

Format for ANSWERING REVIEWERS



August 4, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name 19450-review.doc)

Name of Journal: World Journal of Radiology

ESPS Manuscript NO: 19450

Title: Recovery of serum testosterone following neoadjuvant and adjuvant androgen deprivation therapy in men treated with prostate brachytherapy

Authors List: Hideyasu Tsumura, Takefumi Satoh, Hiromichi Ishiyama, Shuhei Hirano, Ken-ichi Tabata, Shinji Kurosaka, Kazumasa Matsumoto, Tetsuo Fujita, Masashi Kitano, Shiro Baba, Kazushige Hayakawa, Masatsugu Iwamura

Reviewer #1

We thank the reviewer for the insightful comments. We attempted to reply to all of your concerns in the revised text. We would like to respectfully request that this revised manuscript be re-considered for publication in *World Journal of Radiology*

1) *Methods: Define normal and supracastrate testosterone levels.*

We apologize that these information were not correctly included in text. We correctly define normal and supracastrate testosterone levels in text (Methods).

(Page 5, Para 3)

A normal level of T and a castrate T level were defined as ≥ 207 ng/dl and ≤ 50 ng/dl, respectively. A T level of > 50 ng/dl was defined as a supracastrate level. Both supracastrate and normal levels were used for the definition of T recovery.

2) *Results, Patients characteristics, first paragraph, should specify the reasons why 42 patients were removed from the study. My suggestion is to mention "42 patients were removed for reasons detailed in Figure 1: PSA failure during AHT (n=13), severe disease (n=1), missing data (n=17), AHT duration deviation from treatment protocol (n=11)".*

We really appreciate your suggestion. We add information about reason why 42 patients were removed from study in text.

(Page 7, Para 3)

Patient characteristics

Figure 1 provides the characteristics of the 216 patients who were candidates for the present study. Data for the 174 who were eligible for inclusion in the efficacy analysis were analyzed, and 42 patients (19.4%) were removed for reasons detailed in Figure 1: PSA failure during AHT (n=13), severe disease (n=1), missing data (n=17), and ADT duration deviation from study protocol (n=11).

- 3) *Methods: detail what type of EBRT was given, what type of fields (target prostate only, or regional nodes), indicate if testicular dose was computed or not.*

We apologize that these information were not included in text. We add information about type of EBRT and type of field in text.

(Page 6, Para 3)

HDR brachytherapy and hormonal therapy

We previously mentioned about our protocol and procedure for HDR brachytherapy and hormonal therapy in high-risk prostate cancer [12, 13]. Briefly, the mean dose to 90% of the planning target volume was 6.3 Gy/fraction of ¹⁹²Ir HDR brachytherapy. After five fractions of HDR treatment, EBRT with 10 fractions of 3 Gy was administered. Patients received EBRT using a dynamic-arc conformal technique, administered with high-energy photons comprising 10-MV X-rays. The radiation field was limited to the prostate gland with or without proximal seminal vesicles with a 7-mm leaf margin using multileaf collimators. Testicular dose was not computed.

- 4) *The study should take into consideration that pelvic radiotherapy might cause higher scattered dose to the testes, see for example the commenting review and discussion in King and Kapp, JCO 2009;27:6076-8. My suggestion is to insert into Table 2 a comparison of EBRT versus no EBRT.*
- 5) *If EBRT is statistically significant, insert into the Discussion: the results might have been confounded by EBRT, because patients receiving 36 months AHT also received EBRT.*

We really appreciate your very insightful suggestion. However, all patients in long-term usage group were treated with combination of HDR brachytherapy and EBRT (Please see Figure 1). Thus, we could not compare factors associated with testosterone recovery between EBRT and no EBRT in Table 2. We hope you will understand this study populations.

- 6) *Discussion: the statement "In these cases, we have difficulty judging whether radiotherapy provides a cure" appears inexact. I suggest to replace with "In these cases, we have difficulty judging whether cure is attributable to radiotherapy, to sustained castration, or to both".*

We really appreciate your suggestion. We replace the sentence as follow.

(Page 9, Para 3)

In these cases, we have difficulty judging whether cure is attributable to radiotherapy, to sustained castration, or to both.

Please understand and we hope you will satisfy with the latest version of our manuscript.

If you have any further questions, please do not hesitate to contact me. Thank you for this courtesy.

Sincerely,

Hideyasu Tsumura, M.D.

Department of Urology

Kitasato University School of Medicine

1-15-1 Kitasato Minami-ku, Sagamihara, Kanagawa 252-0374, Japan

TEL: +81-42-778-9091

FAX: +81-42-778-9374

E-mail: tsumura@med.kitasato-u.ac.jp