Author’s response to reviews

Title: Clinically Significant Prostate Cancer Diagnosed Using a Urinary Molecular Biomarkerbased Risk Score: Two Case Reports

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Author’s response to reviews:

Dear editor,

We would like to thank the reviewer Dr Rubio-Briones for his comments, and we have taken them all into account. Below his comments are copied and we added behind his comments in italic what amendments we have made.

Reviewers comments: Jose Rubio-Briones (Reviewer 1): This is a simple case report on 2 men with one of the commonest conundrum a urologist face in every day practice, that of a persistent suspicion of Prostate Cancer but a negative biopsy, with the corresponding anxiety at the patient side

Although its simplicity, it stress the need of utilizing all the tools EUA Guidelines propose to individualize the need for a second biopsy

The authors propose SelectMDx in a clear way in these two cases as an easy tool to help in this decision, combined with mpMRI for its optimization. It could be argued the role of direct mpMRI after a negative previous biopsy, but as the second case shows, targeted biopsies do not always find the tumor and should be done together with mapping biopsies, as Guidelines recommend

Having said this, the authors;

- in the abstract, normal DRE findings should be mentioned: Abstract section, line 24, “had normal DRE findings”
- have to further explain the role of mpMRI in the introduction: Background section, line 63-67, added Multiparametric MRI (mpMRI) is the most accurate imaging modality for localization of PCa. The use of mpMRI before biopsy could indicate whether the patient requires a biopsy because of a significant cancer identified on mpMRI or whether biopsy could be avoided. The EAU guideline committee recommends the use of mpMRI before repeat biopsy to allow targeted biopsies of suspicious lesions in addition to standard biopsies. However, the risk of missing 16.2% to 39.7% clinically significant prostate cancers using mpMRI targeted biopsy for PI_RADS ≥3 stresses the need to use RCs or biomarker-based tests for an improved risk stratification for a repeat biopsy [6].

- have to limit comments such as "However, routine TRUS biopsy can miss some cancers in 20-30% of the cases because it is systematic, non-targeted, and directed toward the peripheral gland";

"the physician is challenged by the lower diagnostic yield upon repeat biopsy (10-35%) and the additional anxiety, physical discomfort and complication risk a biopsy will cause " ; I think these comments should be done at the introduction or the discussion

These have been moved to the background section line 48 and 48 for ““because it is systematic, non-targeted, and directed towards the peripheral gland”

"the physician is challenged by the lower diagnostic yield upon repeat biopsy (10-35%) and the additional anxiety, physical discomfort and complication risk a biopsy will cause " has been removed entirely.

- the cases can be shortened: Case presentations have been shortened based on reviewers comments as much as possible in lines Case presentation sections 1 and 2 lines 102-161, which is at least 20 lines shorter than in the version the reviewer had.

- UTI should be ruled out in the second rise of PSA. We added this to line 108 “and there was no sign of a urinary tract infection”.

- Should avoid repeating recommendations on when to biopsy following ERSPC RC in the text (exposed in case reports and discussion)... We have removed all these lines from the cases sections.

Due to the simplicity of the message, but its role in managing daily consultations, the CASE REPORT paper should be shortened as much as possible. We shortened the cases as suggested. Case presentations have been shortened based on reviewers comments as much as possible in lines Case presentation sections 1 and 2 lines 102-161, which is at least 20 lines shorter than in the version the reviewer had.

Kind regards,

Dr Daphne Hessels