

Point by point responses to the Reviewers' Comments on Manuscript - "Engineering 3D-Printed Bioresorbable Scaffold to Improve Non-Vascularised Fat Grafting: Proof of Concept Study"

Reviewer 1

The paper provides comprehensive information on the use of 3D-printed PLCL scaffolds for adipose tissue engineering and discusses the advantages and limitations of PLCL scaffolds, including biocompatibility, degradation rate, manufacturing processes, and regulatory approval. This offers readers vital insights into the crucial factors in selecting PLCL scaffolds for adipose tissue engineering. Here are specific review comments:

1. The paper's structure is clear and well-organized. Each section provides experimental design, methods, results, and discussion to ensure that readers fully grasp various aspects of the research.

R: We thank reviewer #1 for his/her supportive comment

2. The language in most parts of the article is clear and precise, but there are some areas that could be further edited for readability and clarity. In particular, when describing experimental design and data analysis, ambiguity in wording should be minimized to ensure that readers completely understand the methods and results.

R: Thank you for your valuable feedback. I agree that ensuring readability and clarity, especially in sections detailing experimental design and data analysis, is crucial for the comprehensive understanding of the methods and results by the readers.

I have revisited these sections (see highlighted text) and strived to refine the language, focusing on simplifying complex sentences, using more specific terminology.

3. The discussion section offers a thorough analysis of the research results, highlighting the advantages and limitations of the materials used. The discussion also presents potential applications and future research directions. This is a good approach but may need to emphasize the novelty and significance of the research more to capture the reader's interest.

R: I'm pleased to hear that you found the analysis of the research results, along with the evaluation of the materials' advantages and limitations, to be thorough. Your point about the need to more strongly emphasize the novelty and significance of our research is well-taken and appreciated.

In response to your suggestion, I have made several modifications to both the introduction and discussion sections of the paper. In the introduction, I have now included a more detailed explanation of the context and background.

In the discussion section, I have also made an effort to more explicitly connect our results to broader scientific and practical implications, thereby underscoring their significance.

4. In the in vivo experiments, besides conducting safety checks on the implantation site, it is recommended to perform safety assessments on important organs of the animals to ensure the biocompatibility of the material.

R: In another project using a scaffold in the same polymer but with a different design, we measured the presence of polymer residues in the excretory organs of minipigs after 21 months of implantation (quasi-complete resorption). As you can see below, there are none left, indicating that resorption has left no residues in the body. This work is currently being finalized and will be published in another paper soon.

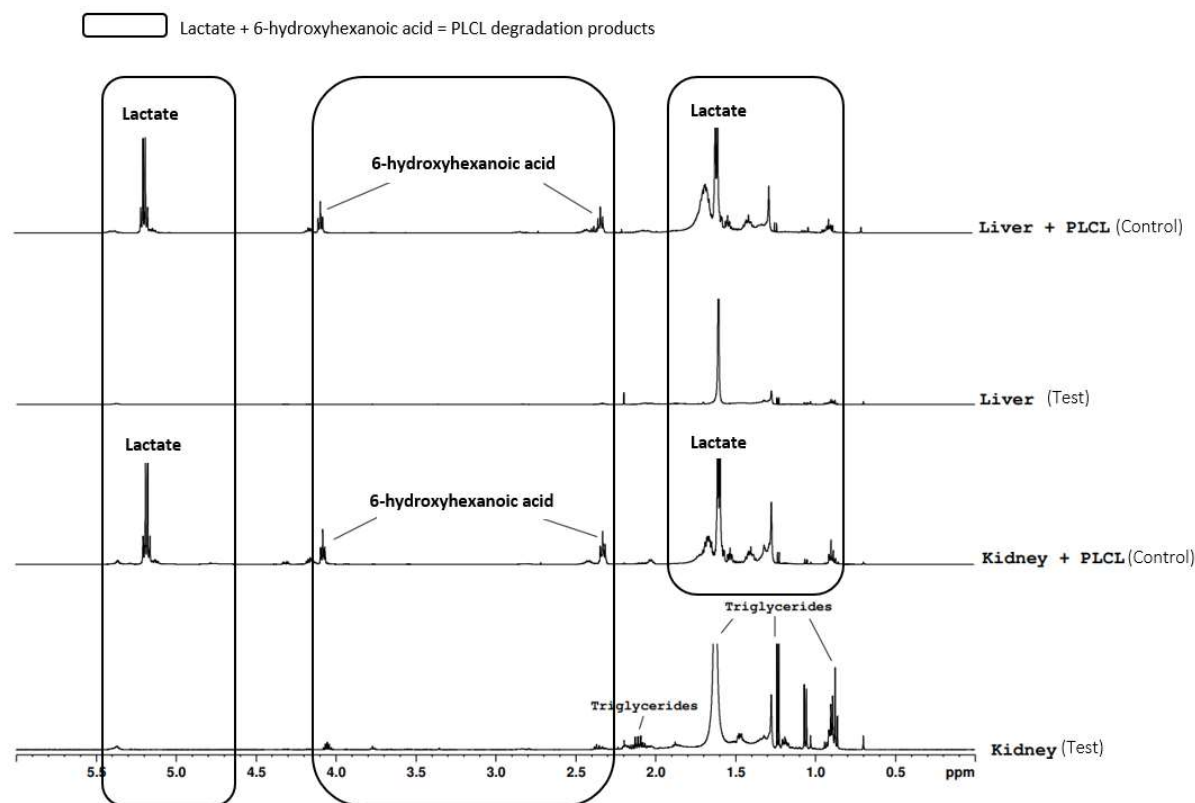


Figure 1: NMR analysis of PLCL TEC degradation products in liver and kidney after 21 months of implantation. Detection of scaffold degradation products was carried out in the liver and kidneys after 21 months of implantation (Fig.1, test conditions in comparison to positive Control conditions which are represented by organs with addition of PLCL). NMR (1H-Nuclear Magnetic Resonance) analysis revealed no degradation products in these two organs after 21 months of implantation. This demonstrates the absence of accumulation of degradation products which are probably eliminated by natural ways.

5. In addition to biodegradable scaffolds, hydrogels have extensive potential applications in the field of biorepair materials. It is recommended to introduce relevant literature on hydrogels and make comparisons with biodegradable scaffold materials to make the content of the paper more comprehensive. Relevant hydrogel literature is as follows:

- 1) A Bionic-Homodimerization Strategy for Optimizing Modulators of Protein-Protein Interactions: From Statistical Mechanics Theory to Potential Clinical Translation
- 2) Biomimetic peptide dynamic hydrogel inspired by humanized defensin nanonets as the wound-healing gel coating

R: Thank you for your valuable suggestion to include information on hydrogels in our paper. I agree that this addition would provide a more comprehensive understanding of the field of biorepair materials.

In response to your recommendation, I have updated the introduction to incorporate a discussion on hydrogels. This should offer readers a broader perspective on the current state and future directions of biorepair material research.

Regarding the literature references you provided, I have carefully evaluated both. The second reference, 'Biomimetic peptide dynamic hydrogel inspired by humanized defensin nanonets as the wound-healing gel coating,' was found to be highly relevant and directly applicable to our paper. It has been included in the paper to support the points made about the advancements and potential of hydrogel technology in wound healing and tissue repair.

After thorough consideration, I concluded that the first reference, 'A Bionic-Homodimerization Strategy for Optimizing Modulators of Protein-Protein Interactions: From Statistical Mechanics Theory to Potential Clinical Translation,' while interesting and highly valuable in its field, did not align closely with the specific focus of our manuscript. Therefore, to maintain the relevance and coherence of our paper, I decided not to include this particular reference in our paper.

I appreciate your guidance in enhancing the depth and breadth of our manuscript. I hope that these modifications align with your expectations and contribute to the overall quality and comprehensiveness of the work.