

# Histology results of systematic prostate biopsies by in-bore magnetic resonance imaging vs. transrectal ultrasound

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## Abstract

**Introduction:** We aimed to compare systematic biopsies (SBs) of in-bore magnetic resonance-guided prostate biopsy (MRGpB) with those performed under transrectal ultrasound (TRUS) guidance in the clinical setting.

**Methods:** Data on all 161 consecutive patients undergoing prostate biopsy at our institution between November 2017 and July 2019 were retrospectively collected. The patients were referred to biopsy due to elevated prostate-specific antigen (PSA) and/or abnormal digital rectal examination (DRE) and/or at least one Prostate Imaging Reporting and Data System (PI-RADS) lesion score of  $\geq 3$  on multiparametric magnetic resonance imaging (mpMRI). We included patients with PSA levels  $\leq 20$  ng/ml and those with 8–12 core biopsies. Histology results of SBs performed by in-bore MRGpB were compared to TRUS SBs. Chi-squared, Fischer's exact, and multivariate Pearson regression tests were used for statistical analysis (SPSS, IBM Corporation).

**Results:** In total, 128 patients were eligible for analysis. Their median age was 68 years (interquartile range [IQR] 61.5–72), mean prostate size  $55 \pm 29$  cc, and mean PSA and PSA density levels  $7.6 \pm 3.5$  ng/ml and  $0.18 \pm 0.13$  ng/ml/cc, respectively. Thirty-five patients (27.3%) had suspicious DRE findings. Both biopsy groups were similar for these parameters. Thirty-eight (62.3%) MRGpB patients had a previous biopsy vs. five (7.1%) TRUS-SB patients ( $p < 0.0001$ ). The number of patients diagnosed with clinically significant and non-significant disease was similar for both groups. High-risk disease was more prevalent in the TRUS-SB group (22.4% vs. 4.9%,  $p < 0.01$ ).

**Conclusions:** Our data suggest that in-bore MRGpB is no better than TRUS for guiding SBs for the detection of clinically significant prostate cancer.

## Introduction

The transrectal ultrasound (TRUS)-guided systematic biopsy (SB) had long been the standard diagnostic procedure for prostate cancer detection.<sup>1,2</sup> Multiparametric magnetic resonance imaging (mpMRI) has now become the leading tool for diagnosing clinically significant prostate cancer, and the magnetic resonance-guided prostate biopsy (MRGpB) is considered superior to a TRUS-guided biopsy for the purpose of histological diagnosis.<sup>2–4</sup> The combination of mpMRI to locate and define suspected lesions, together with their being targeted by an MRGpB, has succeeded in increasing the rate of detection of clinically significant disease and lowering the detection of non-significant prostate cancer.<sup>2</sup> Much of these data were acquired by comparing SBs to targeted MRGpBs, aiming solely at suspected lesions.<sup>5</sup> The actual advantage of combining an SB with a targeted MRGpB had been unclear until newly published data confirmed that targeted-MRGpB followed by TRUS-SB conferred the best chance for diagnosing clinically significant cancer.<sup>6–9</sup> Supporting this combined approach would therefore imply that all SBs performed by diverse imaging guidance systems will achieve equivalent results, for example, ultrasound (US)/MRI fusion or in-bore MRGpB (the latter being considered by some to be a superior technique<sup>10</sup>).

We sought to compare SBs performed in the clinical setting by means of in-bore MRGpB with those performed under TRUS guidance to better substantiate the superiority — or lack thereof — of one technique over the other.

## Methods

Following Helsinki approval and waiver of informed consent, we retrospectively collected data from 161 consecutive patients who underwent prostate biopsy at our institution between November 2017 and July 2019. The patients were referred to biopsy due to elevated prostate-specific antigen (PSA) serum levels and/or abnormal digital rectal examination (DRE) and/or  $\geq 1$  suspicious area on an mpMRI scan defined as score of  $\geq 3$  according to the Prostate Imaging Reporting and Data System (PI-RADS version 2) (for MRGpB patients). We included patients with PSA levels  $\leq 20$  ng/ml and 8–12 cores taken at systematic sampling. Two of 63 MRGpB and 31 of 98 TRUS biopsy patients were excluded applying these criteria. A final total of 128 patients were eligible for analysis, of whom 61 underwent an in-bore MRGpB and 67 underwent a TRUS-guided systematic prostate biopsy (TRUS-SB).

All the study patients had SBs taken with the intention of performing a formal 12-core template: two samples (on each side) from the prostate base, two from mid-gland, and two from the apex. All biopsies were performed transrectally following the administration of prophylactic antibiotics.

In-bore MRGpBs were carried out using 3T MRI scanners and external coil application. Imaging during the biopsies included T2-weighted images, and diffusion series were used as necessary at the radiologist's discretion. In-bore MRGpB patients were placed in a prone position and administered general anesthesia. A DRE was performed to determine if there were any anatomical or pathological conditions that could hinder transrectal biopsy and to approximate the position of the gland. Axial and sagittal T2-weighted images were obtained to visualize the prostate and identify the target lesion. A non-magnetic portable biopsy device (DynaTRIM; Invivo, Gainesville, FL) and a dedicated software package for device tracking and target localization (DynaCAD; Invivo) were also used as previously described.<sup>11</sup> Suspected clinically significant target lesions that were detected by MRI were sampled first, followed by an SB using the last MR image acquired to mark needle coordinates for all 12 cores. SBs were precluded when a large lesion seen on MR left insufficient space for non-targeted sampling of an anatomical location.

The TRUS-SB patients were placed in left lateral decubitus position. A DRE was performed to evaluate prostate volume, nodularity, and pathological lesions. Lidocaine 2% was then administered under TRUS guidance (7.5-MHz transducer, Brüel & Kjær, Nærum, Denmark) for local prostatic nerve block. Transverse and axial imaging of the prostate was used to evaluate its size and structure, and to define the peripheral zone, transitional zone, and seminal vesicles. TRUS-SBs were taken as previously described.<sup>12</sup>

Biopsies were performed by two senior urologists. In-bore MRGpBs were carried out by a dedicated uro-radiologist with over eight years' experience in prostate MRI reading,

an anesthesiologist, a fellowship-trained urologic oncologist, and an experienced nurse and technician. TRUS-SBs were done by a highly experienced urologist with over 20 years' experience in this form of biopsy and a dedicated nurse. All biopsies took place in our tertiary center.

The biopsy specimens were processed by routine pathological fixation with formalin solution and evaluated by a single dedicated uro-pathologist with over 20 years' experience. The retrieved cancer cells were used as the reference standard to determine the positivity of the biopsy. We stratified the SB results according to levels of clinically significant disease, defined as a Gleason score of  $\geq 7$  (International Society of Urological Pathology [ISUP]  $\geq 2$ ); non-clinically significant disease, defined as a Gleason score of 6 (ISUP 1); and high-risk disease, defined as a Gleason score  $\geq 8$  (ISUP  $\geq 4$ ).

Chi-squared, Fischer's exact, and multivariate Pearson regression tests were used for statistical analysis (SPSS, IBM Corporation).

## Results

We retrospectively collected data on all 161 consecutive patients who underwent a prostate biopsy in our institution during the study period. The total of 128 patients who met the inclusion criteria and were eligible for analysis included 61 patients who underwent MRGpBs and 67 who underwent TRUS-SBs. The median age was 68 years (interquartile range [IQR] 61.5–72), mean prostate size  $55 \pm 29$  cc, and mean PSA and PSA density levels  $7.6 \pm 3.5$  ng/ml and  $0.18 \pm 0.13$  ng/ml/cc, respectively. Thirty-five patients (27.3%) had suspicious DRE findings. Both biopsy groups were similar for these parameters. Thirty-eight (62.3%) MRGpB patients had a previous biopsy vs. five (7.1%) TRUS-SB patients ( $p < 0.0001$ ). (Table 1). Sixteen of the 38 MRGpB patients (42%) and three of the five TRUS-SB patients (60%) were formerly diagnosed with prostate cancer ( $p = \text{non-significant}$ ).

Non-significant disease (Gleason 6) was diagnosed in all former biopsies except one MRGpB patient, diagnosed with Gleason 7 (3+4) disease, within the MRI region of interest (ROI) only. The median number of cores per current biopsy systematic samplings was 12 (IQR 0) for both groups. The number of patients diagnosed with clinically significant and non-significant disease was similar for both groups' systematic sampling. High-risk disease was more prevalent in the TRUS-SB group (22.4% vs. 4.9%,  $p < 0.01$ ) (Table 2).

Subgroup analysis of biopsy-naïve patients showed no difference between MRG-SBs and TRUS-SB patients in non-significant, clinically significant, and high-risk disease diagnosis (Supplementary Table 1).

**Table 1. Patient characteristics**

Variable	All patients		MRGpB		TRUS-SB		p <sup>†</sup>
Age, years (IQR)	67	61.5–72	67	61–72	67	61.7–72	NS
Prostate size*, cc, mean (SD)	55	29	54	29	55	30	NS
Pre-biopsy PSA, ng/ml, mean (SD)	7.6	3.5	7.0	3.2	8.1	3.7	NS
PSAD, ng/ml/cc, mean (SD)	0.18	0.13	0.16	0.12	0.19	0.13	NS
DRE							
Non-suspicious (T1c)	87	68.0	43	70.5	44	65.7	NS
Suspicious (T2a)	35	27.3	15	24.6	20	29.9	
NA	6	4.7	3	4.9	3	4.5	
Previous biopsy							
No	84	65.6	22	36.1	62	92.5	<0.0001
Yes	43	33.6	38	62.3	5	7.5	
NA	1	0.8	1	1.6	0	0.0	

\*Measured on MRI or TRUS. †Calculated for MRGpB vs. TRUS-SB. DRE: digital rectal exam; MRGpB: magnetic resonance imaging-guided prostate biopsy; NS: non-significant; PSA: prostate-specific antigen; PSAD: PSA density (calculated according to prostate size as measured on MRI or TRUS); TRUS-SB: transrectal ultrasound-guided systematic prostate biopsy.

## Discussion

The technique for performing a prostate biopsy is known to substantially influence clinical outcomes. As such, much effort is expended to achieve improved prostate imaging technologies and to use imaging-directed biopsies most effectively.<sup>2–4</sup> mpMRI-guided biopsies were reportedly superior to TRUS-guided biopsies for diagnosing clinically significant prostate cancer, with an added benefit of approximately 12%,<sup>2–4</sup> which was attributed to targeted lesion sampling. Applying combined MRI-targeted lesion sampling and an SB was recently found by several studies to confer the best chance of diagnosing clinically significant cancer.<sup>6–9</sup> In-bore MRGpB is a feasible alternative for MRI-guided prostate biopsy, and it has been considered to be superior to the TRUS/MRI fusion biopsy.<sup>10</sup> While an SB at the time of TRUS/MRI fusion are directed by sonography, SBs performed at the time of in-bore MRGpBs are taken under MRI guidance. This variation in testimonies raises the question of which imaging modality is superior for guiding SBs.

Our MRGpB cohort included a higher percentage of patients with a prior prostate biopsy ( $p < 0.0001$ ), in line with updated guideline recommendations.<sup>13,14</sup> It has been verified

that patients who undergo repeated biopsies have lower cancer detection rates compared to first prostate biopsy candidates.<sup>13,15</sup> Furthermore, we intentionally avoided sampling lesions that were considered suspicious on MRI and that were located within the SB field (described above in Methods). Taken together, one would expect our results to indicate a lower detection rate of clinically significant cancer on MRG-SBs compared to TRUS-SBs, but our analysis did not find any overall increase in the rates of clinically significant disease in the TRUS-SB group, although the rates of ISUP  $\geq 4$  disease were significantly higher in that group. Considering that a higher Gleason's score is reportedly correlated with mpMRI findings,<sup>16,17</sup> we believe our exclusion of the mpMRI lesions that were visualized on systematic sampling explains the higher rate of high-risk detection rather than a true advantage of TRUS-SBs over MRG-SBs. The fact that many of the MRGpB patients underwent repeated biopsies probably further supports the lower high-risk cancer detection rate on MRG-SBs. Indeed, subgroup analysis for biopsy-naïve patients showed no such difference (Supplementary Table 1). Several reports have demonstrated that the diagnostic rate of TRUS biopsies correlated with tumor location within various anatomical zones, and showed false-negative rates to

**Table 2. Histology of MRG-SB vs. TRUS-SB**

Variable	All		MRG-SB		TRUS-SB		p
	n	%	n	%	n	%	
Clinically significant disease (Gleason $\geq 7$ , ISUP $\geq 2$ )	60	46.9	30	49.2	30	44.8	NS
Base*	52	40.6	24	39.3	28	41.8	NS
Mid-gland*	51	39.8	25	41.0	26	38.8	NS
Apex*	50	39.1	22	36.1	28	41.8	NS
Non-clinically significant disease (Gleason=6, ISUP=1)	16	12.5	9	14.8	7	10.4	NS
High-risk disease (Gleason $\geq 8$ , ISUP $\geq 4$ )	18	14.1	3	4.9	15	22.4	<0.01

\*Many biopsies identified clinically significant disease in more than one anatomic location, and percentage is calculated per specific location for the relevant cohort (all, MRG-SB, and TRUS biopsy). ISUP: International Society for Urological Pathology grading; MRG-SBs: magnetic resonance imaging-guided systematic biopsies; NS: non-significant; TRUS-SBs: transrectal ultrasound-guided systematic biopsies.

correlate with prostate zones.<sup>18-20</sup> More accurate sampling of prostate zones achieved with MR-SBs may therefore suggest that a higher cancer detection rate will follow. In opposition to this proposed added benefit of MRG-SBs over TRUS-SBs, our results did not support any general advantage for an MR-SB diagnosis of cancer, either overall or for per-zone subgroups. Rather, these data indicate that TRUS is not different from MR in identifying prostatic anatomical zones and in aiming a biopsy needle towards them, and they do not support either the superiority or inferiority of MRG-SBs over TRUS-SBs. Detecting significant cancer in accordance with the reported literature, for both groups, further supports lack of such difference.<sup>6,21</sup>

This study is limited by its retrospective nature and possible bias resulting from patient selection. Except for a prior biopsy, however, our analysis showed similarity of all relevant covariates between the groups assessed by the two imaging systems. Furthermore, our multivariate analysis controlled for alleged variability and did not find any difference between the systems in the capability of detecting clinically significant prostate cancer.

## Conclusions

Our data suggest that in-bore MRGpB is no better than TRUS for guiding SBs for the detection of clinically significant prostate cancer. We believe this work provides sound groundwork for future analysis of this high-end technology.

**Competing interests:** The authors report no competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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**Supplementary Table 1. Histology of MRG-SB vs. TRUS-SB (biopsy-naïve patients only)**

Variable	All (n=85)		MRG-SB (n=23)		TRUS-SB (n=62)		p
	n	%	n	%	n	%	
Clinically significant disease (Gleason $\geq 7$ , ISUP $\geq 2$ )	41	48.2	12	52.2	29	46.8	0.8
Non-clinically significant disease (Gleason=6, ISUP=1)	5	5.9	1	4.3	4	6.5	1
High-risk disease (Gleason $\geq 8$ , ISUP $\geq 4$ )	15	17.6	1	4.3	14	22.6	0.06

ISUP: International Society for Urological Pathology grading; MRGSBs: magnetic resonance imaging-guided systematic biopsies; NS: non-significant; TRUS-SBs: transrectal ultrasound-guided systematic biopsies.