ADC Mapping of Whole Excised Human Prostate

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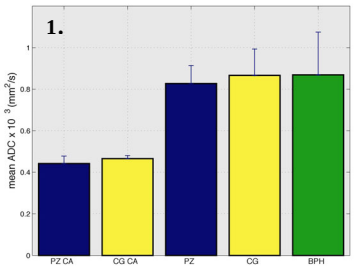
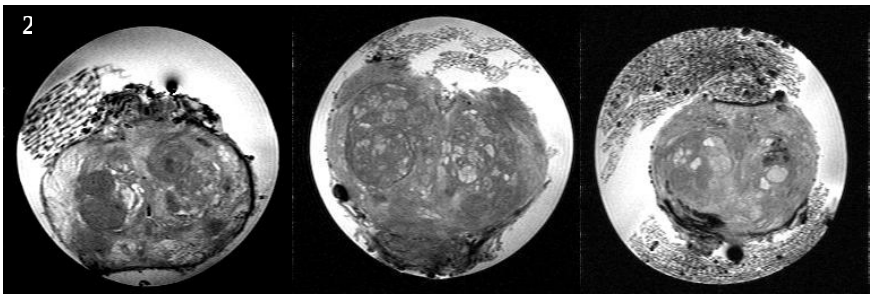
Introduction: Although prostate cancer is the second leading cause of cancer deaths among American men, clinical debates frequently arise over the best treatment choice and whether treatment is necessary for some patients (1). The main reason for the debate is that current methods of prostate cancer staging are inaccurate and the imaging techniques often do not determine the location and extent of cancer within the prostate (2). Many studies have provided compelling evidence that the measurement of apparent diffusion coefficients (ADC) has potential for characterization of lesions in brain, liver and prostate. This method has not been validated to determine the usefulness of these values alone for evaluating cancer.

Purpose: To evaluate the use of ADC maps for distinguishing prostate carcinoma from normal and hypertrophied tissue in excised human prostates and to correlate these parameters with Gleason score from prostate histology.

Materials and Methods: Eight patients with biopsy proven prostate cancer and no prior therapy underwent radical prostatectomy surgery, and their prostates were scanned post-excision. The mean Gleason score of the patients at biopsy was 6.6 ± 0.9 (range: 6 – 8) and their mean serum prostate-specific antigen (PSA) level was 6.98 ± 4.5 (range: 1.7 – 20). The median patient age at the time of surgery was 59.9 ± 5.9 years (range: 49 – 70). Each gland underwent MR imaging at 7.0T. High resolution anatomical images were collected from the entire volume of the prostate sample (typically 40 1-mm slices) with a T2 weighted spin-echo sequence (TE/TR 40 ms/6000 ms, 256 x 128, 6 x 6 cm FOV). Diffusion-weighted imaging was performed over the same volume (typically 20 2-mm slices) using at least three orthogonal diffusion-weighting directions, Δ=20 ms, δ=10 ms, and b-values of 0 and 1000 s/mm^2. After imaging, whole mount slides were prepared and regions representing cancer were identified by a pathologist and outlined on the cover-slip. Digital images were then made of the pathology slides, from these images, topographic relationships were made. Whole mount section histological tumor maps were then used to differentiate carcinoma from normal tissue on the ADC maps (seen in fig. 3).





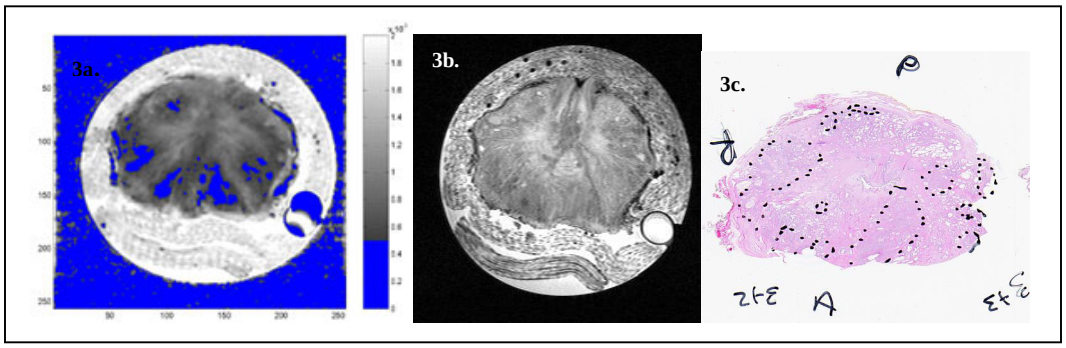


Figure 1: mean ADC values found in various tissue types of excised prostates examined. **Figure 2**: three different examples of the heterogeneity of human prostate tissue seen at 7T using a T2 weighted spin-echo sequence. Each sample is imaged in a vessel of saline and supported by gauze (also seen in the periphery of the images) **Figure 3: (a)** The ADC map of one patient's prostate with an overlay that highlights areas within the limits of ADC values found to illustrate cancer. **(b)** T2 weighted image of the same prostate again illustrating the heterogeneity of human prostate tissue. **(c)** Represents the corresponding histology of this patient.

Results/Discussion: From seven of the eight patients, where pathologically defined regions of carcinoma could be co-registered between histology and anatomical MRI**,** mean ADCs were found to be 0.44 ± 0.04 mm^2/s in the peripheral zone and a similar 0.47 ± 0.01 mm^2/s in the central gland (as shown in figure 1). These values were significantly lower than mean ADC values found across the same zones without carcinoma identified (0.83 ± 0.09 mm^2/s and 0.87 ± 0.13 mm^2/s, respectively) and across regions of benign hyperplasia (0.87 ± 0.21 mm^2/s). These measures represent sample to sample variation, and may prove representative of low-resolution ADC values acquired in vivo prior to surgery. However, the high resolution data provided from excised prostates at 7T reveal tremendous heterogeneity in mean ADC values within normal tissue of each of the aforementioned regions (as illustrated in figures 2 and 3). As such, regions of peripheral zone and central gland tissue may exhibit mean ADCs at or below those of cancerous tissue. Our preliminary data and histology also suggest that the inclusion of fractional anisotropy data may help distinguish cancerous tissue from fibrous tissue with similarly low mean ADCs. A more detailed voxel-by-voxel comparison of ADC and histology will be a valuable next step in understanding the potential of ADC for identifying prostatic carcinomas.

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