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A Multi-Reader Exploratory Evaluation of Individual Pulse Sequence Cancer Detection on Prostate Multiparametric MRI

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Abstract

Purpose—To determine independent contribution of each prostate multiparametric MRI (mpMRI) sequence to cancer detection when read in isolation.

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Methods—Prostate mpMRI at 3T with endorectal coil from 45 patients (n=30 prostatectomy cases, n=15 negative MRI/biopsy controls) were retrospectively interpreted. Sequences (T2W, DWI, DCE MRI) were separately (N=135) distributed to 3 radiologists at different institutions. Readers evaluated each sequence blinded to other mpMRI sequences. Findings were correlated to whole-mount pathology. Cancer detection sensitivity, positive predictive value for whole prostate (WP), transition zone (TZ) and peripheral zone (PZ) were evaluated per sequence by reader, with reader concordance measured by index of specific agreement (ISA). Cancer detection rates (CDR) were calculated for combinations of independently read sequences.

Results—44 patients were evaluable (cases median PSA 6.83 [1.95–51.13] ng/mL, age 62 [45–71] years; controls PSA 6.85 [2.4–10.87] ng/mL, age 65.5 [47–71] years). Readers had highest sensitivity on DWI (59%) versus T2W (48%) and DCE (23%) in WP. DWI-only positivity (DWI+/T2W–/DCE–) achieved highest CDR in WP (38%), compared to T2W-only (CDR 24%) and DCE-only (CDR 8%). DWI+/T2W+/DCE– achieved CDR 80%, an added benefit of 56.4% from T2W-only and of 42% from DWI-only ($p<0.0001$). All 3 sequences interpreted independently positive gave highest CDR of 90%. Reader agreement was moderate (ISA: T2W=54%, DWI=58%, DCE=33%).

Conclusions—When prostate mpMRI sequences are interpreted independently by multiple observers, DWI achieves highest sensitivity and CDR in TZ and PZ. T2W and DCE MRI both add value to detection, mpMRI achieves highest detection sensitivity when all 3 mpMRI sequences are positive.

Keywords

Multiparametric; MRI; prostate; sequence; PI-RADSv2

Introduction

Prostate multiparametric MRI (mpMRI) has become an established method for localizing clinically significant prostate cancer and for informing subsequent treatment planning decisions (1–3). The technique combines anatomical data from T2-weighted MRI (T2W) with functional data from diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) MRI to provide up to 90% reported sensitivity in detection of significant disease (4). mpMRI interpretation inherently relies on findings across multiple sequence images; however, the degree to which each pulse sequence contributes to overall detection sensitivity remains unclear.

Perception of the contribution of each pulse sequence has evolved. Initial Prostate Imaging-Reporting and Data System (PI-RADS) guidelines for standardization of prostate MRI interpretation assumed equal diagnostic weight for each of the 3 sequences, while the current PI-RADSv2 has weighted sequences differently depending on the lesion location within the prostate (5). The change was based on expert consensus and zone-focused data reflecting possibly optimal cancer detection in the transition zone (TZ) from T2W sequences and in the peripheral zone (PZ) from DWI sequences (6–9). However, these studies, along with recent PI-RADSv2 validations, are almost always based on mpMRI evaluations using complete multiparametric MRI sets (10–13). In this context, conclusions about the value of

individual sequences in cancer detection are subject to innate reader bias as each sequence validates the other in the reader's mind. Moreover, such studies are often based on a single institution's experience. As a result, there is continued uncertainty about the true value of each mpMRI sequence in cancer detection. Therefore, the purpose of this work was to determine the independent contribution of each prostate mpMRI sequence to cancer detection when read in isolation.

Materials and Methods

Study Population

This Health Insurance Portability and Accountability Act-compliant retrospective evaluation of prospectively acquired data was approved by local ethics committee. Written informed consent was given by all patients. Flow-diagram illustrating patient exclusion and inclusion is given in Figure 1. All patients underwent complete mpMRI [T2W, DWI (ADC map, *b*-2000 DWI acquisition), DCE MRI] at 3-Tesla with endorectal coil performed at one institution. In population of consecutive patients imaged between April 2012 and June 2015 considered for inclusion, 179 underwent radical prostatectomy and 92 had no lesions detected on mpMRI and subsequent negative 12-core systematic biopsy guided by mpMRI-transrectal ultrasound fusion technique using the Uronav platform. Patients were excluded for receiving any prior treatment, artifacts arising from hip prostheses, or if acquired mpMRI was missing any sequences. Cases were additionally excluded if whole mount specimen mapping with lesion-specific Gleason scores was not available (total exclusions n=69 cases, n=3 controls). From remaining eligible patients, 45 (n=30 cases, n=15 controls) were randomly selected in a 2:1 ratio of cases:controls for study inclusion. Indications for imaging included rising PSA with prior negative biopsy (n=12 controls), high measured PSA without prior biopsy (n=3 controls), referral for fusion-guided biopsy and cancer staging (n=29 cases), and referral for cancer staging after a positive biopsy (n= 1 case). Patients originally presented to [Institution] as part of accrual for an [Institute]-sponsored approved protocol.

Study Design

As this method of studying independent sequence cancer detection did not suggest an ideal set-point for facilitating statistical powering, the study was conducted as a small pilot study and the sample size utilized reflects its exploratory purpose. The patient population is a subset of patients from a larger ongoing multi-reader study of a computer-aided diagnosis system.

Three radiologists participated as readers. All were from different institutions, highly experienced with prostate mpMRI (>2000 cases each in last 2 years), and familiar with reading endorectal coil mpMRI. Readers were blinded to clinical and pathologic data while conducting reads. Readers were asked to independently evaluate each sequence in the following manner:

Each complete mpMRI data per patient was split into three individual MR sequences and separately anonymized within the following groupings: T2W (axial and sagittal sets), DWI

(ADC map and $b=2000$ DWI sets), and DCE MRI (raw data of time points at each slice location). The resultant set of 135 anonymized pulse sequence datasets were randomly ordered and distributed to readers for interpretation.

MRI Technique

All MR images were acquired at 3-Tesla (Achieva 3.0T-TX, Phillips Healthcare, Best, Netherlands) using an endorectal coil (BPX-30, Medrad, Pittsburgh, PA, USA) filled with 45 mL perfluorocarbon-based fluid (Fluorinert, 3M, Maplewood, MN, USA) and anterior half of a 32-channel cardiac SENSE coil (InVivo, Gainesville, FL, USA). All patients underwent complete mpMRI protocol, which consisted of the following sequences: T2W (axial, coronal, sagittal), DWI (Apparent diffusion coefficient (ADC) map calculated from five evenly spaced b -values between 0–750 sec/mm^2 and an acquired high b -value image of $b=2000 \text{ mm/sec}^2$), and DCE MRI. Full mpMRI parameters are given in Table 1.

MRI Interpretation

Readers were instructed to use RadiAnt DICOM Viewer to view images (14). All 135 sequences were randomized per reader, and provided in this order with a read-out form designed with Microsoft Access (15). Within this programmed form, shown in Figure 2, readers recorded up to 4 detected lesions per sequence. Readers identified suspicious regions on each sequence utilizing visual patterns characteristic for tumor as outlined in PI-RADSv2 (5). For each lesion detected, readers recorded lesion location (zone and side of prostate), annotated the provided MRI sequence to delineate the diameter of the identified lesion, and uploaded a screenshot. All data was recorded in a linked Microsoft Access database.

Pathology Correlation

After mpMRI, case patients underwent robotic-assisted radical prostatectomy. For optimal image-pathology correlation, all prostate specimens were processed with patient specific MRI-based 3D-printed molds with sections cut spanning apex to base (16). One highly experienced genitourinary pathologist annotated the location of cancerous regions and lesion-specific Gleason scores ($\leq 3+3$) were assigned. A prostate mpMRI-focused research fellow performed radiologic-pathologic correlation using screenshot annotations of detected lesions from each reader. MR lesions detected were correlated to the pathology maps using visible prostate landmarks and lesion morphology. Lesions outlined on pathology but not detected by any readers were noted as false negative reads in subsequent analysis.

Statistical Analysis

Lesions were considered detected by a reader if a screenshot was uploaded showing clear annotation of the lesion on the sequence, with a category assigned. Reader-based lesion detection sensitivity was evaluated for each sequence. Concordance of lesion detection across readers was measured by index of specific agreement (ISA), defined as the conditional probability of an individual reader, randomly selected, detecting a lesion in the same location as a blinded, independent reader. Pairwise ISAs were calculated over three pairs of readers and average ISA was reported. Cancer detection rate (CDR) was defined as the proportion of true positive lesions among all detected lesions (sum of true positives and

false positives), and was calculated as the weighted average of reader CDRs. For example, a single unique lesion detected by all readers would be considered as three total lesions. This weighted average serves to minimize the variability of CDRs in categories where the number of lesions was small. All detected lesions were classified based on independent positivity read from all three sequences, lending to seven possible combinations of sequence detection positivity for each reader: T2W+/DWI-/DCE- (T2W-only), T2W-/DWI+/DCE- (DWI-only), T2W-/DWI-/DCE+ (DCE-only), T2W+/DWI+/DCE- (T2W+ DWI+), T2W+/DWI-/DCE+ (T2W+ DCE+), T2W-/DWI+/DCE+ (DWI+ DCE+), and T2W+/DWI+/DCE+ (all positive). Sensitivity and CDR is reported for whole prostate (WP), transition zone (TZ) and peripheral zone (PZ) separately.

Standard errors and 95% Confidence Intervals (CI) were estimated from 2000 bootstrap samples by random sampling on the patient-level to account for intra-patient correlation arising from multiple-readers, multiple lesions, and multiple sequences. Proportion of case and control patients were maintained in the bootstrap resampling procedure. The 95% confidence limits were taken from the 2.5% and 97.5% percentiles of the bootstrap distribution and the Wald test was used to test the difference in CDRs across combinations of sequence positivity. All p-values correspond to two-sided tests, with a p-value <0.05 considered to represent a significant difference.

Results

Patient and Lesion Characteristics

The final study population consisted of 44 patients. 1 control patient was excluded after positive biopsy result (Gleason 3+3) following initial inclusion. Median age for cases and controls was 62 [range 45–71] and 65.5 [47–71] years, median PSA for cases and controls was 6.83 [1.95–51.13] and 6.85 [2.4–10.87] ng/ml. Median time between MRI and radical prostatectomy was 3 [0.67–13] months for case patients. For control patients, median time between MRI and negative biopsy was 37.1 [0.07–104.2] months.

A total of 232 unique lesions were detected across all 3 readers on all individual sequences, of which 128/232 (55.1%) were PZ lesions, 103/232 (44.4%) were TZ lesions, and 1 lesion spanned both zones. Histopathologically, 30.2% (70/232 lesions) of identified lesions were tumor-positive. Mean histologic lesion size was 7.2 [0.1–271.7] ml. Of these 70 lesions, 57, 10, 2, 1 were Gleason 3+4, 4+4, 4+5, 5+4, respectively.

Reader-Based Individual Sequence Sensitivity and Agreement

Reader agreement was moderate for all sequences; ISA was highest for DWI at 58%, followed by T2W at 54%, and DCE at 33% (Figure 3). Analysis of pairwise ISA showed higher concordance between Readers 1 and 2 for lesion detection on DCE (Table 2).

Lesion zonal breakdown with individual true positive detection, used for sensitivity analysis, is given in Table 3. For whole prostate, reader sensitivity was highest with DWI (average 59%, range [51–71%]), followed by T2W (48%, [39–59%]), and then DCE (23%, [13–36%]). This pattern remained consistent across zones, with DWI achieving highest average sensitivity of 50% in the PZ, and 69% in the TZ (Figure 4).

Individual and Additive Value of MRI Sequences for Cancer Detection

As a single sequence, DWI showed highest individual CDR in WP, PZ and TZ at 38%, 36% and 40% respectively. When DWI and T2W independently identified the same lesion, CDR in WP, PZ and TZ rose to 80%, 80%, and 81% respectively. Highest CDR in the TZ was seen when the same lesion was identified independently on T2W and DCE (100% for N=4 lesions). When the same lesion was independently identified on all three sequences CDRs for WP, PZ, TZ were 90%, 85%, 94%, respectively (Figure 5). Examples of single sequence and independent identification on 2 sequences are shown in Figure 6.

Added benefit to CDR of each sequence combination (CDR) is given in Table 4. Overall in the WP, DWI was a significant addition to T2W-positive and DCE-positive lesions, adding 56.4% and 59% to the detection rates, respectively ($p<0.0001$). Similarly, T2W positivity was a significant addition to DWI-positive lesions (42% increased CDR, $p<0.0001$) and DCE-positive lesions (42.3% increased CDR, $p=0.03$). Together, DWI was the most significant addition to lesions detected both on T2W and DCE independently, adding 40% to CDR ($p=0.03$).

The effect of different combinations of independently interpreted pulse sequences on zone-based detection is given in Table 4. In the PZ, DWI consistently added the greatest benefit to positive T2W or DCE lesions ($p<0.0001$ and $p<0.01$, respectively) (Table 4). Only modest benefit was observed when a positive DCE lesion was also seen independently on T2W (16.3% CDR increase, $p=0.38$, N=6 lesions). In the TZ, the addition of DCE positivity added significant benefits to T2W-positive lesions (77.4% increased CDR, $p=0.02$, N=4 lesions). In cases in which lesions were detected by two independently positive sequences, no significant addition to detection was achieved by the addition of the third sequence in the TZ (Table 4).

Discussion

It can be difficult to distinguish individual contribution of a pulse sequence in a multiparametric study when the study pulse sequences are viewed simultaneously, as the results of one sequence can bias the reader's opinion on other sequences. Such studies often conclude that DCE MRI adds little to mpMRI of the prostate. This study compares individual pulse sequences in a completely independent interpretation manner using different readers from different institutions, and suggests that when maximizing detection of prostate cancer with mpMRI, all sequences in multiparametric MRI are contributory in an independent fashion. We found that while DWI consistently provided the highest sensitivity and independent cancer detection rate, this was closely matched by the sensitivity and cancer detection rate of T2W. DCE added moderate increases in CDR, and in some cases these were quite significant when added to the findings of T2W and DWI. Our data suggests that identifying a dominant sequence or discounting the value of a certain sequence based on zone potentially reduces the impact of mpMRI.

DWI and T2W are generally considered key sequences for clinically significant cancer detection on mpMRI (12, 17, 18). The high predictive values reported for these two sequences are confirmed in this study, with both exhibiting relatively high reader sensitivity,

ranging from 39–59% and 51–71%, respectively, across all readers. Additionally, both sequences significantly added to the CDR in combination with other sequences, suggesting T2W and DWI are the two most essential sequences for maximizing cancer detection. We also report that out of all three sequences, reader agreement was highest in T2W and DWI, indicating that readers are able to most commonly identify lesions on these two sequences. While overall reader agreement was moderate and prior studies have reported lesion detection agreement as high as 74–93%, given the completely independent reads utilized in the present study in contrast to multiparametric application, the clinical scenarios cannot be reasonably compared (4).

Throughout the whole prostate and by zones, DWI achieved the strongest performance for reader sensitivity and for additive value to other sequences. DWI characteristics are well known to be moderately inversely correlated with tumor Gleason score, and the association with likelihood of clinically significant disease is strongest in the PZ (21–25). These findings are also confirmed by our data, which shows high sensitivity and detection in the PZ. In the TZ, DWI sequence interpretation is confounded by signal patterns from benign prostatic hyperplasia (BPH) (26). However, DWI-positive lesions in the TZ achieved a CDR of 40% compared to T2W-positive lesions interpreted independently which achieved a CDR of only 23%. This finding raises some questions regarding the “dominance” of T2W in the PZ and set forth in PI-RADSv2 (5). This is supported by other lines of evidence such as recent studies that have shown promise in using DWI signal difference to distinguish between tumor and benign tissue in the TZ, suggesting that perhaps DWI can play a more prominent role in detection of clinically significant cancer (23, 27–29).

Some studies recommend dropping DCE altogether from mpMRI of the prostate (12, 30–33). In PI-RADSv2, the role of DCE is minimized with readers simply evaluating for positive enhancement or lack of enhancement, and its role in determining overall PI-RADS categorization is limited to equivocal PZ lesions. In our analysis, reader detection on DCE, although inferior to T2W and DWI, nevertheless was contributory when read independently. In combination with other sequences, DCE added value to cancer detection, ranging from 9.6%–28.3% in WP, 0.4%–24.4% in PZ, and 13.3%–77.4% in TZ. The small number of lesions that were positive on DCE, both alone and in combination with other sequences, limited the statistical power for evaluating its added benefit. However, the additional gain in CDR from DCE observed in this study suggests that excluding DCE MRI completely from the prostate mpMRI evaluation would compromise the efficacy of mpMRI.

While the very first PI-RADS schema assumed equal diagnostic weight among all mpMRI sequences, the idea of a zone-based “dominant sequence” for optimal weighting was adopted in PI-RADSv2 (5, 6). Initial studies validating PI-RADSv2 show some limitations in capturing optimal detection of clinically significant disease especially in PI-RADS “4” lesions (10, 29, 34). Further investigation has suggested that the zone-based weighting system is imperfect, with some suggesting equal weighting of the 3 sequences had greater diagnostic performance than PI-RADSv2 in the PZ (35). Additionally, Rosenkrantz et al. found that assigning DWI more weight in the TZ than what is given in current PI-RADSv2 recommendations improved cancer detection (29). The data we have provided in this study suggests that there is likely no clear dominant sequence in each zone and further research

remains to be done for designing the optimal weighting schema for prostate mpMRI interpretation.

As all pulse sequences were read independently, a false positive in one sequence would not add to overall false positivity by other sequences. The aim of this study was to elucidate detection and sensitivity of each sequence independently and without reader bias. However, the best way to truly assess combination detection and effect of each sequence on overall false positive rate would be to test all bi-parametric and tri-parametric combinations of imaging sequences in a prospective reading study, in addition to testing single sequence detection as is done here. Despite this, we have shown that false positive findings are lower in combinations of independent positivity, as demonstrated by higher CDR.

Our study has some limitations. First, our study cohort had only case patients who underwent subsequent radical prostatectomy and therefore harbored possibly higher-grade cancers, leading to a selection bias compared to an average population of all patients undergoing mpMRI. Our definition for cancer was Gleason score $\geq 3+3$, and the randomly selected lesion population consisted of only Gleason 3+4 disease and above. We included control patients so as to reduce this effect. However, control populations are somewhat inherently limited by being only biopsy-proven since surgery cannot be offered to these patients. Additionally, as this was an exploratory evaluation with no set predicted detection rate for each sequence, the population used in this study was relatively small at 45 patients. Our results should be validated in a similar, optimally larger cohort. Moreover, this experimental read out study included 3 expert readers, but it may be more ideal to include readers with a greater diversity of experience. The readers' detection guidelines followed a framework outlined in PI-RADSv2 to optimize standardization across readers, but at the cost of standardization, perhaps detection instructions could be broadened to include in-house interpretation practices and central zone lesion identification.

In conclusion, when multiple observers independently read individual pulse sequences on prostate MRI, DWI achieves the highest cancer detection in both prostate zones, however, T2W and DCE MRI also add independent value to prostate cancer detection. These findings can serve as groundwork for future refinement of diagnostic criteria for mpMRI of the prostate.

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Abbreviations

mpMRI	Multiparametric MRI
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T2W	T2-weighted MRI
DWI	Diffusion-weighted imaging
DCE	Dynamic contrast-enhanced MRI
PI-RADSv2	Prostate Imaging-Reporting And Data System, version 2
WP	Whole prostate
TZ	Transition zone
PZ	Peripheral zone
PSA	Prostate-specific antigen
ADC	Apparent diffusion coefficient
ISA	Index of specific agreement
CDR	Cancer detection rate

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Figure 1. Study design

Flow diagram shows exclusion criteria as well as random selection of patients for inclusion in study. mpMRI = multiparametric MRI imaging.

The application window is titled 'frmTimer' and contains the following sections:

- Left Sidebar:**
 - Sequence ID: 12670285
 - Name: [Empty]
 - Image Type: DCE
 - Buttons: Start, Pause, End
 - Timer On: [Green Circle]
 - Notes: [Text Area]
 - Completed?: [Empty]
 - Sequence 1 Of 135
 - Navigation: Prev [Left Arrow] Next [Right Arrow]
- Main Area: Evaluation of mpMRI Individual Sequences**
 - Number of Lesions:** 0 1 2 3 4
 - Lesion 1 (Green Panel):**
 - Screenshot (Double Click): [Paperclip]
 - L1 Zone: TZ PZ B
 - L1 Side: R L Midline
 - L1 T2W or DWI score: NA 1 2 3 4 5
 - L1 DCE score: NA (+) (-)
 - Dominant Lesion?: []
 - L1 EPE?: Yes No
 - Lesion 2 (Purple Panel):**
 - Screenshot (Double Click): [Paperclip]
 - L2 Zone: TZ PZ B
 - L2 Side: R L Midline
 - L2 T2W or DWI score: NA 1 2 3 4 5
 - L2 DCE score: NA (+) (-)
 - Dominant Lesion?: []
 - L2 EPE?: Yes No
 - Lesion 3 (Orange Panel):**
 - Screenshot (Double Click): [Paperclip]
 - L3 Zone: TZ PZ B
 - L3 Side: R L Midline
 - L3 T2W or DWI score: NA 1 2 3 4 5
 - L3 DCE score: NA (+) (-)
 - Dominant Lesion?: []
 - L3 EPE?: Yes No
 - Lesion 4 (Blue Panel):**
 - Screenshot (Double Click): [Paperclip]
 - L4 Zone: TZ PZ B
 - L4 Side: R L Midline
 - L4 T2W or DWI score: NA 1 2 3 4 5
 - L4 DCE score: NA (+) (-)
 - Dominant Lesion?: []
 - L4 EPE?: Yes No

Figure 2. Reader data collection

Microsoft Access-designed application used to collect data from each reader. All patient sequence IDs and names are anonymized, and all 135 sequences appeared in random order to the reader. Readers could identify up to 4 lesions per sequence, and gave lesion information using form buttons. Each lesion's paperclip box represents where the reader would attach each lesion screenshot.

Figure 3. Inter-reader Specific Agreement

Inter-reader Specific Agreement (ISA) in the whole prostate (WP) for each sequence, evaluated for all identified lesions.

Figure 4. Reader-specific and average detection sensitivities per sequence

Reader detection sensitivity for T2-weighted (T2W), diffusion-weighted imaging (DWI), and dynamic contrast-enhanced (DCE) MRI sequences for whole prostate (WP), peripheral zone (PZ), and transition zone (TZ) lesions. Average across three readers is indicated by wide solid bars for WP, PZ, TZ, with individual reader-based sensitivities and 95% confidence intervals overlaid as narrower bars. From left to right, the narrow bars indicate results for Reader 1 (R1), Reader 2 (R2), and Reader 3 (R3), respectively. True positive and condition positive findings from which these results were derived are available in Table 3.

Figure 5. Cancer detection rates of sequence positivity combinations

Cancer Detection Rates (CDR) in (A) whole prostate (WP), (B) peripheral zone (PZ), and (C) transition zone (TZ) for all 7 combinations of sequence positivity, with 95% confidence intervals calculated from bootstrapping. Observed true positive (TP), false positives (FP), and CDR are listed below each combination. Differences in CDR between combinations are presented in Table 4.

Figure 6. Panels 6A–6D: Example T2W-only detection

58-year old man with a serum PSA of 7.09 ng/ml. All readers identified a lesion on axial T2W MRI which shows a hypointense lesion in the left anterior transition zone (arrow, A). Only one of three readers identified this lesion on diffusion imaging, including ADC map (B) and b2000 DW MRI (C). No readers detected this lesion on DCE MRI (D). Patient underwent radical prostatectomy and subsequent pathology mapping revealed Gleason 3+4 within this lesion.

Panels 6E–6H: Example DWI-only detection. 51-year old man with a serum PSA of 4.47 ng/ml. No readers reported findings on T2W MRI in this patient (E). All readers detected a lesion in the right apical anterior transition zone on with restricted diffusion on ADC (F) and b2000 (G) DW imaging. No readers detected this lesion on DCE MRI (H). Patient underwent radical prostatectomy and subsequent pathology mapping revealed Gleason 3+4 within this lesion.

Panels 6I–6L: Example T2W+/DWI+ detection. 66-year old man with serum PSA of 8.9 ng/ml. All readers reported a lesion on axial T2W MRI (I) in the right mid anterior transition zone. All readers additionally reported this lesion (arrows) on DW imaging, including ADC map (J) and b2000 DW MRI (K). No readers detected this lesion on DCE MRI alone (L). Pathology mapping after radical prostatectomy revealed Gleason 3+4 within this lesion.

Table 1
Multiparametric MRI acquisition parameters given for prostate imaging at 3-Tesla (3T)
with use of an endorectal coil

Sequences acquired include T2 weighted, diffusion-weighted imaging (DWI) which includes apparent diffusion coefficient (ADC) map calculation and a high *b*-value sequence, and dynamic contrast enhanced (DCE) MRI.

Multiparametric MR Imaging Sequence Parameters at 3T				
Parameter	T2 Weighted	DWI [*]	High <i>b</i> -Value DWI [†]	DCE MR Imaging [‡]
Field of view (mm)	140 × 140	140 × 140	140 × 140	262 × 262
Acquisition Matrix	304 × 234	112 × 109	76 × 78	188 × 96
Repetition time (msec)	4434	4986	6987	3.7
Echo time (msec)	120	54	52	2.3
Flip angle (degrees)	90	90	90	8.5
Section thickness (mm), no gaps	3	3	3	3
Image reconstruction matrix pixels)	512 × 512	256 × 256	256 × 256	256 × 256
Reconstruction voxel imaging resolution (mm/pixel)	0.27 × 0.27 × 3.00	0.55 × 0.55 × 2.73	0.55 × 0.55 × 2.73	1.02 × 1.02 × 3.00
Time for acquisition (min:sec)	2:48	4:54	3:50	5:16

^{*} For ADC map calculation. Five evenly-spaced *b* values (0–750 sec/mm²) were used

[†] *b* = 2000 sec/mm²

[‡] DCE MRI obtained, before, during, and after a single dose of gadopentetate dimeglumine 0.1 mmol/kg at 3 mL/sec. Each sequence obtained at 5.6 s intervals

Table 2
Pair-wise Inter-reader Specific Agreement (ISA) in the whole prostate

ISA is given for all reader combinations for each sequence type.

	Reader 1–2	Reader 1–3	Reader 2–3
T2W	0.51	0.55	0.56
DWI	0.59	0.59	0.57
DCE	0.46	0.24	0.30

Observed number of true positives for each reader, by zone and within each sequence

Table 3

Sensitivities calculated for Figure 4 were derived from the ratio of number of true positives to number of pathologically confirmed lesions (condition true).

Zone	Number of Pathologically Confirmed Lesions	Reader-detected True Positives											
		T2W			DWI			DCE					
		R1	R2	R3	R1	R2	R3	R1	R2	R3	R1	R2	R3
PZ	38	14	16	23	23	18	16	11	9	3			
TZ	32	19	11	18	27	18	21	14	5	6			
All	70	33	27	41	50	36	37	25	14	9			

Table 4
CDR benefit (CDR) in whole prostate (WP), peripheral zone (PZ), and transition zone (TZ)

CDR is calculated as the difference in CDR between combinations of varying sequence positivity. Of note, CDRs for all sequence combinations are illustrated in Figure 5. For example, the baseline CDR for T2W-only in WP is 24.0% and the combined CDR for T2W+/DWI+ in WP is 80.4%, giving a CDR (DWI benefit to T2W-only) of 56.4% $p<0.0001$.

Positive sequence combination	WP			PZ			TZ		
	Baseline	Added	Baseline CDR	CDR	p-value	Baseline CDR	CDR	p-value	Baseline CDR
T2W+/DWI+/DCE-	T2W-only	DWI+	24.0%	56.4%	<0.0001	24.6%	55.4%	<0.0001	22.6%
	DWI-only	T2W+	38.3%	42.0%	<0.0001	35.6%	44.4%	0.0002	40.3%
T2W+/DWI-/DCE+	DCE-only	T2W+	7.7%	42.3%	0.03	8.7%	16.3%	0.38	5.9%
	T2W-only	DCE+	24.0%	26.0%	0.17	24.6%	0.4%	0.98	22.6%
T2W-/DWI+/DCE+	DCE-only	DWI+	7.7%	59.0%	<0.0001	8.7%	51.3%	0.001	5.9%
	DWI-only	DCE+	38.3%	28.3%	0.03	35.6%	24.4%	0.16	40.3%
T2W+/DWI+/DCE+	T2W+/DCE+	DWI+	50.0%	40.0%	0.03	25.0%	59.6%	0.002	100.0%
	DWI+/DCE+	T2W+	66.7%	23.3%	0.08	60.0%	24.6%	0.20	80.0%
T2W-/DWI+/DCE+	T2W-/DCE+	DCE+	80.4%	9.6%	0.24	80.0%	4.6%	0.73	80.8%