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ARTICLE

Pelvic phased-array mpMRI versus saturation biopsy: a diagnostic performance analysis in men with suspected advanced prostate cancer

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ABSTRACT

Objective: Saturation biopsy is more sensitive than transrectal biopsy in the detection of prostate cancer but is an invasive method and has a risk of overdiagnosis. Multiparametric magnetic resonance imaging (mpMRI) provides imaging and working information of the prostate. The purpose of the study was to compare the performance of pelvic phased-array mpMRI against saturation biopsies in men with suspected advanced prostate cancer considering pathology of the surgical specimen as the reference standard.

Materials and methods: Data of men ($n = 81$) with prostate-specific antigen >10 ng/mL, low free-to-total ratio <0.1, and/or prostate-specific antigen density >0.15 who underwent mpMRI and saturation biopsy prior to radical prostatectomy were reviewed. The mpMRI was characterized as per Prostate Imaging Reporting and Data System v2.1. Gleason scores $\geq 3+4$ were considered as prostate cancer. The beneficial score was evaluated for each diagnostic method for the decision-making of prostatectomy.

Results: mpMRI was positive in 72 men, while saturated biopsies reported 57 men with positive prostate cancer. The histopathology of the surgical specimen reported prostate cancer in 76 men. mpMRI and saturated biopsies reported 0.934 and 0.737 sensitivities and 0.926 and 0.741 specificities, respectively. mpMRI had cancer detectability between 0.55 and 0.965 diagnostic confidence and saturation biopsies had cancer detectability between 0.85 and 0.952 diagnostic confidence. Above 0.965 and 0.952 diagnostic confidence, mpMRI and saturation biopsies had the risk of overdiagnosis.

Conclusions: mpMRI can provide additional information for the detection of prostate cancer before saturation biopsies.

Level of Evidence: III.

Abbreviations: mpMRI: Multiparametric magnetic resonance imaging; STROBE: strengthening the reporting of observational studies in epidemiology; T2WI: T2-weighted image; DWI: diffusion-weighted image; ADC: Apparent diffusion coefficient; DCE: Dynamic contrast-enhanced; STROCSS: Strengthening the reporting of cohort studies in surgery.

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KEYWORDS
Multiparametric magnetic resonance imaging; overdiagnosis; prostate cancer; prostatectomy; saturation biopsy

Introduction

The Chinese population has a higher risk of advanced prostate cancer than low and intermediate-risk prostate cancer [1]. For advanced prostate cancer, the widespread use of the prostate-specific antigen testing [2] and mass screening protocols have led to an increase in the detection rate of prostate cancer [3] but extended transrectal-ultrasound guided-biopsy and saturation biopsy are suggested for detection of prostate cancer [4]. Saturation biopsy is more sensitive than transrectal biopsy in the detection of prostate cancer [5]. Repeated prostate biopsies have the risk of overdiagnosis [2]. Also, it may miss insignificant tumors [4] and detect small low grades of cancer which have no risk over men's survival [3,6]. Also, biopsies have the risk of hematuria, urinary retention, urosepsis, urinary tract infections, hematospermia and sepsis [7]. Therefore, there is a requirement to reduce unnecessary biopsies to diagnose prostate cancer. Multiparametric magnetic resonance imaging (mpMRI) may provide valuable information regarding suspected prostate cancer among older men [6,8]. Also, it provides imaging and working information of the prostate [9]. However, there are many factors, for example, blood perfusion, different mpMRI sequence, temperature of body and magnetic susceptibility in the tissue, that may affect the results of the mpMRI. Also, the presence of prostatitis, hemorrhage, benign prostatic hyperplasia and fibrosis may increase the difficulties of mpMRI in the detection of prostate cancer [10].

The objective of the study was to compare sensitivities and specificities of pelvic phased-array mpMRI against saturation biopsies in men with suspected advanced prostate cancer (high risk of prostate cancer) considering the pathology of the surgical specimen as the reference standard.

Materials and methods

Ethics approval and consent to participate

The designed protocol (QUH/CL/26/19, dated 28 May 2019) of the established study was approved by the Qingdao

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University review board. The study reporting adheres to the law of China, strengthening the reporting of observational studies in epidemiology (STROBE) statement: cross-sectional studies, and the V2008 Helsinki Declaration. All the enrolled men signed an informed consent form regarding diagnosis, anesthesia, pathology, biopsies, radiology, surgeries and publication of the study, including personal images and data, irrespective of time and language during hospitalization.

Study population

From 1 May 2016 to 1 June 2019, a total of 81 men with prostate-specific antigen more than 10 ng/mL, a low free-to-total ratio less than 0.1, and/or a prostate-specific antigen density more than 0.15 underwent mpMRI and saturation biopsy prior to radical prostatectomy (laparoscopic or robot-assisted) at the department of urology of the Affiliated Hospital of Qingdao University, Qingdao, China. Men's data were reviewed for the clinical history of patients.

Multiparametric magnetic resonance imaging

mpMRI was performed 1-week before saturation biopsies. mpMRI examinations were performed using 3.0 T equipment (Ingenia 3.0 T, Philips Medical system, Amsterdam, the Netherlands) in the supine position of the patient using a surface 16 channels phased-array coil placed around the pelvic area of the men. Multiplanar turbo spin-echo T2-weighted images (T2WI), axial diffusion-weighted imaging (DWI), axial apparent diffusion coefficient (ADC) images, axial dynamic contrast-enhanced (DCE) imaging and spectroscopy were performed for each patient. 0.1 mL/kg Gadobutrol (Gadovist, Bayer Schering Pharma, Leverkusen, Germany) was injected at a rate of 3 mL/s followed by 15 mL of normal saline flash for DCE images [11]. Radiologists (a minimum of 3 years of experience) of the institute performed mpMRI.

Image analyses

The mpMRI was characterized as per Prostate Imaging Reporting and Data System v2.1 [12]. The presence of a circumscribed, low signal intensity lesion (hypointense) in T2WI, foci showing early and intense enhancement in DCE imaging, and any area where the choline-citrate ratio was $\geq$ 3.0 standard deviations above the mean healthy value in spectroscopy were considered as positive lesions [13]. Radiologists (a minimum of 5 years of experience in prostate imaging) of the institute were involved in image analysis.

Saturation biopsy

Saturation biopsies were performed through a Tru-cut 18 G needle (Merit Medical Systems, Inc., South Jordan, Utah, USA) and 7 MH_Z transrectal probe (GE Healthcare, Chicago, IL, USA) in a transperineal way under general anesthesia [13]. An average of 12 (range = 10–15) cores from the apex, middle zone and the base of the prostate and an average three (range = 2–4) cores from the anterior zone and transition zone were collected [3]. The samples were sent to the pathologist for evaluation. Pathologists (a minimum of 3 years of experience) of the institute performed biopsies.

Histopathology

Gleason scores $\geq 3+4$ were considered as prostate cancer [14,15]. Pathologists of the institute performed histopathological analyses.

Surgical method

Laparoscopic or robot-assisted radical prostatectomy was performed by urologists (a minimum of 3-years of experience) of the institute. The resected surgical specimens were sent to pathological departments for histopathological analyses (whole-mount step section method). The surgeries had been reported in line with the STROCSS (strengthening the reporting of cohort studies in surgery) criteria [16].

Beneficial score analysis

The beneficial score was evaluated for each diagnostic method for decision-making of prostatectomy as per equations (1) and (2) [1]:

$$\begin{aligned}&\text{Beneficial score}\\&= \frac{\text{Accurate positive prostate cancer detected}}{\text{Men subjected to prostatectomy}}\\&- \left(\frac{\text{False}-\text{positive prostate cancer detected}}{\text{Men subjected to prostatectomy}}\right.\\&\left.\times \text{Risk of overdiagnosis}\right.\end{aligned} \tag{1}$$

$$\begin{aligned}&\text{Risk of overdiagnosis}\\&= \frac{\text{Diagnostic confidence above which prostatectomy was performed}}{1-\text{Diagnostic confidence above which prostatectomy was performed}}\end{aligned} \tag{2}$$

Statistical analyses

InStat 3.0 GraphPad (San Diego, CA) was used for statistical analyses. Fisher's exact test [17] was performed for statistical analysis between ordinal data. The results were considered significant at a 95% confidence level.

Results

Clinical parameters

All men had normal digital rectal examinations. The other clinical parameters of men are reported in Table 1.

Table 1. Demographical and clinical parameters of men.

Parameters	Value
Data of men included in analyses	81
Age	
Minimum	51
Maximum	65
Mean ± SD	50.49 ± 4.15
Ethnicity	
Han Chinese	72 (89)
Mongolian	8 (10)
Tibetan	1 (1)
PSA (prostate specific antigen) (nG/mL)	
Minimum	10.11
Maximum	17.12
Mean ± SD	14.12 ± 3.45
*Prostate volume (cm^3)	45.57 ± 5.55
Radical prostatectomy	
Laparoscopic	39 (48)
Robot-assisted	42 (52)

Ordinal data are presented as frequency (percentage) and numerical data are presented as mean ± SD.
*Detection of fresh specimen.

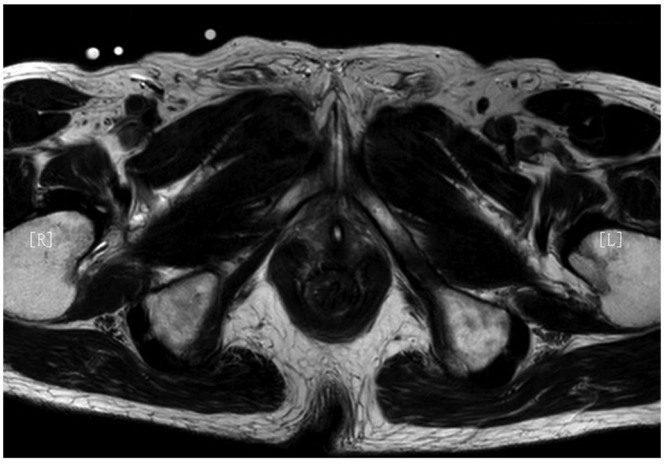

Figure 1. Axial multiplanar turbo spin-echo T2-weighted images. Age = 58 years. PSA = 13.15 ng/mL.

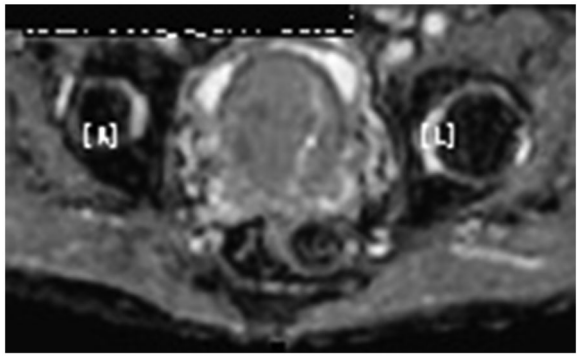

Figure 2. Axial diffusion-weighted image. Age = 58 years. PSA = 13.15 ng/mL.

Imaging analyses

T2WI clearly showed enhancement patterns to detect prostate cancer (Figure 1). DWI provided an aggressiveness of tumor (Figure 2). The ADC image correlated negatively with the Gleason score of pathological findings (Figure 3). DCE imaging provided a clear vision of contrast-enhancement (Figures 4 and 5).

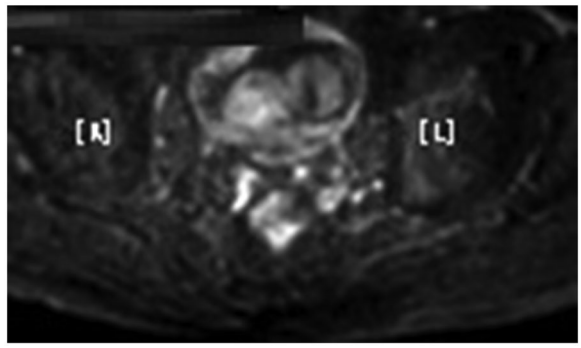

Figure 3. Axial apparent diffusion coefficient image. Age = 58 years. PSA = 13.15 ng/mL.

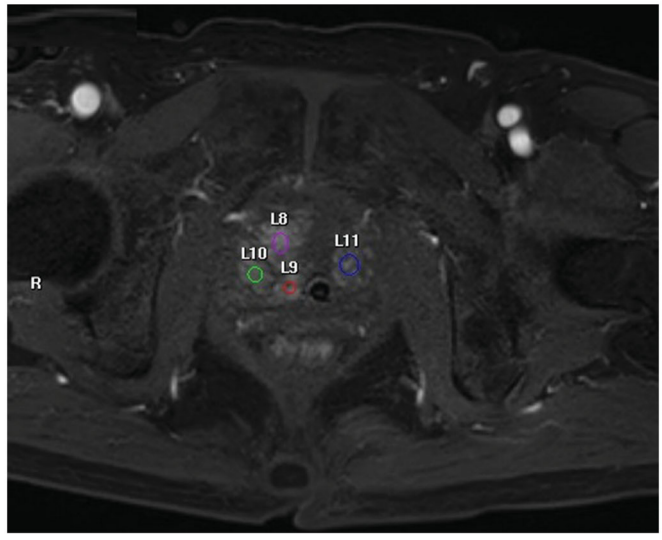

Figure 4. Axial dynamic contrast-enhanced image. Age = 58 years. PSA = 13.15 ng/mL.

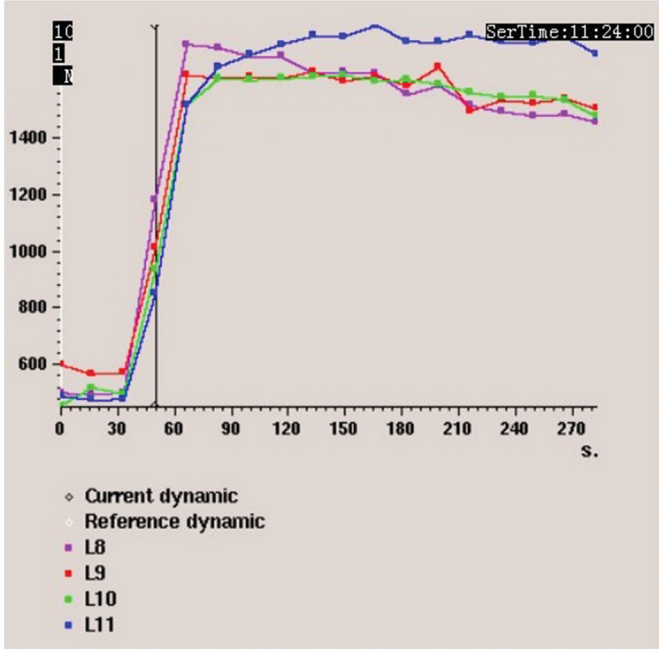

Figure 5. Dynamic chart. Age = 58 years. PSA = 13.15 ng/mL.

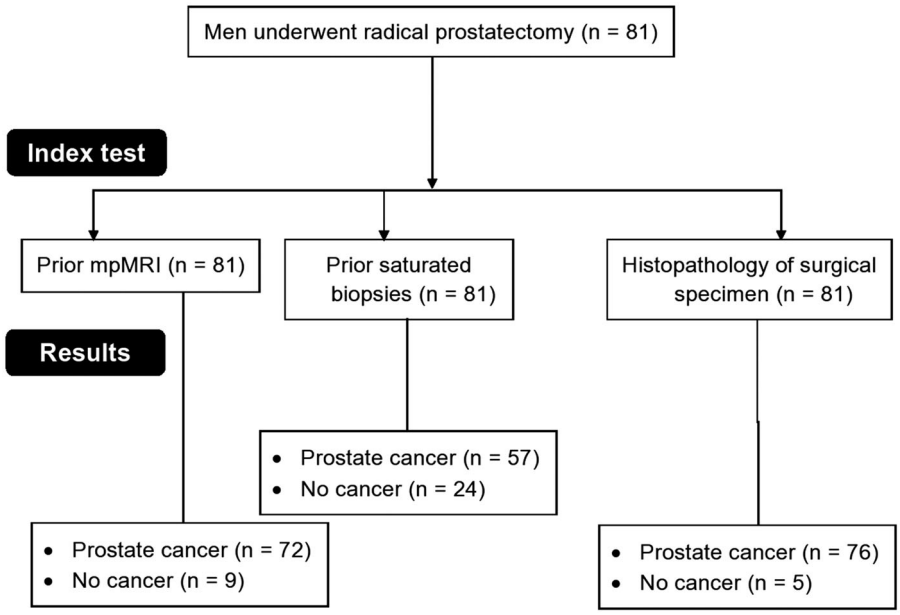

Figure 6. Flow chart of the study.

Table 2. Diagnostic parameters.

Parameters	The histopathology of the surgical specimen	Multiparticulate magnetic resonance imaging		Saturated biopsies	
Data of men included in analyses	81	81	p**	81	p**
True positive prostate cancer detected	76 (94)	71 (88)	0.278	56 (69)*	< 0.0001
True negative prostate cancer detected	5 (6)	4 (5)	1.0	4 (5)	1.0
False positive prostate cancer detected	0 (0)	1 (1)	1.0	1 (1)	1.0
False negative prostate cancer detected	0 (0)	5 (6)	0.059	20 (25)*	< 0.0001
Sensitivity	1	0.934	0.278	0.737*	< 0.0001
Accuracy	1	0.800	1.0	0.800	1.0
Specificity	1	0.926	1.0	0.741*	< 0.0001

Ordinal data are presented as frequency (percentage) and numerical data are presented as mean.
Fisher's exact test was performed for statistical analysis.
A p-value of less than 0.05 was considered statistically significant.
*Statistical difference with reference to the histopathology of the surgical specimen.
**With reference to the histopathology of the surgical specimen.

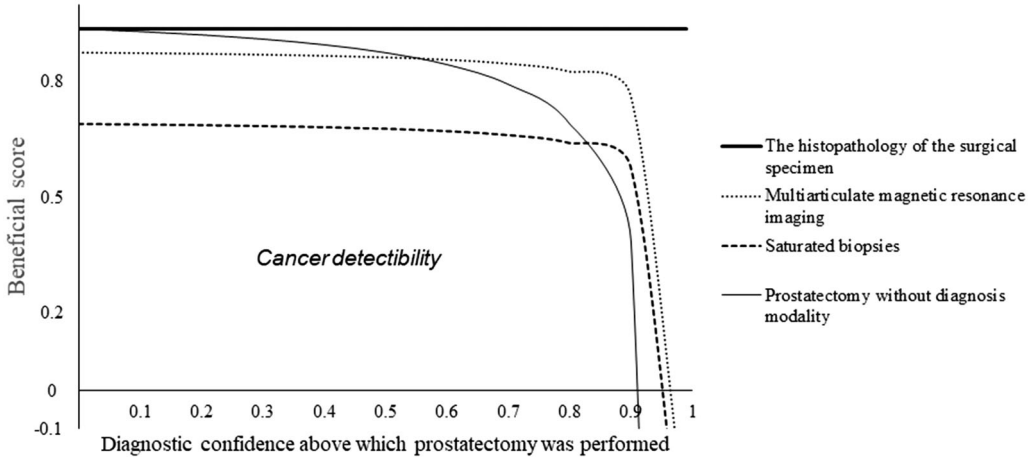

Figure 7. Beneficial score analyses. Making surgery without confirmation of prostate cancer diagnosis is imaginary for evaluation purposes only.

Diagnostic parameters

mpMRI was positive in 72 men while saturated biopsies reported 57 men with positive prostate cancer. Urologists decided on radical prostatectomy in all 81 men. However, the histopathology of the surgical specimen reported prostate cancer in 76 men (Figure 6). mpMRI and saturated biopsies reported 0.934 and 0.737 sensitivities and 0.926 and 0.741 specificities, respectively. The detailed diagnostic parameters are reported in Table 2.

Beneficial score analysis

mpMRI had cancer detectability between 0.55 and 0.965 diagnostic confidence and saturation biopsies had cancer detectability between 0.85 and 0.952 diagnostic confidence (Figure 7). Above 0.965 and 0.952 diagnostic confidence mpMRI and saturation biopsies had the risk of overdiagnosis. Also, below 0.55 and 0.85 diagnostic confidence mpMRI and saturation biopsies had no diagnostic importance for the decision-making of prostatectomy, respectively.

Discussion

Saturation biopsies had 0.737 and 0.741 sensitivity and specificity, while mpMRI had 0.934 and 0.926 sensitivity and specificity. The results of the study were parallel with the population-based prostate cancer screening study [3,6], the prospective study [4] and retrospective reviews [9,13]. In saturation biopsies, there are higher chances of biopsy-related complications because higher numbers of cores are collected [5] and Gleason scores 6 and 7 have close proximity [4]. Besides saturation biopsies, mpMRI should be performed for the detection of cancer in men with suspected advanced prostate cancer.

The study reported that cancer detectability was higher for mpMRI and saturation biopsies had a higher risk of overdiagnosis. In saturation biopsies, there is a need for detection of every small cancer focus, which leads to overdiagnosis [5]. mpMRI is the preferred imaging technique for the detection of prostate cancer before surgery.

mpMRI and saturation biopsies detected five and 20 false-negative lesions. Large numbers of collections of cores in saturation biopsies do not guarantee high sensitivity and specificity [5]. 3.0 T mpMRI using a surface coil is a more accurate and non-invasive technique in predicting prostate cancer than pathological findings.

mpMRI and saturation biopsies detected one lesion each as false-positive lesions. Inflammation of the prostate may act as ghost prostate cancer in a mpMRI scan and inadequate histopathology may lead to false-positive cancer in saturation biopsies [1]. mpMRI may have a high success rate in the detection of prostate cancer.

In the limitations of the study, for example, mpMRI has a higher cost than saturation biopsies [18], but the cost factor was not evaluated in the study. Inter- and intra-observer agreement were not performed. The small sample size leads to an issue of generalizability.

In conclusion, for men with suspected advanced prostate cancer, mpMRI can provide additional information for the detection of prostate cancer before saturation biopsies. A combination of mpMRI and saturation biopsies may increase the detection rate of prostate cancer.

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Disclosure statement

The authors declared that they have no conflict of interest or any other competitive interest regarding results and/or discussion reported in the research.

Authors' contributions

Both authors read and approved the manuscript for publication. GL was the project administrator, contributed to conceptualization, methodology, validation, software and literature review of the study. TY contributed to the investigation, literature review, supervision, data curation and formal analysis of the study and drafted, reviewed and edited the manuscript for intellectual content. The authors agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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