Reviewer’s report

Title: Assessment of lower urinary symptom flare with overactive bladder symptom score and International Prostate Symptom Score in patients treated with iodine-125 implant brachytherapy: Long-term follow-up experience at a single institute

Version: 0 Date: 25 Apr 2017

Reviewer: Jonathan Tward

Reviewer’s report:

The authors have investigated the performance of a relatively new Patient Reported Outcome (PRO) measure (the OABSS) relative to that of the almost ubiquitous IPSS scale that has traditionally been used to assess LUTS. Although the authors were not attempting to demonstrate superiority of one PRO vs the other, the potential advantages of the OABSS relative to the IPSS is that it is a shorter questionnaire, and has a urinary incontinence domain. The results were reported over a 5 year time interval and assessments were made annually.

When one eyeballs the shape and magnitude of the curves of IPSS vs OABSS domains (figure 1), they almost look superimposable. Which suggests that these instruments perform similarly. Nevertheless, the authors indicate that an additional 11% of persons with clinically significant GU bother (symptom flare specifically) can be identified by adding the OABSS to an IPSS evaluation. They performed statistical analyses to create prognostic cutpoints for symptom flare, settling on a 12 point increase over nadir for IPSS and 6 point over nadir for OABSS to prognosticate those more likely to flare. They also evaluated the relationship of the flare phenomenon to PSA bounce, and found no correlation.

The major value of the work to this reviewer is that it validates that the OABSS is a clinically useful PRO, that performs similarly, but can provide some independent information to the IPSS. However, prior to publication, the author's need to address the following concerns:

1) The authors indicate they performed a "threshold sensitivity analysis" to choose their cutpoints for symptom flare. They do not provide enough detail about the statistical methods to allow a reviewer to criticize if these methods were valid. As the authors indicate, they chose different threshold values of clinical significance than others (Cesaretti et al and Keyes et al.) I believe the authors need to add more detail, and the journal should have a statistician review the methodology in the revised manuscript.

2) In the results section, the author's state

"To evaluate the correlation between IPSS flare and OABSS flare, the number of additional points (peak subtracted by nadir) in total IPSS and total OABSS were plotted and examined using Spearman’s correlation (Figure 3A). There was a STROONG correlation between the increased points of total IPSS and total OABSS ( □ = 0.49, P < 0.0001)."
However, a correlation coefficient of 0.49 is a MODERATE correlation at best. in fact, many would read this as somewhat discordant between IPSS and OABSS scoring. Since my interpretation of the main conclusion of the author's is that 11% of additional people may be identified as at flare risk on OABSS, this lack of excellent correlation may better support their argument, and they should revise the wording. If the OABSS and IPSS were truly concordant (which they are not) there would be no clinical utility of also getting OABSS in addition to IPSS.

3) the author's emphasize that 11% of people with flare were identified by OABSS but not IPSS. Figure 3 reveals highly implies that a similar number of people were identified with flare on IPSS but not OABSS. The authors should report this finding as well.

4) The fact that a certain percentage of people will be independently discovered as flare on OABSS and IPSS, without overlap, is the major finding to support addition of OABSS to either clinical use or as a PRO measure on clinical trials. This should be made a little more clear.

5) Gleason score was found to be significant for predicting flare, as was Biologically equivalent dose (BED). However, GLeason 9 and 10 patients were almost certainly likely to receive EBRT + Brachy instead of brachy alone, which means that Gleason 9 and 10 could merely be a surrogate for high BED. The author's do state that they tried to do analyses to exclude the effect of EBRT, but it was not clear to this reviewer if their analyses addressed this potential interaction. I recommend a statistician address the issue of whether or not BED and High Gleason score (or high D'amico risk group) had a statistical interaction confounding the significance testing.

In summary, This work currently shows that OABSS and IPSS can be independently prognostic for symptom flare, but reveals no predictive information (i.e. that intervening when a point rise is noted in either instrument would change the outcome). It also revelas that the PSA bounce phenomenon is independent of symptom flare, an important observation.

This work would add to the body of literature that OABSS can be used as a validated PRO to assess bladder dysfunction after brachytherapy, but should not replace the IPSS.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I recommend additional statistical review

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