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TOPIC PAPER

# MRI-guided in-bore biopsy for prostate cancer: what does the evidence say? A case series of 554 patients and a review of the current literature

**Morgan Pokorny[1] · Boon Kua[1] · Rachel Esler[1] · John Yaxley[1,4] · Hemamali Samaratunga[3] · Nigel Dunglison[1] · Troy Gianduzzo[1] · Geoff Coughlin[1] · Ross Holt[2] · Barbara Laing[2] · Darren Ault[2] · Nicholas Brown[2] · Rob Parkinson[2] · Les Thompson[1]**

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## Abstract

**Purpose** To review our experience with MRI-guided in-bore prostate biopsy (MRGB) and present a review of the literature on MRGB.

**Methods** A retrospective review of patients presenting for MRGB between 2013 and 2018. Diagnostic and biopsy MRI scans were reviewed to collect data on scan dates, procedure times, characteristics of MRI targets (PI-RADS™ score, target size, ADC value and location). A review of the literature on MRGB for the period 2013–2018 was performed.

**Results** 607 targets in 554 men were biopsied. Overall and significant cancer detection rate were 80% and 55% at a patient level, and 76 and 59% at the target level, respectively. Prostate cancer (CaP) detection in men with prior negative biopsy was 60% while 50% of men on active surveillance were upgraded to clinically significant disease (CSD). Lesion location did not predict for presence of CaP or CSD. PI-RADS™ score, age and PSAD were predictors of CSD at biopsy on multivariate analysis. Literature review identified 23 reports reporting on MRGB cohorts (~4000 patients). Overall cancer detection ranged from 23 to 74% and CSD in 63% overall. CaP detection in PI-RADS™ 3 targets was substantially lower in our series and the literature than for PI-RADS™ 4–5 targets.

**Conclusions** MRGB in PI-RADS™ 3–5 targets yields high rates of cancer diagnosis. High detection rates are also seen in men with prior negative biopsy and AS cohorts. PI-RADS™ score, age and PSAD can reliably predict CSD detection. The number of published series is small and the role of MRGB in PI-RADS™ 3 targets needs further study.

**Keywords** In-bore biopsy · MRI-guided biopsy · Multiparametric MRI · Prostate cancer

## Abbreviations

| | |
|---|---|
| ADC | Apparent diffusion co-efficient |
| AS | Active surveillance |
| CaP | Prostate cancer |
| CCL | Cancer core length |
| CSD | Clinically significant disease |
| DICOM | Digital imaging and communications in medicine |
| IQR | Inter-quartile range |
| ISUP | International Society of Urological Pathology |
| mpMRI | Multiparametric magnetic resonance imaging |
| MRGB | In-bore MRI-guided biopsy |
| MRI | Magnetic resonance imaging |
| PI-RADS™ | Prostate Imaging-Reporting and Data System |
| PZ | Peripheral zone |
| TRUS | Transrectal ultrasound (guided) |

✉ Morgan Pokorny
pokornyurology@gmail.com

[1] The Wesley Hospital Urology Department, Brisbane, Australia

[2] Wesley Medical Imaging, The Wesley Hospital, Brisbane, Australia

[3] Aquesta Uropathology, Brisbane, Australia

[4] School of Medicine, University of Queensland, Brisbane, Australia

## Introduction

In the last 5 years multiparametric prostate MRI (mpMRI) has revolutionized the diagnosis of prostate cancer and has gained widespread adoption by urologists in their management of patients with suspected or known prostate cancer. Although prostate MRI has been available for over two decades, recent advances in technology, including the development of 3 T magnets, development of multiparametric anatomical and functional scanning protocols, and a standardized reporting framework in PI-RADS™ [1] (Prostate Imaging-Reporting and Data System) has meant that prostate mpMRI has become a reliable tool in the evaluation of men at risk of prostate cancer, monitoring of low grade disease and treatment planning [2–4]. Prostate MRI is now a recommended tool at various steps of the patient pathway, and position statements on its use have been published by the American Urological Association [5] and by the National Institute for Health and Care Excellence in the UK [6]. Urologists, working in concert with radiologists, have become very familiar in reviewing prostate MRI scans and understanding MRI sequences [7].

Prostate MRI has provided a reliable tool to visualize suspicious regions of the prostate prior to biopsy and has helped urologists develop targeted biopsy techniques to ensure a high chance of diagnostic accuracy. These techniques include cognitive fusion, ultrasound-guided MRI-fusion, and finally "in-bore" or "in-gantry" MRI-guided biopsy (MRGB), in which the patient undergoes a prostate biopsy in the MRI machine. Each of these techniques has its own set of advantages and disadvantages [4]. MRGB can be performed under conscious sedation in an outpatient setting, and procedure times have been reported as short as 25 min [8]. The technique allows immediate registration of needle position in the target of interest, enabling a high degree of certainty in the event of negative biopsy results. The drawback to MRGB is relative cost compared to an office-based prostate biopsy, and access to MRI scanning time. In addition, it is usually not possible to perform template biopsies of the rest of the prostate, and biopsy of additional targets can add 10–15 min per lesion to overall procedure time.

The first aim of this study was to report our experience with MRGB, which began in 2011 when the senior author (LT) introduced mpMRI and MRGB to our institution with the assistance of colleagues from the Department of Radiology, Radboud University, Nijmegen, The Netherlands. This allowed our unit to perform the first prospective trial comparing MRGB and standard transrectal sextant ultrasound (TRUS) guided prostate biopsy [8]. Since that time MRGB has been available and utilized for both routine biopsy and for biopsy of challenging targets in patients referred through our unit and from external institutions as a "tertiary" referral.

The second major aim was to compare our results to the international literature, and to assess the current utilization and experience of MRGB across the world, especially in the last 5 years. Although most centres still use sextant TRUS biopsy, more recently transperineal cognitive biopsy and ultrasound fusion biopsy are becoming increasingly popular. However, we believe there is still a role for MRGB, specifically in targeting small regions of interest (5 mm diameter and under), targets in very large glands, or targets in regions of the prostate known to harbour missed tumours, such as the anterior gland, extreme base, and anterior apex [9]. Therefore, the second part of this paper comprises a literature review and assessment of current practice patterns around the world.

## Patients and methods

### Patients

This was a retrospective review of consecutive men referred for in-bore MRI-guided prostate biopsy at our institution between December 2012 and May 2018. Patients included those referred by urologists within our institution and those referred as tertiary referrals from outside centres. Exclusion criteria included prior treatment for prostate cancer, poor detection MRI quality if performed at another institution, and insufficient clinical data (PSA, prior biopsy status or histology results). This cohort did not include any patients from our previously reported clinical trial [8], but did include 249 patients from a recent retrospective cohort series [10].

### Multiparametric MRI

Multiparametric prostate MRI was performed on a 3.0-T MRI scanner (Siemens Skyra, Siemens Healthcare, Erlangen, Germany) using a pelvic phased-array coil. The MRI protocol was adjusted and optimized over the course of the study period by in-house MR radiographers, but always complied with the PI-RADS™ criteria. The current MRI detection protocols are listed in Table 1. MRI scans were read by one of four radiologists with at least 2 years of mpMRI prostate imaging experience by the time of study commencement. One radiologist had completed a prostate MRI fellowship prior to the era of mpMRI; all four radiologists were mentored over 12 months by Prof Jelle Barentsz from Radboud University through second-reading of MRI scans via high-capacity data link and reciprocal site visits during our previous clinical trial from 2012 to 2013 [8]. MRI scans were reported according to the PI-RADS™ v1 or v2 system. All MRI scans were also co-read by the treating urologist. All MRI-identified target locations were coded to one of seven regions by the reporting radiologist, and

**Table 1** MRI scanning protocols

| | | TR (ms) | TE (ms) | Averages | Slice thickness (mm) | Field of view (mm) | *b* values (s/mm$^2$) |
|---|---|---|---|---|---|---|---|
| T2W | Sagittal | 3120.0 | 106.0 | 4 | 3.0 | 185 | n/a |
| | Axial | 3500.0 | 110.0 | 1 | 3.0 | 180 | n/a |
| | Coronal | 3000.0 | 106.0 | 1 | 3.0 | 185 | n/a |
| DWI | Axial | 3800 | 63.0 | 6 | 3.0 | 256 | 50,400,800<br>Calculated $b = 1400$ |
| DCE | Axial | 4.84 | 1.87 | n/a | 3.0 | 260 | n/a temporal resolution = 4.96 s |
| T1 | Axial 2° | 4.09 | 1.39 | 8 | 3.0 | 260 | Flip angle 2° |
| T1 | Axial 15° | 4.09 | 1.39 | 6 | 3.0 | 260 | Flip angle 15° |

*TR* repetition time; *TE* echo time; *T2W* T2-weighted; *DWI* diffusion-weighted imaging; *DCE* dynamic contrast-enhanced imaging

verified by the principal author for each target—peripheral zone (PZ) base, PZ mid-gland, PZ apex, transition zone, anterior gland, anterior horn of the PZ, and seminal vesicle/central zone.

MRI images were reviewed and relevant findings extracted, including date of diagnostic MRI and biopsy MRI, patient age at time of MRI, PI-RADS™ classification of identified targets and location in the prostate, biopsy target largest diameter on axial T2 and ADC images, lowest target ADC value, and correlation of needle biopsy positions in the prostate with histology reports for each patient and target. Lesions were only measured in the axial plane as this is what is visualized during biopsy.

## MRI-guided biopsy

In-bore MRI-guided biopsy was performed at a subsequent session to the MRI diagnostic study. Patients were prepared with a rectal enema on the morning of the procedure as well as preoperative antibiotics for 1–3 days prior (usually ciprofloxacin) at the discretion of the biopsy surgeon. Patients were kept fasted for 3 h prior to the biopsy and received 1 g IV ceftriaxone 30 min prior to biopsy. Biopsy was performed prone on the MRI scanner with IV sedation using fentanyl 1 µg/kg. The MR-compatible DynaTRIM adjustable needle-guide device (Invivo Corp, Gainesville, FL, USA) was used to guide needle placement. The needle guide was inserted into the rectum lubricated with 1% lignocaine gel and mounted in the DynaTRIM device. All biopsy cores were sampled using an MRI-compatible 17.5-cm, 18G fully automatic biopsy gun (Invivo). Concurrent systematic biopsies were not performed in this cohort.

The scanning protocol was commenced with a sagittal T2 localizer sequence to adjust the needle guide placement at commencement, after which a series of axial and sagittal TRUFI (true fast imaging with steady-state free precession) images are obtained to guide manual needle adjustments toward the target of interest. When the needle guide is aimed toward the target based on axial and sagittal correlation, a DWI sequence is run to allow accurate biopsy targeting of the region of the target containing the lowest ADC value(s). After completing the DWI sequence, further corrections are made using short sequence axial and sagittal TRUFI scans, and the target is co-located using workstation crosshairs correlated to the ADC map. When targeting is complete, distance to target from the tip of the needle guide is measured to guide depth of needle placement prior to firing the biopsy device. After the first needle core is fired, the needle gun is left deployed in the prostate and an axial and sagittal TRUFI scan is captured to confirm needle location for later correlation if required. All biopsies were performed by one of four urologists trained in the procedure, together with the MR radiographers. Procedure biopsy time was coded per target, using the DICOM time stamps, from the time of the first T2 localizer scan, till the final TRUFI scan showing the deployed biopsy needle position, recorded in min:s. For patients with more than one MRI target, the second target was timed from the scan showing final needle position of the preceding target to the last TRUFI scan showing needle deployment in the second target.

## Pathology analysis

Biopsy cores were analysed and reported at a specialist uropathology laboratory by one of three expert uropathologists, according to the standards of the 2005 or 2014 [11, 12] ISUP (International Society of Urological Pathology) Consensus Conference at the time of reporting. Pathologists were blinded to the MRI results, and were supplied with standard clinical information (PSA, DRE status). Biopsy cores were reported for Gleason score/ISUP grade, biopsy core length, and biopsy cancer core length (CCL, in mm or percentage of core involved by cancer). Clinically significant disease (CSD) was defined as at least one core containing Gleason 3 + 4 (ISUP grade 2) or greater prostate cancer.

## Ethical requirements

Institutional ethics approval was granted for this retrospective database review. All patients signed informed consent forms for the MRGB procedure.

## MRGB literature review

### Search strategy

A PubMed database search was carried out on 29 April 2018 by a single reviewer to find English language articles describing patient series undergoing in-bore MRI-guided prostate biopsy, via transrectal or other routes. Only articles published from Jan 2013 were included, to focus on current practice in the last 5 years during which prostate mpMRI has become more widely available. The following medical subject headings were used: "prostate, MRI, magnetic resonance, in-bore, in-gantry, MRI-guided, biopsy". In addition, references from selected articles were scanned to identify additional papers not listed in the search results. Abstracts were reviewed for relevance to the subject.

Inclusion criteria included English language reports of patients undergoing MRGB (prospective or retrospective) published from January 2013 onwards. Exclusion criteria included failure to report cancer detection rates, studies reporting only on TRUS- or fusion-biopsy, systematic reviews, consensus statements, cost analyses, experimental reports, technical reports, ex vivo or in vitro series. Where one group or institution published more than one series, an attempt was made to exclude articles reporting duplicate cohorts, or earlier cohorts, and to include only the largest reported series. Where it was not possible to be certain whether authors had reported duplicate cohorts, both reports were included for analysis. Study authors were not contacted during the process of this review.

### Data extraction

A standardized form was used to collect data for the outcomes of interest, including year of publication, city and country of institution, patient characteristics, MRI and biopsy platform, overall and clinically significant cancer detection rates, detection rates in biopsy-naïve, active surveillance, and prior negative biopsy cohorts, and where available, data on cancer detection by PI-RADS™ target score.

## Statistical analysis

Descriptive statistics were used to present population characteristics and the results of MRGB. Continuous variables were reported as median and inter-quartile range (IQR) while categorical variables were reported as absolute and relative frequencies. Student's $t$ test was used to compare the means of independent groups. Significance level was set at $p \leq 0.05$. Univariate and multivariate logistic regression analysis was performed to determine predictors of detecting any cancer, and clinically significant cancer at biopsy. Odds ratios and 95% confidence intervals were computed. The Hosmer–Lemeshow goodness of fit test was used to test the quality of the fitted model, with a $p$ value $> 0.05$ considered to be a good fit. Statistical analysis was performed using SPSS v25 (IBM Corporation, Armonk, NY, USA).

# Results

## Patient characteristics

In total, 607 target lesions biopsied from 554 men were included in the study. 479 men had no prior prostate biopsy, while 53 men had undergone at least one negative transrectal or transperineal ultrasound-guided prostate biopsy. Twenty-two men were included who were on active surveillance for low-risk prostate cancer, 21 for Gleason 3 + 3 prostate cancer and one man with Gleason 3 + 4 disease. As shown in Table 2, the median age for the cohort was 65 years, median PSA 5.6 ng/mL, and median prostate volume was 43 mL. Full patient characteristics for the cohort, subgroups and target distribution are also shown in Table 2. Of the 607 targets identified in the cohort, 88, 402 and 117 were PI-RADS™ 3, 4 and 5, respectively. A median of 2 biopsy cores was taken per target.

## Biopsy results and target characteristics

Table 3 shows the biopsy results at a per patient and per target level. Overall 443 men (80%) were found to have any prostate cancer on biopsy, and 55% (307) had clinically significant disease. A total of 1416 biopsy cores were taken, of which 69% (977) harboured cancer. When analysed per target, PI-RADS™ 3, 4 and 5 targets demonstrated cancer in 36, 79 and 97% of targets, and clinically significant disease was present in 18, 60 and 85%, respectively. Median target diameter in the axial plane was 10 mm, with median cancer core length involvement of biopsy cores 1 and 2 of 5 mm and 4 mm, respectively. The mean ADC value of PI-RADS™ 5 targets (527) was significantly lower than that of PI-RADS™ 4 targets (661, $p < 0.001$). Similarly, the mean ADC value of PI-RADS™ 4 targets was lower than that of PI-RADS™ 3 targets (661 vs 760, $p < 0.001$).

**Table 2** Patient characteristics

| | All patients | Biopsy naïve | Prior negative biopsy | Active surveillance |
|---|---|---|---|---|
| Patients, *n* | 554 | 479 | 53 | 22 |
| Age (years), median (IQR) | 65 (60–69.5) | 65.5 (59–70) | 63 (59–69) | 66.5 (64–68.8) |
| PSA (ng/mL), median (IQR) | 5.6 (4–7.7) | 5.4 (3.8–7.6) | 6.7 (4.8–9.4) | 6.8 (4.9–8.9) |
| Prostate volume (mL), median (IQR) | 43 (34–57) | 42 (33–55) | 53 (40–68) | 53 (40–74) |
| MRI targets, *n* | 607 | 532 | 53 | 22 |
| PI-RADS™ 3 | 88 | 74 | 8 | 6 |
| PI-RADS™ 4 | 402 | 348 | 41 | 13 |
| PI-RADS™ 5 | 117 | 110 | 4 | 3 |
| Biopsies per target, median (IQR) | 2 (2–3) | 2 (2–2) | 2 (2–3) | 2 (2–3) |

*PSA* prostate-specific antigen; *IQR* inter-quartile range; *PI-RADS*™ Prostate-Imaging Reporting and Data System

**Table 3** Biopsy results by patients and Pi-Rads™ targets

| | Total, *n* | Any prostate cancer on biopsy, % (*n*) | CSD on biopsy % (*n*) (Gleason ≥ 3 + 4 or ISUP > 1) | Total biopsy cores, *n* | Cores involved, % (*n*) | Target T2 diameter, median (mm) | Lowest ADC value, mean | CCL biopsy core 1 mean (mm) | CCL biopsy core 2 mean (mm) |
|---|---|---|---|---|---|---|---|---|---|
| All patients | 554 | 80% (443) | 55% (307) | 1416 | 69% (977) | 10 | 652 | 5 | 4 |
| MRI targets, *n* | 607 | 462 | 357 | | | | | | |
| PI-RADS™ 3 | 88 | 36% (32)[a] | 18% (16) | 194 | 30% (59) | 9 | 760[b] | 2 | 2 |
| PI-RADS™ 4 | 402 | 79% (317)[c] | 60% (241) | 961 | 70% (674) | 9 | 661[d] | 5 | 4 |
| PI-RADS™ 5 | 117 | 97% (113) | 85% (100) | 261 | 93% (244) | 19 | 527 | 9 | 9 |

*CSD* clinically significant disease; *ADC* apparent diffusion co-efficient; *CCL* cancer core length

[a] $p < 0.001$ for Chi-square test, PI-RADS™ 3 vs PI-RADS™ 4

[b] $p < 0.001$ for *t* test comparison of means, PI-RADS™ 3 vs PI-RADS™ 4

[c] $p < 0.001$ for Chi-square test, PI-RADS™ 4 vs PI-RADS™ 5

[d] $p < 0.001$ for *t* test comparison of means, PI-RADS™ 4 vs PI-RADS™ 5

## Distribution of Gleason Grade groups by target PI-RADS™ score and prior biopsy history

Table 4 displays the breakdown of the distribution of cancers detected for each PI-RADS™ group by ISUP Grade. Of the 32 cancers detected in PI-RADS™ 3 targets, 31 were ISUP Grade 1 or 2 cancers, while 1 target was an ISUP Grade 5 cancer (Gleason 4 + 5, 8 mm core involvement). Most PI-RADS™ 4 targets in the cohort contained ISUP Grade 2 cancer (37%), while for PI-RADS™ 5 targets the predominant diagnoses were ISUP Grade 2 (29%), Grade 3 (20%) and Grade 5 (27%) prostate cancer.

Cancer was detected in 32/53 (60%) of men with a prior negative biopsy, of which 26/32 (81%) were CSD. For men on active surveillance, 11/22 (50%) were upgraded after MRGB to clinically significant disease. All 22 of these men had been recruited to active surveillance following a previous standard template biopsy.

## Tumour location

Table 5 shows the cancer detection rate for each location in the prostate stratified by PI-RADS™ score. It can be seen that PI-RADS™ 3 targets had an appreciably lower rate of cancer detection for each location, compared to PI-RADS™ 4 and 5 targets. No PI-RADS™ 3 targets harboured cancer in the apical region or anterior horn of the peripheral zone, while for other locations cancer detection rate ranged from 33 to 57%, compared to detection rates of 69–86% for PI-RADS™ 4 lesions (HR 0.42–0.66 for PI-RADS™ 3 lesions harbouring cancer).

**Table 4** Summary of biopsy findings by ISUP grade and cohort

| | All MRI targets % (*n*) | Biopsy naïve % (*n*) | Prior negative biopsy % (*n*) | Active surveillance % (*n*) |
|---|---|---|---|---|
| PI-RADS™ 3 | 88 | 74 | 8 | 6 |
| No cancer | 63.6 (56) | 62.1 (46) | 75.0 (6) | 67.0 (4) |
| ISUP 1 | 18.2 (16) | 21.6 (16) | 0 (0) | 0 (0) |
| ISUP 2 | 17.0 (15) | 14.9 (11) | 25.0 (2) | 33.0 (2) |
| ISUP 3 | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| ISUP 4 | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| ISUP 5 | 1.1 (1) | 1.4 (1) | 0 (0) | 0 (0) |
| PI-RADS™ 4 | 402 | 348 | 41 | 13 |
| No cancer | 21.0 (85) | 19.3 (67) | 36.6 (15) | 23.1 (3) |
| ISUP 1 | 19.0 (75) | 19.5 (68) | 12.2 (5) | 15.4 (2) |
| ISUP 2 | 37.0 (150) | 39.4 (137) | 22.0 (9) | 30.7 (4) |
| ISUP 3 | 12.5 (50) | 11.2 (39) | 17.0 (7) | 30.7 (4) |
| ISUP 4 | 2.5 (10) | 2.3 (8) | 4.9(2) | (0) |
| ISUP 5 | 8.0 (32) | 8.3 (29) | 7.3 (3) | (0) |
| PI-RADS™ 5 | 117 | 110 | 4 | 3 |
| No cancer | 3.4 (4) | 3.6 (4) | 0 (0) | 0 (0) |
| ISUP 1 | 11.1 (13) | 9.1 (10) | 25.0 (1) | 66.7 (2) |
| ISUP 2 | 29.1 (34) | 29.1 (32) | 50.0 (2) | 0 (0) |
| ISUP 3 | 20.5 (24) | 20.9 (23) | 25.0 (1) | 0 (0) |
| ISUP 4 | 8.5 (10) | 9.1 (10) | 0 (0) | 0 (0) |
| ISUP 5 | 27.4 (32) | 28.2 (31) | 0 (0) | 33.3 (1) |

*ISUP 1* International Society of Urological Pathology Grade 1 prostate cancer (Gleason 3+3); *ISUP 2* Gleason 3+4 prostate cancer; *ISUP 3* Gleason 4+3 prostate cancer; *ISUP 4* any Gleason sum 8 prostate cancer; *ISUP 5* Gleason sum 9 and 10 prostate cancer

Table 6 presents a summary of all targets bearing CSD and their locations. For the entire cohort, 40% (144/358) of clinically significant tumours were located in the anterior half of the gland (anterior gland or anterior fibromuscular stroma, transition zone or anterior horn of peripheral zone). For biopsy-naïve men, this figure was 36.7% (118/321), while for patients with a prior negative biopsy it was 73% (19/26), and for men on active surveillance, 63% (7/11).

## Biopsy procedure time

Median procedure biopsy time across the cohort was 20 min 39 s per target (IQR 16 m 27 s to 26 m 25 s; range 8 m 32 s to 1 h 0 1 m 42 s). Two patients had a total procedure time of 1 h or longer—one had 3 separate targets biopsied, and the second had 6 cores taken of an apical PZ target.

## Smallest targets positive for cancer

Table 7 shows the MRI targets 5 mm and smaller in T2 axial diameter and the detection rates for prostate cancer. In total, 52/79 (65.8%) targets were found to be malignant and 35/79 (44%) targets met the criteria for CSD. Ten of the 79 targets (13%) were Gleason $\geq 4+3$ tumours.

## PSA density and cancer detection rate

The relationship of PSA density (PSAD) and prostate cancer detection was examined for lower PSAD cut-offs of 0.12 and 0.15, following recent reports of a possible role for PSAD in stratifying PI-RADS™ 3 patients for biopsy [13]. These results are shown in Table 8. For PI-RADS™ 3 patients with a PSAD below 0.12, 37% had prostate cancer detected and 15% had CSD (compared to 67 and 45% for all patients). When a PSAD below 0.15 was selected, 39% of patients were found to have CaP on biopsy with 20% showing CSD. No PI-RADS™ 3 patients below PSAD 0.15 were found to have ISUP 3 or higher prostate cancer.

## Predictors for detection of cancer and CSD

Binary logistic regression analysis was performed to assess whether certain clinical and MRI-based variables could predict the presence of any prostate cancer on biopsy, and the presence of CSD. The variables PSA density, age at biopsy, target location, PI-RADS™ score, target T2 diameter and lowest ADC value were entered into the model. On univariate analysis, all variables except target location were significant predictors of both cancer

**Table 5** Cancer detection rate stratified by target location and PI-RADS™ score

| Location | PI-RADS™ score | No cancer % (*n*) | Cancer % (*n*) | *p* (Pearson Chi-square) | HR | CI |
|---|---|---|---|---|---|---|
| Anterior gland/FMS | 3 | 42.9 (6) | 57.1 (8) | 0.008 | 0.66 | 0.42–1.05 |
| | 4 | 13.3 (10) | 86.7 (65) | | | |
| | 5 | 0 | 100 (33) | | | |
| Transition zone | 3 | 60 (15) | 40 (10) | 0.01 | 0.52 | 0.30–0.88 |
| | 4 | 22.3 (5) | 77.3 (17) | | | |
| | 5 | 0 | 100 (11) | | | |
| PZ anterior horn | 3 | 100 (6) | 0 | 0.001 | 3.25[a] | 2.26–4.68 |
| | 4 | 30.8 (20) | 69.2 (45) | | | |
| | 5 | 0 | 100 (8) | | | |
| PZ base | 3 | 66.7 (8) | 33.3 (4) | 0.001 | 0.42 | 0.19–0.95 |
| | 4 | 21.2 (14) | 78.8 (52) | | | |
| | 5 | 0 | 100 (11) | | | |
| PZ mid-gland | 3 | 54.5 (12) | 45.5 (10) | 0.001 | 0.58 | 0.36–0.93 |
| | 4 | 21.6 (24) | 78.4 (870 | | | |
| | 5 | 8.8 (3) | 91.2 (31) | | | |
| PZ apex | 3 | 100 (9) | 0 | < 0.001 | 5.3[a] | 3.16–8.74 |
| | 4 | 19 (12) | 81 (51) | | | |
| | 5 | 5.6 (1) | 94.4 (17) | | | |

*FMS* fibromuscular stroma; *PZ* peripheral zone; *HR* hazard ratio; *CI* confidence interval

*p* values shown for Pearson Chi-square test for proportions of targets in each location found to contain cancer, for PI-RADS™ 3 vs PI-RADS™ 4. HR < 1 signifies lower chance of cancer detection in PI-RADS™ 3 target for that location

[a]The hazard ratio for target being negative in this location for PI-RADS™ 3 compared to PI-RADS™ 4 (0 targets positive for cancer for PI-RADS™ 3 for these locations)

**Table 6** Summary of clinically significant cancer locations, by cohort

| Location | All CSD targets (*n* = 358) % (*n*) | Biopsy-naïve patients (*n* = 321) % (*n*) | Prior negative biopsy (*n* = 26) % (*n*) | Active surveillance (*n* = 11) % (*n*) |
|---|---|---|---|---|
| Anterior gland | 23 (81) | 21 (66) | 50 (13) | 18 (2) |
| Transition zone | 7 (24) | 6 (19) | 11. % (3) | 18 (2) |
| PZ anterior horn | 11 (39) | 10 (33) | 11. %(3) | 27 (3) |
| PZ base | 16 (57) | 17 (55) | 4 (1) | 9 (1) |
| PZ mid-gland | 28 (101) | 30 (98) | 11.5 (3) | 0 (0) |
| PZ apex | 15 (54) | 15 (48) | 11.5 (3) | 27 (3) |
| Central zone/SV | 0.6 (2) | 0.6 (2) | 0 (0) | 0 (0) |

*PZ* peripheral zone; *SV* seminal vesicles; *CSD* clinically significant disease

detection and CSD detection on biopsy. However, on multivariate analysis, only PI-RADS™ score (OR 5.33, $p < 0.001$) and lowest ADC value (OR 0.99, $p < 0.001$) were significant predictors for detection of any cancer (Table 9), while for predicting CSD, PSA density, age at biopsy, PI-RADS™ score, and lowest ADC value were significant predictors (Table 10).

## MRGB literature review

The literature search returned 248 abstracts based on the MeSH search terms. Sixty-four records were excluded on first pass as they were outside the timeframe of the study period (prior to 2013, $n = 58$) or non-English language publications (6 records). A further 124 records were then

**Table 7** Detection rate of prostate cancer in targets with T2 axial diameter ≤ 5 mm

| T2 diameter | *n* | % |
|---|---|---|
| 3 mm | 6 | 100 |
| No cancer | 3 | 50 |
| ISUP 1 | 2 | 33.3 |
| ISUP 2 | 1 | 16.6 |
| ISUP 3 | 0 | 0 |
| ISUP 4 | 0 | 0 |
| ISUP 5 | 0 | 0 |
| 4 mm | 37 | 100 |
| No cancer | 10 | 27 |
| ISUP 1 | 9 | 24.3 |
| ISUP 2 | 14 | 37.8 |
| ISUP 3 | 4 | 10.8 |
| ISUP 4 | 0 | 0 |
| ISUP 5 | 0 | 0 |
| 5 mm | 36 | 100 |
| No cancer | 14 | 38.9 |
| ISUP 1 | 6 | 16.7 |
| ISUP 2 | 10 | 27.8 |
| ISUP 3 | 4 | 11.1 |
| ISUP 4 | 1 | 2.8 |
| ISUP 5 | 1 | 2.8 |

*ISUP 1* International Society of Urological Pathology Grade 1 prostate cancer (Gleason 3 + 3); *ISUP 2* Gleason 3 + 4 prostate cancer; *ISUP 3* Gleason 4 + 3 prostate cancer; *ISUP 4* any Gleason sum 8 prostate cancer; *ISUP 5* Gleason sum 9 and 10 prostate cancer

**Table 8** Prostate cancer detection by PSA density stratification, by PI-RADS™ 3 patients and all patients

| | PSAD < 0.12 | | PSAD < 0.15 | |
|---|---|---|---|---|
| | PI-RADS™ 3 | All patients | PI-RADS™ 3 | All patients |
| *n* | 59 | 289 | 69 | 372 |
| CaP | 22 (37%) | 195 (67%) | 27 (39%) | 262 (70%) |
| CSD | 9 (15%) | 131 (45%) | 12 (20%) | 184 (49%) |
| ISUP ≥ 3 | 0 | 47 (16%) | 0 | 69 (18%) |

*PSAD* PSA density; *CaP* prostate cancer; *CSD* clinically significant disease (≥ Gleason 3 + 4); *ISUP* International Society of Urological Pathology

excluded based on title and abstract review (Fig. 1). Thirty-six records underwent full review, after which 13 papers were excluded as they reported cohorts that were reported in larger publications at a later date or analysed different research questions using the same dataset. This left 23 studies reporting cohorts undergoing in-bore MRI-guided prostate biopsy (Table 11). Twenty-one series reported biopsies using the transrectal route, while one series reported a transgluteal approach and one series a transperineal approach.

**Table 9** Binary logistic multivariate analysis for predictors of any cancer detected on MRGB

| Variable | OR (95% CI) | *p* |
|---|---|---|
| PSA density | 11.21 (0.83–150.54) | 0.068 |
| Age at biopsy | 1.01 (0.97–1.03) | 0.648 |
| Target location | 0.93 (0.82–1.07) | 0.313 |
| PI-RADS™ score | 5.34 (3.32–8.58) | < 0.001 |
| T2 diameter | 0.97 (0.92–1.02) | 0.169 |
| Lowest ADC | 0.997 (0.996–0.998) | < 0.001 |

*OR* odds ratio; *CI* confidence interval; *PSA* prostate-specific antigen; *PI-RADS*™ Prostate-Imaging Reporting and Data System; *ADC* apparent diffusion co-efficient

**Table 10** Binary logistic multivariate analysis for predictors of clinically significant cancer (CSD) detected on MRGB

| Variable | OR (95% CI) | *p* |
|---|---|---|
| PSA density | 43.82 (4.55–421.74) | 0.001 |
| Age at biopsy | 1.03 (1.00–1.05) | 0.031 |
| Target location | 1.06 (0.95–1.19) | 0.289 |
| PI-RADS™ score | 3.70 (2.38–5.75) | < 0.001 |
| T2 diameter | 0.99 (0.95–1.04) | 0.791 |
| Lowest ADC | 0.998 (0.997–0.999) | 0.003 |

*OR* odds ratio; *CI* confidence interval; *PSA* prostate-specific antigen; *PI-RADS*™ Prostate Imaging-Reporting and Data System; *ADC* apparent diffusion co-efficient

### Country of origin, publication rate, protocols and patient demographics

Overall, the 23 series came from 7 countries—Germany (7 reports), the USA (6), Australia (5), The Netherlands (2), Denmark (1), Austria (1) and Italy (1). There has been a steady increase in the number of publications annually since 2013, with a rise from 4 publications in 2016 to 9 in 2017. Four studies from 2018 met the inclusion criteria for this review. Siemens MRI machines were the most popular scanning platform (16 studies), followed by Philips (4) and GE (1). Most centres used 3 T magnets (17/23, 74%). Virtually all centres used the DynaTRIM (Invivo, Gainesville, Florida) MRI-compatible biopsy device to hold and guide the MRI-compatible needle-guide used for targeting. In addition, almost all of these centres used the accompanying DynaCAD software to guide adjustment of the DynaTRIM device to position and align the needle guide. Only 9 centres explicitly reported their antibiotic protocol, and most of these used fluoroquinolone prophylaxis (7/9, 78%). Eleven centres reported on their use of sedation and analgesia during

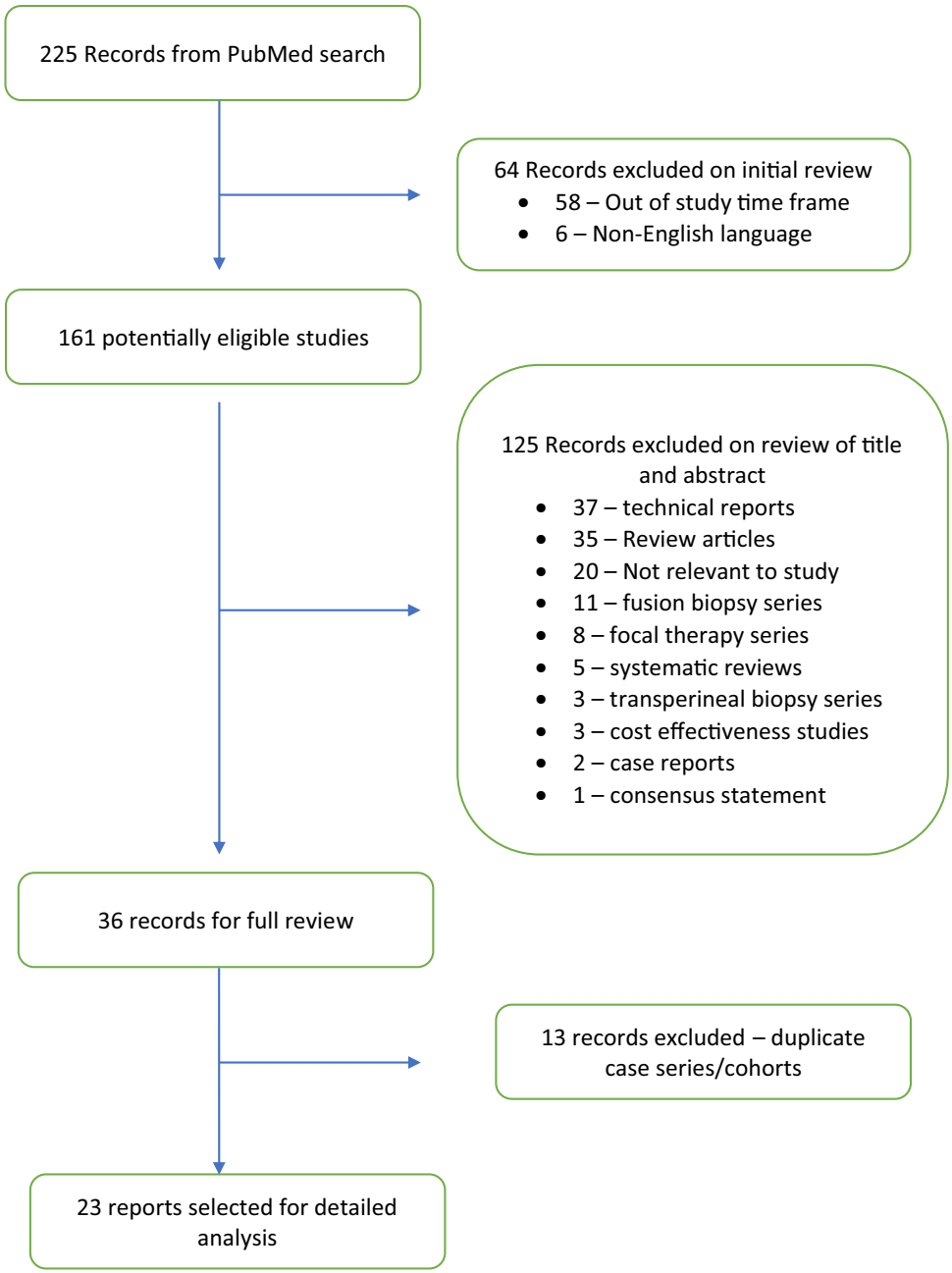


**Fig. 1** Flow diagram showing search strategy and selection for literature review

biopsy, with most centres using either fentanyl or midazolam, or a combination, for conscious sedation during the procedure.

Overall, 4061 patients underwent MRGB in the 23 reported series. Median patient age in the series ranged between 62 and 68 years, with reported median PSA ranging from 5.3 to 13 ng/mL. Median prostate volumes showed a fairly wide range, from 36 to 79 mL. Detailed patient demographics and protocol variations are listed in Table 11.

### Biopsy cores and procedure times

Thirteen papers reported the number of cores taken per target, with a range of 1–6 cores per target, and 2 cores per MRI target being the most common practice. Median biopsy time was reported by 6 studies, ranging from 24 to 63 min.

**Table 11** Study and patient details of 23 studies reporting MRI-guided in-bore prostate biopsy cohorts

| First author | Year | References | City, country | MRI platform | Magnet strength, *T* | Biopsy guide | Antibiotic prophylaxis | Analgesia/sedation | Study commencement | Patients, *n* | MRGB patients, *n* | Median age, years | Median PSA, ng/mL | Median prostate volume, mL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Transrectal | | | | | | | | | | | | | | |
| Durmus | 2013 | [35] | Berlin, Germany | Siemens Magnetom Avanto | 1.5 | DynaTRIM | NS | NS | Jan 2008 | 87 | 87 | 66 | 10.1 | NS |
| Mouraviev | 2013 | [36] | Cincinnati, USA | GE Signa | 3 | DynaTRIM | Ciprofloxacin 500 mg | NS | NS | 32 | 10 | NS | NS | NS |
| Pokorny | 2014 | [8] | Brisbane, Australia | Siemens Skyra | 3 | DynaTRIM | Ceftriaxone, ciprofloxacin | Fentanyl | July 2012 | 223 | 142 | 63 | 5.3 | 41 |
| Garmer | 2015 | [37] | Bochum, Germany | Siemens Espree | 1.5 | InVivo | NS | NS | Nov 2007 | 177 | 177 | 66 | 8 | 36 |
| Liddell | 2015 | [38] | Canberra, Australia | Philips Ingenia | 3 | DynaTRIM | NS | NS | Jan 2013 | 118 | 65 | 62 | 6.5 | 78.4 |
| Felker | 2016 | [39] | Los Angeles, USA | Multiple | 3/1.5 | DynaTRIM | Oral 1–3d pre and post | Midazolam/fentanyl | NS | 461 | 461 | 66 | 7.5 | 54 |
| Kasel-Seibert | 2016 | [40] | Jena, Germany | Siemens Magnetom Avanto | 1.5 | DynaTRIM | Fluoroquinolones | NS | Jul 2013 | 82 | 82 | 65 | 13 | NS |
| Schimoller | 2016 | [41] | Dusseldorf, Germany | Siemens Magnetom Trio | 3 | DynaTRIM | NS | NS | Jan 2012 | 290 | 290 | 66 | 8.2 | 58 |
| Tewes | 2016 | [42] | Hannover, Germany | Siemens Skyra | 3 | DynaTRIM | NS | LLA gel PR | Dec 2012 | 54 | 54 | 69 | 8.7 | 52 |
| Addicott | 2017 | [15] | Portland, USA | Philips Ingenia | 1.5 | DynaTRIM | Ciprofloxacin | Fentanyl/midazolam | Aug 2013 | 50 | 50 | 66 | 12 | NS |
| Elkjaer | 2017 | [14] | Skejby, Denmark | Siemens Skyra | 3 | DynaTRIM | NS | NS | Oct 2014 | 78 | 78 | 66 | 6.3 | 45 |
| Jyoti | 2017 | [20] | Canberra, Australia | Philips Ingenia | 3 | DynaTRIM | NS | NS | NS | 137 | | 63 | 6.4 | 73 |
| Osses | 2017 | [43] | The Hague, The Netherlands | NS | 3 | NS | 750 mg ciprofloxacin | NS | Jan 2013 | 155 | 155 | 68 | 11.1 | 61 |
| Schiavina | 2017 | [44] | Bologna, Italy | Philips Achieva XR | 1.5 | DynaTRIM | Ciprofloxacin 3d | Peripros-tatic block | July 2015 | 70 | 70 | 63 | 6.9 | 50 |

**Table 11** (continued)

| First author | Year | References | City, country | MRI platform | Magnet strength, *T* | Biopsy guide | Antibiotic prophylaxis | Analgesia/sedation | Study commencement | Patients, *n* | MRGB patients, *n* | Median age, years | Median PSA, ng/mL | Median prostate volume, mL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tan | 2017 | [45] | Los Angeles, USA | Siemens Skyra, Trio, Verio | 3 | | Ciprofloxacin 3d | Fentanyl/midazolam | May 2013 | 106 | 106 | 66 | 7.9 | 53 |
| Venderink | 2017 | [13] | Nijmegen, The Netherlands | Siemens Skyra | 3 | DynaTRIM | NS | NS | Jan 2012 | 1057 | 1057 | 66 | 10.4 | 53 |
| Yaxley | 2017 | [10] | Brisbane, Australia | Siemens Skyra | 3 | DynaTRIM | Ceftriaxone, ciprofloxacin | Fentanyl | Jan 2012 | 249 | 249 | 64 | 5.5 | 42 |
| Bastian Jordan | 2018 | [46] | Brisbane, Australia | Siemens Skyra/Verio | 3 | DynaTRIM | Surgeon preference | IV sedation | NS | 343 biopsies | 343 | NS | NS | NS |
| Elfatairy | 2018 | [47] | Atlanta, USA | Siemens Magnetom trio | 3 | DynaTRIM | NS | NS | NS | 7 | 7 | 62 | 5.9 | 47 |
| Friedl | 2018 | [34] | Vienna, Austria | Siemens Skyra | 3 | DynaTRIM | Fluoroquinolones | Nalbuphine HCl | Mar 2014 | 142 | 142 | 68 | 8.9 | 51 |
| Kaufmann | 2018 | [48] | Tübingen, Germany | Siemens Skyra | 3 | | NS | NS | Oct 2014 | 156 | 45 | 67 | 9 | 45 |
| Transgluteal | | | | | | | | | | | | | | |
| Steureer | 2017 | [49] | Hamburg, Germany | Siemens Magnetom Avanto | 1.5 | NS | NS | Diazepam, skin LA | May 2013 | 960 | 301 | 65 | 7 | 39 |
| Transperineal | | | | | | | | | | | | | | |
| Penzkofer | 2015 | [50] | Boston, USA | Siemens Verio | 3 | In house | NS | Midazolam and fentanyl | Jan 2011 | 90 | 90 | 66 | 12.4 | 54 |

*MRI* magnetic resonance imaging; *MRGB* MRI-guided in-bore biopsy; *PSA* prostate-specific antigen; *NS* not stated; *LA* local anaesthetic; *PR* per rectum

**Table 12** Cohort breakdown and biopsy results from 23 studies analysed for MRGB

| First author | Year | Biopsy naïve, *n* | Prior negative biopsy, *n* | AS, *n* | Median biopsy time, min | Biopsy cores per lesion, *n* | All CaP diagnosed, *n* (%) | CSD diagnosed, *n* (%) | Insignificant CaP, *n* (%) | CaP in biopsy naïve, *n* (%) | CaP in prior negative biopsy, *n* (%) | Upgrading in AS, *n* (%) | CaP in PI-RADS™ 3, *n* (%) | CaP in PI-RADS™ 4, *n* (%) | CaP in PI-RADS™ 5, *n* (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Transrectal | | | | | | | | | | | | | | | |
| Durmus | 2013 | – | 87 | – | – | 3 | 36/87 (42%) | 31/36 (86%)[a] | 5/36 (14%) | – | 36/87 (42%) | – | | | |
| Moura-viev | 2013 | 3 | – | 7 | – | NS | 8/10 (80%) | 0/10 | 8/10 (80%) | – | – | – | | | |
| Pokorny | 2014 | 142 | – | – | 25 | 2 | 99/142 (69.7%) | 93/99 (93.9%)[b] | 6(6%) | – | – | – | 5/33 (15%) | 94/109 (86%) | incl. with PI-RADS 4 |
| Garmer | 2015 | – | – | – | – | NS | 64/177 (36%) | 32/64 (50%)[c] | 32/64 (50%) | – | – | – | | | |
| Liddell | 2015 | – | – | – | – | NS | 4/65 (6%) | 2/6 (33%)[c] | 4/6 (67%) | – | – | – | 4/65 (6%) | | |
| Felker | 2016 | 381 | – | 80 | 41-55 | 2 | 233/461 (51%) | 151/461 (33%)[c] | 82/233 (35%) | 178/381 (47%) | 79/234 (34%) | 27/80 (34%) | 74/451 (16.4%) | 130/225 (57.8%) | 78/81 (96.3%) |
| Kasel-Seibert | 2016 | – | – | – | – | NS | 31/82 (38%) | 21/82 (26%)[c] | 10/31 (32%) | – | – | – | | | |
| Schi-moller | 2016 | 157 | 133 | – | – | 2 | 145/290 (45%) | 54/145 (37%)[d] | 91/145 (63%) | 87/157 (55%) | 58/133 (44%) | – | 4/37 (11%) | 52/152 (34%) | 89/101 (88%) |
| Tewes | 2016 | 18 | 36 | – | – | 2 | 31/54 (57%) | 19/31 (61%)[e] | – | – | – | – | | | |
| Addicott | 2017 | 5 | 30 | 14 | 49 | NS | 37 (74%) | 31 (62%)[c] | 6/37 (16%) | 5 (100%) | 18/30 (60%) | 10/14 (71%) | | | |
| Elkjaer | 2017 | – | – | 78 | – | 2 | 18/78 (23%) | 17/18 (94%)[f] | 1/18 (5%) | – | – | 8/78 (10%) | | | |
| Jyoti | 2017 | – | 56 | – | – | NS | NS | – | NS | – | 12/56 (21%) | – | | | |
| Osses | 2017 | – | – | – | – | NS | 100/155 (65%) | 63/100 (63%)[c] | 37/100 (37%) | – | – | 15/26 (58%) | 3/29 (10%) | 65/84 (77%) | 32/36 (89%) |
| Schi-avina | 2017 | 29 | 41 | – | 51 | 2 | 32/70 (45.7%) | 24/32 (75%)[c] | 8/32 (25%) | 15/29 (52%) | 17/41 (41.5%) | – | 8/32 (25%) | 13/25 (52%) | 11/13 (85%) |
| Tan | 2017 | 23 | 34 | 49 | – | 3 or 4 | 63/106 (59%) | 49/72 targets (68%)[c] | – | 11/23 (48%) | 13/34 (38%) | 18/49 (37%) | 6/31 (19.4%) | 39/50 (78%) | 24/29 (82%) |
| Vender-ink | 2017 | 184 | 649 | 224 | – | 2 | 757/1057 (72%) | 506/757 (67%)[c] | 251/757 (33%) | 141/184 (77%) | 439/649 (67.6%) | 95/224 (42%) | 55/156 (35%) | 223/373 (60%) | 479/528 (91%) |

**Table 12** (continued)

| First author | Year | Biopsy naïve, *n* | Prior negative biopsy, *n* | AS, *n* | Median biopsy time, min | Biopsy cores per lesion, *n* | All CaP diagnosed, *n* (%) | CSD diagnosed, *n* (%) | Insignificant CaP, *n* (%) | CaP in biopsy naïve, *n* (%) | CaP in prior negative biopsy, *n* (%) | Upgrading in AS, *n* (%) | CaP in PI-RADS™ 3, *n* (%) | CaP in PI-RADS™ 4, *n* (%) | CaP in PI-RADS™ 5, *n* (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Yaxley | 2017 | – | – | – | – | 2 | 221/298 lesions (74%) | 203/298 (68%)[b] | 18/221 (8%) | – | – | – | 22/45 (49%) | 139/190 (73%) | 60/63 (95%) |
| Bastian Jordan | 2018 | – | – | – | – | 2 | 231/343 (67%) | 171/231 (74%)[c] | 60/231 (26%) | – | – | – | 19/75 (25%) | 101/133 (76%) | 109/117 (93%) |
| Elfatairy | 2018 | – | 2/7 | 3/7 | – | NS | – | – | | – | – | – | | | |
| Friedl | 2018 | – | – | – | 24-26 | NS | 81/142 (57%) | – | | – | – | – | | | |
| Kaufmann | 2018 | – | 156 | – | – | NS | 23/45 (51%) | 18/45 (40%)[g] | 5/23 (22%) | – | – | – | | | |
| Transgluteal | | | | | | | | | | | | | | | |
| Steureer | 2017 | – | 63 | – | – | 6 | 197/301 (65%) | 164/197 (83.2%)[c] | 33/197 (17%) | – | – | – | | | |
| Transperineal | | | | | | | | | | | | | | | |
| Penzkofer | 2015 | 52 | – | 13 | 63.8 | 1-5 | 51/90 (56.7%) | 43/51 (84%)[c] | 7/51 (13.7%) | 25/52 (48%) | – | 5/13 (38.5%) | | | |

*CaP* prostate cancer; *CSD* clinically significant disease; *AS* active surveillance; *NS* not stated; *PI-RADS*™ Prostate Imaging-Reporting and Data System

Definitions of clinically significant disease for each study:

[a]D'Amico intermediate or high risk

[b]Gleason 3 + 3 > 6 mm 1 core, or 2 cores any length; Gleason 3 + 4 > 4 mm in 1 core, or 2 cores any length; Gleason 4 + 3 any length in 1 core

[c]Gleason ≥ 3 + 4

[d]Gleason ≥ 4 + 3

[e]D'Amico criteria

[f]Gleason 3 + 3 ≥ 6 mm, or higher

[g]Gleason ≥ 3 + 4 or any tumour length > 5 mm

### Biopsy outcomes and prostate cancer detection after prior negative biopsy and men in active surveillance programmes

Table 12 shows a detailed breakdown of the study cohorts in these series and the cancer detection outcomes, both for overall prostate cancer detection and clinically significant disease, and where reported, by PI-RADS™ target category (PI-RADS™ 3, 4 or 5). Most centres now appear to use a definition of significant disease as Gleason 3 + 4 or higher on biopsy core analysis. As is to be expected, the reported series included heterogeneous cohorts, with a mixture of biopsy-naïve patients, patients with prior negative biopsy, and patients on active surveillance protocols. Eight studies included patients on AS, with a total of 468 patients. Eleven studies included patients with one or more prior negative prostate biopsy, totalling 1287 patients.

There was a wide variation in reported prostate cancer detection rates, with overall prostate cancer detection ranging from 23% in an active surveillance cohort [14] to studies reporting 72–74% detection rates for any CaP [10, 13, 15]. There was a trend for larger series to report overall higher detection rates. All but three studies reported the detection rate for clinically significant disease, which ranged from 26 to 94%. Overall, CSD was found in 1661/2632 patients (63%) from studies which explicitly reported patient figures for CSD. Eight studies reported on detection of CaP in patients with prior negative biopsy, with cancer found in 21–67% of men undergoing MRGB. Overall, 672/1264 men (53%) undergoing MRGB after prior negative biopsy were found to have prostate cancer.

Six studies provided detailed information on men included from an active surveillance protocol, and in these studies between 10 and 71% of men were upgraded to a higher Gleason score following MRGB. In total, 173/471 men (36.7%) were upgraded to a higher Gleason score compared to that on their enrolment to active surveillance.

### Cancer detection according to target PI-RADS™ score

Only 9 of 23 studies provided information on prostate cancer detection according to MRI target PI-RADS™ classification. Detection of prostate cancer in PI-RADS™ 3 targets ranged between 6 and 49%, and overall 195/921 men (21%) with PI-RADS™ 3 targets were found to have cancer on MRGB. For PI-RADS™ 4 targets, detection of CaP ranged between 34 and 77%, while for PI-RADS™ 5, overall CaP detection ranged between 82 and 96%.

## Discussion

To our knowledge we present here the second largest published cohort of patients undergoing MRGB in a single centre ($n = 554$). The results demonstrate that MRGB can be performed in an outpatient setting with a 20-min procedure time for single targets, and detection rates for cancer are very high for PI-RADS™ 4 and 5 targets. Our overall prostate cancer detection rate was 80% and detection of significant cancer was 55%. This is in contrast to rates of 30–50%, and 10–40%, respectively, for most 12-core TRUS series reported in a recent systematic review of randomized trials of prostate biopsy techniques by Wang [16]. This is to be expected in the modern era with the benefits of MRI imaging and targeted biopsy. The biopsy needle efficiency is high, with 69% of cores positive for cancer. Additionally, we observed a high detection rate for cancer of 65.8% in targets 5 mm in size or smaller, with 44% of such targets harbouring CSD. Unlike cognitive biopsy techniques, MRGB provides validation that the biopsy core has passed through the target, thereby allowing the operator to have high confidence in the histology results, particularly for smaller targets. Our overall biopsy results are largely comparable to the published literature, as can be seen by reviewing Table 12.

Our data and that of other series show the value of MRGB in biopsy of men with prior negative prostate biopsy, or on active surveillance. Sixty percent of men with a prior negative biopsy in our cohort were found to have cancer, with a large proportion of these in the anterior half of the gland (73%), and 81% of these tumours were CSD. It is now well established that the anterior gland is poorly sampled, or difficult to sample with standard TRUS biopsy, and MRI-based cognitive targeting assists in finding these previously missed tumours [17]. Similarly, 50% of men on AS were upgraded to CSD following MRGB. The literature review demonstrated similar findings, with detection rates for CaP in the order of 21–67%. Within the limitations of a retrospective review with potential selection bias, overall our cohort demonstrated anteriorly located tumours in 40% of cases. We would argue therefore that blind TRUS biopsy without a prior diagnostic MRI can no longer be considered an adequate diagnostic technique, as many men would have CSD missed by a single round of TRUS biopsy. This position is supported by the results of two recently published, prospective, large studies showing the superiority of an MRI-based triage pathway for prostate biopsy over standard TRUS biopsy. The PROMIS study [18] showed that up to 27% of men could avoid a biopsy if they had an MRI first, with up to 18% more CSD being detected if biopsy was guided by MRI findings, and 5% fewer clinically insignificant

cancers being found. The PRECISION study [19] was a multicentre, randomized, non-inferiority study in which 500 men were randomized to MRI followed by targeted biopsy if a suspicious target was seen, or TRUS biopsy without an upfront MRI. Clinically significant cancer was detected in 38% of the MRI group compared to 26% of the TRUS biopsy group. Clinically insignificant cancer was detected in 9% of the MRI arm, compared to 22% of the TRUS arm. Overall the analysis favoured the MRI pathway as superior to TRUS biopsy.

A controversial area requiring further study is how to manage PI-RADS™ 3 targets. It is well known that the detection rate for prostate cancer in PI-RADS™ 3 targets is much lower than for PI-RADS™ 4 targets. Our cohort had a 36% detection rate for any prostate cancer, and 18% overall had CSD. Other studies examined in this review also show a low rate of detection, from 6% [20] to 49% [10], and 21% overall for the reported series. Part of the variability will no doubt stem from the impact of modification of a PI-RADS™ 3 target in PI-RADS™ v2, and many of these targets would now either be downgraded to PI-RADS™ 2 or upgraded to PI-RADS™ 4, compared to the original PI-RADS™ v1 criteria. Many reported series have cohorts which spanned the transition from PI-RADS™ v1 to v2, making it difficult to extract these details from published papers. However it can be argued, as Venderink [13] have done in their paper, that perhaps other discriminators such as PSA density (PSAD) can be used to better triage those patients who would be the best candidates for targeted biopsy of PI-RADS™ 3 targets. Their data showed that using a PSAD $\geq$ 0.15 would allow 42% of men with PI-RADS™ 3 targets to avoid biopsy, and only 6% of CSD would be missed. Using a PSAD cut-off of 0.12 would change the figures to 26% avoiding biopsy and no CSD being missed. However, our own analysis from this cohort showed that PI-RADS 3 patients with a PSAD below 0.12 still had a 15% rate of CSD, and below 0.15, 20% of all patients were found to have CSD. This may be explained in part by different patient selection between the two centres, and a change in patterns of PI-RADS™ 3 reporting over time. The total number of PI-RADS™ 3 patients in this series was only 88 patients. Alternatively, it could be argued that men with a PI-RADS™ 3 target should have both template and targeted biopsy using ultrasound guidance. However, prospective studies with large patient cohorts are required to answer this question. It would seem difficult to justify the use of an expensive resource like MRGB to biopsy patients with a detection rate of around 20% for CSD. However, the cost-effectiveness of MRI has been examined by a number of groups [21–23] and found to be favourable when the endpoint is Quality Adjusted Life Years.

A further important point that deserves mention is that urologists now have an array of biomarker options to help determine which men should undergo biopsy or repeat biopsy. These include the 4K score, Prostate Health Index (PHI), Apifiny assay, PCA3 score, Michigan Prostate Score, SelectMDx and Confirm MDx. A recent review highlights these biomarkers, however many are also hampered by low specificity (30–50%), similar to prostate MRI [24]. We assessed the utility of clinical and MRI parameters to predict CSD at biopsy, and on multivariate regression analysis, PSAD, age, PI-RADS™ score and lowest ADC value were predictive for the presence of CSD. However, the hazard ratio for lowest ADC was only marginally below 1.0, likely reflecting a large cohort of cases with a high pre-test probability for cancer, and therefore this parameter is less useful and needs further validation in a less skewed population. Other groups have also confirmed that age, PSAD and PI-RADS™ score were predictive of CSD [25, 26].

## Strengths

This large series represents the experience of a single high-volume centre with very high co-operation levels between urologists and radiologists, including a weekly MDT meeting in which prostate MRI features prominently. All patients underwent diagnostic and biopsy imaging on the same 3T machine, ensuring consistency of image quality and reporting. In addition, all pathology was reported by a single group of expert uropathologists.

## Weaknesses

Our MRGB cohort does have some weaknesses. This was a retrospective review of cases referred for MRGB over a 5-year period, and therefore there is inherent selection bias which may not reflect the spectrum of patients presenting to a general urology practice. The tertiary nature of the referral service means our cohort is likely to contain a larger number of smaller and anterior tumours than would be seen in all men undergoing a diagnostic prostate MRI. The specific skillset and experience of the radiologists and use of a 3T platform is not available in all centres, limiting the generalizability of our results somewhat. In-bore MRGB results may not reflect what is achievable with cognitive or software fusion techniques, although a large review did not find differences in cancer detection between MRGB and fusion or cognitive biopsy [27]. One important reason for this is that MRI often underestimates true tumour size, and therefore any targeting mis-registration by various techniques is nullified by the fact that that target is actually larger than seen on MRI [28].

No template biopsies were performed in our patients, and there was no attempt at correlating biopsy results with radical prostatectomy histology, as patients were referred from multiple urologists, often in other centres. Therefore, we cannot comment on the accuracy of MRGB for predicting

the highest grade of disease present, nor correlation with final Gleason score on prostate whole mount examination. However, other groups have examined these questions, many using fusion or cognitive biopsy approaches [29–32]. Finally, we were not able to collect data on complications in this retrospective review. However, it has been reported that sepsis following a 2-core transrectal MRGB with antibiotic prophylaxis is very rare [33, 34].

The literature review was not conducted as a formal systematic review, and therefore is limited in that a single reviewer conducted a search of one database limited to the English language.

## Conclusion

Use of MRGB in our cohort resulted in a high detection rate for CaP of 80%, and of CSD in 55% of all patients. Overall cancer detection rate did not differ by target location in the prostate, and PI-RADS™ 3 targets were significantly less likely to harbour cancer than PI-RADS™ 4/5 targets. 41% of all CSD targets were located in the anterior half of the prostate. PI-RADS™ 3 lesions remain a diagnostic challenge, with 20% of patients with PSAD under 0.15 having CSD. Multivariate regression analysis showed age, PSAD, PI-RADS™ score and lowest target ADC value all predict CSD at biopsy. Finally, MRGB can be performed in an outpatient setting with a short procedure time and can be performed reliably by both urologists and radiologists.

**Authors' contributions** MP: project development, data collection, data management, data analysis, manuscript writing and editing. BK: data collection, manuscript editing. RE: data collection, manuscript editing. JY: data analysis, manuscript editing. HS: data collection, manuscript editing. ND: manuscript editing. TG: manuscript editing. GC: manuscript editing. RH: data collection, data management, manuscript editing. BL: manuscript editing. DA: manuscript editing. NB: manuscript editing. RP: data analysis, data collection, manuscript editing. LT: data collection, manuscript editing.

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### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

**Ethical approval** All procedures performed in this study involving human participants were in accordance with the ethical standards of the institution and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Institutional ethics committee approval was obtained from Uniting Care Health's Human Research Ethics Committee for the conduct of this study.

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