10.1148/radiol.2019181705

Appendix E1

Materials and Methods

Patients

Due to overlap in study periods from September 2014 to April 2016, 16 patients with 16 transition zone lesions targeted with cognitive biopsy were derived from the patient dataset used in a prior publication (19), but the previous publication only included patients with peripheral zone lesions undergoing TRUS and/or cognitive targeted biopsy and compared normal peripheral zone with peripheral zone cancers and prostatitis (19). No transition zone lesions were included in the published cohort.

MR Fingerprinting Acquisition and Processing

MR Fingerprinting settings were as previously described and included: FOV 400 × 400 mm^2, TR 11–13 ms, flip angle 5–75° and resolution 1 × 1 × 5 mm^3. The whole prostate was covered with an acquisition time of 39 seconds per slice. Total scan time ranged between 5–10 minutes, depending on the number of slices needed to cover the entire gland. For MR Fingerprinting data processing, a dictionary containing expected signal evolutions was calculated with T_1 of 20–2950 msec and T_2 of 9–500 ms. Pattern matching was performed pixelwise to generate coregistered T_1 and T_2 maps (18).

Results

Patient Characteristics

The age (mean ± SD) of 67 patients included in analysis was 65.5 years ± 7.4 years. 33 patients had cancers and 34 patients had noncancers. Patients with cancers had higher PSA density (P = .006) and lower prostate volume (P = .004) compared with patients with noncancers. There was no difference in age (P = .94) and PSA (P = .49) between the two groups (Table 2). The time between diagnostic MRI and targeted biopsy was similar in cancers and noncancers groups (P = .56 for in-gantry biopsy, P = .28 for cognitive biopsy) (Table 2). All 16 patients undergoing cognitive targeting were biopsy naïve while 29/51 in-gantry patients had one or more previous TRUS biopsies. For in-gantry patients with prior TRUS biopsy (n = 29), there was no difference in time between TRUS and in-gantry biopsy between the two groups (Table 2).

Lesion Characteristics

Final lesion analysis included 75 lesions with 37 cancers (14 Gleason score 3+3 = 6, 23 Gleason score ≥ 7) and 38 noncancers (22 prostatitis, 16 biopsy-proven benign prostatic tissue). 37 lesions were PIRADSv2 Category 3 lesions (31 noncancers and 6 cancers) and 38 lesions were PIRADSv2 Category 4/5 lesions (31 cancers and 7 noncancers) (Fig 1). Lesion size for cancers was significantly higher than noncancers (P = .006) while ROI sizes were comparable for both cancers and noncancer lesions (P = .72) (Table 2). MR Fingerprinting T_1 and T_2 numbers were

available for all 75 lesions while ADC measurement was not available for one lesion due to distorted ADC map.

Table E1: Sequence details for In-gantry Biopsy

Sequence	TR (ms)/ TE (ms)	Field of View (mm)	Spatial Resolution (mm)	Matrix	Flip angle (degrees)	Slice thickness (mm)	NEX	b Value (s/mm^2)	Sequence Duration (minutes)
Localizer	1000/67	420 × 315	1.7 × 1.3	190× 320	137	3	1		0.16
Coronal turbo spin echo T_2w image to guide	2000/67	420 × 315	1.7 × 1.3	190× 320	150	3	1		0.10
Sagittal turbo spin echo T_2w image to guide	6200/95	256 × 256	1.2 × 1.0	215× 256	150	3	1		1:04
Transverse turbo spin echo T_2w image	4020/120	220 × 220	1.0 × 0.9	215× 256	150	3	2		3:41
Diffusion weighted imaging	3900/96	100 × 240	2.4 × 2.4	102 × 102	—	3	2	50, 600, 1000, 1400	3:23
MR Fingerprinting	13–15	400 × 400	1 × 1	400 × 400	5–75	5	1		0.39 per slice
Quick Sagittal localizer	2000/69	420 × 315	1.7 × 1.3	190 × 320	150	4	1		0.10
Oblique coronal turbo spin echo T_2w image to guide	3500/95	256 × 256	1.2 × 1.0	215 × 256	150	3	1		0.37
Transverse single shot T_2w image post biopsy	2000/94	304 × 248	1.2 × 1	205 × 320	150	5	1		0.40

Abbreviations: TR: Time of Repetition, TE: Time of Echo, NEX: Number of excitations.

Table E2: Summary of Means of Two-Reader T_1, T_2 and ADC values of normal transition zone and different histologic groups

Group (Number of samples)	T_1 (ms) Mean ± SD	T_2 (ms) Mean ± SD	ADC (×10^{-3}mm^2/s) Mean ± SD
Normal Transition Zone (*n* = 66)	1800 ± 150	65 ± 22	1.13 ± 0.19
Prostate Cancers (*n* = 37)	1450 ± 110	36 ± 11	0.57 ± 0.13
Non-Cancers (*n* = 38)	1620 ± 120	47 ± 16	0.82 ± 0.13
Clinically significant cancers/Gleason score ≥ 7 (*n* = 23)	1440 ± 140	37 ± 12	0.58 ± 0.14
Clinically insignificant lesions (Low-grade cancers + Noncancers) Gleason score ≥ 7 (*n* = 52)	1580 ± 120	44 ± 15	0.75 ± 0.17

Table E3: Best-performance cut-off values from regression models based on the means of two-reader values for T_1, T_2, and ADC. The numbers indicate sensitivity (Sn) and specificity (Sp) with 95% CI for respective cut-off values. For univariate regression models, the individual cut-off values contributed independently to overall diagnostic performance

Groups Compared	T_1 (ms) (Sn, Sp)	T_2 (ms) (Sn, Sp)	ADC (×10^{-3}mm^2/s) (Sn, Sp)
PCa (*n* = 37) vs NTZ (*n* = 66)	1610 msec (100% (37/37), 91% (60/66))	43 msec (86% (32/37), 88% (58/66))	0.83 × 10^{-3}mm^2/s (97% (35/36), 95% (62/65))
PCa (*n* = 37) vs Non-PCa (*n* = 38)	1510 msec (76% (28/37), 87% (33/38))	35 msec (54% (20/37), 82% (31/38))	0.70 × 10^{-3}mm^2/s (86% (31/36), 84% (32/38))

Gleason score ≥ 7 PCa (*n* = 23) vs Low grade PCa+Non-PCa (*n* = 52)	1500 msec (70% (16/23), 77% (40/52))	Regression model not significant	0.66 × 10^{-3}mm^2/s (87% (20/23), 71% (36/51))
PIRADS 3 Non-PCa (*n* = 31) vs PCa (*n* = 6)	1600 msec (100% (6/6), 61% (19/31))	Regression model not significant	0.73 × 10^{-3}mm^2/s (80% (4/5), 77% (24/31))

Clinically significant cancers: Gleason score ≥ 7 Prostate cancer.

Clinically insignificant lesions: Gleason 6 prostate cancers +Noncancers.

Table E4: Individual best-performing AUCs for Reader 1 and Reader 2 for clinically relevant comparisons*

Groups Compared	T_1 AUC		T_2 AUC		ADC AUC		Highest AUC#		
	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2	Reader 1	Reader 2	Based on mean of two-reader values
PCa (*n* = 37) vs NTZ (*n* = 67)	0.98 (0.96–1.00)	0.96 (0.92–0.99)	0.90 (0.84–0.96)	0.87 (0.80–0.94)	0.99 (0.98–1.00)	0.97 (0.93–1.00)	**0.99 [ADC,T_2] (0.98–1.00)**	**0.98 [ADC,T_2] (0.95–1.00)**	**0.99 [ADC, T_2] (0.98,1.00)**
PCa (*n* = 37) vs Non-PCa (*n* = 38)	0.88 (0.80–0.95)	0.82 (0.71–0.91)	0.70 (0.53–0.82)	0.63 (0.44–0.77)	0.88 (0.80–0.95)	0.89 (0.81–0.96)	**0.95 [ADC,T_1] (0.91–0.99]**	**0.92 [ADC,T_1] (0.86–0.98)**	**0.94 [ADC, T_1] (0.88,0.98)**
PIRADSv2 Category 3 Non-PCa (*n* = 31) vs PCa (*n* = 6)	0.78 (0.67–0.94)	0.74 (0.38–0.99)	0.29 (0.00–0.63)	0.28 (0.00–0.65)	0.79 (0.42–0.98)	0.62 (0.00–0.98)	**0.79 [ADC] (0.42–0.98)**	**0.74 [T_1] (0.38–0.99)**	**0.79 [T_1] (0.57,0.96)**

* Performed 1000 bootstrap resamples with replacement from the data and leave-one-out cross validation. Numbers in parentheses are the bootstrap 95 percentile confidence intervals.

Variables in the models with the highest AUC are given in brackets.

NTZ: Normal Transition Zone, PCa: Prostate Cancer, Non-PCa: Non–cancers, AUC: Area Under Curve.