

# High Resolution IVIM Parameter Maps in the Presence of Rician Noise

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**INTRODUCTION:** The Intravoxel Incoherent Motion (IVIM) method of diffusion imaging presents a noninvasive technique for capturing information about the structure and flow characteristics of the microcirculation *in vivo* [1]. While modeling the motions of blood through the capillary bed as a pseudodiffusive process leads to a straightforward parameter estimation problem, in reality, Rician noise present in magnitude images [2] impedes reliable estimation of the spatial distribution of IVIM parameters. IVIM parameters have been shown to change pre and post-treatment in clinical glioblastoma cases [3], but determining the spatial distribution of the changes remains an open challenge. However, while the presence of noise poses challenges, use of a maximum penalized likelihood estimate (MPLE) [4] to incorporate the noise model and spatial regularization can improve the quality of the estimation of the IVIM parameters relative to the conventional assumption of Gaussian noise as in the commonly used least-squares (LSQ) estimation.

**THEORY:** The IVIM method models both the signal decay due to microcirculatory flow and diffusion in tissue as:  $S_b = S_0 f \exp(-bD^*) + S_0(1 - f) \exp(-bD)$  [1]. In the model,  $D^*$  is the pseudodiffusion coefficient,  $D$  is the passive diffusion coefficient,  $f$  is the blood perfusion fraction, and  $S_0$  is the estimated image intensity at a  $b$ -value of zero. Most of the challenge in obtaining spatially resolved IVIM estimates lies in estimating  $f$  and  $D^*$ , with  $D^*$  being particularly difficult to estimate [2]. Given the low perfusion fraction (less than 10% in human white matter) the influence of the pseudodiffusive signal relative to the Rician noise is extremely small. From the Rician PDF [5],  $M_b$ , the noisy magnitude pixel value,  $\sigma$  the noise level and  $S_b$  the pixel value according to the IVIM model, a log-likelihood function,  $\mathcal{L}(M_b|S_b, \sigma)$ , can be formed using the PDF, the data, and the IVIM model. A MPLE is found by solving  $\arg\min_{\theta} \mathcal{L}(M_b|S_b(\theta), \sigma) + \sum_{i=1}^4 R(\theta_i)$ , where  $R(\theta_i)$  are roughness penalties over the parameter estimates, for the IVIM parameters,  $\theta$ , for each pixel.  $\sigma$  must be estimated in this formulation either jointly with the IVIM parameters or separately.

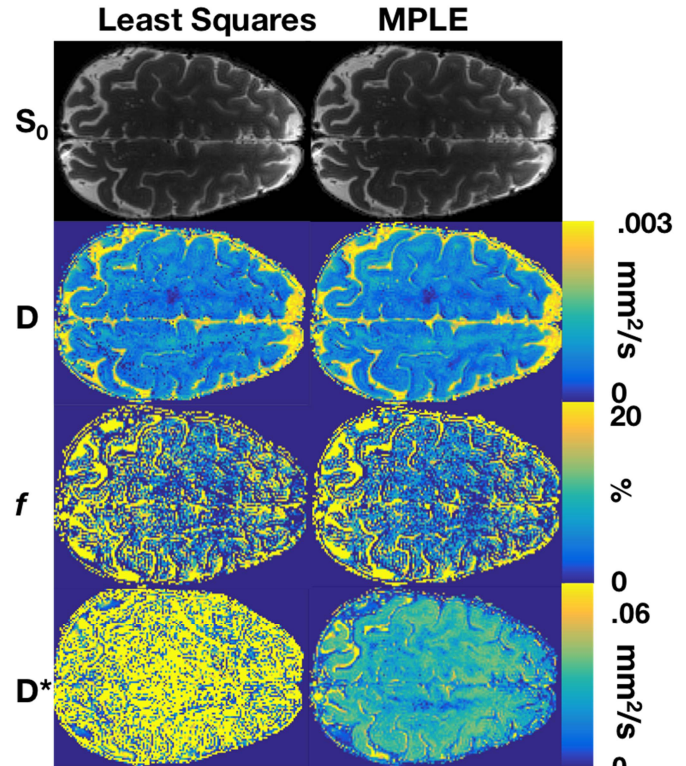
**METHODS:** Data was acquired on a Siemens Trio 3T magnet with 32 channel head coil using a 3D multi-shot motion corrected spiral acquisition [6] with field corrected SENSE reconstruction using the NUFFT [7]. Experimental parameters were: a resolution of 1.04 mm by 1.04 mm x 1.3 mm, TE/TR of 60/10000ms,  $\delta/\Delta$  of 14.91/28.71 ms, and a TA of 28 min. One repetition of the data was acquired with 14  $b$ -values between 1.2 and 700 s/mm<sup>2</sup>. The KNITRO v7.0.0 nonlinear optimizer through a MATLAB interface was used to minimize the resulting MPLE objective function for 1000 iterations. Rician noise levels were estimated following the procedure in [8]. LSQ estimates used the trust region nonlinear fitting method in the MATLAB Curve Fitting Toolbox. Gray matter and white matter was segmented using FSL FAST [9] from a T2-weighted overlay image for comparing white and gray matter.

**RESULTS:** Estimates for  $f$ ,  $D^*$ ,  $D$ ,  $S_0$ , for each pixel were obtained using the method above and are shown in Figure 1. The MPLE maps in Figure 1 show good correlation between the structure of the underlying  $S_0$  image and the boundaries between CSF and tissue. Structure is readily apparent in the MPLE estimates of  $D^*$  where as the structure in the LSQ estimates of  $D^*$  is difficult to find. As shown in Table 1, the spread between 25<sup>th</sup> and 75<sup>th</sup> percentiles of the voxel by voxel estimates of the IVIM parameters is tighter for the MPLE estimates for  $f$  and  $D^*$  suggesting higher reliability of the estimates from the MPLE method compared to the LSQ method based on the assumption that tissue types should exhibit some amount of spatial homogeneity within the microvasculature.

For  $D$ , the MPLE and least squares method returns similar estimates for both the average  $D$  value and the 25<sup>th</sup> and 75<sup>th</sup> percentile estimates.

**CONCLUSIONS:** MPLE estimation shows improved resolution and reliability of IVIM parameter estimates at high spatial resolution as compared to LSQ estimates of the IVIM parameters. For  $D^*$  and  $f$ , use of the MPLE based estimator enhances the quality of spatially resolved IVIM parameter estimates. Future work will explore the variations in the microvasculature across the brain across different cortical and subcortical structures.

**REFERENCES:** [1] Le Bihan, et al., *Radiology*, 1988,168(2):497-505; [2] Zhang, et al. IEEE Eng Bio Med Symp,2013:511-514 [3] Kim, et al., *AJNR Am J Neuroradiol*,2014,35:490-497; [4] LaRiccia, et al., *Maximum Penalized Likelihood Estimation*, 2009, Springer; [5] Aja-Fernandez, et al., *Magn Reson Med*,2009,27(10):1397-1409; [6] Sutton, et al. *IEEE Sig Process*,2003, 51(2):560-574; [7] Holtrop, et al. ISMRM 2013:2064; [8] Rajan, et al., *Phys Med Bio*, 2010, 55(16):N441; [9] Zhang, et al., *IEEE Med Imag*, 2001, 20(1):45-57;



**Figure 1:** Comparison between least squares fitting and the MPLE estimate for IVIM parameter estimation.

**Table 1:** Mean and 25<sup>th</sup> and 75<sup>th</sup> percentile levels for the voxel by voxel IVIM parameter estimates over the slice for white matter and gray matter after segmentation using MPLE and least squares (LSQ).

|              | D (10-4 mm <sup>2</sup> /s)                       |             | f (%)   |                               | D* (10-2 mm <sup>2</sup> /s)                      |             |
|--------------|---|-------------|---|-------------------------------|---|-------------|
|              | (25 <sup>th</sup> , 75 <sup>th</sup> ) Percentile |             | (25 <sup>th</sup> , 75 <sup>th</sup> ) Percentile |                               | (25 <sup>th</sup> , 75 <sup>th</sup> ) Percentile |             |
|              | MPLE  | LSQ         | MPLE  | LSQ                           | MPLE  | LSQ         |
| White Matter | 7.52  | 7.03        | 6.33  | 8.29                          | 2.72  | 6.68        |
|              | (5.38,8.92)                                       | (4.97,8.63) | (0.49,8.88)                                       | (2.1x10 <sup>-2</sup> ,11.31) | (2.33,3.20)                                       | (1.82,10.0) |
| Gray Matter  | 12.29   | 12.0        | 11.32   | 13.52                         | 2.67  | 6.19        |
|              | (6.72,16.61)                                      | (6.30,16.0) | (0.12,17.63)                                      | (7x10 <sup>-4</sup> , 21.44)  | (1.82, 3.33)                                      | (1.49,10.0) |