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Non-Gaussian water diffusion kurtosis imaging of prostate cancer

Shiteng Suo [a,1], Xiaoxi Chen [a,1], Lianming Wu [a], Xiaofei Zhang [a], Qiuying Yao [a], Yu Fan [a], He Wang [b], Jianrong Xu [a,*]

[a] Department of Radiology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200127, China
[b] Global Applied Science Laboratory, GE Healthcare, Shanghai 201203, China

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ABSTRACT

Purpose: To evaluate the non-Gaussian water diffusion properties of prostate cancer (PCa) and determine the diagnostic performance of diffusion kurtosis (DK) imaging for distinguishing PCa from benign tissues within the peripheral zone (PZ), and assessing tumor lesions with different Gleason scores.
Materials and Methods: Nineteen patients who underwent diffusion weighted (DW) magnetic resonance imaging using multiple b-values and were pathologically confirmed with PCa were enrolled in this study. Apparent diffusion coefficient (ADC) was derived using a monoexponential model, while diffusion coefficient (D) and kurtosis (K) were determined using a DK model. Differences between the ADC, D and K values of benign PZ and PCa, as well as those of tumor lesions with Gleason scores of 6, 7 and ≥8 were assessed. Correlations between parameters D and K in PCa were analyzed using Pearson's correlation coefficient. ADC, D and K values were correlated with Gleason scores of 6, 7 and ≥8, respectively.
Results: ADC and D values were significantly ($p < 0.001$) lower in PCa (0.79 ± 0.14 μm^2/ms and 1.56 ± 0.23 μm^2/ms, respectively) compared to benign PZ (1.23 ± 0.19 μm^2/ms and 2.54 ± 0.24 μm^2/ms, respectively). K values were significantly ($p < 0.001$) greater in PCa (0.96 ± 0.20) compared to benign PZ (0.59 ± 0.08). D and K showed fewer overlapping values between benign PZ and PCa compared to ADC. There was a strong negative correlation between D and K values in PCa (Pearson correlation coefficient $r = -0.729$; $p < 0.001$). ADC and K values differed significantly in tumor lesions with Gleason scores of 6, 7 and ≥8 ($p < 0.001$ and $p = 0.001$, respectively), although no significant difference was detected for D values ($p = 0.325$). Significant correlations were found between the ADC value and Gleason score ($r = -0.828$; $p < 0.001$), as well as the K value and Gleason score ($r = 0.729$; $p < 0.001$).
Conclusion: DK model may add value in PCa detection and diagnosis. K potentially offers a new metric for assessment of PCa.

1. Introduction

Prostate cancer (PCa) is the second most common cancer and the sixth leading cause of cancer deaths in men [1]. Prostate-specific antigen (PSA) testing is most commonly used to initially diagnose PCa, although transrectal ultrasonography (TRUS) guided biopsy is the gold standard. Biopsy samples can be evaluated based on the Gleason score, a histopathological grading system used to predict PCa prognosis [2]. However, both of these tests have their drawbacks. PSA testing lacks specificity in some circumstances, as patients with benign prostatic hyperplasia (BPH), for example, may also demonstrate elevated PSA levels [3]. Furthermore, transrectal biopsy, in which several cores are taken from the prostate in a nontargeted way, may result in undersampling, which often leads to incorrect cancer localization and inaccurate Gleason score.

Prostate magnetic resonance (MR) imaging is a promising technique for the diagnosis of PCa. Traditional T2-weighted MR imaging provides tissue's anatomic information but cannot precisely discriminate PCa from other benign diseases such as prostatitis and BPH [4]. Many other MR functional imaging modalities such as dynamic contrast-enhanced (DCE) MR imaging, MR spectroscopy and diffusion-weighted (DW) imaging have evolved to supplement T2-weighted MR imaging [5–8]. Thus, multiparametric MR imaging has been shown to contribute to the detection and staging of PCa [3].

Of all the MR imaging modalities, DW imaging, which measures the variation in water diffusion among different tissues, has shown great potential to improve PCa diagnosis. Most previous studies have used a simple monoexponential model to describe signal decay with a range of increasing b-values and these results have shown that the

* Corresponding author at: Department of Radiology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, No. 160, Pujian Rd, Pudong, Shanghai 200127, China. Tel.: +86 2168383570.
E-mail address: xujianrong_renji@163.com (J. Xu).
[1] Shiteng Suo and Xiaoxi Chen contributed equally to this work.

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apparent diffusion coefficient (ADC) is typically lower in PCa than in benign prostate tissues [9–12]. A lower ADC value suggests restricted diffusion, which indicates that the Brownian motion of water molecules in tumor tissue is not as free as in normal tissue, likely due to changes in cells and organelles. One limitation of the monoexponential model is that it assumes Gaussian behavior of water thermal motion. However, water diffusion follows a non-Gaussian distribution when restrictions are present, such as in human tissues. Therefore, signal decay is no longer monoxeponential with b-values, as demonstrated by a number of studies [4,13–15]. Diffusion kurtosis (DK) imaging, as an extension of traditional DW imaging, is based on non-Gaussian water diffusion and can better describe complex tissue microstructure [16,17]. In the DK model, a new measure called kurtosis represents the deviation of water diffusion from a Gaussian distribution. DK imaging was first employed to characterize neural tissue, and it has been commonly applied in brain abnormalities such as cerebral infarction [18] and gliomas [19]. Furthermore, DK imaging can be achieved from a standard DW acquisition with more than 3 b-values, with a maximum b-value of 2000 sec/mm^2 necessary to guarantee that diffusional non-Gaussianity has a sufficiently large effect on the DW signal [14].

The purpose of this study was to investigate the impact of non-Gaussian diffusion in PCa using DK imaging as well as determine the capacity of this technique to differentiate between PCa and benign tissues, and assess tumor lesions with different Gleason scores.

2. Materials and methods

2.1. Patient population

This study was approved by the local institutional review board, and written informed consent from patient was not necessary on account of its retrospective nature. Between March 2012 and August 2012, 72 consecutive male patients with biopsy-proven PCa underwent MR examination. The inclusion criteria were as follows: (a) available DICOM datasets including a multiple b-value DW imaging sequence and clinical records; (b) reliable image quality without significant artifacts; (c) less than 3 months between MR examination and prostatectomy; (d) definite pathological record of cancer in the peripheral zone (PZ) and (e) no treatment such as endocrine therapy, external-beam radiotherapy or brachytherapy before MR examination. The study population consisted of 19 male patients (mean age 68 years, range 51–81 years) who underwent 3 Tesla prostatic MR imaging and subsequently received prostatectomy (mean time interval 16 days, range 1–73 days). The mean postoperative Gleason score of the patients in this study was 7 (range 6–9). Nine patients had a Gleason score of 6, 6 had a Gleason score of 7 and the remaining 4 had a Gleason score greater than 7 ($\geq$8). The mean preoperative PSA level was 16.9 ng/ml (range 3.26–115 ng/ml).

2.2. MR imaging

MR imaging was performed on a 3 Tesla MR scanner (HDxt; GE Medical Systems, Waukesha, WI, USA) using a body phased-array coil. All patients underwent a prostatic MR protocol including axial T1-weighted imaging, T2-weighted imaging in 3 orthogonal planes and axial multi-b DW imaging parallel to the corresponding set of T2-weighted images. The main imaging parameters were as follows: for axial T1-weighted imaging, TE = 7 ms, TR = 740 ms, matrix size = 352 × 192, FOV = 280 mm, slice thickness/gap = 3/1 mm, echo train length = 3; for axial T2-weighted imaging, TE = 106 ms, TR = 3940 ms, matrix size = 320 × 224, FOV = 280 mm, slice thickness/gap = 3/1 mm, echo train length = 20; for DW imaging, TE = 106 ms, TR = 3940 ms, matrix size = 128 × 128, FOV = 280 mm, slice thickness/gap = 3/1 mm, echo train length = 20, number of averages = 4, b-values = 0, 500, 800, 1200, 1500 and 2000 sec/mm^2. Total acquisition time was about 20 min. Parameters for T1-weighted imaging and T2-weighted imaging were slightly floating due to individual differences. DW imaging was obtained using a fat suppressed single-shot echo-planar sequence. Low b-values (less than 200 sec/mm^2) were not used in order to minimize microcirculation effects [14]. For each b-value, 3 orthogonal directions were employed to generate rotationally invariant trace images. Dynamic contrast-enhanced (DCE) MR imaging was performed in most of the patients (14/19), but was not analyzed in this study. DW imaging was performed before DCE MR imaging in patients who received both procedures.

2.3. Image interpretation and data analysis

All patients received prostatectomy after MR examination. Transverse prostatectomy specimens were sliced from apex to base at 3-mm intervals. All slices were reviewed by an experienced pathologist who was blinded to the MR results, and regions of PCa were delineated.

MR data were transferred to a PC for further calculation and analysis, and were post-processed using in-house software written in Matlab (version R2011b; MathWorks, Natick, MA, USA). With histopathological examination used as the reference standard, MR data were interpreted by a radiologist with 8 years of experience in diagnosing pelvic MR images. Regions of interest (ROIs) were placed within the largest proven PCa lesion on T2-weighted images and DW images. The size and extent of the lesion ROI were chosen to ensure that the ROI matched, as closely as possible, the tumor size and extent as indicated by histological examination [20]. Another ROI was placed within contralateral benign tissue for comparison. Nineteen data points were obtained with a ROI size of 65.93 ± 43.80 mm^2 (range, 15.55–196.21 mm^2) in PCa and 70.59 ± 39.05 mm^2 (range, 27.52–142.37 mm^2) in benign PZ. To improve the signal-to-noise ratio (SNR), a nonlocal-means filter for image denoising was employed before curve-fitting. The multi-b DW images were fitted voxel-by-voxel using the DK signal decay equation by means of a nonlinear least squares algorithm:

$$S(b) = S_0 \times \exp\left(-bD + \frac{1}{6}b^2D^2K\right). \quad (1)$$

In this equation, S(b) is the signal intensity at a certain b-value; S_0 is the signal intensity at b = 0; D is the diffusion coefficient; and K is the excess kurtosis. K describes the degree to which molecular motion deviates from the perfect Gaussian distribution. When K is equal to 0, equation (1) degrades to conventional monoexponential equation:

$$S(b) = S_0 \times \exp(-b \times ADC) \quad (2)$$

The difference between D and ADC is that D is a corrected form of ADC for use in non-Gaussian circumstances. Both equations (1) and (2) were fitted in the software and 3 parameter maps for ADC, D and K were produced. ROIs were pasted from DW images to the parameter maps for data analysis.

Additionally, SNRs of benign PZ and PCa were recorded on DW images with a b-value of 2000 s/mm^2. Mean intensities were measured on the ROIs of both benign PZ and PCa. The standard deviation of background intensity was also calculated by placing a