Comparison of conventional histology and diffusion weighted microimaging for estimation of epithelial, stromal, and acinar volumes in prostate tissue

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Target audience Researchers and clinicians interested in the biophysical basis of diffusivity variations in normal and pathological glandular tissue.

Purpose Diffusion weighted (DW) microimaging of fixed prostate tissue reveals distinct diffusivity differences between epithelium, stroma, and acinal spaces[1]. In normal glandular tissue changes in the relative volumes of epithelium and stroma explain ~60% of the variation in signal fraction of a biexponential model of diffusion signal decay[2]. We hypothesise that microscopic tissue volume changes may also explain the observed strong correlation between cancer Gleason grade and apparent diffusion coefficient measured in vivo. In this pilot study we used semi-automated morphometry methods to quantify partial volumes of epithelium, stroma and acinal space in H&E-stained histological images of benign and cancerous prostate tissue and compared these results with segmentation and statistical analysis of diffusion weighted microimages of normal tissue.

Methods DW images were obtained from a previous study in which six normal glandular tissue samples from five patients were formalin fixed and imaged with 40 μm isotropic voxels at 16.4 T[1]. In the previous work partial volumes were estimated by fitting three Gaussian curves to voxel diffusivity histograms[1]. Five diffusion- weighted images per specimen were manually segmented into epithelium, stroma and acinal space (Fig. 1.). For light microscopy 63 20× images (14 normal, 17 Gleason-3, 32 Gleason-4) from two patients were manually segmented into epithelium, stroma and lumen components. For cancer samples the field of view was cropped to ensure the presence of a single Gleason grade only. Segmentation of the light microscopy images was based on separate selection of epithelial tissue or acinal space with the magic wand tool in Adobe Photoshop followed by manual correction of obvious errors.

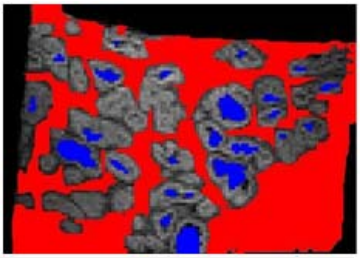

Fig. 1. *Manually segmented diffusion weighted microimage of a 3-mm diameter core of normal glandular tissue. Voxel size = 40 μm³ Red = stroma. Blue = acinal space. Black = not tissue. Remainder = epithelium.*

Results Fig. 2. compares partial volumes of epithelium, stroma and acinal space estimated by DWI and histology in our study and two earlier histology studies. Normal tissue volumes estimated by segmentation of DW images are similar to those obtained by voxel diffusivity statistics of the same samples. When compared with histology images DWI appears to underestimate the volume of acinal space.

Normal tissue volumes estimated by segmentation of our histology samples show more variability than previous studies based on morphometry of histology samples[3,4].

Our histology-based segmentation demonstrated significant differences in the volumes of epithelium, stroma and acinal space between normal, Gleason 3, and Gleason 4 samples ($p<0.05$, one-way ANOVA).

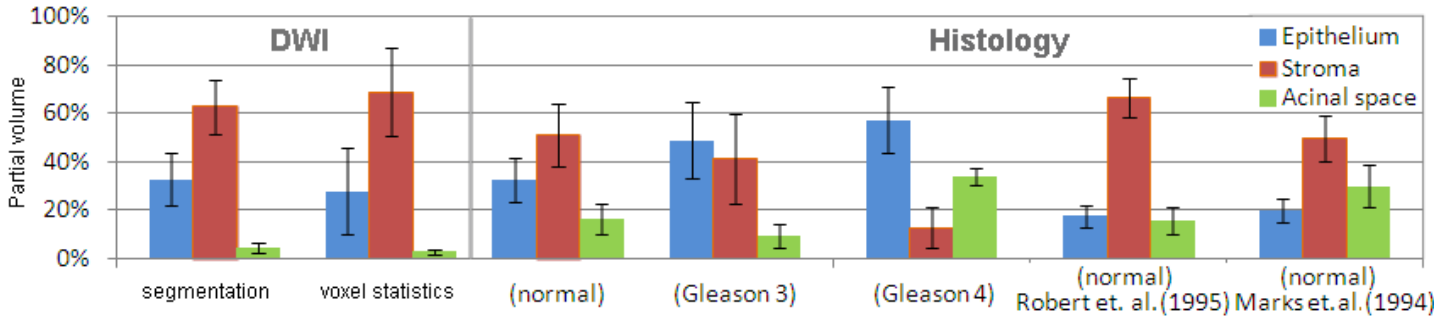

Fig. 2. Volumes of epithelium, stroma, and acinal space estimated from segmentation and statistical analysis of DW images, and by morphometry of histology images. Error bars = ± 1 SD.

Conclusion There is broad agreement between estimated partial volumes of epithelium and stroma obtained from diffusion-weighted microimages and histology. The relatively low estimate of acinal space obtained from DWI may be the result of partial volume effects as the thickness of the epithelial layer of most glands (15 – 20 μm) is typically smaller than the 40 μm voxel dimension in our DWI data. The increasing volume of low diffusivity epithelial tissue and decreasing volume of high diffusivity stroma that occurs with increasing Gleason grade may explain the clinically observed decrease in ADC with increasing Gleason grade[5]. This pilot study is the first step towards a validated measurement of microscopic tissue compartment volumes that can be used for development of models for diffusion of water in prostate tissue.

References 1) Bourne R, Kurniawan N, Cowin G, et al. Microscopic diffusivity compartmentation in formalin fixed prostate tissue: Preliminary findings. Magnetic Resonance in Medicine 2012. 68(2): 614-620. 2) Bourne R, Kurniawan N, Cowin G, et al. Biexponential Diffusion Decay in Formalin Fixed Prostate Tissue: Preliminary Findings. Magnetic Resonance in Medicine. 2012;68(3):954-959. 3) Robert M, Costa P, Bressollef F, et al. Percentage area density of epithelial and mesenchymal components in benign prostatic hyperplasia: comparison of results between single biopsy, multiple biopsies and multiple tissue specimens. British journal of urology 1995;75(3):317-324. 4) Marks L, Tretger B, Dorey F, et al. Morphometry of the prostate: I. Distribution of tissue components in hyperplastic glands. Urology 1994;44(4):486-492. 5) Turkbey B, Shah VP, Pang X, et al. Is Apparent Diffusion Coefficient Associated with Clinical Risk Scores for Prostate Cancers that Are Visible on 3-T MR Images? . Radiology. 2011;258:488-495.

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