ADC Decrease in Histology Identified Prostate Cancer


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Introduction
The ability to accurately localize prostate carcinoma (PCa) within prostate gland non-invasively can dramatically improve PCa diagnosis and treatment. However, conventional T2 weighted (T2W) imaging has not proven sensitive or specific enough to localize gland-confined PCa. Recently substantial decrease of mean water apparent diffusion coefficient (ADC), due to disruption of the prostate ductal structures by PCa, provides a unique contrast for tumor localization. This promising ADC contrast has been explored in vivo, as recently summarized by Pickles et al. [1]. Nevertheless, none of the reports to date validated the suspected PCa region, either diagnosed by T2W, ADC contrast, or biopsy, with the “gold standard” histology. Herein, we propose a co-registration strategy to determine the in vivo ADC of histology identified PCa.

Material and methods
Patients Twelve radical prostatectomy patients (mean age 62 yrs, range 46 – 76 yrs) without any preoperative treatment were enrolled in this study.

MRI In vivo diffusion tensor imaging (DTI) measurement (resolution = 2x2x2.5 mm) and T2W imaging (resolution = 1x1x2.5 mm) were performed prior to scheduled prostatectomy surgery [1]. After surgery, prostatectomy specimens were fixed in formalin for more than 24 hours and step-sectioned at 4-mm intervals using a custom-made slicer. The regrouped 4-mm tissue blocks underwent ultra high resolution (0.5x0.5x0.5 mm) ex vivo DTI measurement [3].

Histology Individual 4-mm sections were carefully labeled to ensure correct identification of each section within the prostate. The sectioned slabs were then completely embedded in paraffin and sampled in 4-µm thick slices for hematoxylin and eosin (H & E) staining. Regions of PCa and BPH were identified and outlined in blue and red, respectively, by a urologic pathologist.

Image registration A two-dimensional (2D) thin plate spline (TPS) warping was performed using 10 – 20 control points (Fig 2, A and B) to transform histology to the coordinate of ex vivo ADC map (Fig. 1, T1). By using a rigid body 3D affine transformation (Fig. 1, T2), the ex vivo ADC maps were further manually co-registered with the in vivo T2W images through intraglandular structure alignment. The in vivo ADC maps were also co-registered with the in vivo T2W images using a 3D affine transformation (Fig. 1, T3). In this manner, all the images were mutually aligned in the coordinate space of the standard in vivo T2W images.

Results and Discussions
The ultra high resolution ex vivo diffusion anisotropy map (Fig. 2B), revealing exquisite intraglandular structure, affords accurate placement of the control points in the corresponding histology slide (Fig. 2A). The ex vivo ADC map, exhibiting similar tissue contrast as the in vivo T2W images, provides a critical link to the in vivo ADC map. Excellent co-registration results were achieved despite some manual procedures involved (Fig. 3). The registration results may be further improved by utilizing mutual information based automatic procedures [4]. After image registration, cancerous (Fig. 2D) and normal (Fig. 2C) tissues in the PZ were mapped from the histology slides onto the standard “histology. Herein, we propose a co-registration strategy to determine the in vivo ADC of histology identified PCa.


Figure 1. Overview of histology and in vivo ADC co-registration.

Figure 2. Representative control points that drive the 2D TPS warping in the T1 transformation are enlarged in both the H&E slide (A) and the ex vivo diffusion anisotropy map (B). Cancerous (marked blue in A) and non-cancerous PZ, identified by pathologist, are magnified to show the more cellular PCa (D) comparing to the normal ductal tissues (C).

Figure 3. Registration results at three transformation stages (rows, T1 - T3). The transformed source images (left column) were overlaid onto the target images (right column) to highlight alignment results in checkerboards (center column). The transformation pairs are A) TPS warped H&E and C) ex vivo ADC; D) transformed ex vivo ADC and F) in vivo T2W; and G) transformed in vivo ADC and I) in vivo T2W.

Figure 4. Decreased ADC values were observed in in vivo patients, ex vivo human prostatectomy specimens, and an in vivo mouse model of PCa. All results were determined by histopathology identified tissue categories. Error bars represent mean standard deviation. Statistical significance was accepted for p < 0.0001.