Reviewer Comments:

Comment 1: The title is inadequate and does not reflect the content of the manuscript.

Reply: Thank you. We have changed the title of the paper to: “Subtotal Surgical Therapy for Localized Prostate Cancer: A Single-Center Precision Prostatectomy Experience in 25 Patients, and SEER-Registry Data Analysis”.

Comment 2: The name “precision prostatectomy” is catchy and imprecise. The proper name for this procedure is partial prostatectomy for prostate cancer.

Reply: Thank you for your comment. However, we respectfully disagree with the reviewer. It is not partial prostatectomy, as partial implies that a non-specific part of prostate gland is being left behind in-situ, but in practice, we are leaving behind precisely the part of the prostate that we intend to. We understand that there is operator error, but so is the case for all procedural interventions. The excision we perform is done with intention and diligent planning. Hence, partial or subtotal resections are imprecise and unfair terms for this procedure. Further, the basis for using the name “precision prostatectomy” has been detailed in our first publication on this subject (Sood A, Jeong W, Taneja K, et al. The Precision Prostatectomy: an IDEAL Stage 0, 1 and 2a Study. BMJ Surgery Intervention Health Technologies, 2019). Here is an excerpt from that paper for reviewer’s review: “Nomenclature: A focus group of 30 men, including those in this report, were asked to come up with a name for the procedure or to choose from a menu of options: focal surgery, focal prostatectomy, subtotal prostatectomy, precision surgery, precision prostatectomy or capsule preserving prostatectomy. The consensus of the men was precision prostatectomy (29/30 men) …"
Comment 3: Data collection under IRB-approval is inadequate for this kind of study. Partial prostatectomy is VERY controversial, it is far from standard of care. Therefore, any study reporting partial prostatectomy should be performed under strict regulations of prospective clinical trials. Therefore, there is a MAJOR concern regarding to ethics for this study.

Reply: Thank you.

1. We agree that precision prostatectomy is experimental, and we believe that we have not stated anywhere in the manuscript that precision prostatectomy is standard-of-care (we double checked to ensure this during the revision process). Further, we have detailed in the methods section the consenting process for these patients emphasizing the experimental nature of this procedure, which we have also published previously (Eur Urol Focus. 2020 Mar 15;6(2):227-230).

2. This study was done under the guise of a prospective trial (HFH-IRB #12507). We have now clarified this in more detail: “Data collection was done under an ongoing research protocol approved by the Henry Ford Hospital Institutional Review Board for the prospective trial of image-guided diagnosis and treatment of prostate cancer (HFH-IRB#12507), and in compliance with HIPAA regulations.”

3. Lastly, the Institutional Review Board has the ultimate authority in approving or disqualifying a study based on scientific or ethical concerns. Merely registering a study with a clinical trials registry does not grant the study a higher ethical standard. We have innovated several surgical procedures including the first trials of robotic radical prostatectomy, robotic kidney transplantation, robotic cystectomy, and robotic partial nephrectomy. We have also published 2 surgical randomized controlled trials – both these trials were registered with ClinicalTrials.gov. We were among the first group to introduce IDEAL guidelines to the field of Urology in collaboration with Prof. Peter McCulloch (See Eur Urol publications 2013 and 2014 in renal transplantation). IDEAL guidelines do not mandate registration of early studies of surgical innovation outside of the IRB. Finally, we have a grant for an NCI funded randomized trial pending (FOA PAR-21-033),
and we cannot register the trial at ClinicalTrials.gov until that grant has been decisioned. Hence, we believe that we have adhered to proper standards and ethics while undertaking this study, and find it rather unfair on the reviewer’s behalf to suggest it otherwise.

Comment 4: How many patients were converted from partial to radical prostatectomy? “Completion prostatectomy was performed if the frozen biopsies showed residual cancer.”

Reply: Among the first 26 patients done, one patient was converted to radical prostatectomy. That patient was excluded from this report as we wanted to report on patients that completed the precision prostatectomy procedure. We have now noted this in the results section “One patient, not part of this report, was excluded due to positive intraoperative biopsy necessitating conversion to radical prostatectomy.”

Comment 5: “Huber criteria for focal therapy”. This BCF criterion does not apply for partial prostatectomy. This was performed on patients undergoing HIFU PGA and needs validation.

Reply: Agree with the reviewer. This is the reason why we used 3 separate criteria to assess biochemical failure in these patients. Details are in the paper already (of note, Huber criteria has not been validated in HIFU either, it has merely been investigated once so far).

Comment 6: There are SEVERAL and SEVERE concerns and limitations about the methodology that were not described... I would spend long time listing all of them, therefore, I will list some:
A. How you select the patients? B. Systematic + target biopsy? C. Systematic biopsy only? D. How many cores were taken? E. Did you use MRI? What was the protocol for MRI? F. What are the details of the biopsy for diagnosis?

Reply: Details on selection criteria are listed in the manuscript already. The patients reported here underwent transrectal 12-core biopsy at the minimum, with/without MRI guidance (Table 1 provides details on the number of cores, laterality, etc. already). MRI was not a pre-requisite for entry into this study.
We agree with the reviewer that a lack of standardization of pre-surgery biopsy technique and sparse utilization of MRI is a drawback of our study. In light of this, in the more recent patients (not reported here, patient #51 onwards), we have employed use of 3D ultrasound guided transperineal biopsies with/without MRI guidance, and in the most recent patients (patient #110), we are employing MRIs regularly. Although this is a drawback, we believe that by using more precise and thorough biopsy methods moving forward, we will improve our oncological outcomes only more. We have now stated this in the discussion: “However this evaluation of our technique is not devoid of limitations, within the bounds of which our results should be interpreted. These limitations include single-center design, and lack of long-term follow-up. However, the goal of this paper was to report on early results of the technique especially the functional results. Another limitation of our study is that patients selected for precision prostatectomy did not routinely undergo mp-MRI imaging, PSMA-PET imaging, or saturation biopsies to better characterize the burden and topography of CaP within the gland. Although this lack of standardization is a drawback of our current study, it is also an opportunity for further improvement of our oncological outcomes in the future.”

G. How did you do suprapubic biopsies for frozen intraoperatively? H. How many cores did you take intraoperatively? I. What are the results of the intra-OP frozen cores? J. Did you convert any partial to radical prostatectomy based on biopsy results?

Reply: These details are already listed in Table 2. We have added a footnote on suprapubic biopsies in Table 2: “Intra-op biopsies were performed with either transperineally or suprapubically; suprapubic biopsies were performed via a 14 or 16 Gauge angiocath passed through the suprapubic region, through which a 18 Gauge Bard biopsy needle was passed and cores obtained under visual guidance via the robotic camera.”
K. How did you do the follow up? L. How often did you follow up? M. Did you do biopsies on follow up?

Reply: Details are already in the paper.

Briefly, the patients were followed-up as per standard time intervals for a radical prostatectomy using PSA monitoring. The only thing different in follow-up was need for a biopsy at 12-18 months from surgery, in patients who had a detectable PSA (>=0.1 ng/mL).

N. Did you use MRIs on follow up?

Reply: Thank you for your comment. No. We do not believe that it adds value. It has been shown to be a poor predictor of residual disease in focal HIFU literature. See paper by Mortezavi et al J Urol 2019 “multiparametric magnetic resonance imaging (14.3% sensitivity) performed poorly to predict positive biopsies”. Furthermore, MRI use is not validated in patients post treatment of any kind. Please refer to the most recent version of the PIRADS manual. Thus biopsy of the remnant remains the gold standard for now to detect clinically-significant disease.

O. Where did take the RALP from? P. How did you select patients for RALP?
Q. Did you use the same criteria as for partial prostatectomy? R. What are these patients’ characteristics, demographics, histology, pathology?

Reply: Thank you. Yes these were 100 patients who met criteria for focal therapy but decided to have radical prostatectomy (these are the same 100 patients that we have reported on in our earlier paper: Sood A, Jeong W, Taneja K, et al. The Precision Prostatectomy: an IDEAL Stage 0, 1 and 2a Study. BMJ Surgery Intervention Health Technologies, 2019). Their baseline and clinical characteristics are not listed due to limitations of space, but they are available in the aforementioned paper. Thank you for pointing out this omission. We have added this sentence to Figure 1 legend: “Figure 1: Preoperative rankings of the relative importance of the 10 mutually exclusive quality-of-care indicators, provided by 100* and 25 consecutive patients undergoing robot-assisted radical prostatectomy and precision prostatectomy, respectively”
Note: the 10 questions are mutually exclusive, that is a patient can only assign a score of 10 (highest score) to one item, and then the next item, in order of priority, will receive a score of 9, and so on; “the 100 patients reported here for radical prostatectomy fulfilled the criteria for focal therapy but decided to undergo radical treatment (data on clinical and pathological details of these patients not shown [available in ref 10])”

Comment 7: Using SEER database is incorrect and inadequate for comparison. The SEER database does not discriminate partial or whole-gland ablation. The SEER database does not provide details that can be retrieved and used for comparison.

Reply: We agree with the reviewer that SEER does not provide detailed information regarding the type of treatment, however, we are not comparing among different types of gland ablation, but rather gland ablation to other forms of subtotal therapy. And whether a partial or total gland ablation, it is undertaken with curative intent. A similar investigation has already been done “Roy S, Morgan SC. Who Dies From Prostate Cancer? An Analysis of the Surveillance, Epidemiology and End Results Database. Clin Oncol (R Coll Radiol). 2019;31(9):630-6.”, using this methodology, and we followed the methodology listed in that paper. But here in the current paper we wanted to focus on non-radical treatments, hence, we limited our population to that. Further we have listed the potential drawbacks of SEER analysis in detail, and discussed our results in context of those drawbacks. Also we focused on cancer specific mortality rather than overall mortality given the fact that comorbidity information is lacking in SEER.

Comment 8: This technique is very controversial and not widespread. Therefore, please provide pictures and videos of the technique.

Reply: We apologize that we cannot provide pictures or videos for the current paper as we are in the process of submitting a surgical video along with
pictures to another journal. We are including a link to a YT video here for reviewer’s consideration: https://youtu.be/b60kst7lbCQ

**Comment 9:** Honestly, if you like to get these data published, I advise to remove all SEER data and all RARP data from the manuscript. Don’t even mention SEER or RALP. Just try to make this a pilot study of safety and feasibility of a surgical technique based only on the 25 patients that underwent partial prostatectomy. Please be very clear with the data and report as much details as possible. Please rename “precision prostatectomy” to partial prostatectomy for PCa.

**Reply:** Thank you again for your review and suggestions to help improve our study. Hopefully the aforementioned edits and arguments have answered the reviewer’s relevant concerns.