Author’s response to reviews

Title: Computer-aided transrectal ultrasound: Does prostate HistoScanningTM improve detection performance in repeat biopsies?

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Author’s response to reviews: see over
Dear editors,

On behalf of all authors, I am hereby sending you the revised manuscript (MS: 1000047284159681) with the title “Computer-aided transrectal ultrasound: Does prostate Histo-Scanning TM improve detection performance of prostate cancer in repeat biopsies”, Biomedcentral Urology.

We would like to thank the reviewers for their efforts and valuable comments which have helped us to improve this manuscript. We have revised the manuscript accordingly. Our responses to the reviewers comments (in italics) are as follows:

Reviewer:
Ahmet Kursad Poyraz

1. One concern of this current manuscript is the subjects are the men at risk of prostate cancer who had at least one previous set of TRUS-guided prostate Bx. Prior biopsy can produce false positive signals in histoscanning and reduce the accuracy.

   We thank the reviewer for this valuable remark. To minimize interference with previous procedures, rescanning was scheduled with a prolonged time interval. We have clarified this crucial point in the “Methods” section. (p. 4, ll. 83-85).

Abstract
2. Change “objective” to “background”
3. Change “conclusion” to “conclusions”

   We have corrected this both. (p. 2, ll. 31 and 43)

4. Page 2, line 40: Please give the p value after the sentence “Detection rate in tBx was significantly higher”

   P values now are given in this section.
Background:
5. Change title to background

We have corrected this. (p. 3, l. 52)

6. Authors should add some information about Histoscanning.

We have re-organized the “Methods” sections and added information on HistoScanning technique. (p. 4, ll. 92-104).

7. Page 3, line 60: change “magnet resonance” to “magnetic resonance"

We have corrected this. (p. 3, l. 61)

Patients and Methods:
8. Change title to methods

We have corrected this. (p. 4, l. 76)

9. Did single operator perform all the histoscanning & biopsies and how many years of experience did operator had?

We have clarified this in the “Methods” section. (p. 6, ll. 123-124)

10. If different operators performed the histoscanning & biopsies what was the degree of inter operator variability?

We have added this in the “Results” section. (p. 10, ll. 233-4).

Results and discussion:
11. There is a limitation of this study. The operator performed targeted Bx firstly and then standard Bx was performed. Knowing the abnormal regions of prostate
before the standard Bx can affect the operator’s decision.

*We have mentioned this crucial point as a limiting factor in the “Discussion” section. (p. 10, ll. 231-233).*

**Conclusions:**
12. Change title to conclusions

*We have corrected this. (p. 11, l. 258)*

**References:**
13. Authors should rewrite the references according to BMC Urology reference Style

*Corrections are made accordingly.*

**Figures:**
14. Authors should add some figures showing examples of histoscanning and targeting.

*We added a figure showing HistoScanning report and perineal biopsy setting. (Figure 1, p.5, l. 119; p. 21)*

**Reviewer:**
Mehmet Ruhi Onur

1. **Title:** ‘Computer-aided transrectal ultrasound: Does prostate HistoScanning™ improve detection performance in repeat biopsies?’ Do authors mean detection of prostate cancer? If so, they should add ‘prostate cancer’ in title.

We changed the title accordingly.

2. **Abstract**
   a. Objective: Appropriate
b. Methods:
- Page 2 Line 35: Please start sentence with ‘three’ instead of ‘3’

*We have corrected this. (p. 2, l. 35)*

- ‘3 PHS positive foci were defined in accordance with 6 bilateral prostatic sectors.’ May authors explain why this statement is settled in methods section?

*It is stated, because the limited (up to a maximum of three) extract of target regions represents a general methodological background in the study in contrast to the systematic backup approach.*

c. Results:
- ‘Detection rate in tBx was significantly higher.’ May authors add a statistical value after this statement?

- ‘Detection rate in tBx and sBx did not differ on patient level.’ May authors add a statistical value after this statement?

*P values now are given in this section.*

3. Introduction:
a. Page 3 Line 55-56: ‘However, the power to identify, and in particular to exclude cancer reliably is limited due to low PCa specificity of grey scale ultrasound patterns’ Please add a reference after this statement.

*We have added a reference to this statement. (p. 3, l. 56)*

b. In the introduction section, it would be better to briefly describe the prostate histoscanning method.

*We have re-organized the “Methods” sections and added information on HistoScanning technique. (p. 4, ll. 92-104).*
4. Patients and Methods

a. Page 4 line 77: ‘At one center, data was collected from 97 consecutive men ----’ Please add age range and mean age of patients as stated in the abstract.

_We have corrected this. (p. 4, ll. 77-78)_

b. Page 4 line 93 - 95: ‘Based on the PHS image, the physician defined the most prominent (largest) target regions, up to a maximum of three.’ May authors explain how they defined target regions on PHS? How was the appearance of target areas on PHS?

_We have added information on HistoScanning appearance (p. 5, ll. 102-104) and in addition drafted a figure showing HistoScanning report and perineal biopsy setting. (Figure 1, p.5, ll. 109,119; p. 21)_

5. Results

a. Page 7 Line 143 – 145: ‘Detection rate for each PHS positive region was significantly higher in both targeted transperineal and targeted transrectal Bx compared to systematic Bx.’ Please add a statistics number (P ----) after this statement.

_We apologize the omission. P values now are given in this section._

b. Did authors search the efficiency of PHS guided biopsy in different regions of the prostate? For example prostate base, apex, transitional zone, peripheral zone? Was there any difference between sensitivity and specificity of PHS guided biopsy in terms of prostate zones?

_We thank the reviewer for this comment, but data was not analyzed in this respect. Due to the limited number of prostate carcinomas in the cohort and the unknown number of occult cancers we excluded these considerations a priori for statistical reasons. Never the less, we might be able to answer your much valued question by future studies following comparable designs._
6. Discussion
May authors explain why transperineal PHS guided biopsy yielded more accurate results than transrectal PHS guided prostate biopsy?

Following your helpful remark, we have discussed this crucial point in the “Discussion” section. (p. 10, ll. 216-223).

7. References: OK
8. Figures: It would be better to add PHS figures which demonstrate sectors with prostate abnormality.

We added a figure showing HistoScanning report and perineal biopsy setting. (Figure 1, p.5, l. 119; p. 21)

We hope that the revised version of our manuscript can now be accepted for publication in Biomedcentral Urology. We are pleased to have been given the opportunity to improve the manuscript and we appreciate the editors’ and the reviewers’ time dedicated to the consideration of our paper.

Yours sincerely

Moritz Franz Hamann, on behalf of all authors