Peer Review File

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Reviewer A

The editorial addresses a very topical discussion in radiotherapy for prostate cancer. I only have minor comments:

The authors state at the end that radiation dose is the key factor. In my opinion, this message would become even stronger when it is pointed out that AHT in high-risk patients is essential for disease control outside the prostate (as previously proven in several RCTs), and that now as an important next step, disease control inside the prostate should be addressed by increasing BED. Furthermore, it might be relevant to mention studies that aim at increasing focal dose levels to defined areas within the prostate (based on functional imaging), like in the Dutch FLAME trial.

Reply: Now I have incorporated RCT references showing advantage of long-term usage of ADT in combination with EBRT: See page 2, Text lines 1-3.

Concerning the discussion on disease control of inside and outside of the prostate: The concept of prostate cancer with clinical organ confined or extra-prostatic extension is obscure and putative.

This cannot be clearly judged before radiotherapy or treatment. On the other hand, this author has invented and published a methodology: a quality LDR method of high BED which can treat both inside and outside of the prostate with or without ADT. Therefore, I have incorporated this point in the text: See the bottom of page 5.

Reviewer B

I recommend the author clearly define the topic of the Review at the beginning of the manuscript (the relevance of the recovery of testosterone levels when evaluating effectiveness, and the impact of BED on oncologic effectiveness). Moreover, the literature may confirm the impact of BED on oncologic effectiveness. However, the determinant role of BED cannot be concluded from the RTOG0521 trial as it is not one of its objectives and there is no comparison referring to this topic.

Reply: Now I have clearly described the topic of this review at the beginning of the text: See page 2, lines 4-7.

The reviewer's point out that role of BED and duration of ADT are not the aim of the RTOG 0521 is correct. Therefore, this author has mentioned on this point: See page 7, lined 3-4. I have incorporated a recent RCT literature showing that high BED has demonstrated g good oncological outcome regardless of duration of ADT: See the bottom of page 6 and the top of page 7, ref 18.

The reason why this author has accepted the offer writing the present editorial comment is that current design of RTOG has not been well done.

This author feels that I should give a warning opinion that a similar attempt to repeat RTOG 0521 will just result in the waste of time and resources.: See page 7, lines 4-6.

Now, I hope that every physician involved in prostate cancer should go forward to the standpoint that prostate cancer treatment should be conducted with at most care and attention to avoid recurrence: See the video abstract, Ten-step method of high-dose LDR 125I brachytherapy for intermediate-risk prostate cancer - Okamoto - 2021 - Journal of Applied Clinical Medical Physics - Wiley Online Library.