Magnetic Resonance Diffusion Characteristics of Histologically Defined Prostate Cancer in Humans

J. Xu1, P. A. Humphrey2, A. S. Kibel1, A. Z. Snyder4, V. R. Narra4, J. J. Ackerman4, and S-K. Song4

1Chemistry, Washington University, St. Louis, MO, United States, 2Pathology & Immunology, Washington University, St. Louis, MO, United States, 3Surgery, Washington University, St. Louis, MO, United States, 4Radiology, Washington University, St. Louis, MO, United States

Introduction

The contrast provided by diffusion sensitive magnetic resonance (MR) in organ-confined human prostate cancer (PCa) offers the promise of improved detection and localization.[1] By employing an image co-registration procedures to align "gold standard" histology slide with ex vivo, and, subsequently, in vivo diffusion sensitive MR images,[2] the MR diffusion characteristics of histologically defined human prostate cancer were studied.

Material and methods

Patients Twelve radical prostatectomy patients (mean age 62 yrs, range 46 – 76 yrs) were enrolled in this study. MRI In vivo diffusion tensor imaging (DTI) (resolution = 2x2x2.5 mm³) and T2-weighted (T2w) images (resolution = 1x1x2.5 mm³) were performed prior to prostatectomy surgery. After surgery, prostatectomy specimens were fixed in formalin and step-sectioned at 4-mm intervals using a custom-made slicer. The regrouped 4-mm tissue blocks underwent ultra high resolution (0.5×0.5×0.5 mm³) ex vivo DTI measurements.[3] Histology Individual 4-mm sections were carefully labeled and then completely embedded in paraffin and sampled in 4-µm thick slices for hematoxylin and eosin (H & E) staining. The histology slides and MR images were mutually aligned in the coordinate space of the standard in vivo T2w images.[2]

Results and Discussions

After MR and histology image co-registration for each slice, the PCa region and the benign tissue region in the peripheral zone (PZ) were translated from the histology slide (Fig. 1E) to both the ex vivo (Fig. 1D) and in vivo apparent diffusion coefficient (ADC) maps (Fig. 1A). The ADC value of PCA tissue (0.43 ± 0.06 µm²/ms) was significantly lower than that of the non-cancerous PZ tissues (0.99 ± 0.16 µm²/ms), and 1.66 ± 0.21 µm²/ms in vivo). Microscopically, normal prostate has a branching duct-acinar glandular architecture embedded in a dense fibromuscular stroma (Fig. 1G). This duct-acinar structure underlies the diffusion MR characteristics of the prostate gland in human. In prostate carcinoma, tightly packed tumor cells disrupt the duct-acinar structure leading to the decreased ADC in tumor due to the loss of tissue anisotropy.

Figure 1. Co-registered images illustrate the tissue microstructure underpinning the MR diffusion characteristics. A) in vivo ADC, B) in vivo T2w, C) in vivo color coded sRA, D) ex vivo ADC, E) H & E slide, and F) ex vivo sRA. The cancerous and BPH regions in the H & E slide were marked in blue and red, respectively, by a urologic pathologist. Blue and red arrows indicate regions of PCa and stromal BPH, respectively, as diagnosed by histology. The white arrow in panel B indicates a T2 hypointense region that could be mistaken for PCa without the additional co-registered diffusion data. The peripheral zone region was delineated in panel B and mapped onto panel C in magenta. High resolution H & E examinations reveal the microstructures of different types of tissues (G) benign peripheral zone, H) PCa, and I) stromal BPH (10x magnification, scale bar = 100 µm).

Figure 2. DTI images were co-registered with step-section histology slides from six representative specimens (each column) with different tumor sizes. PCa identified on the volume rendered DTI, ex vivo (panel A; projected view) and in vivo (panel B; projected view with a representative T2w image as background), closely correlated with those seen in histology. The histologically defined PCa extents and stages (from left to right in each panel) are 40% T3b, 16% T2c, and 4% T2c for ex vivo, and 15% T3a, 40% T3a, and 20% T3a for in vivo. The cancerous and BPH regions in the H & E slides were marked in blue/black and red, respectively, by a urologic pathologist. In the MR images, the ADC and diffusion anisotropy values were imported into the yellow-orange and green-blue channels, respectively. Bright yellow-orange regions in the MR images were identified as carcinoma determined by ADC threshold (ex/in vivo PCA mean ADC ± standard deviation). Red and blue arrows indicate regions of fibromuscular and carcinoma tissues, respectively, as identified by histology and their co-registered diffusion (red in the MR images. In ex vivo DTI images (panel A), pairs of ejaculatory ducts with high ADC value (color scale irrelevant) are segmented from the ADC map separately.

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