factors (CGFs) developed by Sacco in 2006 are produced by a centrifuge device (Medifuge Silgradent srl, Italy) in a similar manner to PRF but with different speeds. Compared with PRF, the fibrin matrix of CGFs is larger, denser and richer in growth factors. Therefore, CGFs could be expected to have better properties for clinical manipulation and regenerative potential.

- Fiber band --&gt; are you using rigid fixation ?, please elaborate
Answer: Thank you for your suggestion. All the transplanted teeth were stabilized with fiber-splint which were carried out with a multi-layer fiber-glass band.

Post operative --&gt; follow up
- page 6 line 17 change to according to the criteria described by Tsukiboshi
Answer: Thank you for your suggestion. We had change the sentence to “The primary success criteria of the transplanted tooth were followed according to the described by Tsukiboshi”.

Results:
should be presented as a case series
have a look on (DOI 10.1016/j.oooo.2013.01.025) for reference
Answer: Thank you for your suggestion. We had change the structure of the results section to three parts: “Preoperative evaluation, Surgical procedure, and Clinical and radiographic evaluation”, and rewritten it.

Discussion
please rewrite
Include key papers on CBCT guided transplantation as mentioned above
Answer: Thank you for your suggestion. We had rewritten the discussion section, and add the key papers on CBCT guided transplantation as you mentioned above, especially the reference of EzEldeen M 2019 and Shahbazian 2013.

Conclusion:
1 year is too short for such a strong conclusion please rephrase

Answer: Thank you for your suggestion. We kept following up the patients. We got the dates of two years until now and we had added it to the manuscript. Although the study is a short time observation retrospective case series, the 3D replica can reduce the extra-oral time and made the surgery easier can be inferred. The present study also had it meaning.