Reviewer's report

Title: Stereotactic Body Radiotherapy for Organ-Confined Prostate Cancer

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Reviewer: Michael Papagikos

Reviewer's report:

The authors are to be commended for amassing detailed toxicity and QOL data for a large number of patients treated with SBRT for organ confined adenocarcinoma of the prostate. This will certainly add to the emerging data on this new and experimental therapy. The manuscript is well written and easy to understand and the references are appropriate. My criticisms are listed below.

Discretionary Revisions:

1) The reference to the Sanda paper in the background suggesting that ED is identical between RP and EBRT is misleading. The abundance of the QOL data presented in that paper regarding sexual function suggest that EBRT patients had much less decrements from baseline than RP. Perhaps a more nuanced handling of that very important reference would be beneficial.

2) Given the very short follow-up period for what is a cohort of men with mostly low and intermediate risk prostate cancer, presentation of the QOL and Toxicity data first, followed by the PSA and efficacy data would be more appropriate so as not to overestimate the strength of the data with regards to biochemical control, which the authors acknowledge will require much longer follow-up.

Minor Essential Revisions:

1) Explain precisely what version of the ASTRO biochemical failure definition was used. I assume the Phoenix definition but a brief sentence describing the definition for the reader would be helpful.

2) Multiple references are made to 75% of patients completing their EPIC QOL questionnaires. It should be noted in the manuscript that this 75% refers to patients who have been followed for at least 18 months, i.e. 145 patients or 48% of the entire cohort.

3) The % of high-risk patients in table 1 is incorrect 12/304 is 3.9% not 0.7%

4) Figure 2: The number of patients at risk for the 6, 12, and 18 month data points if you combine A and B and combine C and D don't match as would be expected?

5) Figure 3: The x-axis should be in 6 month increments to match the text.
Major Compulsory revisions:

1) There are two major problems I have with this paper. The first is that there are 4 groups of patients defined by two variables that potentially have impact on efficacy and perhaps toxicity and they are the radiation dose and the use/duration of ADT. The second problem is the very short follow-up period, which not as critical with respect to toxicity and QOL, but is terms of biochemical control rates. The 35Gy cohort (n=50) has a median follow-up of only 30 months. I would prefer allowing the data to mature until the minimum potential follow-up period is at least 24 months, but in a primary toxicity paper I think it is fine to show some efficacy data. I would argue that the strength of this paper is the toxicity and QOL data and the authors should treat lightly when making reference to biochemical outcomes. For cohort 2 (n=254), the median follow-up is only 17 months! When this fact is combined with ~20% of patients receiving a variable duration of ADT, any reference to efficacy or biochemical control in this cohort is not appropriate. I would suggest that the authors report their data as follows:

a. Acute toxicity: include all patients with data from the 5 month follow-up.

b. Late toxicity: include all patients with data from the 12 month follow-up.

c. Efficacy (i.e. biochemical control data): limit this to patients with a minimum potential follow-up of 12 months and exclude those patients that had received ADT. The authors point out that the median duration of ADT was only 7 months and that the impact of this will be mitigated with longer follow-up which is true but this report does not have that longer follow-up and thus the issue needs to be addressed and the purest way to do that would be to exclude those patients from the efficacy portion of the analysis. Reporting a crude recurrence rate of 1.3% (4/304) is not informative when only 250 (or 239 depending on what graph you use) patients even had their 6 month PSA drawn by the time of the analysis.

d. If biochemical control rates are going to be given the Kaplan-meier estimates with CIs should be provided.

2) What type of study was this? The methods state that patients were treated “under internal review board approval”. If this was a prospective study then they should state as such as well as the inclusion and exclusion criteria and sample size calculations and the primary endpoint and assumptions and mention that patients signed a study specific informed consent. If this is an IRB approved retrospective study of patients treated off protocol but with the intention of being published at a later date, that should be stated as well. If the later, then it would also be helpful to know how many patients treated during the study time frame are not included in this analysis.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests