A Simplified Intravoxel Incoherent Motion Model for Diffusion Weighted Imaging in Prostate Cancer Evaluation: Comparison with Monoexponential and Biexponential Models

Qing Yuan[1], Daniel N Costa[1,2], Julien Sénégas[3], Yin Xi[1], Andrea J Wiethoff[2,4], Robert E Lenkinski[1,2], and Ivan Pedrosa[1,2]

[1]Radiology, UT Southwestern Medical Center, Dallas, TX, United States, [2]Advanced Imaging Research Center, UT Southwestern Medical Center, Dallas, TX, United States, [3]Philips Research Laboratories, Hamburg, Germany, [4]Philips Research North America, Briarcliff Manor, New York, United States

Target Audience: Investigators interested in intravoxel incoherent motion (IVIM) diffusion imaging of prostate cancer

Purpose: Diffusion-weighted imaging has become an essential tool for detection and characterization of prostate cancer in a multiparametric MRI (mpMRI) study. The apparent diffusion coefficient (ADC) calculated using a monoexponential model has been widely used in a clinical setting. However, diffusion signal decay with increasing b-values is influenced by pure tissue water diffusion as well as the microcirculation of blood within the voxel. The intravoxel incoherent motion (IVIM) diffusion model [1] consisting of fast and slow decay components should improve prostate tissue diffusion assessment [2]. In practice, the IVIM approach requires multiple b-value acquisition, which increases scan time, therefore is prone to motion artifacts and patient discomfort. Alternatively, a simplified IVIM model as originally proposed in [1], which uses b-values selected above a suitable threshold where perfusion can be neglected, has shown promise in liver diffusion evaluation in a more time-efficient manner [3]. The goal of this work was to compare this simplified IVIM model with commonly used monoexponential and original biexponential IVIM models in characterization of prostate cancer and noncancerous prostate tissues.

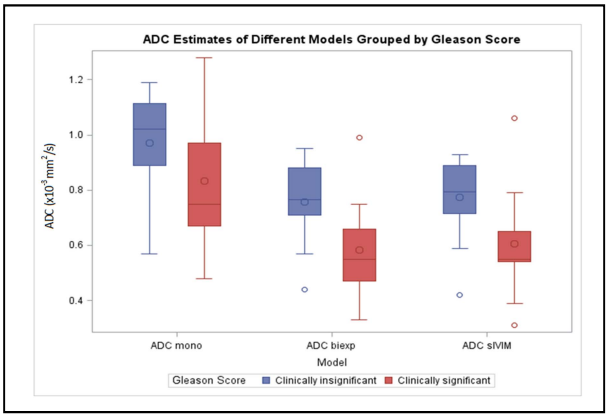
Methods: In this IRB-approved retrospective study, eighteen consecutive patients who underwent mpMRI of prostate followed by targeted biopsy and radical prostatectomy between February and August, 2014 were evaluated. All MRI exams were performed on a 3T dual-transmit MRI scanner (Achieva, Philips Medical Systems, Cleveland, OH) with a 6-channel cardiac coil (Philips Medical Systems) and an endorectal coil (Bayer Healthcare, Medrad Inc., Indianola, PA). Axial diffusion images were acquired using a single-shot spin-echo echo-planar imaging sequence with b-value = 0, 10, 25, 50, 100, 250, 450, 1000, 1500, and 2000 s/mm^2. Quantitative diffusion parametric maps were calculated using three different models with nonlinear least squares algorithm: (1) monoexponential model (mono): $S(b) = S_0 \cdot e^{-b \cdot D}$; (2) biexponential IVIM model (biexp): $S(b) = S_0 \cdot \left((1-f) \cdot e^{-b \cdot D} + f \cdot e^{-b \cdot D^*}\right)$; and (3) simplified IVIM model (sIVIM): $S(b) = S_0 \cdot \left((1-f) \cdot e^{-b \cdot D} + f \cdot \delta_0(b)\right)$, in which the perfusion effect is modeled by a Delta function for b = 0 s/mm^2. S_0 is the initial signal intensity, f is the perfusion fraction, D is the apparent diffusion coefficient representing pure molecular diffusion, D^* is the perfusion-related pseudo-diffusion coefficient, representing incoherent blood circulation in the capillary network. All b-values were used for monoexponential and biexponential models, whereas only b-values of 0, 250, 450, 1000, 1500, and 2000 s/mm^2 were used for the simplified IVIM model as indicated in [1] and [3]. Using anatomic co-registration from targeted biopsies and histopathologic findings after prostatectomy, three regions of interest (ROI) were identified in each patient on high-resolution T2-weighted images and DWI images: prostate tumor, noncancerous central gland and peripheral zone. These ROIs were then copied to the parametric maps of D, D^* and f to measure the mean and SD values for each ROI. Linear mixed models (SAS 9.3) were used to test the difference in the mean of diffusion measurements between different regions of interest and different models. Wilcoxon rank sum tests were performed to evaluate the difference in diffusion parameters based on Gleason score and tumor stage. P values < 0.05 are statistically significant.

Results: A total of twenty-one prostate tumors in 18 patients were included in this study. Based on post-prostatectomy findings, fourteen tumors were organ-confined (pT1a to pT2c), and seven were locally advanced (i.e., extracapsular extension and/or seminal vesicle invasion, pT3a or pT3b). We classified Gleason score of 3+3 (n = 3) and 3+4 (n=9) as the clinically insignificant group; and 4+3 (n=7) and 4+5 (n=2) as the clinically significant group.

ADC estimates of three different ROIs using three different models showed ADC values lowest in tumor, intermediate in central gland, and highest in peripheral prostate tissue (p < 0.0001) (see Table). Monoexponential model yields significantly higher ADC values compared to biexponential model and the sIVIM model for all three tissue types (p < 0.0001), suggesting that ADC values from monoexponential fitting was overestimated due to the intravoxel perfusion effect. No significant difference was found between ADC values estimated from biexponential and sIVIM models. Perfusion fraction was also calculated using biexponential and sIVIM models (see Table). The sIVIM model yields lower perfusion fraction for all three tissue types compared to the biexponential model (p = 0.015 for tumor, p < 0.001 for noncancerous tissues). Only sIVIM model showed significant difference of perfusion fraction among tumor and noncancerous prostate tissues (overall p = 0.03), and significantly lower perfusion fraction in tumor compared to peripheral zone (p = 0.03).

Comparing the quantitative diffusion measures with the histologic findings, both biexponential and simplified IVIM models showed significant lower ADC values in tumors with clinically significant Gleason scores (p = 0.03 and 0.04, respectively) (Figure), and significant lower ADC values in locally advanced tumors (p = 0.012 and 0.015, respectively). However, no significant correlations were found for ADC from monoexponential model. No significant correlation was found for perfusion fraction.

ROIs	ADC (x10^{-3} mm^2/s)						Perfusion Fraction (%)			
	Monoexponential Model		Biexponential Model		sIVIM Model		Biexponential Model		sIVIM Model	
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Tumor	0.91	0.23	0.68	0.19	0.70	0.20	22.05	6.92	19.64	6.85
Central Gland	1.86	0.38	1.46	0.38	1.50	0.38	22.16	6.61	16.62	6.56
Peripheral Zone	2.27	0.23	1.86	0.37	1.93	0.33	19.98	11.96	13.16	9.49



Discussion and Conclusion: IVIM diffusion imaging allows the assessment of "pure" tissue diffusivity by minimizing the effect of tissue perfusion. However, application of the IVIM method in a routine clinical study is limited due to the time constraints and the challenges of biexponential fitting in image post-processing. Compared to the conventional biexponential IVIM model, the simplified IVIM model uses fewer b-values for image acquisition, which would have resulted in reduced scan time from 6 min to 4.5 min using our clinical protocol. Moreover, our results demonstrated that the sIVIM model provided ADC estimates in prostate cancer and noncancerous prostate tissues that were equivalent to the biexponential model, and showed significant correlations with tumor aggressiveness. Previous application of the simplified IVIM model in liver indicated that organ-specific b-values significantly improved the performance of this method [3]. Future studies are necessary to investigate an optimized b-value scheme for prostate diffusion imaging with an acceptable scan time in a clinical setting.

References: 1. Le Bihan, el al, Radiology 168:497-505 (1988); 2. Shinmoto H, et al, AJR 199:W496-W500 (2012); 3. Sénégas J, et al, ISMRM: 1891 (2012).