

## Unsupervised multi-characteristic framework for DW-MRI prostate cancer localization

Raisa Z Freidlin<sup>1</sup>, Harsh K Agarwal<sup>2</sup>, Sandeep Sankineni<sup>3</sup>, Anna M Brown<sup>3</sup>, Marcelino Bernardo<sup>3,4</sup>, Peter A Pinto<sup>3</sup>, Bradford J Wood<sup>3</sup>, Deborah E Citrin<sup>3</sup>, Peter L Choyke<sup>3</sup>, and Baris Turkbey<sup>3</sup>

<sup>1</sup>NIH/CIT, Bethesda, Maryland, United States, <sup>2</sup>Philips Research, New York, United States, <sup>3</sup>NIH/NCI, Maryland, United States, <sup>4</sup>Leidos, Maryland, United States

**PURPOSE:** Multiparametric MRI (mpMRI) is becoming an increasingly important tool for localizing prostate cancer. Common mpMRI sequences include T<sub>2</sub>-weighted (T2W), dynamic contrast-enhanced (DCE), and diffusion-weighted (DW) MRI. Recent work has identified DW-MRI as helpful for improving prostate cancer detection. Additionally, several studies have established a correlation between apparent diffusion coefficient (ADC) values and tissue morphology of prostate cancer. Prostate tissue diffusion properties do not follow a mono-exponential diffusion decay model at b-values above 600-700 s/mm<sup>2</sup>. Therefore, more complex models such as bi-exponential, intravoxel incoherent motion (IVIM), kurtosis, and statistical models have been proposed for better characterization of DW-MRI signal attenuation in the prostate. Studies exploring these models reported different values for diffusion parameters in cancerous and normal tissue regions of interest (ROIs). However, none of these studies used an unsupervised approach to localize prostate cancers using DW-MRI. Our goal is to assess the feasibility of a novel unsupervised multi-characteristic framework for localizing prostate cancers using a combination of two well-established diffusion models, IVIM and kurtosis.

### MATERIALS AND METHODS:

**Diffusion models:** IVIM<sup>1</sup> and kurtosis<sup>2</sup> models for DW-MRI are shown in equations (1) and (2):

$$S(b) = S_0[(1-f) \cdot e^{-\alpha} + f \cdot e^{-\beta}], \quad (1)$$

where  $S_0$  represents signal intensity at  $b=0$  s/mm<sup>2</sup>,  $f$  is the fraction of signal dominated by the pseudo-diffusion ( $D^*$ ),  $\alpha = b \cdot D$  and  $\beta = b \cdot (D^* + D)$  where  $b$  is an experimental design vector derived from the gradients used to acquire DW-MRI scans (b-values) and  $D$  is an estimation of self-diffusion.

$$S(b) = S_0[f \cdot e^{-\gamma}], \quad (2)$$

where  $\gamma = b \cdot D - b^2 D^2 K/6$ ,  $K$  is kurtosis, and  $D$ ,  $S_0$  and  $b$  are as in Equation 1.

**Unsupervised multi-characteristic framework:** Previous work has reported that cancerous tissue exhibits lower diffusion<sup>3</sup> parameters and higher kurtosis<sup>4</sup> values. We have utilized this information in our unsupervised multi-characteristic framework. Voxels with  $D^*$ ,  $D$ , and  $f$  (defined in the IVIM model, Equation 1) below the pre-defined threshold were selected. Next, the selected voxels with kurtosis above a pre-defined threshold were labeled as “cancerous” while selected voxels with kurtosis below the threshold were marked as “tumor suspicious”. A threshold was set at one standard deviation away from the mean value calculated over the entire prostate.

**Patient population:** Ten patients with mean age of 65 years (range 54-78) and mean serum PSA of 21.9 ng/mL (range 4.8-44.8 ng/mL) with moderate or high clinicopathological risk for prostate cancer who underwent mpMRI followed by MRI/TRUS fusion-guided biopsy were analyzed in this study. Multi-echo DW-MRI was acquired with 16 equidistantly spaced b-values in the range 0-2,000 s/mm<sup>2</sup> (TE=58ms; TR=3990ms; spatial resolution 2.19×2.19×2.73mm<sup>3</sup>, slices = 26, FOV = 140×140mm, slice gap = 0.27mm, NSA = 2). All images were acquired using a 3T clinical MR scanner (Achieva 3.0T-TX, Philips Healthcare, Best, NL) with the anterior half of a 32-channel SENSE cardiac coil (Invivo; Gainesville, FL, USA) and an endorectal coil (BPX-30, Medrad, Pittsburgh, PA, USA).

**Evaluation:** One experienced radiologist and two radiology trainees evaluated the unsupervised multi-characteristic framework maps on consensus blinded to histology and mpMRI results. For each patient, regions suspicious for cancer were recorded and these areas were correlated to each patient's 12-core systematic and MRI/TRUS fusion-guided biopsy results.

**RESULTS:** 25 lesions were identified using the unsupervised multi-characteristic framework approach. There were 14 true positives, resulting in a 56% tumor detection rate on lesion-based analysis. The most aggressive (index) lesion was identified on all patients' framework maps with a resultant 100% detection rate on patient-based analysis. The index lesions were coded as the most suspicious lesion on framework maps in 9 out of 10 patients.

**DISCUSSION AND CONCLUSION:** This novel multi-characteristic framework applied to diffusion parameters obtained using the IVIM and kurtosis models has high patient-based sensitivity with a 100% detection rate for identifying the index lesions. Further analysis on larger patient population is warranted to expand this technique from a proof-of-concept to a clinically utilizable tool.

**REFERENCES:** [1]. Le Bihan, Breton E, Lallemand D, et al. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. Radiology 1986; 161 (2): 401-7. [2]. Jensen JH, Helpern JA, Ramani A, et al. Diffusional kurtosis imaging: the quantification of non-gaussian water diffusion by means of magnetic resonance imaging. Magn Reson Med 2005;53(6):1432-1440. [3]. Riches SF, Hawtin K, Charles-Edwards EM, de Souza NM. Diffusion weighted imaging of the prostate and rectal wall: comparison of biexponential and monoexponential modeled diffusion and associated perfusion coefficients. NMR Biomed 2009; 22:318-325. [4]. Rosenkrantz AB, Sigmund EE, Johnson G, et al. Prostate Cancer: Feasibility and Preliminary Experience of a Diffusional Kurtosis Model for Detection and Assessment of Aggressiveness of Peripheral Zone Cancer. Radiology. 2012 Jul;264(1):126-35.

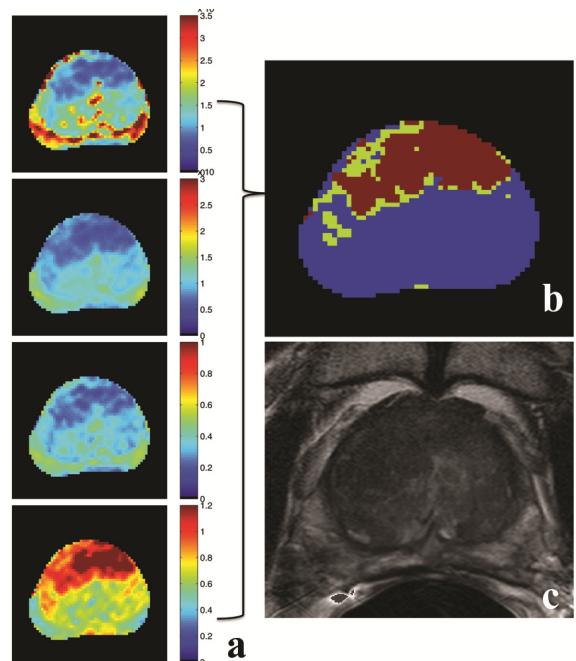


Fig 1: A 60 year old patient with a PSA of 44.81 ng/mL with prior negative systematic biopsy. Parametric maps localize the lesion to the midline apical-mid anterior transition zone of the prostate (a); framework map identifying lesion voxels marked in red and green (b); axial T2-weighted MR image confirming the midline apical-mid transition zone lesion with broad capsular base (c); MRI/TRUS fusion-guided biopsy confirmed Gleason 4+4 disease.