

Non mono-exponential Analysis of DW-MRI data for the Detection of Prostate Cancer

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INTRODUCTION: A monoexponential diffusion model requires at least two acquisitions with different b-values to generate apparent diffusion coefficient (ADC) maps. Although straightforward, this model ignores the contribution from microperfusion to the signal decay at low b-values and results in ADC values that are sensitive to the b-value selection. In biological tissues, microscopic motion detected by DW-MRI includes both diffusion of water molecules, influenced by the structural components of the tissue, and microcirculation of blood in the capillary network (perfusion). Comparing biexponential and monoexponential models of diffusion signal in the prostate, Riches et al (1) showed that the effects of perfusion in the diffusion signal results in a fast component of signal decay. The purpose of our study is to retrospectively compare the accuracy of monoexponential and non-monoexponential DWI parameters for identifying malignant regions of interest (ROIs), using whole-mount histopathology as the reference standard.

MATERIALS AND METHODS: Our institutional review board waived the requirement for informed consent for this retrospective study, which was compliant with the Health Insurance Portability and Accountability Act. Between May and December 2008, forty-four patients (median age, 61 years; age range, 42–85 years) who had an MRI exam were identified who met the inclusion criteria for our study, which were as follows: biopsy-proven prostate cancer; no prior hormonal or radiation treatment; and at least one peripheral zone lesion with volume > 0.1 cm³ on whole-mount pathology. MRI examinations were performed on a 1.5-T whole-body MRI unit (GE Medical Systems, Milwaukee, WI). A body coil was used for excitation, and a pelvic four-channel phased-array coil combined with a commercially available balloon-covered expandable endorectal coil (Medrad, Pittsburgh, PA) was used for signal reception. DW-MR images were obtained using a spin-echo echo-planar imaging (SE-EPI) sequence. **Imaging parameters:** TR = 4000–5475 ms, TE = 77.6–110.3 ms, FOV = 14×14 cm², 3 mm slice thickness, no inter-slice gap; b-values were 0, 400, and 700 s/mm². **Analysis:** 1) The mean values (ADC₄₀₀ and ADC₇₀₀ from monoexponential and D and f from non-monoexponential) of the malignant ROIs were compared using paired t-tests. Receiver operating characteristic (ROC) curves and the corresponding areas under the curves (AUCs) were estimated non-parametrically for the detection of cancer for each ROI. 2) We developed a predictor of cancer status based on the MRI variables. A logistic regression modeling approach using generalized estimating equations (GEE) with an independence working correlation matrix to account for the correlated data was used.

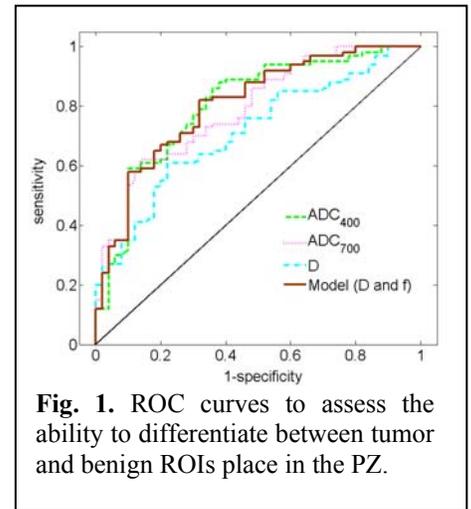


Fig. 1. ROC curves to assess the ability to differentiate between tumor and benign ROIs place in the PZ.

RESULTS AND DISCUSSION: The ROC curves (Fig. 1) evaluate the ability of mean ADC₄₀₀ (AUC= 0.81, 95% CI (0.72, 0.89)), mean ADC₇₀₀ (AUC= 0.79, 95% CI (0.71, 0.87)), D (AUC= 0.71, 95% CI (0.62, 0.81)) and combined D and f (AUC = 0.82, 95% CI (0.74, 0.90)) to differentiate between malignant and benign ROIs. The mean ADC values measured monoexponentially at two

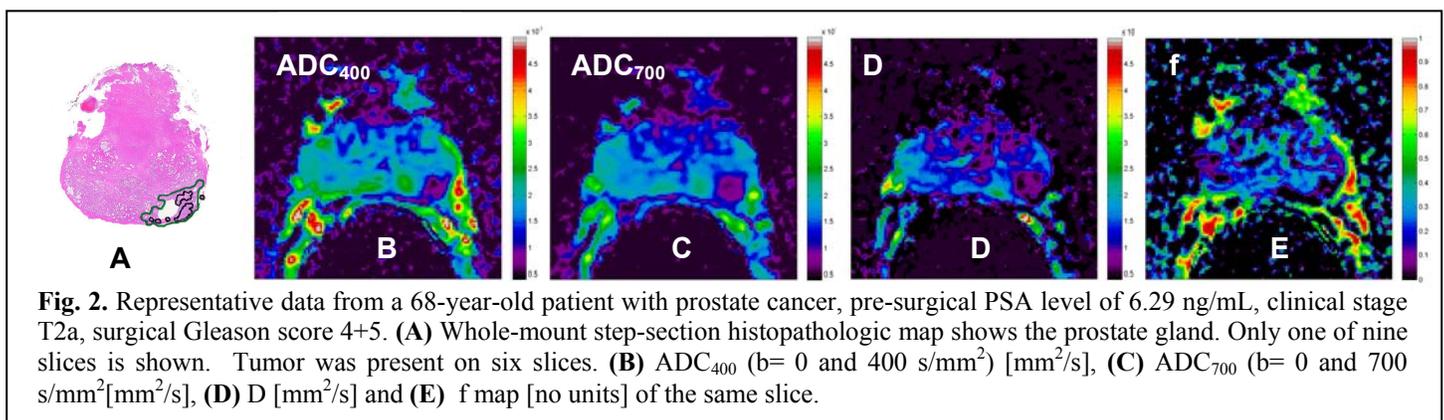


Fig. 2. Representative data from a 68-year-old patient with prostate cancer, pre-surgical PSA level of 6.29 ng/mL, clinical stage T2a, surgical Gleason score 4+5. (A) Whole-mount step-section histopathologic map shows the prostate gland. Only one of nine slices is shown. Tumor was present on six slices. (B) ADC₄₀₀ (b= 0 and 400 s/mm²) [mm²/s], (C) ADC₇₀₀ (b= 0 and 700 s/mm²) [mm²/s], (D) D [mm²/s] and (E) f map [no units] of the same slice.

different b-values from benign and malignant lesions were significantly different ($p < 0.0001$). The true diffusion estimate which is less sensitive to perfusion effects was also significantly different ($p = 0.0001$). The perfusion fraction was not significantly different for benign and malignant regions ($p = 0.28$) (Fig. 2). Furthermore, the AUC for the combination of D and f was significantly higher than that for D alone, but not significantly different than either one of the ADC values in the detection of prostate cancer. True diffusion coefficient measured with three b-values is significantly different than the corresponding benign tissue which at the same time providing an additional parameter that has reduced sensitivity to the selection of b-value making a more useful and consistent parameter for multicenter diffusion studies.

REFERENCES: [1] Riches SF, et al. NMR in biomedicine. 2009; 22(3):318-25.