

Diffusion-Weighted MR Imaging of Prostate with A Fractional Order Calculus Model

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Target audience: Clinicians including radiologists, urologists, oncologists and MR physicists with an interest in diffusion models.

Purpose: Recently, a novel non-Gaussian diffusion model based on fractional order calculus (FROC) was successfully applied to diffusion MRI of pediatric brain tumors¹. Taking into account of anomalous diffusion in locally heterogeneous tissue structures and environment, FROC diffusion model produces two new diffusion parameters β and μ^2 . This model has demonstrated improved ability to differentiate low- and high- grade pediatric brain tumors, when compared to the mono-exponential model which produces apparent diffusion coefficient (ADC) maps¹. Our present study is aimed at expanding the utility of FROC model to prostate diffusion MRI. Specifically we investigated the performance of FROC diffusion model in differentiating normal, benign and malignant prostatic tissues including normal peripheral zone, areas of chronic prostatitis, benign prostatic hypertrophy (BPH), and prostate cancer.

Methods: A retrospective study was carried out on 25 male patients (age range: 53-67 years), who had prostate cancer diagnosed by transrectal-ultrasound-guided biopsy and underwent prostate MRI examination followed by radical prostatectomy treatment. Prostate MRI was carried out at 3.0 Tesla with a 16-channel phased-array pelvic coil, including T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI) and dynamic contrast enhanced (DCE) T1-weighted imaging. DWI was performed using a single-shot EPI sequence with multiple b-values ($b = 50, 500, 1500, \text{ and } 2000 \text{ s/mm}^2$). Key acquisition parameters for DWI were: TR/TE = 1538 ms/69.8 ms, slice thickness = 4 mm, matrix size = 128x128, FOV = 18x18 cm², number of slices = 6, and total scan time = 3.5 minutes. The FROC diffusion model was applied to fitting the multi-b-value DWI dataset on a pixel-by-pixel basis using the following equation: $S/S_0 = \exp\{-D\mu^{2(\beta-1)}(\gamma G_0 \delta)^{2\beta} [\Delta - (2\beta-1)\delta / (2\beta+1)]\}$, where the spatial fractional order β (dimensionless) is correlated to the degree of tissue heterogeneity and the spatial quantity μ (in units of μm) is related to the diffusion mean free length in tissue¹⁻². In data fitting, the initial value of D was estimated by a mono-exponential fit using data acquired at b-values $\leq 1000 \text{ sec/mm}^2$, allowing a direct comparison to ADC. All data analyses were performed using customized software developed in Matlab (Mathworks, Inc, Natick, MA). MRI images were reviewed by two board-certified radiologists to identify four types of tissues:

normal peripheral zone, areas of chronic prostatitis, BPH, and prostate cancer, based on T2WI, DWI and DCE signal characteristics. Imaging findings were correlated with

histopathologic results

from prostatectomy specimens reviewed by two pathologists. Regions of interests (ROIs) were placed on MR images of each tissue type for all the patients, followed by quantitative calculation of D and β . Since a strong correlation between D and μ has been reported previously¹, our analysis was limited to D and β . The values of D and β were compared using Mann-Whitney U test with a statistical significance set at $p < 0.05$. All statistics was conducted using SPSS (SPSS Inc, Chicago, IL).

Results: Representative image datasets are shown in Fig. 1 from a patient with prostate cancer (white arrow) and in Fig. 2 from a patient with BPH (red circle) and prostatitis (white oval). For all 25 patients, D and β values for four different tissue types are summarized in Fig. 3. Statistically extracted p values are shown in Table 1, by comparing D and β values between the four different tissue types. Statistically significant differences in D and β values are observed, between prostate cancer and normal tissue, and between prostate cancer and prostatitis or BPH. In addition, there is significant difference in D and β values between prostatitis/BPH and normal tissue. No significant difference is shown in D and β values between prostatitis and BPH, suggesting similar diffusion patterns for both benign processes.

Discussion and Conclusion: Similar to changes in ADC, decreased D in prostate cancer likely corresponds to increased cellularity and decreased extracellular space as compared to normal tissue³. The new parameter β , as a tissue heterogeneity/complexity indicator, likely reflects the underlying histologic organization of prostate, with cancer cells packed more tightly and homogeneously when compared to the normal/benign zonal tissues mostly composed of glands and fibromuscular stroma. It is of significant clinical relevance to improve the differentiation of normal, benign, and malignant process in prostate gland by obtaining new diffusion parameters based on the FROC model, in addition to conventional ADC map, which can be used as potential imaging biomarkers in prostate cancer diagnosis, staging, treatment selection and monitoring for treatment response.

References: 1. Sui Y, et al., ISMRM, 2012. 2. Zhou XJ, et al., MRM, 2010. 3. Gibbs P, et al., Inv Radiology, 2009.

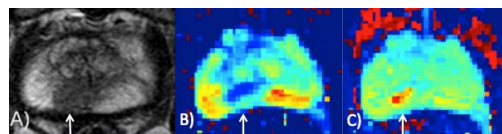


Figure 1 A set of images from a patient with confirmed prostate cancer. (A): T2-W image; (B): D map; (C): β map. The arrows point to the cancer lesion.

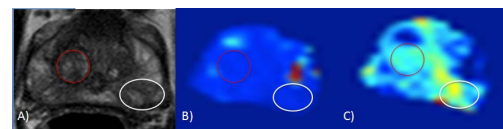


Figure 2 A set of images from a patient with proven BPH (red circle) and prostatitis (white oval). (A): T2 weighted image; (B) D map; (C) β map.

	Cancer vs.Normal	Cancer vs.BPH	Cancer vs.Prostatitis	BPH vs.Normal	Prostatitis vs.Normal	BPH vs.Prostatitis
P(β)	0.000	0.000	0.000	0.001	0.002	0.380
P(D)	0.000	0.000	0.000	0.000	0.000	0.073

Table 1 Extracted p values using Mann-Whitney U test comparing different pairs of tissue types. The greater statistical significance ($P < 0.01$) was observed when comparing cancer to normal and BPH/prostatitis.

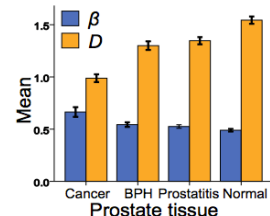


Figure 3 Mean and standard deviation of the diffusion parameters based on the FROC model over ROIs in different tissue types.