

Manuscript 74366

Peer review point-by-point response:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This is an interesting and meaningful study, and I recommend accept.

Response: Thank you very much for your comments. We hope our study is a starting point for further meaningful research for the application of this technology to prevent and treat orthopedic implant related infections.

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This laboratory study looked at the influence of AC on adhesion of bacteria to a titanium model and concluded that AC may have a role in reducing biofilm formation and bacterial adhesion in implant infection. The approach was novel with satisfactory methodology. The results show better activity for S aureus compared to E coli. Additionally there was some electrocoagulation of the medium suggesting that in vivo application may cause cytotoxicity. The results are definitely worth publishing but my main concerns are: 1 The clinical application seems difficult. When and how would AC be applied to an implant, considering that bacterial adhesion probably occurs within 14 days of contamination and presumably attacking the first phase of bacterial adhesion would be the most important. the authors do comment on this aspect as a limitation but do they have any suggestions on how it could be clinically implemented? 2 The cytotoxicity of AC is also a major limitation. I would like to know from the authors how that could be investigated and what are the potential mechanisms to achieve this? Do they suggest external AC or some implantable mechanism? Although the English was satisfactory there were a few grammatical errors that need to be addressed.

Response: Thank you so much for taking the time to review our manuscript and for your interesting questions:

- 1) This is the first experimental study performed for a thesis project. We have continued to work on several variables that have allowed us to design methods that are potentially viable for clinical application. A patent protects these methods and unfortunately, some information cannot be shared at the moment.
- 2) Although DC has shown greater success in preventing bacterial adhesion, its major drawback is the high amount of energy transferred during the tests. For this reason, we believed low intensity AC could perform similarly, under the appropriate conditions, allowing for a smaller energy transfer. This smaller energy transfer would be key in

preventing a cytotoxic effect in an *in vivo* scenario. We have been working with other electrical conditions and models that seem to prevent this cytotoxic effect. However, until *in vivo* trials are not completed, we will not be able to have definitive data.

Editorial Office's Comments:

Specific Comments To Authors: The authors focused on orthopaedic implant associated infection (OIRI) and found that AC electric field can reduce the bacterial adhesion on titanium surface. Respected authors, this is a well written paper and covers an interesting topic. Nevertheless, there are a number points that may deserve some revisions. However, the choice of the references is outdated. How does the author think about the cytotoxicity of AC? Scientific Quality:Grade A Language Quality:Grade B Recommendation:Conditional acceptance.

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