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Combined prostate diffusion tensor imaging and dynamic contrast enhanced MRI at 3T — quantitative correlation with biopsy☆

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Abstract

The purpose of this work was to compare diagnostic accuracy of Diffusion Tensor Imaging (DTI), dynamic contrast-enhanced magnetic resonance imaging (DCE MRI) and their combination in diagnosing prostate cancer. Twenty-five patients with clinical suspicion of prostate cancer underwent MRI, prior to transrectal ultrasound-guided biopsies. MRI data were correlated to biopsy results. Logistic regression models were constructed for the DTI parameters, DCE MRI parameters, and their combination. The areas under the receiver operator characteristic curves (AUC) were compared between the models. The nonparametric Wilcoxon signed rank test was used for statistical analysis. The sensitivity and specificity values were respectively 81% (74–87%) and 85% (79–90%) for DTI and 63% (55–70%) and 90% (85–94%) for DCE. The combination "DTI or DCE MRI" had 100% (97–100%) sensitivity and 77% (69–83%) specificity, while "DTI and DCE MRI" had 44% (37–52%) sensitivity and 98% (94–100%) specificity. The AUC for DTI+DCE parameters was significantly higher than that for either DTI (0.96 vs. 0.92, P=.0143) or DCE MRI parameters (0.96 vs. 0.87, P=.00187) alone. In conclusion, the combination of DTI and DCE MRI has significantly better accuracy in prostate cancer diagnosis than either technique alone.

Keywords: Diffusion tensor imaging; Dynamic contrast enhanced MRI; Prostate cancer; 3T; Biopsy; Logistic regression analysis

1. Introduction

Non-invasive identification and localization of prostate cancer remains challenging. Magnetic resonance imaging (MRI) is arguably the best non-invasive diagnostic method available. Relatively low sensitivity and specificity of the traditionally used T_2-weighted images can be improved to some degree with other MRI techniques such as Diffusion Tensor Imaging (DTI) [1,2], dynamic contrast-enhanced (DCE) MRI [3,4] and MR spectroscopic imaging (MRSI) [5,6]. Recently, a number of studies suggested that a combination of several MRI techniques can further improve the MRI capability of diagnosing prostate cancer [7–14]. Most of these techniques, however, were based on the qualitative assessment of the MRI exams by an experienced reader.

In this study we used a combination of DTI and DCE MRI with quantitative analysis, using biopsy as a reference standard, to test whether this combination improves the sensitivity and specificity over either technique alone. The presence or absence of cancer was evaluated based on the numerical values of 5 MRI parameters calculated from DTI and DCE MRI data. In addition, logistic regression modeling was used to construct a predictor that can estimate the probability of any pixel within parametric maps representing cancer.

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In a previous study at 1.5 T, we have shown that a combination of the diffusion-weighted (DW) and DCE MRI provides higher sensitivity in diagnosing prostate cancer than either technique alone [14]. In this study, we tested whether with the expected improvement in data quality at a higher field of 3.0 T, the combination of diffusion and DCE MRI remains more accurate in prostate cancer diagnosis that either of these techniques alone.

2. Materials and methods

2.1. Patient selection and biopsy technique

This prospective study was approved by the institutional human ethics board, and all participants gave signed consent prior to entering the study. Twenty-five patients with a high clinical suspicion for prostate adenocarcinoma due to an elevated prostate specific antigen (PSA) and/or palpable prostatic nodule, with no prior treatment, were consecutively recruited to this study. Standard MRI exclusion criteria (e.g., pacemaker, metallic implants, known allergy to MRI contrast agent, etc.) were applied during patients' selection process. Unlike in most prostate MRI studies, subjects recruited to this study underwent MRI examination prior to transrectal ultrasound (TRUS)-guided biopsies. Such recruitment process ensures that the study is truly prospective in its assessment as a diagnostic tool, and that no artifacts resulting from biopsies are present in the MRI images.

TRUS biopsies of the prostate were performed on a GE Logic 9 ultrasound machine (GE Healthcare, Milwaukee, WI, USA). The patients were examined with gray scale imaging in the axial and sagittal planes with a 5-MHz transrectal probe. All patients had an enema and were given prophylactic antibiotics prior to performing the prostate biopsies. The biopsies were performed under local anesthetic and the number of biopsies obtained from the peripheral zone (PZ) was determined by prostate gland size. In patients with a prostate gland of 30 cc or less, eight biopsies (base: right and left; midgland: right lateral, left lateral, right medial, left medial; apex: right and left) were taken. For prostate glands ranging 31–60 cc, 10 biopsies (base: right lateral, left lateral, right medial, left medial; midgland and apex biopsies as above) were obtained. For prostate glands greater than 60 cc, 12 biopsies were obtained (apex: right lateral, left lateral, right medial, left medial, base and midgland biopsies the same as the 10 biopsy scheme).

2.2. MRI examinations

All MRI examinations were performed on a 3-T MRI scanner (Achieva, Philips Healthcare, Best, the Netherlands). MRI signals were acquired with a combination of an endorectal coil (Medrad, Pittsburgh, PA, USA) and a cardiac phased-array coil (Philips Healthcare, Best, the Netherlands). Fast spin-echo T_2-weighted images (repetition time TR=1851 ms, effective echo time TE=80 ms, field of view (FOV)=14 cm, slice thickness=4 mm with no gap, 284×225 matrix, three averages) were acquired in the axial and coronal planes to provide anatomical details of the prostate. From this sequence, 12 axial slices covering the entire gland were then selected and used for the DTI and DCE MRI scans.

DTI data were acquired using a diffusion weighted single shot echo planar imaging (EPI) sequence (TR/TE=2100/74 ms, FOV=24 cm, slice thickness=4 mm with no gap, 128×115 matrix, 6 non-collinear gradient directions, *b*-value=0 and 600 s/mm^2, 18 averages, total acquisition time of 8 min; the relatively low *b*-value of 600 s/mm^2 was chosen to ensure sufficient SNR for quantitative measurements of DTI parameters).

DCE MRI was performed using a 3D T_1-weighted (T1W) spoiled gradient echo sequence (TR/TE=3.4/1.06 ms, flip angle=15°, FOV=24 cm, 256×163 matrix, two averages). Initially, proton density (PD) images (TR/TE=50/0.95 ms, flip angle=4°) were acquired to allow calculation of the contrast agent concentrations in the prostate [15]. Next, a series of 75 T1W images were acquired prior to (three images) and following (72 images) a bolus injection of Gd-DTPA (Magnevist, Berlex Canada; 0.1 mmol/kg injected with a motorized power injector within 10 s followed by a 20 ml flush of saline). This resulted in a time resolution of 10.6 sec per 12 slices. The total time of the MRI examination was approximately 45 min.

2.3. Data processing

The DTI data were processed off-line. Diffusion weighted images were registered to the non-weighted *b*=0 image with a mutual information algorithm prior to calculating the eigenvalues of the diffusion tensor and generating maps of the average diffusivity (<*D*>) (i.e., trace of the diffusion tensor) and fractional anisotropy (FA) with the proprietary DTI processing toolbox PRIDE (Philips Healthcare, Best, the Netherlands).

DCE MRI data were processed off-line with software procedures developed in house using Matlab (Mathworks, Natick, MA, USA) and Igor Pro (WaveMetrics, Portland, OR, USA). Prior to further processing, T1W and PD images were registered to one another using PRIDE. Contrast agent concentration maps were calculated from the T1W and PD images as described in [15]. Arterial Input Functions (AIFs) were extracted from voxels in the external iliac or femoral arteries in the central slice for each patient [16]. It has been shown that even with relatively low temporal resolution of 10 seconds per time point used in this study, the patient-specific AIF provides more accurate fitting in highly enhancing areas than the population average AIF [17]. Pharmacokinetic parameters: volume transfer constant (K^{trans}), fractional volume of the extra-vascular extra-cellular space (v_e), and fractional plasma volume (v_p), were calculated by fitting the contrast agent concentration vs. time curves to the extended Kety model [18].