

## Peer Review File

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### Reviewers Comments

**Comment 1: Please include in Results section the themes of the 8 questions in which there was a significant difference (ie, satisfaction with treatment, treatment speed, treatment duration, etc).**

*Reply 1:* This has been addressed in the Results section with the addition of the themes of the 8 questions in which there was a significant difference.

*Changes in the text:* "There was a significant difference in mean survey responses for 8 of the 11 questions in the EDITS questionnaire between the RP group and the radiation group ( $p < 0.05$ ). For all 8 of these questions surveying key satisfaction metrics, the RP group had a significantly higher mean score versus the radiation group. These survey themes with a significant difference in mean score were overall treatment satisfaction (Question 1), likelihood to continuing use of treatment (Question 3), satisfaction with how quickly the treatment works (Question 5), satisfaction with how long the treatment works (Question 6), confidence regarding ability to engage in sexual activity (Question 7), perceived satisfaction of their partner with the device (Question 8), naturalness of the erection with the treatment (Question 10), and naturalness of the erection in terms of hardness (Question 11)."

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**Comment 2: Results - Can you perform a subset analysis for patients who were not on ADT? Are baseline, pre-treatment IIEF scores available?**

*Reply 2:* We unfortunately do not have IIEF scores available. If the reviewers would like, we can do subset analysis for pts with no ADT history, however it would be a small sample size, about 12 pts in radiation group vs 42 RP. Could include as supplemental figure/table if desired.

*Changes in the text:* N/A

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**Comment 3: Discussion - Please hypothesize why radiation patients may have subjective decreased penile length. Need to include discussion on side effects of ADT and how they may contribute to erectile function and satisfaction with erectile function.**

*Reply 3:* We have included in the Discussion section additions regarding why radiation patients may have subjective decreased penile length. Lengthy discussion regarding ADT and its side effects have been expanded upon in additional revisions below as well.

*Changes in the text:* “The role that ADT may play in sexual satisfaction, or lack thereof, in our patient cohort is important in interpretation of our results. In our study, patients with any history of ADT use, including pre-PPS, were included in the “yes” category for both the RP and radiation cohorts. ADT use has been well-documented as increasing the risk for erectile dysfunction and decreased libido in patients. In some instances, it has also been noted to cause ED following discontinuation of use, which guided our rationale in defining ADT use as that of any point prior to survey (24, 25). Furthermore, the downstream effects of ADT use, including the blockade of testosterone (T) production, leading to decreased sexual desire and satisfaction may impact the results of our study (26). The radiation-only cohort had a higher proportion of patients with any history of ADT use, and additionally, as a limitation, we did not have T levels at time of survey to be included in our analysis. Furthermore, the risk of hypogonadism in pelvic irradiation provides another possible factor in the decreased satisfaction our radiation only cohort reported. We hypothesize that this may relate to the greater proportion of the radiation cohort reporting subjectively decreased penis size post-operatively, which has been found as being more common in patients undergoing RT/ADT versus RP (27, 28).”

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**Comment 4: Please identify the directional difference towards RP/RT in Table 2 as well so that readers do not have to look at Figure 2.**

*Reply 4:* Table 2 updated with columns added listing mean values for all questions so directional difference can be observed without referring to Figure 2.

*Changes in the text:* Table 2 updated; changes tracked.

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**Comment 5: Firstly, though literature already exists comparing satisfaction with penile prostheses among men with varying etiologies of ED, I fail to see how this effectively helps men who are considering penile prosthesis as a treatment for ED, or for those surgeons counselling them on ED treatment options. The patient cannot control the cause of their ED, and in this case, it seems unlikely that a patient would base their decision on how to treat their prostate cancer given the possible satisfaction of a prospectively needed ED treatment years down the line. It strikes me that the comparison of satisfaction based on type of prostate cancer treatment is being made because it can be, not because it provides any meaningful insight.**

*Reply 5:* Thank you to the reviewer for this excellent and insightful suggestion. This was a limitation in our initial draft and we have done our best to address this in the Discussion section below. As we have addressed in the changes in the text, the goal of this study was not to drive treatment changes. As even if treatment satisfaction may vary between modalities, it is unreasonable and perhaps even unsafe to expect cancer

treatment options to change under the supposition of post-treatment ED. However, the goal, in addition to building off prior work our team has published, is to (at least in our initial single site findings) establish a conversation regarding any unique considerations we may utilize in the future to increase the PPS satisfaction of a group (like the radiation group) that may have reduced satisfaction post-op versus other patients.

*Changes in the text:* “However, even with an understanding of why the radiation and RP groups differ in post-PPS sexual satisfaction, asking how this information can and should be applied moving forward to best serve our patients is one of great importance. The goal of our study was not to help guide treatment for a patient’s prostate cancer via observed differences in sexual satisfaction following treatment for ED that may or may not result secondary to their treatment modality. Cancer treatment options should absolutely not change under the supposition of post-treatment ED. The goal, in addition to building off prior work our team has published, is that if there is indeed a difference in sexual satisfaction between the two groups, are there any unique considerations we may utilize in the future to increase the PPS satisfaction of our patients (23).”

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**Comment 6: The authors did a good job of mentioning the flaws of using the currently available validated ED questionnaires in assessing satisfaction with penile prostheses, a limitation which I think has been a hindrance in assessing IPP outcomes for years now. That said, efforts are being made in this domain, so to claim that no questionnaires specifically for penile prosthesis satisfaction assessment exist is wrong-see Carlos et al., J Sex Med. 2020 Nov;17(11):2307-2310. This then leads into the discussion of inherent limitations of retrospective studies, whereby dated questionnaires are being used. A prospective study using contemporary meaningful questionnaires might be of interest.**

*Reply 6:* Discussion regarding SSIPI have been included and extensively addressed as a limitation to the data in our study.

*Changes in the text:* The Satisfaction Survey for Inflatable Penile Implant (SSIPI) has been developed and validated to assess post-PPS patient reported outcomes and satisfaction (36).

There are several limitations to our study in addition to those mentioned above. First, although our institution has a high-volume of patients undergoing PPS, all patients did not complete an EDITS questionnaire. Like as mentioned above, utilizing a validated survey such as EDITS in assessing sexual and device satisfaction is important when evaluating PPS patients (9, 37, 38). Many PPS satisfaction studies are limited by using non-validated assessments in capturing data. And with the promising new development of procedure-specific surveys such as the SSIPI, evaluation of post-

operative outcomes and satisfaction should improve. The retrospective nature of our study introduces limitations, including continued utilization of the EDITS questionnaire which may now be considered a dated evaluation tool with the development of surveys such as the SSIPI. We therefore recommend more frequent utilization of EDITS questionnaires such as the SSIPI to provide greater external validity to future related studies, preferably in prospective studies.

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**Comment 7: Furthermore, I do not understand why the 3 extra, unvalidated questions relating to penile length were included. Finally, given that the EDITS questionnaire was used, a discussion on the minimal clinically important differences (MCID) for this questionnaire would be useful-though there is a statistical difference between the groups, how much of a clinical difference does this represent?**

*Reply 7:* These were three additional questions that were part of a survey patients had completed in addition to the EDITS questionnaire, which was also used in our prior published work, given the retrospective nature we chose to include these answers as well however we have now emphasized that these three questions are unvalidated. Additionally, an important note is that although there may be statistically significant difference, there may not be a clinical difference. The scores were lower vs RP, but patients still did report overall positive post-operative satisfaction.

*Changes in the text:* "Subsequently as a limitation, the three additional questions asked of patients following the EDITS questionnaire are currently unvalidated questions but had been used in evaluation of patients in our prior published work (23). Given the retrospective nature of our study we chose to include these answers as well. Additionally, an important note is that although there may be statistically significant difference in EDITS scores, there may not be a clinical difference. The scores of the radiation-only cohort were lower versus the RP group, but as the radiation only cohort did have a mean EDITS score of 76.56, this is still considered an overall positive post-operative satisfaction level, albeit low in relation to the RP group."

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**Comment 8: While a discussion on the impact of age was included, it would have been of interest to assess how duration of ED prior to penile prosthesis implantation impacts on ultimate satisfaction. In this study, men who underwent radiation had almost double the duration of ED. As such, it would seem (though this data was not provided, and would be useful) that those patients would have tried more/different non-surgical ED treatment options prior, with obvious dissatisfaction, as they eventually decided to pursue penile prosthesis. I would think that dissatisfaction with their overall sexual function for years could cloud one's assessment of satisfaction once the penile prosthesis was implanted.**

*Reply 8:* We have addressed all of the following in our Discussion section as reflected in the revision below.

*Changes in the text:* “Also, our radiation-only cohort had a significantly greater period of time from prostate cancer treatment to PPS date. Determining why or what caused this delay in time from treatment to penile prosthesis surgical implantation date may help elucidate the differences in our satisfaction findings. There is a possibility that patients in the radiation-only cohort opted for more non-invasive options for ED treatment with no success prior to finally opting for surgery, although we unfortunately did not have this information to be included in our analysis. Following years of interventions with limited success, this could certainly increase a patient’s dissatisfaction with their sexual function, even following definitive treatment via PPS. This is a limitation to our study and addressing what led to this delay in time from treatment to PPS can help identify ways in which we can streamline our care for our patients.”

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**Comment 9: The main limitation is that the authors did not use the SSIPI validated questionnaire. They note that no validated questionnaire is available but this is incorrect. However, the results are still valuable.**

*Reply 9:* We have made revisions to reflect this, similar to that of Comment 6. Changes to the text listed below is that of Comment 6, as well.

*Changes in the text:* “The Satisfaction Survey for Inflatable Penile Implant (SSIPI) has been developed and validated to assess post-PPS patient reported outcomes and satisfaction (36).

There are several limitations to our study in addition to those mentioned above. First, although our institution has a high-volume of patients undergoing PPS, all patients did not complete an EDITS questionnaire. Like as mentioned above, utilizing a validated survey such as EDITS in assessing sexual and device satisfaction is important when evaluating PPS patients (9, 37, 38). Many PPS satisfaction studies are limited by using non-validated assessments in capturing data. And with the promising new development of procedure-specific surveys such as the SSIPI, evaluation of post-operative outcomes and satisfaction should improve. The retrospective nature of our study introduces limitations, including continued utilization of the EDITS questionnaire which may now be considered a dated evaluation tool with the development of surveys such as the SSIPI. We therefore recommend more frequent utilization of EDITS questionnaires such as the SSIPI to provide greater external validity to future related studies, preferably in prospective studies.”

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**Comment 10: A very small number of patients underwent brachytherapy. This is a limitation.**

*Reply 10:* Addressed in Discussion as a limitation.

*Changes in the text:* Additionally, our radiation-only cohort had a very small number of patients, 6 of the 32, who underwent brachytherapy versus EBRT.

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**Comment 11: Please specify how many RP patients had bilateral nerve sparing vs unilateral vs non-nerve sparing.**

*Reply 11:* Information on nerve sparing in our RP cohort has been included, unfortunately, we did not have specific breakdown of unilateral vs bilateral nerve sparing RP in our data to be included for analysis.

*Changes in the text:* Of the RP group, for those with specific RP operative reports available (n = 44), 91% (n = 40) underwent robotic RP and 81.8% (n = 36) underwent unilateral or bilateral nerve-sparing RP. Specific breakdown of unilateral versus bilateral was unfortunately not available.

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**Comment 12: Patients who underwent radiation had a longer time to prosthesis. The authors should discuss whether this is likely due to differences in timeline of ED after treatment, or perhaps lack of prompt redirection toward curative therapy by radiation oncology. In other words, radiation patients might need to see urology again sooner if having ED.**

*Reply 12:* As reflected in Comment 8 and its subsequent revision, we have included revisions in our Discussion to address this.

*Changes in the text:* “Also, our radiation-only cohort had a significantly greater period of time from prostate cancer treatment to PPS date. Determining why or what caused this delay in time from treatment to penile prosthesis surgical implantation date may help elucidate the differences in our satisfaction findings. There is a possibility that patients in the radiation-only cohort opted for more non-invasive options for ED treatment with no success prior to finally opting for surgery, although we unfortunately did not have this information to be included in our analysis. Following years of interventions with limited success, this could certainly increase a patient’s dissatisfaction with their sexual function, even following definitive treatment via PPS. This is a limitation to our study and addressing what led to this delay in time from treatment to PPS can help identify ways in which we can streamline our care for our patients.”

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**Comment 13: Why was ADT used in some of the RP patients?**

*Reply 13:* We included any history of ADT use as “Yes” for the ADT category in our data versus selection for use at time of EDITS survey evaluation. This has been addressed and updated in the text.

*Changes in the text:* “Androgen Deprivation Therapy (ADT) use at any time prior to completion of EDITS questionnaire was also assessed, with 62.5% (n=20) in the radiation group and 17.6% (n=9) in the RP group noting ADT use at any point, with a significant difference found between the two groups (p<0.001).”

“The role that ADT may play in sexual satisfaction, or lack thereof, in our patient cohort is important in interpretation of our results. In our study, patients with any history of ADT use, including pre-PPS, were included in the “yes” category for both the RP and radiation cohorts. ADT use has been well-documented as increasing the risk for erectile dysfunction and decreased libido in patients. In some instances, it has also been noted to cause ED following discontinuation of use, which guided our rationale in defining ADT use as at any point prior to survey (24, 25). Furthermore, the downstream effects of ADT use, including the blockade of testosterone (T) production, leading to decreased sexual desire and satisfaction may impact the results of our study (26).”

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**Comment 14: Another limitation is that T levels were not assessed. Radiated patients likely have a higher risk of hypogonadism which could impact libido and subsequent satisfaction with sexual performance.**

*Reply 14:* In our revisions, we have now addressed both of the above suggestions as well as additional reference to the limitations this may produce in interpretation of our sexual satisfaction data.

*Changes in the text:* “The role that ADT may play in sexual satisfaction, or lack thereof, in our patient cohort is important in interpretation of our results. In our study, patients with any history of ADT use, including pre-PPS, were included in the “yes” category for both the RP and radiation cohorts. ADT use has been well-documented as increasing the risk for erectile dysfunction and decreased libido in patients. In some instances, it has also been noted to cause ED following discontinuation of use, which guided our rationale in defining ADT use as at any point prior to survey (24, 25). Furthermore, the downstream effects of ADT use, including the blockade of testosterone (T) production, leading to decreased sexual desire and satisfaction may impact the results of our study (26).”

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**Comment 15: Another limitation is lack of info about partner satisfaction**

*Reply 15:* Inclusion of this as a limitation has now been included in the discussion section.

*Changes in the text:* “Another limitation includes lack of information regarding partner satisfaction with treatment in this cohort. Understanding if there is a relationship between partner satisfaction and patient device satisfaction rates is vitally important in post-PPS assessments going forward (39, 40).”

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**Comment 16: Unfortunately, the article needs extensive English revision and in it’s content. Phrases like 52-54; 123-125 discourage further reading and denote a lack of careful review. Repeated words and punctuation errors compromise quality. Useless repetitions (121-122 and 126-127) occupy prime space in the methodology, just to name a few...what made reading painful.**

*Reply 16:* Thank you for this revision, we have made extensive grammatical and structural revisions and deletions throughout the text, marked via tracking changes.

*Changes in the text:* Throughout text

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**Comment 17: But the major limitation, in my opinion, and which compromises the correct interpretation of the results, is the higher prevalence of hormonal blockade in the group under radiotherapy (fact expected by the protocols for RT) and that obviously impacts on sexual satisfaction. There is no line about it.**

*Reply 17:* We have made revisions (also addressed in various of the previous Comments) regarding ADT and hormonal blockade as a limitation in interpretation of our results.

*Changes in the text:* The role that ADT may play in sexual satisfaction, or lack thereof, in our patient cohort is important in interpretation of our results. In our study, patients with any history of ADT use, including pre-PPS, were included in the “yes” category for both the RP and radiation cohorts. ADT use has been well-documented as increasing the risk for erectile dysfunction and decreased libido in patients. In some instances, it has also been noted to cause ED following discontinuation of use, which guided our rationale in defining ADT use as that of any point prior to survey (24, 25). Furthermore, the downstream effects of ADT use, including the blockade of testosterone (T) production, leading to decreased sexual desire and satisfaction may impact the results of our study (26). The radiation-only cohort had a higher proportion of patients with any history of ADT use, and additionally, as a limitation, we did not have T levels at time of survey to be included in our analysis. Furthermore, the risk of hypogonadism in pelvic irradiation provides another possible factor in the decreased satisfaction our radiation only cohort reported. We hypothesize that this may relate to the greater proportion of the radiation cohort reporting subjectively decreased penis size post-operatively, which has been found as being more common in patients undergoing RT/ADT versus RP (27, 28).

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