Received:
23 December 2015

Revised:
13 April 2016

Accepted:
18 April 2016

<http://dx.doi.org/10.1259/bjr.20151076>

Cite this article as:

Wu L-M, Zhao Z-Z, Chen X-X, Lu Q, Suo S-T, Liu Q, et al. Comparison of T_2^* mapping with diffusion-weighted imaging in the characterization of low-grade vs intermediate-grade and high-grade prostate cancer. *Br J Radiol* 2016; **89**: 20151076.

FULL PAPER

Comparison of T_2^* mapping with diffusion-weighted imaging in the characterization of low-grade vs intermediate-grade and high-grade prostate cancer

¹LIAN-MING WU, ¹ZI-ZHOU ZHAO, ¹XIAO-XI CHEN, ¹QING LU, ¹SHI-TENG SUO, ²QIANG LIU, ³JIANI HU, ³E MARK HACCKE and ¹JIAN-RONG XU, MD, PhD

¹Department of Radiology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

²Department of Pathology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

³Department of Radiology, Wayne State University, Detroit, MI, USA

Address correspondence to: Prof. Jian-Rong Xu

E-mail: xujianr@yeah.net

Wu and Zhao contributed equally to this work.

Objective: To evaluate the diagnostic value of T_2^* mapping compared with apparent diffusion coefficient (ADC) mapping in the characterization of low-grade (Gleason score, ≤ 6) vs intermediate-grade and high-grade (Gleason score ≥ 7) prostate cancer (PCa).

Methods: 62 patients who underwent MRI before prostatectomy were evaluated. Two readers independently scored the probabilities of tumours in 12 regions of the prostate on T_2^* and ADC images. The data were divided into two groups, i.e. low- vs intermediate- and high-grade PCa, and correlated with the histopathological results. The diagnostic performance parameters, areas under the receiver-operating characteristic curves and interreader agreements were calculated.

Results: For Reader 2, ADC mapping exhibited a greater accuracy for intermediate-grade PCas than for high-grade PCas (0.77 vs 0.83, $p < 0.05$). For both readers,

T_2^* mapping exhibited a greater accuracy for intermediate-grade PCas than for high-grade PCas (Reader 1, 0.86 vs 0.81; Reader 2, 0.83 vs 0.78; $p < 0.05$). The areas under the curve of T_2^* mappings were greater than those of the ADC mappings for the intermediate- and high-grade PCas (Reader 1, 0.83 vs 0.78; Reader 2, 0.80 vs 0.75; $p < 0.05$) but not for the low-grade PCas (Reader 1, 0.86 vs 0.84; Reader 2, 0.83 vs 0.82; $p > 0.05$). The weighted κ value of T_2^* mapping was 0.59.

Conclusion: T_2^* mapping improves the accuracy of the characterization of intermediate- and high-grade PCas but not low-grade PCas compared with ADC mapping.

Advances in knowledge: T_2^* mapping exhibited greater diagnostic accuracy than ADC mapping in the characterization of intermediate- and high-grade PCas. T_2^* mapping exhibited limited value in the characterization of low-grade PCa.

INTRODUCTION

The most frequently observed malignant cancer and the second leading cause of cancer-related death in males¹ is prostate cancer (PCa) and it varies tremendously in terms of clinical behaviour. Therefore, it is necessary to guide therapy in accordance with the severity of the cancer. PCa ranges from non-aggressive, indolent cancers that are best managed with active surveillance protocols to aggressive cancers that are generally treated with radical radiotherapy or prostatectomy.² The Gleason scoring system is globally recognized for tumour grading.³ Cancers are divided into high grade (Gleason score ≥ 8), intermediate grade (Gleason score 7) and low grade (Gleason score ≤ 6). Image-based diagnoses have been improved by the advantages of 3.0-T MRI.^{4–6}

Diffusion-weighted imaging (DWI) has increasingly become a routine component of clinical MRI. The unique soft-tissue contrast mechanism of DWI exploits differences in the motions of water molecules *in vivo* at a biologically meaningful scale. The magnitude of water diffusion is described by the apparent diffusion coefficient (ADC), which is measured in square millimetre per second.⁷ ADC values have been reported to be negatively related to the Gleason scores of PCas.^{8–11} DWI has been demonstrated to have varying accuracy in the detection of PCa with specificities between 61 and 100% and sensitivities between 54 and 94%.^{12–14} Recently, tumour cell densities have been estimated based on the T_2^* relaxation time, which functions as a new quantitative biomarker. In different body regions, T_2^* weighted imaging is applied to many

Table 1. Diagnostic performance parameters for prostate cancer detection with two image sets at 3 T by two readers

Group/diagnostic accuracy	Sensitivity	Specificity	PPV	NPV	Accuracy
Reader 1					
ADC mapping	0.80 (260/327)	0.76 (319/417)	0.73 (260/358)	0.83 (319/386)	0.78 (579/744)
T_2^* mapping	0.87 (286/327)	0.81 (336/417)	0.78 (286/367)	0.89 (336/377)	0.84 (622/744)
Reader 2					
ADC mapping	0.76 (250/327)	0.74 (309/417)	0.70 (250/358)	0.80 (309/386)	0.75 (559/744)
T_2^* mapping	0.83 (272/327)	0.78 (325/417)	0.75 (272/364)	0.86 (325/380)	0.80 (597/744)

ADC, apparent diffusion coefficient; NPV, negative-predictive value; PPV, positive-predictive value.

organs.^{15,16} In addition, sensitivity differences between non-haemorrhagic and haemorrhagic regions can be recognized by T_2^* weighted imaging, as reported by Hardman et al.¹⁷ Moreover, increasing attention has been focused on pulse sequence optimization suitable for prostate MRI. Hardman et al used a rapid three-dimensional T_2^* weighted echoplanar imaging (EPI) sequence to map the local magnetic sensitivity differences on 3.0-T prostate MRIs. However, in this study, the susceptibility of T_2^* was compared with that of the more commonly used T_1 weighted turbo spin echo to examine hints about sequences and haemorrhages that are susceptible to field non-uniformities in addition to MR spectroscopy. The conclusion reached was that the even and uneven regions of sensitivity differences can be recognized with a fast T_2^* EPI sequence, which might be useful for the planning of 3.0-T MRIs. In addition, Korteweg et al¹⁸ demonstrated obvious variations in the average T_2^* relaxation time constants between benign and malignant nodes. Specifically, compared with the non-contrast technology of DWI alone, this method can easily be utilized to enhance the precision of cancer localization.

The use of T_2^* weighted imaging is supported by our previous study data that demonstrated that quantitative T_2^* mapping seems to be a method that is potentially useful for characterizing PCa.¹⁹ T_2^* mapping can provide additional quantitative information that is significantly correlated with the aggressiveness of PCa.¹⁹ Because a substantial number of cancers with Gleason scores of 6 are invisible on ADC and T_2^* mapping, as demonstrated in prior research and our institutional experience, the

diagnostic abilities of T_2^* mapping and DWI are thought to vary according to the Gleason score. Therefore, the purpose of this study was to evaluate the diagnostic ability of T_2^* mapping in the characterization of low-grade vs intermediate- and high-grade PCas compared with DWI.

METHODS AND MATERIALS

Patients

The institutional review board of Renji Hospital approved this retrospective study and informed consent was waived for the review of the data. All patients with histologically confirmed PCa who underwent 3.0-T MR scanning from July 2014 to June 2015 were enrolled in this study. Patients were included if they met the following criteria: (1) MRI conducted <60 days after prostate biopsy, (2) radical prostatectomy performed within 3 months of prostate MRI and (3) the prostate MRI protocol included DWI and T_2^* . Based on the primary criteria, 71 patients met the inclusion criteria. Six of these patients were excluded because they received hormonal treatment before MRI and three patients were excluded because histopathological cancer mapping was unavailable. Consequently, 62 patients (median age of 65 years with a range of 49–73 years) were included in our research. The average prostate-specific antigen (*i.e.* a specific antigen of the prostate) value before surgery was $10.3 \pm 5.9 \text{ ng ml}^{-1}$. The distribution of cancer grades was as follows: 34 (55%) patients had Gleason scores of 6, 24 (38%) patients had scores of 7 and 4 (7%) patients had scores of 8 or higher following radical prostatectomy.

Table 2. Comparison of sensitivity, specificity and accuracy for the detection of low-risk prostate cancer (PCa) [Gleason score (GS) 6] and intermediate- or high-risk PCa (GS 7 or higher)

Diagnostic accuracy/imaging modality		Reader 1			Reader 2		
		GS = 6	GS $\geq$ 7	<i>p</i> -value	GS=6	GS $\geq$ 7	<i>p</i> -value
Sensitivity	ADC mapping	0.78 (119/153)	0.81 (141/174)	0.351	0.74 (113/153)	0.79 (137/174)	0.036
	T_2^* mapping	0.86 (131/153)	0.89 (155/174)	0.152	0.80 (123/153)	0.86 (149/174)	0.028
Specificity	ADC mapping	0.75 (191/255)	0.79 (128/162)	0.063	0.73 (186/255)	0.76 (123/162)	0.216
	T_2^* mapping	0.79 (201/255)	0.83 (135/162)	0.055	0.76 (194/255)	0.81 (131/162)	0.054
Accuracy	ADC mapping	0.76 (310/408)	0.80 (269/336)	0.212	0.73 (299/408)	0.77 (260/336)	0.045
	T_2^* mapping	0.81 (332/408)	0.86 (290/336)	0.053	0.78 (317/408)	0.83 (280/336)	0.012

ADC, apparent diffusion coefficient.

Figure 1. Receiver-operating characteristic (ROC) curves for the detection of prostate cancer (PCa) on T_2^* and apparent diffusion coefficient (ADC) maps in the overall, low-grade PCa (Gleason score 6) and intermediate-/high-grade PCa (Gleason score 7 or higher) groups. (a–c) For Reader 1, the areas under the curve (AUCs) for the T_2^* mappings (0.85) were significantly greater than those for the ADC mapping (0.81) for all tumours regardless of the Gleason score. No significant difference was noted between the ADC (0.84) and T_2^* mappings (0.86) in the detection of low-grade PCa. Regarding the detection of intermediate-/high-grade PCas, the AUC for the T_2^* mapping (0.83) was significantly greater than that for the ADC mapping (0.78). (d–f) For Reader 2, the AUC for the T_2^* mappings (0.82) were significantly greater than those for the ADC mappings (0.78) for all tumours regardless of the Gleason score. No significant difference was noted between the ADC (0.83) and T_2^* mappings (0.82) in the detection of the low-grade PCas. Regarding the detection of the intermediate-/high-grade PCas, T_2^* mapping (0.80) was significantly better than ADC mapping (0.75). $T_2^* = T_2^*$ mapping.

Table 3. Areas under the curve and 95% confidence intervals for prostate cancer (PCa) detection for two readers in low-risk PCas [Gleason score (GS) 6] and intermediate- or high-risk PCas (GS 7 or higher)

Group/imaging modality	Reader 1			Reader 2		
	ADC mapping	T_2^* mapping	<i>p</i> -value	ADC mapping	T_2^* mapping	<i>p</i> -value
Overall	0.81 (0.77–0.85)	0.85 (0.81–0.88)	0.021	0.78 (0.74–0.83)	0.82 (0.77–0.86)	0.035
GS = 6	0.84 (0.80–0.88)	0.86 (0.86–0.92)	0.132	0.82 (0.77–0.86)	0.83 (0.81–0.89)	0.263
GS $\geq$ 7	0.78 (0.73–0.82)	0.83 (0.77–0.85)	0.002	0.75 (0.71–0.80)	0.80 (0.73–0.82)	0.005

ADC, apparent diffusion coefficient.

MRI acquisition

A 3.0-T MR scanner (Philips Medical Systems, Best, Netherlands) which included a pelvic four-passage coil with a phased array was used. The axial and sagittal fast spin-echo T_2 weighted [repetition time/echo time (TR/TE) 2800/80 ms, intersection gap 1 mm, section thickness 3 mm, field of view (FOV) 18 cm and matrix 304×234] and transverse T_1 weighted (TR/TE 827/10 ms, intersection gap 1 mm, section thickness 3 mm, FOV 18 cm and matrix 256×203) sequences were used for the acquisition of the images, and diffusion module and fat-suppression pulses were used for single-shot EPI. The b -values of 0, 50, 500, 800, 1500 and 2000 s mm^{-1} were selected; the in-plane resolution of $1.5 \times 1.5 \text{ mm}$, the parallel imaging factor of 3 and 15–19.3-mm-thick sections were used to measure the three-directional water diffusion. The ADC mappings were computed automatically *via* the MRI workstation and by means of all four b -values. In addition, a multishot fast-field echo sequence was applied to obtain multiecho T_2^* images. At TEs of 2, 4, 7, 10, 13 and 15 ms and TR of 1200 ms, the whole series of 6 sets of images (each set had 16 slices) was acquired, and the images were generated through an FOV of $18 \times 18 \text{ mm}^2$, with a between-slice gap of 1 mm, slice thickness of 3 mm and image matrix of 224×226 . In terms of the acquisition of the T_2^* maps, the six images were exponentially fit pixel by pixel, in accordance with the various TEs of each slice.

MRI analysis

Two readers (WLM, CXX) separately interpreted the T_2^* and ADC maps on a picture archiving and communication system workstation (PiView; INFINTT, Seoul, Korea). In the present study, routine T_2 weighted images were not used for review along with T_2^* or diffusion-weighted images. For the diffusion-weighted images, only the ADC images were evaluated. One reader had worked in this field for 15 years and the other reader has reviewed prostate MRIs for 6 years. At the time of review, the diagnoses of PCa were known, but the grade and location of the tumours were not known. The readers reviewed the ADC and T_2^* maps at 4-week intervals to minimize recall bias. The prostate was divided into 12 segments to systematize the assessments of the prostate MRIs; these segments included the mid-gland, base, transition zones in both the right and left lobes and the apex of the peripheral zone. The PCa in every MRI study was separately localized by the two readers. The DWI criteria according to the prostate imaging reporting and data system (PI-RADS) scoring system were as follows: (1) no reduction in the ADC compared with normal glandular tissue and no increase in signal intensity (SI) on any high b -value image (≥ 800); (2) diffuse, hyper SI on ≥ 800 images with low ADCs without focal features, but

triangular and geographical features were allowed; (3) intermediate appearances not in categories 1 or 2 or 4 and 5; (4) focal area(s) of reduced ADCs but isointense SIs on high b -value images (≥ 800); and (5) focal areas/masses of hyper SI on the high b -value images (≥ 800) with reduced ADCs.

Given these characteristics of T_2^* mapping, regions with low signal intensity, ill-defined margins and an absent capsule in the transition zone on T_2^* mapping and nodular or mass-like low-signal-intensity regions in the peripheral area relative to a normal peripheral area were identified. The following five-point scale was applied to characterize the probabilities of tumours in each section: 0 indicated no tumour, 1 indicated that there was probably no tumour, 2 indicated a possible tumour, 3 indicated a probable tumour and 4 indicated a certain tumour.

Correlation of the image analysis with the histopathology

10% formalin was prepared so that the marked prostatectomy specimens could be fixed for $<24 \text{ h}$. To create operation specimens that could fit on standard slides, the specimens were first axially step sectioned every 4 mm and then divided into four quarters (left, right, posterior and anterior) or two halves (left and right). A reader with 25 years' experience in prostate pathology, who was blind to the MRI results, summarized the tumour foci and gave each slide a Gleason score. Using the slides, a schematic prostate diagram that depicted the tumour foci in the 12 parts of the prostate with cancer mapping was created and compared with the MRI results. A reader performed the cancer mapping with the appropriate ADC and T_2^* maps.

Statistical analysis

The patients were divided into two categories in terms of imaging–histopathological correlation data, based on the Gleason scores for prostatectomies; *i.e.* patients with intermediate- or high-grade PCas (Gleason scores of 7 or greater) and patients with low-grade PCas (Gleason scores of 6). The sensitivity, specificity, accuracy, positive-predictive and negative-predictive values for the presence of cancer were calculated at the prostate region level by choosing a threshold score of 2 or greater. Receiver-operating characteristic (ROC) analyses were performed to evaluate the diagnostic performances with the two MRI sets of each group. The sensitivities, specificities and accuracies of the T_2^* and ADC mappings were compared between the two groups using the Z test. The areas under the curve (AUCs) of the two image sets were then compared between the two groups. The weighted κ , which is an interreader agreement

Figure 2. A 53-year-old male with prostate cancer with a Gleason score of 6. (a) An apparent diffusion coefficient map revealing a focal area of low signal intensity in the peripheral zone of the left mid-gland (2–3 o'clock position, white arrows). (b) The transverse T_2^* map showing the equivocal loss of signal without mass effect in the peripheral zone of the left mid-gland (2–3 o'clock position, white arrows).

statistic, was used for the computation of the agreement between the two readers. A commercially available software (SPSS for Windows v. 18.0; IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) was used for the statistical analyses. Differences with $p < 0.05$ were regarded as statistically significant.

RESULTS

Among the 744 histopathological sections, cancer foci were identified in 327 (43.9%) sections. 4 patients had Gleason 8 cancers in 16 segments, 24 patients had Gleason 7 cancers in 158 segments and 34 patients had Gleason 6 cancers in 153 segments. The ADC and T_2^* mapping specificities, accuracies, sensitivities, negative-predictive and positive-predictive values for the characterization of the tumours for the entire group of 62 patients are provided in Table 1. Reader 2 exhibited a greater precision for the intermediate- and high-grade PCas with the ADC images than for the high-grade tumours (0.77 vs 0.83, respectively; $p < 0.05$). Both readers exhibited a greater precision for the intermediate-grade PCas with the T_2^* maps than for the high-grade PCas (Radiologist 1, 0.86 vs 0.81; Radiologist 2, 0.83

vs 0.78; $p < 0.05$). Therefore, the accuracy for the intermediate- and high-grade PCas based on T_2^* mapping was greater than that for those based on ADC mapping (Table 2). The AUCs and ROC curves for the two image sets of the intermediate- and high-grade PCas and the low-grade PCas for both readers are presented in Figure 1 and Table 3. For both readers, for the intermediate- and high-grade PCas, the predictions based on the T_2^* maps were more accurate than those based on the ADC maps. There was an obvious AUC variation between the ADC and T_2^* maps regarding low-grade PCas. Figures 2 and 3 present typical intermediate-/high-grade and low-grade PCa. In addition, T_2^* mapping exhibited a weighted κ value of 0.59.

DISCUSSION

Other research has demonstrated that the precision of PCa detection increases following the addition of DWI to T_2 weighted imaging (83–88% vs 69–77%).^{20–22} Recently, Portalez et al²³ performed a study that compared DWI and T_2 weighted imaging and demonstrated that a suspicious lesion identified by DWI causes the tumour probability to increase 12-fold in a segment.

Figure 3. A 69-year-old male with prostate cancer with a Gleason score of 8. (a) An apparent diffusion coefficient map revealing a focal area of low signal intensity in the peripheral zone of the left mid-gland (3–5 o'clock position, white arrows). (b) The transverse T_2^* map showing the equivocal loss of signal without mass effect in the peripheral zone of the left mid-gland (3–5 o'clock position, white arrows).

Nevertheless, the applicability of DWI for PCa detection is limited owing to the substantial overlap of ADC values between cancerous and normal areas.^{12,13,24} Quantitative MRI results are strongly influenced by the ratio of independent histological elements.²⁵ Woodfield et al⁸ reported that if the Gleason score is 6, cancer is more likely to be invisible on ADC mapping. To the extent of our knowledge, based on Gleason scores, the augmenting effect of DWI has been assessed only in a single study.²⁶ Nevertheless, in this study, only the sensitivity data and high b -value areas were compared; ADC mapping was not reported, and ROC curve analysis was not conducted.

Various methods can be used to evaluate the accuracy of PCa detection with MRI. For example, the findings of whole-mount histology or transrectal ultrasonography-guided biopsy can be used as reference criteria. The obvious cancer framework for dividing the prostate gland and the endorectal or pelvic coil using a phased array is defined by the tumour dimension cut-off.²⁷ From this perspective, the relationship between the diagnostic performance of MRI in PCa detection and Gleason scores has been the focus of only two studies.^{28,29} Zakian et al²⁹ reported that the sensitivities of detecting Gleason 8 or higher PCas and Gleason 6 PCas with MR spectroscopic imaging are 89.5% and 44.4%, respectively. In addition, Vargas et al³⁰ reported a detection rate of 53–63% for Gleason 6 cancers, whereas Gleason 8 or greater cancers were detected with ADC mapping. Our study demonstrated that the AUC for T_2^* mapping was significantly greater than that for ADC mapping in terms of intermediate- and high-grade PCas, but the AUCs did not differ between T_2^* mapping and ADC mapping in terms of low-grade PCas. These results agree with the above findings and suggest that MR-based detection of PCa is dependent on the Gleason score. It is highly possible that tumours of smaller volume with Gleason scores of 6 and substantial overlap between the ADC and T_2^* values of tumours with Gleason scores of 6 and normal prostate tissues may have influenced the tumour detection sensitivity based on these sets of images. These issues were not assessed in the present study. In addition, for Reader 2, the ADC maps were more accurate for the intermediate-grade PCas than for the high-grade PCas; thus, it is possible that the effects of ADC mapping vary for readers with different levels of experience.³⁰

In the present study, quantitative T_2^* mapping at 3.0 T was evaluated in terms of its clinical value for the detection of PCas. However, in accordance with the small number of research subjects, our results demonstrated an obvious variation in the average T_2^* relaxation times between cancerous and healthy tissues. Therefore, theoretically speaking, cancerous tissues can be quite definitively recognized by shortening of the T_2^* relaxation time.

Nevertheless, the definitiveness of the T_2^* value, which is a parameter that exhibits fundamental variation in PCas, remains unknown. Different physiologic features of the tissue that are not due to PCa but are instead due to other states, including ischaemia, benign prostatic hyperplasia and inflammation, might be reflected. Furthermore, the variability of the T_2^* value in terms of the detection of tumours was demonstrated. Because the body temperature, age and other factors may alter diffusion in some tissues, the threshold T_2^* values used for the discrimination of cancers from healthy tissues might vary, which makes it difficult to apply some common threshold T_2^* values for tumour identification.

However, our research is still limited in the following aspects. First, choice and verification deviations may exist in this retrospective research. Furthermore, it is possible that the readers were biased and exhibited increased sensitivity because they were aware of the diagnoses of PCas owing to the retrospective nature of the MRI data. Moreover, in some slices of the prostate, recall bias related to the presence or absence of a PCa may have appeared in our research. Later MR interpretations might have been affected by reviews of MRs in earlier sessions. Relatedly, we conducted the image review sessions with an interval of 4 weeks to decrease this bias as much as possible, and we randomly assessed the MRI data sets individually in each section. Moreover, choice bias may have been present because we only included patients who had undergone radical prostatectomy; therefore, their lesions were less aggressive and more localized. The κ value result suggested a moderate level of disagreement in the readings of the T_2^* mappings, which is also a limitation of the present study. Finally, owing to the section-by-section method, there were essential drawbacks in terms of the relation between the histological examination and the imaging, which were caused by variations in the angle variations between the histological and MRI slices, in addition to the general reduction of prostate during fixation. In this regard, the prostates were split into 12 sections. Therefore, the assessment of the presence of a PCa in each section was influenced as little as possible by the possible non-conformity between the histological slices and the MRI choices.

In summary, T_2^* values are influenced by Gleason scores. T_2^* mapping improves the accuracy of the characterization of intermediate-/high-grade PCas but not low-grade cancers compared with ADC mapping.

FUNDING

This work was supported by National Natural Science Foundation of China (Youth Program No. 81401403).

REFERENCES

- Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J, Brawley O, et al. International variation in prostate cancer incidence and mortality rates. *Eur Urol* 2012; **61**: 1079–92. doi: <http://dx.doi.org/10.1016/j.eururo.2012.02.054>
- Bill-Axelsson A, Holmberg L, Ruutu M, Garmo H, Stark JR, SPCG-4 Investigators, . Radical prostatectomy versus watchful waiting in early prostate cancer. *N Engl J Med* 2011; **364**: 1708–17. doi: <http://dx.doi.org/10.1056/NEJMoa1011967>
- Bostwick DG, Foster CS. Predictive factors in prostate cancer: current concepts from the college of American readers conference on solid tumor prognostic factors and the World Health Organization second international

- consultation on prostate cancer. *Semin Urol Oncol* 1999; **7**: 222–72.
4. Kobus T, Vos PC, Hambrock T, De Rooij M, Hulsbergen-Van de Kaa CA, Barentsz JO, et al. Prostate cancer aggressiveness: in vivo assessment of MR spectroscopy and diffusion-weighted imaging at 3 T. *Radiology* 2012; **265**: 457–67. doi: <http://dx.doi.org/10.1148/radiol.12111744>
 5. Selnaes KM, Heerschap A, Jensen LR, Tessem MB, Schweder GJ, Goa PE, et al. Peripheral zone prostate cancer localization by multi-parametric magnetic resonance at 3 T: unbiased cancer identification by matching to histopathology. *Invest Radiol* 2012; **47**: 624–33. doi: <http://dx.doi.org/10.1097/RLI.0b013e318263f0fd>
 6. Turkbey B, Pinto PA, Mani H, Bernardo M, Pang Y, McKinney YL, et al. Prostate cancer: value of multiparametric MR imaging at 3 T for detection—histopathologic correlation. *Radiology* 2010; **255**: 89–99. doi: <http://dx.doi.org/10.1148/radiol.09090475>
 7. Mannelli L, Nougaret S, Vargas HA, Do RK. Advances in diffusion-weighted imaging. *Radiol Clin North Am* 2015; **53**: 569–81. doi: <http://dx.doi.org/10.1016/j.rcl.2015.01.002>
 8. Woodfield CA, Tung GA, Grand DJ, Pezzullo JA, Machan JT, Renzulli JF 2nd. Diffusion-weighted MRI peripheral zone prostate cancer: comparison tumor apparent diffusion coefficient gleason score percentage tumor core biopsy. *AJR Am J Roentgenol* 2010; **194**: W316–22. doi: <http://dx.doi.org/10.2214/AJR.09.2651>
 9. Tamada T, Sone T, Jo Y, Toshimitsu S, Yamashita T, Yamamoto A, et al. Apparent diffusion coefficient values in peripheral and transition zones of the prostate: comparison between normal and malignant prostatic tissue and correlation with histologic grade. *J Magn Reson Imaging* 2008; **28**: 720–6. doi: <http://dx.doi.org/10.1002/jmri.21503>
 10. Itou Y, Nakanishi K, Narumi Y, Nishizawa Y, Tsukuma H. Clinical utility of apparent diffusion coefficient (ADC) values in patients with prostate cancer: can ADC values contribute to assess the aggressiveness of prostate cancer? *J Magn Reson Imaging* 2011; **33**: 167–72. doi: <http://dx.doi.org/10.1002/jmri.22317>
 11. Turkbey B, Shah VP, Pang Y, Bernardo M, Xu S, Kruecker J, et al. Is apparent diffusion coefficient associated with clinical grade scores for prostate cancers that are visible on 3-T MR images? *Radiology* 2011; **258**: 488–95. doi: <http://dx.doi.org/10.1148/radiol.10100667>
 12. Gibbs P, Pickles MD, Turnbull LW. Diffusion imaging of the prostate at 3.0 tesla. *Invest Radiol* 2006; **41**: 185–8. doi: <http://dx.doi.org/10.1097/01.rli.0000192418.30684.14>
 13. Kim CK, Park BK, Han JJ, Kang TW, Lee HM. Diffusion weighted imaging of the prostate at 3 T for differentiation of malignant and benign tissue in transition and peripheral zones: preliminary results. *J Comput Assist Tomogr* 2007; **31**: 449–54. doi: <http://dx.doi.org/10.1097/01.rct.0000243456.00437.59>
 14. Yoshimitsu K, Kiyoshima K, Irie H, Tajima T, Asayama Y, Hirakawa M, et al. Usefulness of apparent diffusion coefficient map in diagnosing prostate carcinoma: correlation with stepwise histopathology. *J Magn Reson Imaging* 2008; **27**: 132–9. doi: <http://dx.doi.org/10.1002/jmri.21181>
 15. Ghugre NR, Enriquez CM, Coates TD, Nelson MD Jr, Wood JC. Improved R_2^* measurements in myocardial iron overload. *J Magn Reson Imaging* 2006; **23**: 9–16. doi: <http://dx.doi.org/10.1002/jmri.20467>
 16. Mamisch TC, Hughes T, Mosher TJ, Mueller C, Trattinig S, Boesch C, et al. T2 star relaxation times for assessment of articular cartilage at 3 T: a feasibility study. *Skeletal Radiol* 2012; **41**: 287–92. doi: <http://dx.doi.org/10.1007/s00256-011-1171-x>
 17. Hardman RL, El-Merhi F, Jung AJ, Ware S, Thompson IM, Friel HT, et al. Fast T2*-weighted MRI of the prostate at 3 tesla. *J Magn Reson Imaging* 2011; **33**: 902–7. doi: <http://dx.doi.org/10.1002/jmri.22496>
 18. Korteweg MA, Zwanenburg JJ, Hoogduin JM, van den Bosch MA, van Diest PJ, van Hillegersberg R, et al. Dissected sentinel lymph nodes of breast cancer patients: characterization with high-spatial-resolution 7-T MR imaging. *Radiology* 2011; **261**: 127–35. doi: <http://dx.doi.org/10.1148/radiol.11103535>
 19. Wu LM, Chen XX, Xuan HQ, Liu Q, Suo ST, Hu J, et al. Feasibility and preliminary experience of quantitative T2* mapping at 3.0 T for detection and assessment of aggressiveness of prostate cancer. *Acad Radiol* 2014; **21**: 1020–6. doi: <http://dx.doi.org/10.1016/j.acra.2014.04.007>
 20. Haider MA, van der Kwast TH, Tanguay J, Evans AJ, Hashmi AT, Lockwood G, et al. Combined T2-weighted and diffusion-weighted MRI for localization of prostate cancer. *AJR Am J Roentgenol* 2007; **189**: 323–8.
 21. Lim HK, Kim JK, Kim KA, Cho KS. Prostate cancer: apparent diffusion coefficient map with T2-weighted images for detection—a multireader study. *Radiology* 2009; **250**: 145–51. doi: <http://dx.doi.org/10.1148/radiol.2501080207>
 22. Katahira K, Takahara T, Kwee TC, Oda S, Suzuki Y, Morishita S, et al. Ultra-high-b-value diffusion-weighted MR imaging for the detection of prostate cancer: evaluation in 201 cases with histopathological correlation. *Eur Radiol* 2011; **21**: 188–96. doi: <http://dx.doi.org/10.1007/s00330-010-1883-7>
 23. Portalez D, Rollin G, Leandri P, Elman B, Mouly P, Jonca F, et al. Prospective comparison of T2w-MRI and dynamic-contrast-enhanced MRI, 3D-MR spectroscopic imaging or diffusion-weighted MRI in repeat TRUS-guided biopsies. *Eur Radiol* 2010; **20**: 2781–90. doi: <http://dx.doi.org/10.1007/s00330-010-1868-6>
 24. Pickles MD, Gibbs P, Sreenivas M, Turnbull LW. Diffusion-weighted imaging of normal and malignant prostate tissue at 3.0 T. *J Magn Reson Imaging* 2006; **23**: 130–4.
 25. Langer DL, van der Kwast TH, Evans AJ, Plotkin A, Trachtenberg J, Wilson BC, et al. Prostate tissue composition and MR measurements: investigating the relationships between ADC, T2, K(trans), v(e), and corresponding histologic features. *Radiology* 2010; **255**: 485–94. doi: <http://dx.doi.org/10.1148/radiol.10091343>
 26. Rosenkrantz AB, Mannelli L, Kong X, Niver BE, Berkman DS, Babb JS, et al. Prostate cancer: utility of fusion of T2-weighted and high b-value diffusion weighted images for peripheral zone tumor detection and localization. *J Magn Reson Imaging* 2011; **34**: 95–100. doi: <http://dx.doi.org/10.1002/jmri.22598>
 27. Ahmed HU, Kirkham A, Arya M, Illing R, Freeman A, Allen C, et al. Is it time to consider a role for MRI before prostate biopsy? *Nat Rev Clin Oncol* 2009; **6**: 197–206. doi: <http://dx.doi.org/10.1038/nrclinonc.2009.18>
 28. Girouin N, Mège-Lechevallier F, Tonina Senes A, Bissery A, Rabilloud M, Maréchal JM, et al. Prostate dynamic contrast-enhanced MRI with simple visual diagnostic criteria: is it reasonable? *Eur Radiol* 2007; **17**: 1498–509. doi: <http://dx.doi.org/10.1007/s00330-006-0478-9>
 29. Zakian KL, Sircar K, Hricak H, Chen HN, Shukla-Dave A, Eberhardt S, et al. Correlation of proton MR spectroscopic imaging with Gleason score based on step-section pathologic analysis after radical prostatectomy. *Radiology* 2005; **234**: 804–14.
 30. Vargas HA, Akin O, Franiel T, Mazaheri Y, Zheng J, Moskowitz C, et al. Diffusion-weighted endorectal MR Imaging at 3 T for prostate cancer: tumor detection and assessment of aggressiveness. *Radiology* 2011; **259**: 775–84. doi: <http://dx.doi.org/10.1148/radiol.11102066>