

T2-weighted MR Imaging combined with Diffusion weighted MR Imaging for selection of true active surveillance patients based on stage and Gleason score criteria: a retrospective multireader study.

C. Hoeks¹, P. Vos¹, D. Somford², D. Yakar¹, T. Hambrock¹, S. Heijmink¹, J. Futterer¹, H. Vergunst³, C. Hulsbergen-van de Kaa⁴, F. Witjes², H. Huisman¹, and J. Barentsz¹

¹Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, Gelderland, Netherlands, ²Department of Urology, Radboud University Nijmegen Medical Centre, Nijmegen, Gelderland, Netherlands, ³Department of Urology, Canisius Wilhelmina Hospital, Nijmegen, Gelderland, Netherlands, ⁴Department of Pathology, Radboud University Nijmegen Medical Centre, Nijmegen, Gelderland, Netherlands

Introduction: Active surveillance (AS) of low risk prostate cancer has become a popular alternative for radical treatment. Recent results suggested early progression in AS 1-2 years after diagnosis as a result of transrectal ultrasound guided biopsy undersampling of aggressive cancer as opposed to progression of indolent cancer.¹ T2-weighted (T2w) magnetic resonance imaging (MRI) and Diffusion weighted MR imaging (DWI) respectively have been shown to be a non-invasive tool for determination of prostate cancer stage and aggressiveness, which are both criteria for AS selection.^{2,3} Moreover lower signal intensity on T2w-MRI has been related to higher prostate cancer Gleason score (GS).⁴ The possible role of MRI in patient selection for AS has not been evaluated earlier. In this retrospective multireader study we aim to determine how well T2w-MRI and DWI are able to contribute in patient selection for AS by discriminating AS patients from non-AS patients on T2 weighted MR Imaging in combination with DWI by comparing radiologist reading of stage and Gleason score to prostatectomy stage and GS.

Materials: Between January 2007 and May 2009 83 patients underwent prostatectomy at the RUNMC, or at the CWZ Nijmegen Hospital, the Netherlands (116 patients). 12 prostatectomy patients who met the following criteria were included:

1 radical prostatectomy with step section specimen, 2 inclusion criteria AS⁵: a PSA level of ≤ 10 ng/mL, a PSA density ≤ 0.20 and clinical stage T1 to T2c and preprostatectomy biopsy criteria of $GS \leq 6$ (no pattern 4 or 5 disease) with $< 33\%$ of positive cores and $< 50\%$ volume-extent of cancer in any core, 3 a performed a 3T MRI with use of an endorectal coil and DWI (single-shot EPI TR 2600 ms, TE 91 ms, b-values 0, 50, 500, 800 s/mm², spatial resolution: 1.5 x 1.5 x 3mm).

4 radiologists with 1 year, 3 years and over 6 years of experience in prostate MRI independently scored images. Radiologists were informed on presence of prostate cancer, however they were blinded for PSA levels and biopsy or prostatectomy outcomes. Scoring was performed on an in-house developed system for computer aided diagnosis. Before final measurements started radiologists were trained on 2 cases for measurement procedures. T2w-MRI and T2w-MRI in combination with ADC maps were scored in 2 separate sessions with an interval of two weeks. Staging was scored by a five point scale for probability of presence of a stage $\geq T3$. Radiologists were asked to place a region of interest on the most aggressive part of every separate suspicious lesion and to rank this lesion on five point scales for respectively probability of prostate cancer presence and probability of presence of a Gleason 4 or 5 component. Step section (4 mm) prostatectomy findings were annotated digitally on T2 weighted MRI on a

prostatectomy section basis. Every annotation was represented by a 3D sphere with a diameter of 10 mm to correct for inaccuracy between MRI slices and prostatectomy sections. Coordinates of annotated prostatectomy were compared with reader score coordinates. A reader score was considered true positive if a 3-5 rating was given on probability of cancer and if distance between coordinates was ≤ 6 mm. ROC analysis was performed on patient basis with prostatectomy findings as a ground truth for true AS patients or AS exclusion patients. Reader scores of 4 or 5 were considered positive for a prediction of GS 4 or 5 or stage T3. On a patient level AS criteria were present in either stage T3 or GS4/5 or a combination of both.

Results: Patients had a median transrectal biopsy-surgery interval of 3 months and a median MRI-surgery interval of 3.5 months. 8 prostatectomy cases had a stage $< T3$ and no GS 4 or 5 components. 2 prostatectomy cases had a stage T3 in combination with a GS 4 or 5 component and 2 cases had only a GS 4 or 5 component. For respectively T2w-MRI and T2w-MRI+ADC, 31% and 24% of all cancer-coordinates was found by radiologists. AS exclusion based on stage and/or GS was predicted more correctly by experienced radiologists (100% of cases) in comparison to the inexperienced radiologist (50%). Readers predicted 75-100% of true AS patients correctly. AUC values for T2w-MRI prediction of AS patients varied from 0,812 for the inexperienced reader, 0,812-1,0 for experienced readers and 0,875 for the high experienced reader. Combination of T2w-MRI with ADC-maps did not increase, however even decreased AUC values (inexperienced reader 0,687, both experienced readers 0,625 and experienced reader 0,500).

Discussion and Conclusion: While readers incorrectly excluded up to 25% of AS prostatectomy cases, experienced readers excluded all non-AS prostatectomy cases based on patient level stage and GS reading. T2w-MRI could aid in patient selection for active surveillance.

Within this study DWI did not show to be of additional value for AS patient selection. Low volume ($< 0.5cc$) of 50% of GS 4 or 5 cancers might explain low performance on GS prediction in prediction of AS patients based on T2wMRI+ADC, especially on low spatial resolution ADC maps.

References:

1. Duffield et al. J Urol 2009
2. Futterer et al. Eur J Radiol 2007.
3. deSouza et al. Clin Radiol. 2008.
4. Wang et al. Radiology 2007.
5. Dall' Era et al. Cancer 2008.

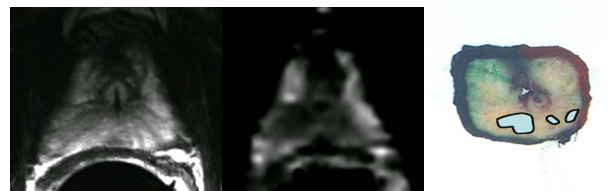


Fig. 1. Right to left: T2w MRI, DWI and prostatectomy section of true AS patient with GS 3+3 and stage $\leq T2$

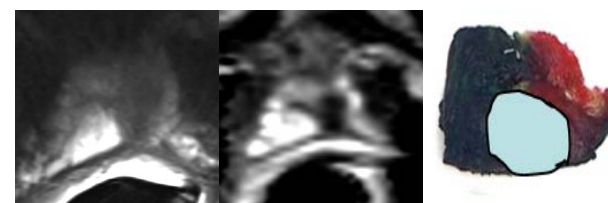


Fig. 2. Right to left: T2-weighted MRI, DWI and prostatectomy section of non-AS patient with GS 5+3 and stage T2

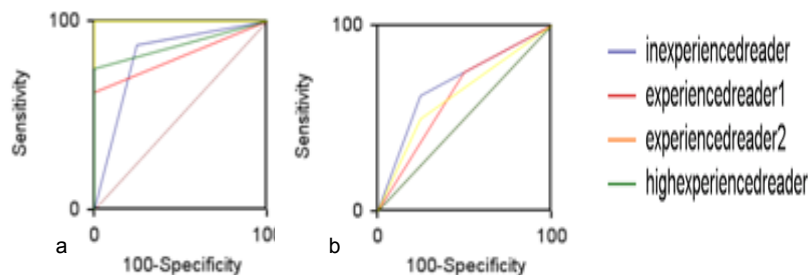


Fig. 3 (a). ROC curve for T2w prediction of true AS prostatectomy patients vs non AS patients. Interreader AUC comparison was significantly different (DeLong et al.) between experienced reader 1 and 2 ($P=0,040$). (b) ROC curve for T2w+ADC prediction of true AS prostatectomy patients vs non AS patients.