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Prostate cancer discrimination in the peripheral zone with a reduced field-of-view T_2-mapping MRI sequence☆

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ABSTRACT

Objectives: To evaluate the performance of T_2 mapping in discriminating prostate cancer from normal prostate tissue in the peripheral zone using a practical reduced field-of-view MRI sequence requiring less than 3 minutes of scan time.
Materials and methods: Thirty-six patients with biopsy-proven peripheral zone prostate cancer without prior treatment underwent routine multiparametric MRI at 3.0 T with an endorectal coil. An Inner-Volume Carr-Purcell-Meiboom-Gill imaging sequence that required 2.8 minutes to obtain data for quantitative T_2 mapping covering the entire prostate gland was added to the routine multiparametric protocol. Suspected cancer (SC) and suspected healthy (SH) tissue in the peripheral zone were identified in consensus by three radiologists and were correlated with available biopsy results. Differences in mean T_2 values in SC and SH regions-of-interest (ROIs) were tested for significance using unpaired Student's two-tailed t-test. The area under the receiver operating characteristic curve was used to assess the optimal threshold T_2 value for cancer discrimination.
Results: ROI analyses revealed significantly ($p < 0.0001$) shorter T_2 values in SC (85.4 ± 12.3 ms) compared to SH (169.6 ± 38.7 ms). An estimated T_2 threshold of 99 ms yielded a sensitivity of 92% and a specificity of 97% for prostate cancer discrimination.
Conclusions: Quantitative values derived from this clinically practical T_2-mapping sequence allow high precision discrimination between healthy and cancerous peripheral zone in the prostate.

1. Introduction

Prostate cancer is the leading cause of non-cutaneous cancer diagnosed among men in the US and is the second most common cause of cancer death, exceeded only by lung cancer [1]. Despite extensive research in the field, many uncertainties remain about this disease, including screening strategies, non-invasive assessment of aggressiveness and treatment options for different grades of cancer. In this setting, prostate MRI has been the focus of extensive research to help improve accuracy in not only ruling out significant disease, but also characterizing and grading tumors, vital information for disease management and treatment stratification.

MRI has been successfully used to stage prostate cancer since the late-1980s, primarily with T_2-weighted (T2W) and T_1-weighted (T1W) imaging sequences. There has been continual improvement in hardware, including the incorporation of endorectal coils, and in software development of pulse sequences suitable for diffusion weighted imaging (DWI), spectroscopy and dynamic contrast enhanced (DCE) studies [2]. Given recent interest in focal therapies and active surveillance as viable options for prostate cancer treatment and the addition of multiparametric imaging capabilities with the technical advances, there is a shifting emphasis toward non-invasive detection, localization and characterization of the disease in addition to staging with MRI.

It is widely appreciated that peripheral zone prostate cancer often has low signal on T2W images [3], making T2W imaging a key, if subjective, assessment for cancer detection. Quantitative measurement of T_2 and the generation of T_2 maps for prostate cancer detection have been previously reported [4–9] but are not routinely used clinically nor are as ubiquitous as mapping of the apparent diffusion coefficient (ADC) value, a quantitative technique used routinely in

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prostate cancer staging and detection, in conjunction with visual impressions from the raw diffusion weighted images [2].

The decrease of signal on T2W images within the peripheral zone that accompanies focal cancer indicates a shortening of the T_2-decay and so it seems somewhat surprising that the use of quantitative T_2 values to discriminate prostate cancer from normal peripheral zone has not been exploited to a greater degree. This may in part be attributed to the prolonged scan times associated with acquiring multiple echo time (TE) data sets required for T_2 evaluation. Our goal in this work was to evaluate the performance of T_2 mapping for discriminating areas of suspected prostate cancer from suspected normal glandular tissue in the peripheral zone when using a practical Inner-Volume Carr-Purcell-Meiboom-Gill (IV-CPMG) imaging sequence.

2. Materials and methods

2.1. Patient population

Patients with newly diagnosed biopsy-proven adenocarcinoma of the prostate without prior treatment undergo routine multiparametric 3 tesla MRI at our institution for the purposes of treatment staging or active surveillance. Between November 2012 and February 2013, 45 consecutive of these patients (median age 60 years; range 50–72 years) had an additional sequence for T_2 mapping added to their MRI protocol. The study was performed under an institutional review board-approved protocol and informed consent was obtained prior to MRI and signed by each patient and a study coordinator.

Of the 45 patients who underwent the additional imaging, four were later excluded from the study either because it was found that there was an absence of a suspicious lesion in the peripheral zone or there was a suspicious lesion but it was in the central gland or anterior fibromuscular stroma (e.g. based on clinical T2W and diffusion-weighted images). Five other patients were excluded because there was significant motion artifact on the T_2 mapping sequence used for the study.

Image data from 36 patients (out of the initial 45 patients that had T_2 mapping) were included in the final study. Of the patients whose data were included, nine had low-risk, 21 had intermediate-risk and six had high-risk prostate cancer (D'Amico's risk criteria [10]). At the time of enrollment, the mean serum prostate-specific antigen (PSA) level was 8.5 ng/mL (range 3.6–21.8 ng/mL). Indications for MRI were mainly for staging ($n = 28$), but also included active surveillance ($n = 8$). The time of biopsy prior to the MRI ranged from 7 to 551 days with a median and standard deviation of 51 and 127 days respectively. Several patients had multiple biopsies.

2.2. Imaging sequences and parameters

All patients included in this study underwent multiparametric MRI under a standard protocol that is used at our institution for the assessment of intra and extra-glandular prostate disease. Imaging was performed using a 3 T Signa HDxt scanner (General Electric Medical Systems) operating under software version 15.0. The MRI protocol, which included the use of an air-filled endorectal coil (Medrad Inc. Indianola, PA, USA) combined with an eight-element flexible torso phased-array coil, has been described previously [2]. Briefly, T1W spoiled gradient recalled echo (SPGR) imaging in the axial plane, T2W fast spin echo (FSE) imaging in all three planes, as well as axial DWI and DCE imaging were performed.

The unique component of this study was the inclusion of an IV-CPMG imaging sequence for T_2 mapping. The manufacturer's clinical FSE sequence includes a CPMG option whereby individual spin echoes in the echo train can be used to obtain images with different TE's in a single acquisition. This sequence was modified in-house to obtain the IV-CPMG sequence used in the study. In the modified sequence, the excitation and refocusing pulses were tilted with respect to each other, as discussed by Rangwala and Zhou [11] and shown schematically in Fig. 1. This tilting has the effect not only of selectively exciting spins in the slice direction but also of restricting the volume of spins excited along the phase encode direction through selective refocusing. The images in Fig. 1 demonstrate the ability of the sequence to select a reduced field-of-view without significant aliasing in the phase-encode direction.

The preferred image orientation for prostate T2W prostate imaging is axial and the R-L direction is normally selected as the phase-encoding direction to avoid having motion artifacts from the rectal wall obscure the prostate. The same axial orientation and selection of phase and frequency directions were adopted for T_2 mapping. Without restricting the selected volume in the phase direction, a field-of-view (FOV) of over 300 mm would be required. However, the IV-CPMG sequence allowed us to greatly reduce the phase FOV (and, thus, the number of phase encoding steps) while avoiding aliasing artifact.

For a tilt angle of ϕ (assuming it is less than ~40^o) the restricted volume in the phase direction equals two times the slice thickness multiplied by tangent (90^o-ϕ). In this study, we used tilts of approximately 4^o to select an 85 mm section in the phase direction for a slice thickness of 3 mm. The FOV in the frequency direction was 140 mm and the selected matrix size was 192×160 in frequency and phase directions respectively. With the phase-encoding FOV set to 62% and with the half-Fourier option added, the actual number of phase encodes was reduced to approximately 50, which included a slight oversampling for the half-Fourier phase correction. Thus, even with a relatively long repetition time (TR), the scan times were only 2.8 minutes compared to almost 9 minutes scans that would be required for a full-FOV, full-Fourier acquisition. A total of 8 spin echoes per slice were acquired at TE's from 18 to 144 ms at intervals of 18 ms. With a TR of 3300 ms, 20 slices could be acquired in one acquisition, allowing for full gland coverage in the axial plane (slice thickness: 3 mm, slice gap: 1 mm). The resultant in-plane resolution was approximately 1×1.5 mm^2.

An undesired side effect due to tilting the spatially selective excitation with respect to refocusing is that the flip angle of the refocusing pulses becomes dependent on the position of the spins not just along the slice direction, as in slice selective CPMG imaging, but also along the phase-encode direction. That is, in standard slice selective CPMG imaging, the variability of the refocusing flip angles within the slice-selection profiles results in contributions from stimulated echoes and a departure of the resulting signal decays with TE from pure T_2 decays. A noticeable feature of this effect is a surprisingly lower signal on first echo images and calculated T_2 values longer than expected due to T_1 contributions. Thus, the estimated T_2 is more aptly referred to as the 'apparent' T_2. In the IV-CPMG sequence used in this study, we expected such effects to be exacerbated due to the additional flip angle variation along the phase-encode direction. This is demonstrated in Fig. 2, which shows T_2 estimates using the standard full-FOV CPMG sequence compared with the T_2 estimates in a doped water phantom (T_2 ~60 ms) obtained using the IV-CPMG sequence. Near the center of the reduced FOV the two methods are in close agreement in terms of the estimated T_2, however, near the edges the difference increases significantly. In the studies reported here, the gland was positioned at the center of the reduced FOV to minimize such effects though they certainly contribute to inaccuracies in T_2 values, which are understood to be "apparent" T_2 values.

2.3. Image analysis

Two radiologists (FIY and TP), aware of all clinical information (indication for the exam, clinical stage, PSA values and biopsy results), reviewed multiparametric MRI data sets (including DWI and DCE images) and identified one suspected cancer (SC) lesion per patient in consensus. When consensus was not reached, a third