Reviewer's report

Title: Minimal percentage of the dose received by 90% of the urethra (%UD90) is the most significant predictor of PSA bounce in patients who underwent seed implantation

Version: 1 Date: 9 June 2012

Reviewer: Peter Black

Reviewer's report:

Review comments:

The issue of distinguishing PSA bounce from PSA failure is an important distinction following radiation treatment for prostate cancer. This study aims to find factors that may contribute to the benign condition of PSA bounce.

The following changes are suggested:

Title

Should include the words “brachytherapy” and “prostate cancer”. The disease prostate cancer is not even mentioned until the Methods section!

Methods/Design

Was the data collected prospectively (implied with statement of patient consent)? This needs to be stated explicitly in the methods.

The treatment is so heterogenous, that it is hard to make sense of the data. Really the authors should limit themselves to the summary in Table 4 (brachy, no ADT) for assessing risk factors.

• While a bounce may be seen with and with ADT and with either form of radiation, it doesn’t make intuitive sense to lump all together and look at bounce.
• 54 months of neoadjuvant ADT, for example, would likely have an effect on bounce! How many patients had more than 12 months of ADT?
• The fact that no patients with adjuvant ADT had bounce implies that this may interfere with a bounce (when given over 2 years). Did the authors measure testosterone recovery?
• It also stands to reason, as shown in the data, that combined brachy and external beam radiation lessen the risk of bounce – so these patients cannot be included in an assessment of risk factors. Higher risk disease was presumably treated with combined therapy, so it would stand to reason that the higher PSA seen in the non-bounce group was a reflection that these patients received combined therapy for their higher risk disease. These associations need to be addressed. The only fair way to look at the long list of potentially confounding factors is with a multivariable analysis.
The longer follow up and more frequent PSA checks are a significant confounder in the PSA bounce group. The lack of follow-up to observe 32 PSA rises come back down to nadir is also a significant limitation.

Did the change from one planning system to another in 2008 have an impact on the results? Dosimetry is measured in part as % of prescribed doses – yet the prescribed dose changed in 2007 – how does this affect the results? Dose is thought to be a predictor of bounce (Stock 2003). The authors would need to include year of treatment in a multivariable analysis. How was dose calculated in patients who received EBRT boost?

The definition of PSA Bounce is controversial. The authors have taken the lowest conceivable threshold (0.1), which may explain why the median height of bounce is so low – presumably in many other series these would never have become bounces. Are the results still significant if rise of >0.4ng/ml is used, or >35% of previous value? The median bounce in this series is less than a 0.4 cut-off.

Discussion

The introduction states that the importance of PSA bounce lies in its confusion with, or delayed diagnosis, of PSA failure. However, the discussion does not attempt to address this issue with the study data or how the data might be useful. PSA bounce is not clinically relevant. Therefore, some attempt should be made to put the usefulness of the data in a clinical context.

Furthermore, no pathobiological explanation of the novel finding is given. Why might an increased dose to the urethra cause a bounce - or is it statistical chance given the multiple comparisons?

Minor points

Table 1 uses mean PSA for non-parametric data; text uses median.

Table 5 uses “confidential interval” instead of confidence.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests