Multi-parametric assessment of prostate cancer in intermediate-risk patients using 3.0 Tesla MR imaging and spectroscopy

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Introduction: Prostate cancer (PC) is the most common cancer diagnosed in men and second oncologic cause of death in older men in the United States. Standard PC diagnosis is based on combination of digital rectal examination (DRE), serum prostate specific antigen (PSA), and biopsy-derived Gleason score (GS). Despite their usefulness, these measures do not provide detailed information about tumor location, aggressiveness, or tissue characterization. In this study, a multi-parametric magnetic resonance imaging / spectroscopy (MRI/MRS) exam was developed and optimized on 3.0T magnetic field. The exam was tested on intermediate-risk PC patients, who show the widest range of treatment outcomes among PC patients, and in whom accurate tumor characterization is expected to improve treatment outcome.

Methods: Ten intermediate-risk PC patients were scanned on a 3.0T Siemens MRI scanner using an optimized imaging protocol that lasted for 40-45 minutes to acquire: 1) three stacks of transaxial, sagittal, and coronal T2-weighted (T2W) images covering the prostate for obtaining relaxivity and morphological information; 2) a stack of transaxial diffusion weighted imaging (DWI) images covering the prostate with different 'b' values; and 3) a 3D chemical shift MRS metabolic and spectral maps (Fig. 1 shows MRS setup). The DWI images were processed to calculate the apparent diffusion coefficient (ADC) map. The MRS data was pre-processed (eddy current correction, removal of water signal, signal filtering (in time domain), zero filling, phase correction, and baseline correction) before calculating the metabolic ratios of choline+creatine/citrate ((Cho+Cr)/Cit) for each voxel inside the volume of interest. An expert semi-automatically analyzed the images to identify regions of suspicious malignancies (low signal intensity on T2W images and ADC maps; high signal intensity on DWI images; and metabolic ratio > 0.8). Image analysis was repeated by the first expert, and conducted by a second expert to measure inter- and intra-observer variabilities using Bland-Altman analysis. Tumor regions determined by different imaging techniques (or repeated measurements by experts) were overlaid on top of each other to calculate the 'degrees of agreement' among different techniques (experts) in determining tumor regions (Fig. 2). The signal intensities of the pixels in the T2W and DWI images were normalized and compared (pixelwise) to metabolic ratios in each tumor region to measure correlations between tumor aggressiveness by different techniques. Correlation analysis was also conducted between PSA, GS, and the 'adjusted malignancy number' inside the whole prostate for each patient. An adjusted malignancy number was calculated for each imaging technique as the summation of all malignant pixels inside the prostate, weighted by the pixel normalized signal intensity (T2W and DWI) or metabolic ratio (MRS).

Results: Results are reported as mean ± standard deviation (SD). Tumors showed low signal intensity in T2W and DWI images; high signal intensity in ADC map; and yellow to red colors on the MRS metabolic map. DWI at b=1500 resulted in better tumor visualization than lower b values. Figure 3 shows images from slices showing tumors. Thirty nine regions (out of total forty four) were detected by all three methods and included in the analysis. Measured tumor areas (mean ± SD) = 101±22 mm^2. The inter-method agreement ratios for all regions were 0.85±0.11, 0.83±0.13, and 0.89±0.09 in the following pairs: (T2W, DWI), (T2W, MRS), and (DWI, MRS). The agreement ratios for inter- / intra-observer measurements were 0.93±0.05 / 0.91±0.06, 0.92±0.06 / 0.92±0.08, and 0.95±0.05 / 0.90±0.08 in the T2W, DWI, and MRS methods. Bland-Altman analysis showed non-significant differences between repeated measurements. Areas were 0.58±5.2 mm^2 and -0.21±4.3 mm^2 for inter- and intra-observer measurements. Absolute correlation coefficients between the degrees of tumor aggressiveness, determined by the three MRI techniques in all regions, were 0.81±0.09, 0.83±0.11, and 0.85±0.10 in the following pairs: (T2W, DWI), (T2W, MRS), and (DWI, MRS). The adjusted malignancy numbers by the three MRI methods showed weak correlations with PSA / GS in all patients: 0.59±0.11 / 0.61±0.13, 0.64±0.13 / 0.62±0.12, and 0.58±0.11 / 0.66±0.10 for T2W, DWI, and MRS.

Discussion: PC management is challenging because of the disease variable clinical and pathologic behaviors. The present study addresses the development, optimization, and implementation of a multi-parametric MRI/MRS exam for evaluating PC in intermediate-risk patients. The developed exam included not only morphologic information, but also functional and metabolic information. The results showed that adding DWI or MRS to T2W increases the technique specificity (precise selection of the common area of identified malignancy). The multi-parametric exam provides more detailed evaluation of the tumor than do classical PSA and GS exams. The images showed differences in the tumor regions determined by different MRI techniques, which reflects the heterogeneous nature of prostate tumors and confirms the fact that different techniques measure different characteristics of the tumor. The strong correlations between different MRI/MRS parameters reflect the concurrent changes that occur in cancerous tissues on the morphological, cellular, and metabolic levels. The low inter- and intra-observer variabilities reflect the high reliability and reproducibility of the proposed multi-parametric MRI technique in differentiating between regions of normal and abnormal activities. The weak correlations between MRI parameters and findings from PSA and GS reflect the important role of MRI/MRS in providing detailed information about PC activity. The use of high-field 3.0T MRI resulted in high resolution image, better spectral separation, and higher signal-to-noise ratio (SNR) in DWI images with high b values, as implemented in the proposed protocol. Intermediate-risk patients were studied in this work because they show the widest range of treatment outcomes. Accurate assessment of the patient stage and tumor characteristics in this group would help in optimizing treatment planning, which not only benefits individual patients but also has important financial consequences. Furthermore, the proposed multi-parametric imaging technique is useful for characterizing prostate tumors that are not easily palpable during DRE and are not routinely targeted during biopsy, e.g. the transitional or anterior peripheral zones.

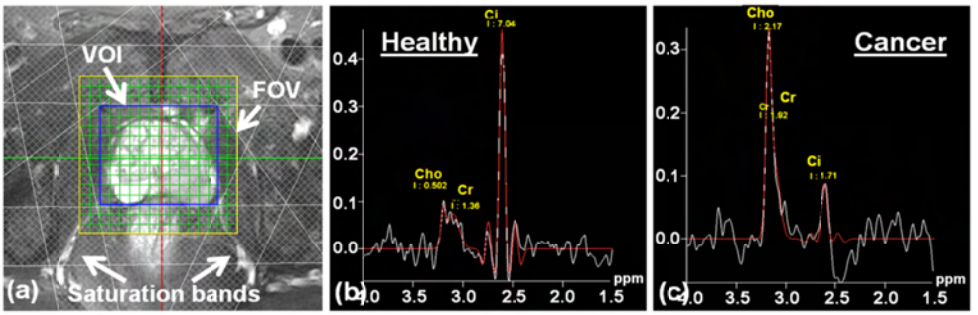

Figure 1. MRS setup. (a) Setup of saturation bands, field of view (FOV), and volume of interest (VOI). (b) Spectrum of healthy tissue (high citrate; low choline and creatine). (c) Spectrum of tumor (low citrate; high choline and creatine).

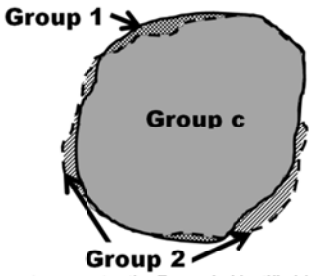

Figure 2. Agreement ratio. Tumor is identified by two MRI techniques: technique 1 (solid line) and technique 2 (dashed line). Group c = common area. Group 1 (2) = area identified by technique 1 (2), but not technique 2 (1). Agreement ratio = # pixels in group c / # pixels in (group c, 1, and 2).

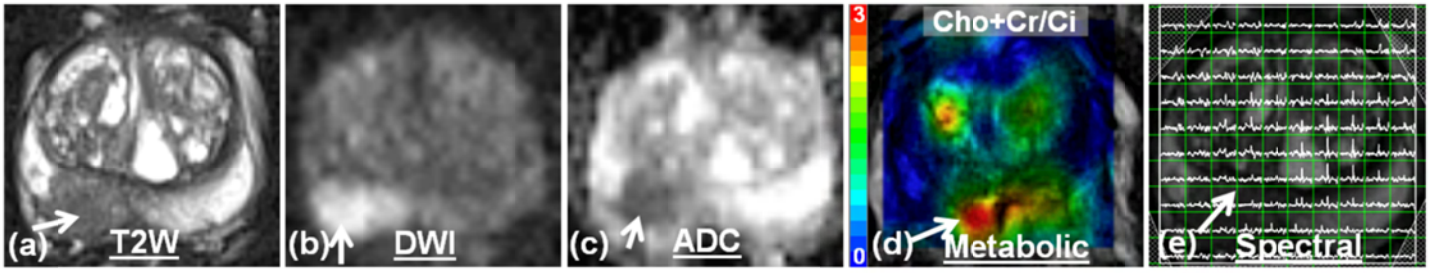

Figure 3. Tumor (arrows). (a) T2W image (tumor has low signal intensity). (b) DWI image (tumor has high signal intensity). (c) ADC map (tumor has low signal intensity). (d) MRS metabolic map, (red core & yellow boundary). (e) MRS spectral map (low citrate; high choline).