Value of combined 3T multiparametric MR Imaging and MR guided biopsy in patient selection for active surveillance within the PRIAS study: initial results of the MRPRIAS study, a prospective multicenter study.

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Introduction: To prevent overtreatment, active surveillance (AS) of low- risk prostate cancer has become a popular alternative for radical treatment[1]. Recent results suggested early 'progression' in AS to be a result of incorrect initial risk-stratification by transrectal ultrasound guided biopsy undersampling of aggressive cancer, as opposed to progression of initial indolent cancer.[2] 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.[3,4] The possible role of MR imaging in selection of prostate cancer patients for AS has not been evaluated earlier. In this prospective study, we aim to evaluate the value of 3T combined multiparametric endorectal MR imaging and magnetic resonance guided prostate biopsy (MRGB) for better selection of prostate cancer patients for AS within the Prostate Cancer Research International Active Surveillance (PRIAS) study[5].

Materials: From November 2009 21 patients were included in the Radboud University Nijmegen Medical Center, the Canisius Wilhelmina Hospital in Nijmegen, the Alysis Zorggroep Hospital and the Andros Mannenkliniek in Arnhem, the Jeroen Bosch Hospital in Den Bosch the Netherlands.
Inclusion criteria were designed in accordance with the PRIAS study inclusion criteria:
- Prostate cancer diagnosis
- PSA ≤10 ng/mL and PSA density <0.2 ng/mL/mL
- Clinical stage ≤ T2
- Diagnostic transrectal ultrasound (TRUS) biopsy (8-10 biopsies): GS ≤6 (no Gleason Grade 4 or 5) and ≤ 2 cores with cancer. Exclusion criteria were:
- Patients with known contradictions to MRI
- Patients with previous therapy for prostate cancer
- Patients who cannot or do not want to receive radical treatment (radiotherapy or radical prostatectomy).
- Patient request for definitive curative intervention

Patients were examined with multiparametric MRI in month 2 and underwent MRGB during month 3 after the date of initial prostate cancer diagnosis upon TRUS biopsy. The images were read in consensus. MRGB was only performed when a suspicious visible lesion was present on MRI. All histopathology examinations were performed by the same experienced pathologist. Triggers for delayed treatment were:
- MRI suspicion of stage ≥ T3 or signs of (nodal) metastasis, which could be confirmed histopathologically
- MRGB GS > 6 (at month 3) or a different cancer localization in comparison to the initial random TRUS biopsy
- Patient request
- Clinical stage ≥ T3

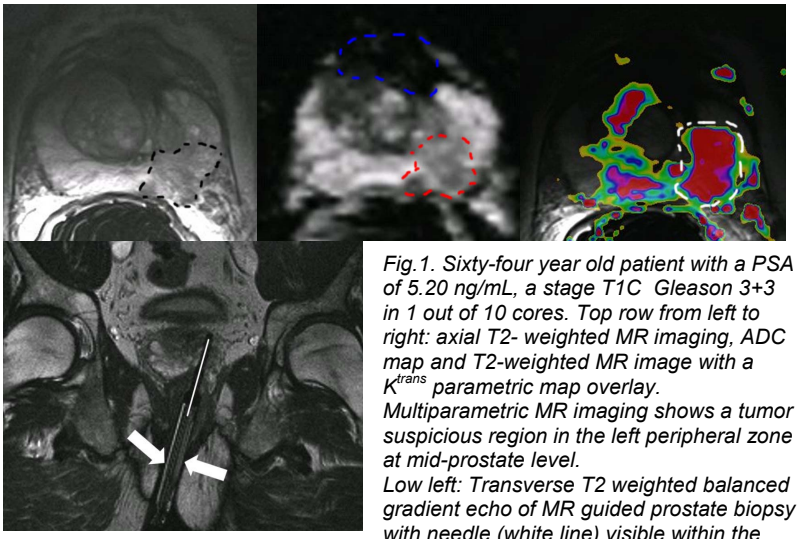

Fig.1. Sixty-four year old patient with a PSA of 5.20 ng/mL, a stage T1C Gleason 3+3 in 1 out of 10 cores. Top row from left to right: axial T2- weighted MR imaging, ADC map and T2-weighted MR image with a K^{trans} parametric map overlay. Multiparametric MR imaging shows a tumor suspicious region in the left peripheral zone at mid-prostate level. Low left: Transverse T2 weighted balanced gradient echo of MR guided prostate biopsy with needle (white line) visible within the needle guide (white arrows). A Gleason 3+4 prostate cancer was found upon MR guided biopsy. The patient underwent prostatectomy, which confirmed a stage T2A, Gleason score 3+4 cancer.

Results: A total of 21 patients were included. Multiparametric MRI showed a median of 2 tumor suspicious regions per patient. In 15 patients, the initial cancer location upon random TRUS biopsy was matching the tumor suspicious region on multiparametric MRI. In one patient MR imaging did not show any tumor suspicious regions and no MRGB was performed. Two patients had suspicion of a stage ≥T3 disease on MRI, which could not be confirmed upon histopathology. A median of 5 MRGB per patient were taken in the 20 patients, who underwent MRGB. Histopathology results are shown in table 1.
In a total of 3 out of 20 patients, a different cancer location in comparison to the initial random TRUS biopsy was confirmed histopathologically. Combined Multiparametric MR imaging and MRGB excluded 5 of 21 patients (24%).

20 patients MR guided prostate biopsy	Outcome histopatholgic analysis biopsy specimen
n=3	Gleason score > 6
n= 6	Gleason score ≤6
n=11	No cancer (prostatitis in 8/11)

Table 1. Histopathology results of MR guided prostate biopsies.

Discussion and Conclusion: Multiparametric MRI and MRGB excluded 24% of AS cancer patients, which had an intermediate to high-risk profile and had initial incorrect initial risk-stratification. Our results support the additional value of multiparametric MRI and MRGB in active surveillance patient selection: initial risk-stratification is improved by better identification of intermediate-to high-risk cancer patients.
Incorporation of MR imaging in active surveillance requires MRGB to evaluate false-positive MR tumor suspicious regions and to improve specificity. Multiparametric MR imaging did not detect the initial cancer in (6/21) 29% of patients. This may be explained by relatively poorer detection of low Gleason Grade prostate cancers by MR imaging[6]. Further follow-up within this study is necessary to evaluate these initial results.

References:

1. Dall' Era et al. Cancer 2008. **2.**Duffield et al. J Urol 2009 **3.** Futterer et al. Eur J Radiol 2007. **4.** deSouza et al. Clin Radiol. 2008. **5.** Van den Bergh et al. Eur Urol 2007. **6.** Ikonen et al. Prostate 2000.