A comparison of intravoxel incoherent motion (IVIM) fitting models in the liver

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Target Audience Researchers and clinicians interested in body/liver imaging and disease, with a particular interest in diffusion imaging.

Purpose The intravoxel incoherent motion (IVIM) technique has been used to model the non-monoexponential signal decay in the liver[1,2]. This technique allows for the extraction of perfusion information from the diffusion-weighted imaging (DWI) signal and includes a faster component thought to represent the microcirculation of blood through capillaries. The IVIM model is biexponential (i.e. a two component model) and includes terms for the fraction of received signal attributed to moving blood (perfusion fraction, f_p), the diffusion of the moving blood (pseudodiffusion, D_p), and the diffusion excluding contributions from moving blood (true molecular diffusion, D_t), (Equation 1). However, the best model for fitting the IVIM signal is still unknown. Previous studies have used several different models and achieved different results. The full model involves using a least squares technique to fit the full range of b-value DWI data to a biexponential equation, with the true and pseudo-diffusion components weighted by fractional perfusion[3]. The segmented technique involves using only high b-values to calculate a perfusion-insensitive diffusion parameter and fractional perfusion[1,2]. Finally, the Bayesian approach uses the least squares data from the full model as a prior distribution and a shrinkage prior model to reduce parameter uncertainty[4]. This study compared the three models in terms of parameter value and repeatability in normal liver parenchyma.

Methods Eight subjects with no known history of abdominal disease participated in this study. Each subject underwent two consecutive respiratory-triggered spin-echo EPI DWI scans on a GE 1.5T scanner. The TR varied based on subjects' breathing and ranged from 6-9s. Additional parameters were: FOV=36-50cm, TE=63.4ms, 3 orthogonal diffusion directions acquired simultaneously (3in1), b = (0, 10, 25, 50, 100, 150, 200, 400, 800) s/mm^2, slice thickness = 8 skip 2mm, and a matrix size of 192x256. The IVIM parameters were calculated using three different fitting models. For the full model, Equation 1 was fit using the full range of b-values. The segmented approach used methods previously published[1,2]. This technique takes advantage of the fact that, since $D_p >> D_t$, its effect can be neglected when b > 200 s/mm^2. Thus, D_t can be estimated by linearly fitting the DWI data obtained at b>200 s/mm^2 with the natural log of Equation 2, and f_p by evaluating Equation 3. Pseudodiffusion can then be calculated by fitting Equation 1, with f_p and D_t already known. For the full and segmented models, curve-fitting analyses were performed in Matlab using a trust region reflective algorithm with constraints (lsqcurvefit). The IVIM parameters had the following constraints: $0<f_p<1$, $0<D_t<10$ μm^2/ms, $0<D_p<500$ μm^2/ms. Finally, the Bayesian model was implemented using a previously published algorithm[4]. This approach, which takes the least squares data from the full model as a prior distribution leads to a shrinkage effect, where outlier values are pinched towards the center of the parameter histogram. Circular ROIs with 20mm radii were drawn in three consecutive slices in the lower right lobe of the liver. Mean values of each parameter were extracted on a voxelwise basis within the ROI and compared across fitting model with a one-way ANOVA and post hoc Tukey's test. Parameter values at the constraints were excluded from further analysis. Repeatability was analyzed via the within-subject coefficient of variation (wCV) and the repeatability coefficient (RC).

	Full		Segmented		Bayesian	
	wCV	RC	wCV	RC	wCV	RC
Fractional Perfusion (f_p)	0.051	0.038	0.075	0.057	0.10	0.065
Molecular Diffusion (D_t)	0.094	0.00028	0.086	0.00026	0.070	0.00022
Pseudodiffusion (D_p)	0.13	0.035	0.14	0.023	0.25	0.089

Table 1. Repeatability of IVIM parameters for the full, segmented, and Bayesian models. Abbreviations: wCV = within subject coefficient of variation; RC = repeatability coefficient

$$\frac{S_b}{S_0} = (1-f_p)\cdot e^{-b\cdot D_t} + f_p \cdot e^{-b\cdot D_p} \quad (1)$$

$$S_b = S_{\text{int}} \cdot e^{-b\cdot D_t} \quad (2)$$

$$f_p = \frac{(S_0 - S_{\text{int}})}{S_0} \quad (3)$$

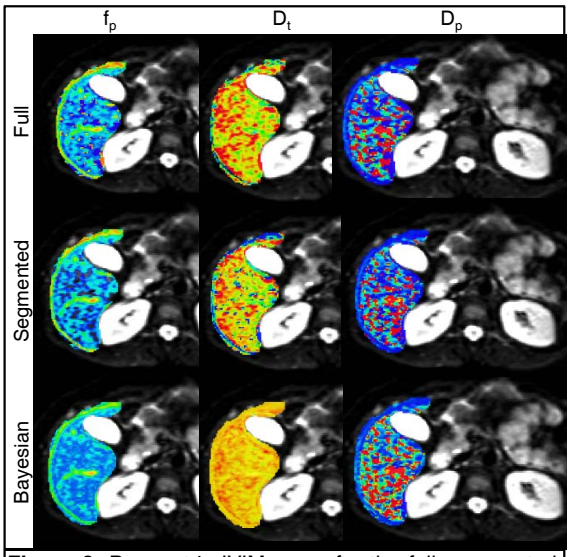

Figure 2. Parametric IVIM maps for the full, segmented, and Bayesian models.

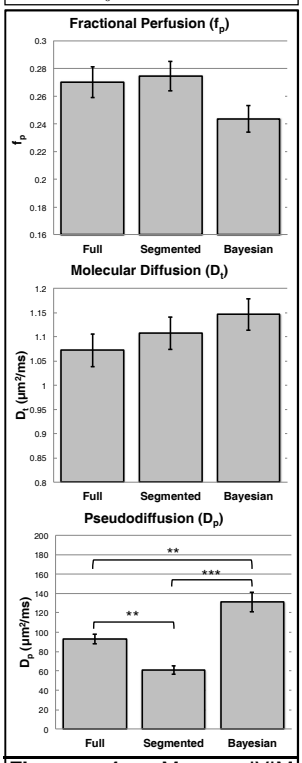

Figure 1. Mean IVIM parameters for the full, segmented, and Bayesian models. Error bars depict standard error.

Results Results are summarized in Table 1 and Figure 1. There were no significant differences across models for f_p and D_t. For D_p, all three models significantly differed with each other. The Bayesian model resulted in the highest D_p, followed by the full model and then the segmented model. Repeatability was comparable for the full and segmented models. The Bayesian model resulted in worse repeatability for f_p and D_p. Example parametric maps are shown in Figure 2. Despite worse repeatability, the Bayesian-derived maps were qualitatively less noisy and cleaner looking than the full or segmented maps.

Discussion Bayesian modeling resulted in less repeatable maps than the full or segmented models, especially for the pseudodiffusion parameter. The Bayesian shrinkage model employed in this study results in a shrinkage effect where outlier voxels get squeezed towards the center of distribution[4]. Therefore, voxels classified as outlier voxels and excluded from further analysis by the full or segmented models get included in the Bayesian analysis. These voxels still tend to have a relatively high D_p and may be the cause of increased D_p and worse repeatability seen with the Bayesian analysis. One remedy could be to use a lower threshold to exclude these voxels from further analysis.

Conclusion The choice of IVIM fitting model affects both the value and repeatability of IVIM parameters, especially for D_p. The full and segmented models were comparable, while the Bayesian technique resulted in higher D_p and lower repeatability, despite less noisy parametric maps.

References **1.** Patel J, Sigmund EE, Rusinek H, et al. J Magn Reson Imaging 2010;31(3):589-600. **2.** Luciani A, Vignaud A, Cavet M, et al. Radiology 2008;249(3):891-899. **3.** Lee Y, Lee SS, Kim N, et al. Radiology 2014:140759. **4.** Orton MR, Collins DJ, Koh DM, Leach MO. Magn Reson Med 2013.

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