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Biexponential apparent diffusion coefficients in prostate cancer

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Abstract

Purpose: The purpose of this study was to investigate the need for biexponential signal decay modeling for prostate cancer diffusion signal decays with b-factor over an extended b-factor range.
Materials and Methods: Ten healthy volunteers and 12 patients with a bulky prostate cancer underwent line scan diffusion-weighted MR imaging in which b-factors from 0 to 3000 s/mm^2 in 16 steps were sampled. The acquired signal decay curves were fit with both monoexponential and biexponential signal decay functions and a statistical comparison between the two fits was performed.
Results: The biexponential model provided a statistically better fit over the monoexponential model on the peripheral zone (PZ), transitional zone (TZ) and prostate cancer. The fast and slow apparent diffusion coefficients (ADCs) in the PZ, TZ and cancer were 2.9±0.2, 0.7±0.2×10^{-3} mm^2/ms (PZ); 2.9±0.4, 0.7±0.2×10^{-3} mm^2/ms (TZ); and 1.7±0.4, 0.3±0.1×10^{-3} mm^2/ms (cancer), respectively. The apparent fractions of the fast diffusion component in the PZ, TZ and cancer were 70±10%, 60±10% and 50±10%, respectively. The fast and slow ADCs of cancer were significantly lower than those of TZ and PZ, and the apparent fraction of the fast diffusion component was significantly smaller in cancer than in PZ.
Conclusions: Biexponential diffusion decay functions are required for prostate cancer diffusion signal decay curves when sampled over an extended b-factor range, providing additional, unique tissue characterization parameters for prostate cancer.

Keywords: MRI; Diffusion; Prostate cancer; Biexponential decay

1. Introduction

Prostate cancer is the third most common cancer in men worldwide, and there has been a large increase in the number of patients during the last two decades [1]. The diagnosis of prostate cancer is basically made by transrectal ultrasonography (TRUS)-guided prostate biopsy; however, the cancer detection rate still remains unsatisfactory [2,3]. Magnetic resonance (MR) imaging of the prostate with a phased array coil and/or an endorectal coil provides excellent anatomical information. Although MR imaging has been considered sensitive for prostate cancer, other lesions such as prostatitis or benign hyperplasia can mimic prostate cancer, which shows low signal intensity on T2-weighted images. To overcome the lack of specificity for prostate cancer, dynamic contrast-enhanced MRI and MR spectroscopy have been applied. Both dynamic contrast-enhanced MR imaging and MR spectroscopy have been shown to improve prostate cancer detection and staging accuracy compared with T2-weighted MR imaging alone [4–8].

Diffusion-weighted MR imaging (DWI) has been proposed as another candidate to improve prostate cancer detection. Recent advances in MR imaging technologies, especially echo planar imaging (EPI) and parallel imaging techniques, make feasible the application of diffusion imaging to abdominal and pelvic organs such as liver, pancreas, ovary and uterus with clinical scanners. Similarly, several papers have been published in which DWI was applied to prostate

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cancer in which apparent diffusion coefficient (ADC) values of prostate cancer have been generally shown to be lower than normal prostate tissues [9–14].

Typically, b-factors used for diffusion imaging of the abdominal and pelvic organs are within the 0 to 1000 s/mm^2 range and ADC values are calculated assuming that the signal decay with b-factor is a monoexponential decay function. However, in normal human brain tissue [15–18] and brain pathologies like tumor [19] and stroke [20], it has been shown that the signal decay with b-factor over an extended b-factor range is better modeled using biexponential decay functions as opposed to monoexponential decay functions. Recently, Mulkern et al. [21] demonstrated that signal decays from normal-appearing peripheral zone and central gland tissue from the prostates of a group of cancer patients were also best modeled with bi- as opposed to monoexponential functions over an extended b-factor range, as previously found for normal and pathological brain tissues [15–20].

In this study, detailed diffusion measurements of prostate cancer using multiple b-factors ranging up to 3000 s/mm^2 have been made. Biexponential fits were applied to diffusion decay curves from cancerous tissues of the prostate and found to be more suitable than monoexponential functions over the extended b-factor range. Biexponential parametrization of the diffusion signal decay curves offers new and unique information to characterize normal prostate tissues and prostate cancer.

2. Materials and methods

All studies were performed with a 1.5-T MR scanner (Signa Excite HD, General Electric Healthcare, Milwaukee, WI, USA) using an eight-channel body array coil. Ten healthy volunteers ages 49–79 years (mean age 64.2 years) and 12 patients with biopsy-proven prostate cancer ages 60–86 years (mean age 71.5 years) were included in this study. Informed consent was obtained from all subjects. Patients were selected using the following criteria: (1) region of cancer was obvious and the cancer formed a bulky mass on T2-weighted images; (2) region of cancer did not contain hemorrhage on T1-weighted images, both as determined from visual inspection by an experienced radiologist. All examinations included axial T1- and T2-weighted images using a 5-mm slice thickness with a 0.5-mm gap, four excitations, an 18-cm field of view and 288×192 (ZIP 512) matrices. Detailed diffusion measurements were performed with a single column variant of the line scan diffusion imaging (LSDI) technique [15,22,23]. A 10×10-mm^2 cross-sectional column passing through the prostate gland was chosen for interrogation. Sixty-four along-column frequency encoding steps were used to sample the echo, resulting in an along-column spatial resolution of approximately 2.8 mm. As a consequence, minimal voxel sizes were 10×10×2.8 mm^3. Diffusion measurements of the tissue column were performed with an inner volume spin-echo sequence. Mutually orthogonal slice selective excitation and refocusing pulses were used to obtain an echo from the intersection of the two slices. The amplitude of the diffusion sensitization gradient, as obtained by simultaneous application along all three orthogonal gradient directions, was exponentially incremented every TR period to cover b-factors from 0 to 3000 s/mm^2 in 16 steps. Consequently, an image consisting of 16 lines, each of which represents a magnitude one-dimensional (1D) image of the column at a different b-factor, was obtained in one acquisition. Scan time was 38 s with TR/TE=2000/91 (ms/ms). In volunteers, a single axial slice that included transitional zone (TZ) and peripheral zone (PZ) was selected for the diffusion measurements. Then, the position of the column was set to pass through the TZ and PZ. In patients, a single slice and the position of a column were selected to pass through the middle of the cancerous tissue to provide regions-of-interest (ROI) which avoided contamination of noncancerous tissue for diffusion measurements (Fig. 1).

The acquired datasets were transferred to a personal computer, and data analysis was performed with OsiriX and in-house software. For the analysis, the ROIs were chosen as large as possible consistent with minimal contamination from unintended tissues by two experienced radiologists (HS, KO) on the basis of exact measurements of the coordinate point on LSDI and T2-weighted images. The ROIs corresponding to TZ and PZ in volunteers and cancerous tissue in patients were extracted and fit with both monoexponential functions and biexponential decay functions of the following form:

$$S = A_{\mathrm{fast}}\exp(-\mathrm{ADC}_{\mathrm{fast}}b) + A_{\mathrm{slow}}\exp(-\mathrm{ADC}_{\mathrm{slow}}b) \qquad (1)$$

Here, S is the signal intensity; b is the b-factor; A_{fast}, A_{slow} are the apparent amplitudes of the fast and slow components; and $\mathrm{ADC}_{\mathrm{fast}}$, $\mathrm{ADC}_{\mathrm{slow}}$ are the fast and slow ADCs, respectively. In both mono- and biexponential fitting, it is understood that the “apparent” amplitudes contain both T1- and T2-weighting where the latter can be considerable due to the long echo time required for the heavy diffusion weightings accessed. Furthermore, the first b-factor (b=0) was excluded from the analyses to decrease contamination from any “perfusion” component. A statistical comparison between monoexponential (A_{slow}=0 in Eq. (1)) and biexponential fits was performed in each individual case by F tests using χ^2 values of each type of fit [21,24]. A statistically improved fit was considered with P<.05 in the F test. In addition, Student’s t tests were performed to assess statistical significance of biexponential parameter differences between tissue types with P values less than .05 considered significant.

3. Results

Detailed diffusion datasets using multiple b-factors ranging up to 3000 s/mm^2 were successfully acquired from all volunteers and patients. Fig. 2 shows semi-log plots of