Peer Review File

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Reviewer A

The authors submit a narrative review of penile implant biofilms. The paper is well-written but suffers from a deficit of legitimate preceding literature on this topic. More specific comments are below.

Thank you for the comment. We have updated our reference list to include more contemporary research studies published within the past 5 years, such as reference 36, 44 and 45.

Title: No issues.

Thank you.

Abstract: It is inaccurate to state that biofilms are believed to be the culprit of penile prosthesis infection. Biofilms are found on devices whether they are infected or not, as seen in publications by one of this paper's coauthors. Microbes are the cause of PP infection; biofilms are communities of bacteria. Conundrum is not an appropriate descriptor in this context.

We thank the reviewer for this clarification. Biofilms are not the culprit of penile prosthesis infection, but rather, they increase the difficulty of treating infections through protecting infectious microbes contained within them from antibiotics and the body's immune responses. We have made changes to the abstract accordingly (page 2, line 50).

> ***While biofilms have shown to support the persistence of microorganisms, the degree by which this matrix is truly pathogenic remains unknown given its high prevalence even in asymptomatic patients.***

We have also replaced the word conundrum with issue as advised by the reviewer in both the abstract (page 3, line 79) and manuscript (page 20, line 394).

> ***Currently, preliminary and experimental biofilm-control strategies are also underway to further address this clinical issue.***

> ***These patients also present with more toxic, systemic infections and ultimately require device removal altogether for source control. While revision washout protocols and antibiotic-coated implants have decreased overall infection rates, testing of preliminary and experimental biofilm-control strategies is necessary to further address this clinical issue.***

Introduction: No concerns.

Thank you.

Methods: There is scant literature on this topic. This may be more appropriate as a scoping review rather than a narrative review.

We thank the reviewer for this comment. Based on the recommendations, we have reformatted our article to a scoping review rather than a narrative review according to the journal guidelines for authors.

> ***Title: A Scoping Review of Penile Implant Biofilms – What Do We Know and What Remains Unknown?***
>
> ***Running title: A Scoping Review of Penile Implant Biofilms***
>
> ***Herein, we aim to provide the readership with a scoping review of the current literature pertaining to biofilm formation in the setting of PP surgeries. We present the following article in accordance with the PRISMA-ScR reporting checklist.***
>
> ***Keyword searches including a combination of the terms "penile prosthetic" OR "penile prosthesis" OR "penile implant" AND "biofilm" OR "revision" OR "removal" OR "infection" OR "explant" were utilized to identify appropriate articles to include in our scoping review.***
>
> ***FOOTNOTE: The authors have completed the PRISMA-ScR reporting checklist.***

Results: There probably should be a results section to specifically talk about the relevant studies found during research.

Thank you for the comment. Based on the guidelines for scoping review, we have included a results section in both the abstract (page 2, line 63) and manuscript (page 7, line 127).

> ***<u>Abstract</u>***
> ***Results: Infected PP yielded a 11% — 100% rate of biofilm presence, while non-infected PP yielded a 3% — 70% rate of biofilm presence. Time to reoperation from initial PP placement were also largely variable, ranging from 2 weeks to over 2 years. Coagulase-negative staphylococcus (i.e., Staphylococcus epidermidis) were the most commonly reported organisms among non-infected implants, however, newer studies have identified a change towards more virulent organisms.***
>
> ***<u>Manuscript</u>***
>
> ***While there were only three studies that explicitly listed the number of biofilms identified in their cohort, we also included several others that mentioned the swabbing and culturing of any bacterial biofilm during revision procedures for both clinically infected and non-infected implants. These results are summarized in Table 2. The percentage of biofilm presence were based on whether the PP were clinically infected or not. When PP were infected, the rate of biofilm presence ranged from 11% — 100%, while biofilm presence ranged from 3% — 70% in non-infected PP. Time to reoperation from initial PP placement were also largely variable, ranging from 2 weeks to over 2 years.***
>
> ***The first study describing biofilms on PP was published by Nickel et al. in 1986 whereby two patients with clinically infected PP harbored rod and coccoid shaped bacterial cells. These***

patients were successfully treated with oral antibiotics. The next study by Silverstein et al. found a 70% rate of biofilm formation among non-infected, non-antibiotic coated implants, 88% of which did have positive cultures. Most recently in 2016, Cifti et al. identified biofilm in 11% of implants removed for non-infectious reasons, all of which grew Staphylococcus epidermidis.

Next, we also noted that for non-infected implants or implants removed secondary to mechanical malfunction, the most common reported organisms were coagulase-negative staphylococcus (i.e., S. epidermidis), which ranged from 15% – 81% in our cohort. Conversely, implants removed for infection harbored other organisms such as P. aeruginosa in 50% of one reported cohort or E. coli in 18% of another cohort.

Discussion: The sections specifically about biofilm are well done. The sections specifically about PP infection are superfluous. These are separate topics.

Thank you for your comment. We have removed several paragraphs that are focused only on PP infection from the discussion section.

Conclusions: Adequate, no concerns.

Thank you.

References: No concerns.

Thank you.

Tables and figures: No concerns.

Thank you.

Reviewer B

Thorough and education review on biofilms in PP surgery. Should be a must-read for implanters interested in learning more about the topic.

Thank you.

Very minor edits/suggestions, but:

1) what did we do before mulcahy protocol? Could you include a line or two about this historical aspect?

We thank the reviewer for this relevant comment. We have included a few lines describing the historical approach of treating penile prosthesis infections prior to the introduction of the Mulcahy protocol (page 14, line 289)

Prior to the introduction of the salvage technique, treatment of PP infection involved the

removal of all prosthetic components along with copious antibiotic irrigation to the PP site. This often resulted in fibrosis and scarring of the corpora cavernosa, complicating subsequent reimplantation in the future. Since the development of the Mulcahy protocol in 1996, other groups have demonstrated promising results with the use of the immediate salvage technique and also modified their techniques with a delayed or malleable salvage method with other antibiotic irrigation solutions.

2) review one more time for minor grammar or flow changes: examples include -
line 349 Aside from targeting the first phase of biofilm formation, adhesion, studies ... might read better as "Aside from targeting adhesion, the first phase of biofilm formation, studies...

Thank you for your comment. We have modified the text accordingly as suggested by the reviewer (page 16, line 343).

Aside from targeting adhesion, the first phase of biofilm formation, studies have attempted to inhibit microcolony formation by disrupting the EPS.

3) 414 PHC consults and receives research support from Boston Scientific and Coloplast - should read consults FOR and receives research support from...

Thank you for your comment. We have modified the text accordingly as suggested by the reviewer (page 20, line 406).

GDH consults for and receives research support from Boston Scientific, MicroGenDx, Coloplast, Signati Medical. PHC consults for and receives research support from Boston Scientific and Coloplast.