Multiparametric prostate MRI and cognitively targeted transperineal biopsy in patients with previous abdominoperineal resection and suspicion of prostate cancer.

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Introduction

Prostate cancer (PCa) is the commonest male cancer as well as the second leading cause of cancer death in men.[1] The standard cancer screening protocol includes serum prostate specific antigen (PSA) testing and digital rectal examination (DRE). If either are abnormal, prostate biopsy with subsequent histopathologic evaluation represents the gold standard for establishing the diagnosis.[2] Prostate biopsy can be performed either by the more traditional transrectal approach or by the increasingly popular transperineal route, using a transrectal ultrasound probe for needle guidance. In both methods, rectal access is essential. Abdominoperineal resection (APR) is a common surgical technique performed in a selected group of patients with inflammatory bowel disease (IBD), carcinoma of the distal rectum or anal canal and familial adenomatous polyposis (FAP). It involves resection of the distal part of the sigmoid colon, rectum, anus and the creation of a permanent end-colostomy.[3] As life expectancy in patients with IBD and FAP is not significantly lower than that of the general population and the 5-year-survival rate in stage T1 and T2 colorectal tumours treated with APR was found to be 78%, it is not uncommon to encounter post-APR patients presenting with a raised PSA and suspicion of prostate cancer.[4] The lack of rectal access means that such patients pose a diagnostic challenge.

Previously described diagnostic approaches in this cohort include biopsy by either a transperineal or transgluteal approach and under the guidance of ultrasound (transperineal, transabdominal or transurethral), magnetic resonance imaging (MRI) or computed tomography (CT). [5-14] Cancer detection rates ranged

from 40 - 82 %,[7-14] but even in the largest cohort, detection of intermediate to high grade prostate cancer (Gleason score ≥7) was low at 43%.[12] However, all studies to date have used a systematic biopsy approach and did not use MRI prior to biopsy to target suspicious areas.

Recently, multi-parametric Magnetic Resonance Imaging (mpMRI) has been shown to be effective for the detection and local staging of prostate cancer and can preferentially detect clinically relevant index tumours of higher grade and a size >5 mm.[15] A normal mpMRI also has a high negative predictive (>90%) for the presence of clinically significant disease.[16] Using transperineal MR/US fusion biopsy, the detection rate for clinically significant disease has been shown to be as high as 72%.[17] The aim of this study was to evaluate if the use of multiparametric MRI and subsequent cognitively targeted US-guided (by visual registration) transperineal biopsy improves cancer detection and particularly detection of significant cancer in patients with abdominoperineal resection and a suspicion of prostate cancer.

Patients and Methods

Study population

This single-institution retrospective study was part of a service evaluation of transperineal prostate biopsies with the need for informed consent for data analysis waived by the local ethics committee (Local audit evaluation number 4058). The study population consisted of 11 consecutive patients who presented to our institution between March 2010 and May 2015 with elevated PSA, a history of abdominoperineal resection of the rectum and undergoing prostate MRI at our institution prior to biopsy.

Magnetic resonance imaging

Patients underwent prostate MRI on a 1.5T MR450 or 3.0T Discovery MR750 HDx (GE Healthcare, Waukesha, USA) with an 8-16 channel surface phased array coil. Axial Fast Spin Echo T1-weighted images of the pelvis, along with T2-Weighted Fast Recovery Fast Spin Echo images of the prostate were acquired in the axial, sagittal and coronal planes (TE/TR = 85/3700-5000 ms; field-of-view (FOV) 24x24 cm; matrix 256x256; slice thickness 3 mm; gap 1 mm). Diffusion-weighted (DW) imaging was performed using a spin-echo echo-planar imaging pulse sequence (TE/TR=60/3000-3400 ms; matrix 256x256; slice thickness 4 mm; gap 0 mm, FOV: 1.5T: 24x24 cm, 3.0T: 28x28 cm; parallel imaging factor of 2; signal averages: 3 for 1.5T and 8 for 3.0T. The following b-values were

acquired: b-150, b-750, b-1,400 s/mm2; apparent diffusion coefficient (ADC) maps were automatically calculated and stored.

Image analysis

The MR images were prospectively reported by body radiologists experienced in reading prostate MRI. T2WI and DWI sequences were evaluated using a Likert scale of tumour probability, based on the Prostate Imaging Reporting and Data System (PI-RADS) structured scoring criteria developed by the European Society of Urogenital Radiology (ESUR).[18] The Likert-based scoring system was as follows: 1 = cancer highly unlikely, 2 = cancer unlikely, 3 = indeterminate for cancer, 4 = cancer likely, 5 = cancer highly likely. A positive MRI was defined as a score of ≥ 3. The location of the lesion was communicated in the report descriptively for earlier cases, and subsequently using the standardized sector map first proposed by Dickinson et al.[19]

Biopsy

Patients with a Likert score of 3-5 underwent transperineal ultrasound-guided biopsies under general anaesthesia. Transperineal biopsies were performed by a urologist (XX) with 29 years experience in prostate biopsy and 8 years experience in transperineal biopsy. The procedure was performed using transperineal ultrasound-guidance from one of two experienced radiologists (XX, XX). Each patient was placed in the lithotomy position, with the scrotum retracted

anteriorly. Bladder filling was not routinely employed as a transvesicular imaging plane was not chosen.

All ultrasound scanning was performed on a Toshiba Aplio 500 machine (Toshiba Medical Systems, UK) using a curved linear array ultrasound transducer with a centre frequency of 3.5MHz, range 1.9-6 MHz. The transducer was enclosed in a rubber sheath with sterilised ultrasound gel for transmission. Direct contact was made to the skin in the midline sagittal plane, to allow lateral transperineal needle access (Figure 1). Biopsies were obtained using an automatic spring driven biopsy device mounted with an 18-gauge biopsy needle (Bard biopsy systems, Tempe, USA) via a caudal approach to the prostate. The needle was directed to target areas by visual registration and systematically to background prostate by the operator, with position confirmed on US prior to sampling (Figure 2).

Histopathology

Biopsies were reviewed by a single sub-specialist uropathologist. Each core was measured, and the total number of cores with cancer and the percentage of cancer recorded. Pathology reports identified the Gleason Score for each side of the prostate, and the target.

Results

11 men with a median age of 68 years (range 63 - 77 years) were included with a median PSA of 9.4 ng/ml (mean 13.6; range 3.2 - 60 ng/mL); **Table 1**. The mean prostate volume was 37.8 ml (median 35; range 24 - 49 ml). Abdominoperineal resection had been performed for ulcerative colitis (7 patients), Crohn's disease, Hereditary nonpolyposis colorectal cancer, rectal carcinoma, and Canada-Cronkheit syndrome. The mean interval from MRI to biopsy was 57.6 days (range 22 - 106 days).

Transperineal ultrasound guided biopsies were successfully completed in 9 cases. On average 16.7 (range 11 - 27) biopsy cores with a median of 5 (range 3-7) target cores were obtained under ultrasound guidance. All patients undergoing biopsy were discharged on the day of procedure, 2/9 patients experienced acute urinary retention after biopsy, 1 described mild perineal discomfort, the other 6 had no ill effects. Of the 9 biopsies performed, 7 (78%) revealed prostate cancer with a Gleason score ranging from 6 - 10. 6/9 (67%) cases revealed a Gleason score of ≥7, 1/9 cases (11%) revealed a Gleason score of 6. Median cancer core length was 2 mm (range 1 - 19mm). Treatment choices in patients with confirmed prostate cancer included open radical prostatectomy in 2 patients, external beam radiation therapy in 2, active surveillance in 2, and androgen deprivation therapy in 1.

9 patients exhibited suspicious lesions on MRI (**Figure 2**). Five patients had suspicious lesions in the posterior peripheral zone and four patients in the anterior transition zone. The median lesion diameter was 15 mm (range 7-25 mm). All 7 patients with highly suspicious lesions (Likert 4-5) on MRI had subsequent biopsy-proven tumour: 6 cases revealed Gleason score ≥7 cancer, with 1 case of Gleason grade 3+3. Biopsies from the target and adjacent area did more often contain cancer than background cores with higher number of positive cores in all seven cases, higher percentages of cancer involvement in all seven cases and/or higher Gleason scores in five cases.

The 2 cases with MR lesions of an intermediate probability score of 3/5 revealed benign tissue at biopsy. Two patients with a negative MRI did not undergo biopsy. The 4 patients with no histological diagnosis of prostate cancer had stable PSA levels at follow-up, with PSA-monitoring performed at 3 months for one year and 6-monthly thereafter; mean follow-up 17.5 months (range 7 - 28 months)

Comment

Our study shows that multiparametric prostate MRI is feasible and useful for targeted transperineal biopsy guided by visual registration in patients with abdominoperineal resection and a suspicion of prostate cancer. The overall cancer detection rate was 7/9 (78%) with 6/9 (67%) cases demonstrating a Gleason score of 7 or higher. This compares favourably to previously published studies without prior MRI, reporting overall cancer detection rates of 20% (2 of 10 patients), 40% (2/5), 43% (3/7), 60% (6/10) and 82 % (23/28).[7-10,12] It has previously been shown that pre-biopsy MR imaging increases biopsy performance in detecting prostate cancer and especially clinically significant cancer, via both a transperineal and transrectal approach using MR/US fusion techniques.[17,20] Although our high detection rate of clinically significant cancers may partially be explained by patients without rectal access presenting with larger and more significant cancers due a delayed diagnosis,[20] our detection rate of 67% for Gleason score ≥7 disease is notably higher than any of the equivalent series that have previously been reported.

Our data suggests that patients with abdominoperineal resection benefit from a pre-biopsy multiparametric MRI and, in the case of suspicious lesions with a Likert score of 4-5, should undergo targeted transperineal biopsy guided by visual registration. In our study population, 6/7 cases with highly suspicious MRI lesions (Likert 4-5) revealed clinically significant adenocarcinomas with a

Gleason score of 7 or higher, with 1 case of low-risk Gleason score 6 prostate cancer. The results are in accordance with a meta-analysis of patients with rectal access undergoing MRI prior to initial targeted biopsy of the prostate with an overall detection rate of 65% for prostate cancer and 49% for significant disease.[21] Additionally, a recent study using targeted transperineal biopsy with rectal access for MR/US fusion found that 85% (89/104) of patients with highly suspicious lesions on MRI were diagnosed with prostate cancer in the biopsy, including 60% (62/104) with high risk cancer of GS of 7 or greater.[17] A fusion approach is not possible in the setting of prior APR and image guidance by visual registration despite its operator-dependence is the only means of biopsy targeting. Previous studies have reported contradicting results when comparing visually-registered and software-registered MR/US fusion targeted transrectal biopsies after prebiopsy MRI: with one demonstrating equivalence,[20] another showing increased detection with software-registration biopsy, especially for smaller lesions,[22] and a third, larger study, concluding that software-registration biopsy was more histologically informative but did not increase cancer detection.[23] An alternative to biopsies guided by visual estimation would be real-time in-bore MRI-targeted biopsies, via a transperineal or transgluteal approach,[24,25]however, this is cost- and time-intensive, requires special MR-safe equipment, and is not available at all centers. In our study, the 2 cases with Likert 3 MR lesions revealed benign tissue upon biopsy. It may therefore be possible to avoid biopsy in patients with intermediate risk MRI, but this is a controversial area. Previous studies in patients without APR, showed a yield of

any cancer of 20-25% in intermediate probability cases, although typically the majority of these are low risk cancers.[26,27]

A limitation of our study is its retrospective nature and the small population size, especially the patients without suspicious lesions on MRI. The lack of prostatectomy as a gold standard in all but two patients is also a limitation, and we therefore cannot exclude some smaller tumours being missed. Another limitation of MRI –targeted transperineal biopsies guided by visual registration is the difficulty of ultrasound guidance. Needle visualisation can be challenging due to lateral entry point of the needle to the ultrasound probe and the off-plane trajectory taken, additionally the beam may be scattered by the fibromuscular layers of the pelvic floor or surgery-related scarring. Theoretically these effects could be exacerbated in glands with larger volume, more heterogeneous transition zone, however, significant BPH was not present in our cohort (gland volume 24 - 49 ml). Patient body mass index (BMI) is less likely to have an affect given the transperineal approach. Steps taken to improve visualisation included small movements of the needle to ascertain position indirectly through tissue motion, incremental tilting and rotation of the probe to change beam position, or even switching to the transverse plane (**Figure 3**). Although not employed here, consideration could also be given to catheterisation to aid urethral land-marking and help establish the prostatic midpoint.

We describe the first use of MRI to aid targeting of prostate biopsies in patients

post APR, with the approach achieving promising results in this challenging patient group. Our findings could also be extended to the group of patients with ileal pouch/anal anastomosis, where transpouch biopsy of the prostate may risk pouch fistulas or abscesses.[28-30]

Conclusions

In conclusion, the use of multiparametric prostate MRI and subsequent targeted transperineal biopsy guided by visual registration can aid in the diagnostic pathway of patients with abdominoperineal resection and a suspicion of prostate cancer.

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Legends to illustrations

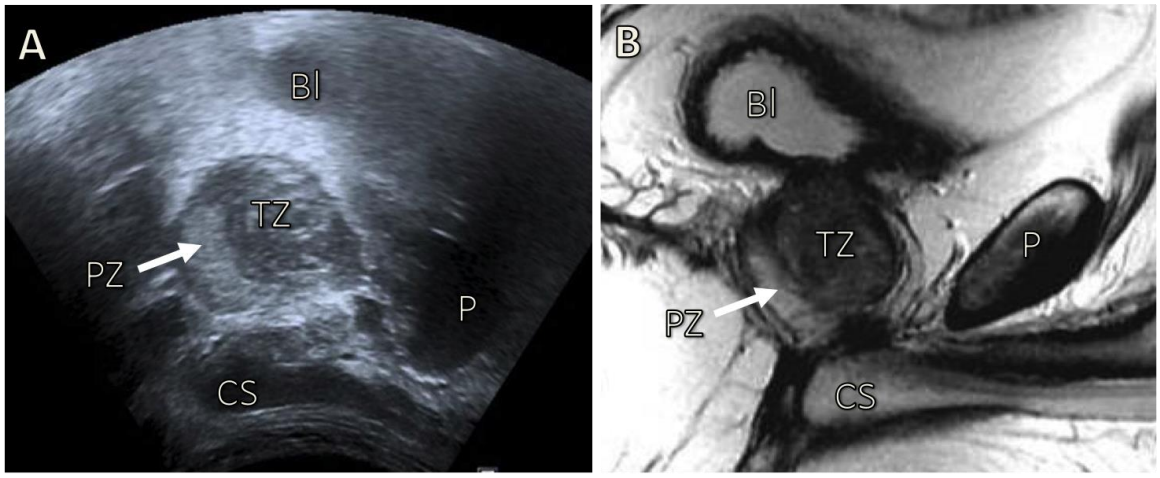

Fig. 1 Transperineal ultrasound views

A: ultrasound image in the sagittal (longitudinal) plane. B: sagittal T2-weighted MR image at the same level. PZ = peripheral zone of prostate; TZ = transition zone; CS = corpus spongiosum; Bl = bladder; P = pubic bone

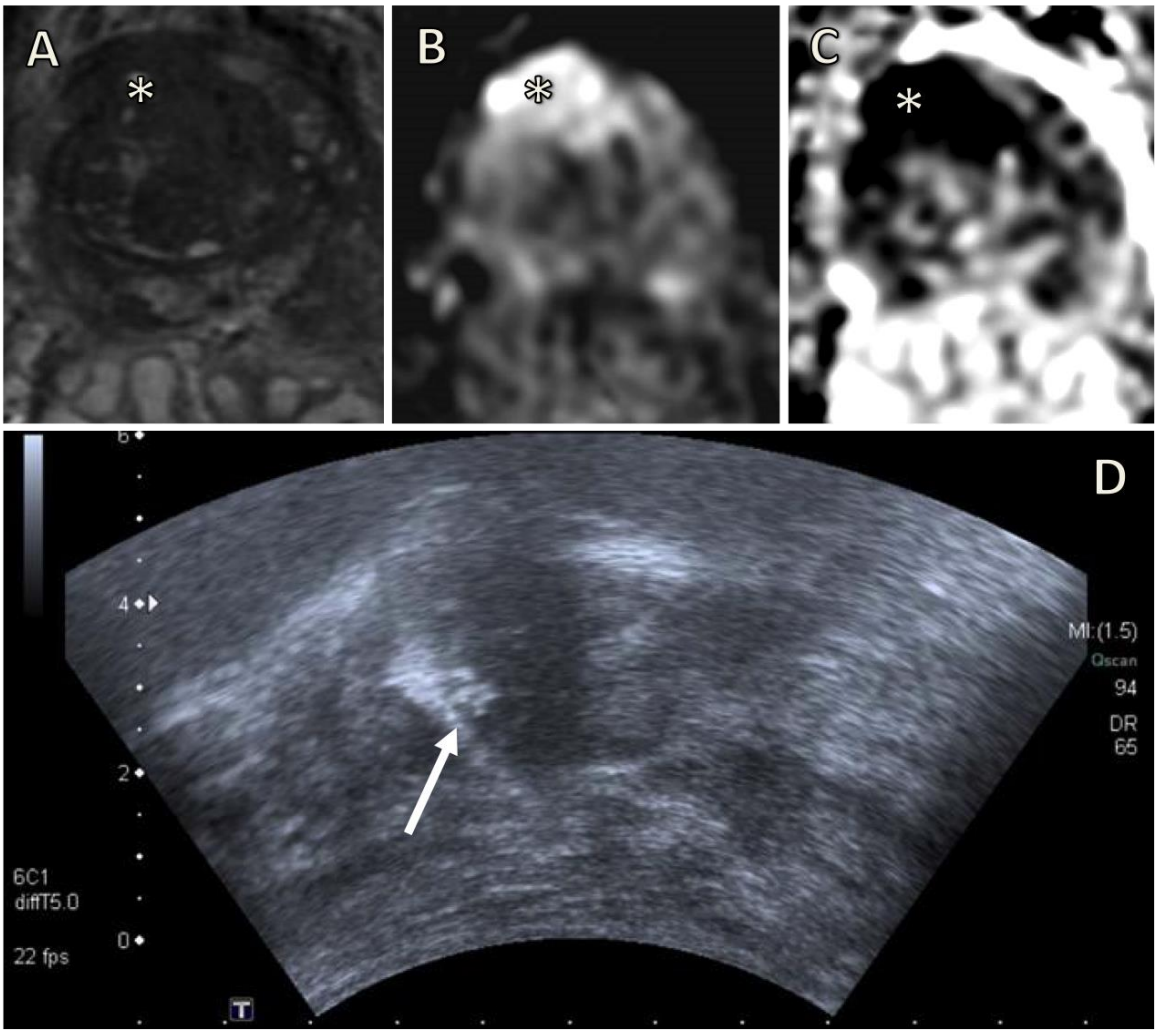

Fig. 2 High probability MRI target

66 year old patient with PSA 11.74 ng/ml and previous total colectomy for Canada-Cronkhite syndrome. A-C: MRI shows a high probability 2.5 cm lesion in the anterior right base transition zone (*) with low T2 signal intensity (A) and restricted diffusion with high signal on the b-1400 images (B) and low ADC value (C). D: Sagittal plane ultrasound image of transperineal biopsy needle (arrow) guided to this region. Subsequent pathology confirmed Gleason 4+3 disease

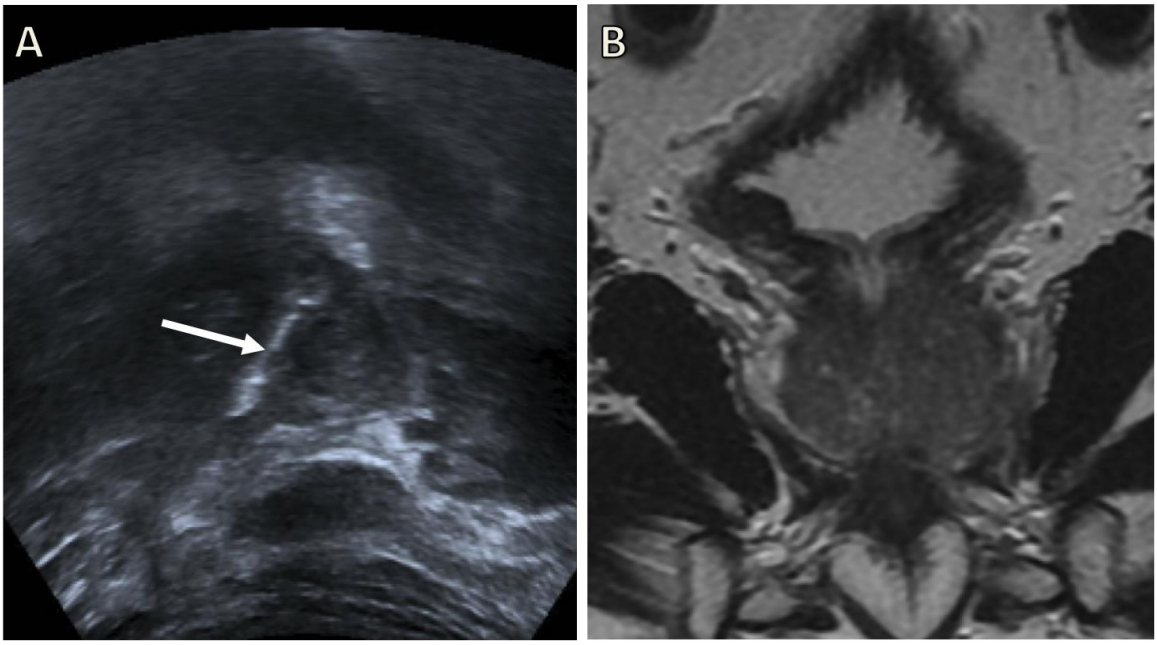

Fig. 3 Ultrasound biopsy guidance: Switching to coronal plane for needle visualisation

68 year old patient with PSA 3.2 ng/ml and strong family history of prostate cancer and low probability MRI. A: Ultrasound switched to coronal (transverse) plane to aid needle visualisation (arrow). B: Coronal T2-weighted MR image at an equivalent position

Tables

Table 1 Results for patients who underwent transperineal prostate biopsy listed in order of date of procedure

Patient	Age (years)	Indication for anorectal resection	Time since resection (years)	PSA (ng/mL)	Volume (mL)	PSA Density (ng/mL/mL)	MRI results	Max Lesion diameter (mm)	Interval MRI to biopsy (days)	Number of Cores (n)	Number of positive Cores (n)	CCL (mm)	Biopsy Result (Gleason score)	Management
1	72	UC	22	60	28	2.14	+	15	22	11	3	3	5+5	ADT
2	77	Rectal Ca	5	15.7	31	0.51	+	16	70	19	6	10	3+5	EBRT
3	77	UC	2	14.8	45	0.33	+	14	34	13	1	1	4+3	Neoadjuvant ADT, EBRT
4	65	UC	43	5.2	24	0.22	+	10	106	12	2	1	3+3	AS
5	65	UC	n/a	7.1	26	0.27	+	9	58	27	0		Benign	PSA Follow-up, stable
6	66	CCS	30	11.7	34	0.35	+	25	83	16	5	2	3+4	AS
7	63	HNPCC	14	3.2	49	0.07	+	7	68	21	0		Benign	PSA Follow-up, stable
8	70	UC	7	9.4	44	0.21	+	15	43	13	5	2	4+5	Neoadj ADT, prostatectomy
9	65	UC	25	3.9	35	0.11	+	16	34	18	12	19	4+5	prostatectomy
10	68	Crohn’s	40	8.8	59	0.15	-							PSA Follow-up, stable
11	68	UC	6	9.6	41	0.23	-							PSA Follow-up, stable

HNPCC = Hereditary nonpolyposis colorectal cancer, UC = ulcerative colitis, CCS = Canada-Cronkheit syndrome, AS = active surveillance, ADT = androgen deprivation therapy, GI = Gleason, EBRT = external beam radiotherapy, PSA = prostate specific antigen