Author's response to reviews

Title: Characterization of prostate cancer detected at repeat biopsy

Authors:

Takeshi Yuasa (yuasa@doc.med.akita-u.ac.jp)
Norihiko Tsuchiya (tsuchiya@med.akita-u.ac.jp)
Teruaki Kumazawa (kuma@doc.med.akita-u.ac.jp)
Takamitsu Inoue (takamitu@doc.med.akita-u.ac.jp)
Shintaro Narita (nari6202@gipc.akita-u.ac.jp)
Mitsuru Saito (mitsaito@med.akita-u.ac.jp)
Yohei Horikawa (horikawa@gipc.akita-u.ac.jp)
Shigeru Satoh (shigerus@doc.med.akita-u.ac.jp)
Tomonori Habuchi (thabuchi@doc.med.akita-u.ac.jp)

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Author's response to reviews: see over
Dear Dr. Scott Edmunds

We were very happy to learn that our paper is of potential interest to *BMC Urology* and revise our manuscript entitled “Characterization of prostate cancer detected at repeat biopsy” by Takeshi Yuasa *et al.* We would like to re-submit our manuscript with the appropriate modifications and revisions for publication as a Research Article in *BMC Urology*

We believe that our manuscript, which has been greatly improved by the reviewer’s helpful comments, will provide valuable information for general urologists as well as urologic oncologists. Your consideration of the revised manuscript for publication in *BMC Urology* is greatly appreciated.

Sincerely yours,

Tomonori Habuchi M.D.Ph.D.
Department of Urology
Akita University School of Medicine
1-1-1 Hondo, Akita, 010-8543, Japan
Phone: +81-18-884-6156
Fax: +81-18-836-2619
E-mail: thabuchi@doc.med.akita-u.ac.jp

Reviewer 1

Comments to the Author

Q1 The cohort is very heterogeneous. As stated in table 2A, 15% of the patients diagnosed with prostate cancer at initial biopsy had M1, but 0 at repeat biopsy. The whole analysis is strongly biased by these patients. I think that the significant p-values in table 2A derive from these patients. I recommend exclusion of M1 patients and to repeat the analysis. This would clearly increase the clinical value.
A To accommodate the helpful comments from Reviewer, we exclude the patients with metastasis from Table 2A, repeated the analysis and added the following sentences.

In order to avoid the selection bias, twenty-nine of the patients with distant metastasis, who were diagnosed at initial biopsy, were excluded in this analysis. As shown in Table 2A, patients who were diagnosed with prostate cancer at a repeat biopsy had significantly higher rates of non-palpable and organ-confined disease than patients who were diagnosed at an initial biopsy (Table 2A).

Q2 How about DRE? The authors show clinical T stage (Table 2A). I highly recommend inclusion of all T stages and not only <=T2b and >=T3a. It is important for the urologist to know, how many DREs were actually positive before repeat biopsy and how many were T1. In addition, the table excludes T2c tumors, but I think that this is a typing error.

A To accommodate the helpful comments from Reviewer, we modified Table 2A.

Q3 The prostatectomy cohort is different from the biopsy cohort. This difference should be somewhere explained in the manuscript and stated how many patients underwent surgery/radiation/hormone ablation etc.

A To accommodate the helpful comments from Reviewer, we added and modified the following sentences in Results section.

Ninety-three and 9 patients who were diagnosed at initial biopsy and seventeen and 2 patients who were diagnosed at repeat biopsy underwent radical prostatectomy and local external beam radiation therapy, respectively. Among these patients, the clinical and pathological variables of 72 patients diagnosed at initial biopsy and 15 patients diagnosed at repeat biopsy, who underwent radical prostatectomy without neoadjuvant or adjuvant therapy, were compared (Table 2B).

Q4 The authors determined a cut-off for PSAV and PSAD by ROC curve analysis. The authors should explain how they determined the cut-off from these ROC graphs (Methods). Therefore, it may be reasonable to include the ROC curves as a Figure and to show the cut-off.
As we mentioned in Materials and Methods section, we ROC curves were constructed by SPSS software and the cut-off points were also recommended by the software. To accommodate the helpful comments from Reviewer, we added the ROC curves as Figure 1.

Q5 The number of cores taken by biopsy was not standardized (6 or 10). To account for this difference, the authors should perform a multivariate logistic regression analysis that controls for this variable.

A To accommodate the helpful comments from Reviewer, we analyzed the difference of the number of cores between the positive and negative results at repeat biopsy. In addition, we performed a multivariate logistic regression analysis that controls for this variable. We added the following sentences in the Results section.

There were no significant differences in age (72.5±7.2 and 69.5±7.2, \( P = 0.085 \)), serum PSA level (12.6±8.6 and 10.5±7.5, \( P = 0.50 \)), prostate volume (30.2±23.6 and 39.7±21.0, \( P = 0.15 \)), PSAD (0.51±0.43 and 0.34±0.35, \( P = 0.13 \)), PSA V (2.6±6.2 and 0.83±6.2, \( P = 0.16 \)), or number of cores taken at repeat biopsy (8.6±2.1 and 8.3±2.3, \( P = 0.43 \)) between patients who had positive and negative repeat biopsies, respectively. In addition, although we performed a multivariate logistic regression analysis, we could not find a significant risk factor for the positive result at repeat biopsy.