Peer Review File
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Review Comments
Reviewer A:
Congratulations on your job. You bring good review, summarizing penile prosthesis scenario regarding infectious complications. There are lots of publicatins and you briefly bring together the most important ones. Considering the preclinical model as the main scope of the article, I think you could explore other publications using different antibiotics and different coating strategies. There are publications about nanoparticle coating, manganese, and zinc coating. You discuss the role of capsule and biofilm formation and mention the elicited shape memory as a prevention mechanism, nanoparticle and metal coatings may play a role in that scenario and could be considered in the discussion and future experiments using your model.

Reply: Thank you for your review and positive feedback regarding our review. We appreciate the suggestion to explore the use of other antibiotics or different coating strategies. Although we did not find additional animal IPP models for this purpose, there were preclinical studies using *in vitro* models or non-penile implant types. We have cited three of these in the discussion section to highlight future avenues for research using an animal model, including studies by Yang, Cazalini, and Towe et al which discuss different nanoparticle, manganese/zinc, and antibiotic coatings. Additionally, we agree that coatings may play a role in capsule formation. We added this comment as outlined in the point below.
Changes in text: Please see references 39-41 on page 17 line 349.

You explain the limitations of this work, it is just a quick off for further experiments, but a valuable one. The main advantage is to access the functionality of the prosthesis, did you do it manually using the pump? Did it get more difficult or rigid throughout the days? One could expect the fibrosis in the subcutaneous tissue would be different from the cavernosum corporae. In fact, explanted mammary prostheses are always encapsulated. Did you explant the prosthesis, and could you evaluate the capsule formation?
I hope I can hear from you really soon. Best regards.

Reply: Thank you for making this important point. Yes, implants were manually inflated/deflated as shown in Figure 1, where we demonstrate an ultrasound image of inflation/deflation cycling, We did not evaluate capsule formation/fibrosis after explantation, although this is a worthwhile point. We added this consideration to the future benefits section of the discussion section. We have also cited a review by Bayston and an animal study of breast implants by di Pompeo et al which studied variations in capsule formation to support this new point.
Changes in text: Please see page 18 lines 370-372: “Of note, we did not evaluate capsule formation upon device explantation. This represents an important area for future study as studies of other implants, particularly in the breast, have shown variance in encapsulation.(44, 45).”

Reviewer B

I would like to congratulate the authors for this rich paper of studies in this area where the options of treatment to a wide variety of different possible to patients. As it has been information by the authors a Penile prosthesis (PPs), including
65 inflatable penile prosthesis (IPPs) and semi-rigid options, are the mainstay treatment for refractory ED, although only 5% of eligible patients receive them.The emergence of new drugs in the late 1990s many researchers thought that this would be a significant number of people but after some years from only a number of people would have been treated from this disease. I think that this research shows new options to try a larger number of different patients.

Reply: Thank you for your positive feedback and review of our manuscript.

Reviewer C

I am curious as to why "rabbit" was not included in the search parameters for the literature review as multiple studies have been published on this, including one in Translational Andrology and Urology. The authors do cite this study by Lima, but their literature review parameters should probably include "rabbit" as that is the model that they're using. This is a small and easily correctable edit.

Reply: Thank you for pointing this out. We have added “rabbit” to the search parameters and repeated the search to ensure that there were no additional studies that were missed in the original search. We did not uncover any new studies that had been originally missed, but we agree that this is an important addition to the search. We added this to the methods.

Changes in text: Please see page 6 line 104.

The rabbit model presented does seem novel and useful for pre-clinical studies. However, the authors should address the differences in rabbit and human microbiomes as well as immune systems.

Reply: Thank you for raising this important point. We have added a statement to the limitations section in the discussion about the differences between rabbit and human microbiomes, and how any in vivo study outside of humans would have this limitation to generalizability when studying infection prevention tools.

Changes in text: Please see page 20 lines 406-408: “It bears noting that there are differences between rabbit and human microbiomes, limiting direct extrapolation of results from any animal study to clinical use.”

Authors should address the lack of perioperative antibiotics in their model.

Reply: We appreciate this comment and recognize why perioperative antibiotics would be important in a clinical model of IPP infections. While we agree that future animal models may incorporate perioperative antibiotics, in this study, we were not attempting to recreate the entire penile implant process. Instead, we sought to evaluate the feasibility and safety of implant placement in a rabbit. We wanted to ensure that the rabbit did not develop any over infection of the implanted device and believed that perioperative antibiotics at this early-stage model would represent a confounder. Future models should certainly consider perioperative antibiotics as a modifiable variable when studying infection prevention strategies. We added this comment

to the discussion section.
Changes in text: Please see page 18 line 358: “Investigators may consider new perioperative antibiotic strategies including PP coatings which specifically attack evolving microorganism profiles or elute greater concentrations of antibiotics (24).”

Finally, the title should better represent the content of the paper.
Reply: We appreciate this suggestion and have revised the title to be more representative and clear regarding the content of the paper. We have changed the title to “Addressing the Need for Preclinical Study of Penile Prosthesis Infection: A New Animal Model and Narrative Review.”
Changes in text: Please see page 1.
aul H. Chung serves as a guest editor for the special issue “Genitourinary prosthetic infection.”