The effect of very low b-values on the IVIM-derived pseudodiffusion parameter in the liver

Alexander D Cohen[1], Moira C Schieke[2], Mark D Hohenwalter[2], and Kathleen M Schmainda[2]
[1]Biophysics, Medical College of Wisconsin, Milwaukee, WI, United States, [2]Radiology, Medical College of Wisconsin, Milwaukee, WI, United States

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

Purpose Diffusion weighted MRI (DWI) has been gaining prominence in abdominal imaging. The intravoxel incoherent motion (IVIM) analysis technique, which uses a biexponential model to extract perfusion-related information from the DWI signal, has been used to diagnose liver cirrhosis[1,2]. This model assumes a voxel can be divided into intravascular and extravascular components and allows for the extraction of perfusion-related components. The faster component is thought to represent the microcirculation of blood through capillaries, with the relatively faster moving blood causing a sharper decrease in the signal with diffusion weighting (b-value). Therefore, the model requires the collection of both low and high b-values as the IVIM effect becomes largely negligible as the b-value is increased beyond about 200 s/mm^2. IVIM studies in the liver have used different b-value distributions and obtained different values for IVIM parameters[1,2,3]. When b-values between 0 and 50 s/mm^2 are not included in the distribution, one parameter, the diffusion caused by moving blood (pseudodiffusion, D_p), has tended to be lower than when b-values between 0 and 50 s/mm^2 are included. Therefore, the goal of this study was to use simulations to examine the effect of very low b-values (0<b<50 s/mm^2) on the value and repeatability of the IVIM-derived pseudodiffusion parameter.

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

$$\sigma_x = \frac{\sqrt{\frac{1}{N}\sum_{i=1}^{N}\left(x_i - x\right)^2}}{x} \quad (2)$$

Methods Simulations were performed to look at the effects of low b-values on IVIM calculations. All simulations were implemented in Matlab (Mathworks, Natick, MA). The procedure was as follows: First, starting with a b-value distribution of b = (0, 50, 100, 150, 200, 400, 800 s/mm^2), b-values were added cumulatively in the range 0<b<50 s/mm^2 in the following order: b = 25, 10, 40 s/mm^2. The signal was generated using Equation 1 with common values for IVIM parameters reported for liver (3,4) of f_p = 0.3, D_t = 1.2 μm^2/ms and D_p = 20, 40, 60, 80, and 100 μm^2/ms. Gaussian noise was added so the SNR of the b = 0 s/mm^2 image was 30. The noisy signal was then fit with Equation 1 using a Levenberg Marquardt algorithm. This was repeated 10000 times and the error was computed from Equation 2, where N = the number of iterations, x_i = the simulated parameter value, and x = the true parameter value. In addition, the mean and median values of each parameter, as well as the percentage of outliers (defined as iterations where the Jacobian matrix was ill-conditioned), were computed for each b-value distribution and IVIM parameter set.

Results Mean and median values for the D_p term, as well as the percentage of outliers, were computed for four b-value distributions and five different simulated D_p values. Results for three D_p values are shown in Table 1. Starting with D_p = 60 μm^2/ms, the simulated D_p was less than the true D_p when there were no b-values between 0 and 50 s/mm^2. When b = 25 s/mm^2 was added to the distribution, the simulated D_p values approached the true values. The percentage of outliers dropped drastically when b = 25 s/mm^2 was added and tended to level off at about 1-2% once b = 10 s/mm^2 was also included. The effects of varying D_p on the IVIM signal as well as histograms of the simulated D_p for two D_p values and varying b-value distributions are shown in Figure 1A,C. The error in the calculated D_p values tended to decrease as more b-values between 0 and 50 s/mm^2 were added to the distribution and leveled off once b = 10 s/mm^2 was included (Figure 1B). This trend was observed for all D_p values, but the largest changes in error were seen for D_p = 40 μm^2/ms (0.21) and D_p = 100 μm^2/ms (0.17).

Table 1. Simulated pseudodiffusion values compared with the true values and the percentage of outliers for different b-value distributions

	D_p = 40 μm^2/ms			D_p = 60 μm^2/ms			D_p = 80 μm^2/ms		
	Mean D_p	Med D_p	% Out	Mean D_p	Med D_p	% Out	Mean D_p	Med D_p	% Out
Low b=(0,50)	41	36	20.4	47	43	37.7	49	45	46.2
Low b=(0,25,50)	44	41	3.3	65	59	9.1	80	73	18.8
Low b=(0,10,25,50)	43	41	1.3	64	61	1.5	86	81	1.4
Low b=(0,10,25,40,50)	43	41	1.3	64	61	1.3	85	81	1.5

The units of the b-values are s/mm^2. Each set of low b-values was in addition to a b-value distribution of b=(100,150,200,400,800) s/mm^2. Abbreviations: D_p = Pseudodiffusion, % Out = Percentage of outliers, Med = median.

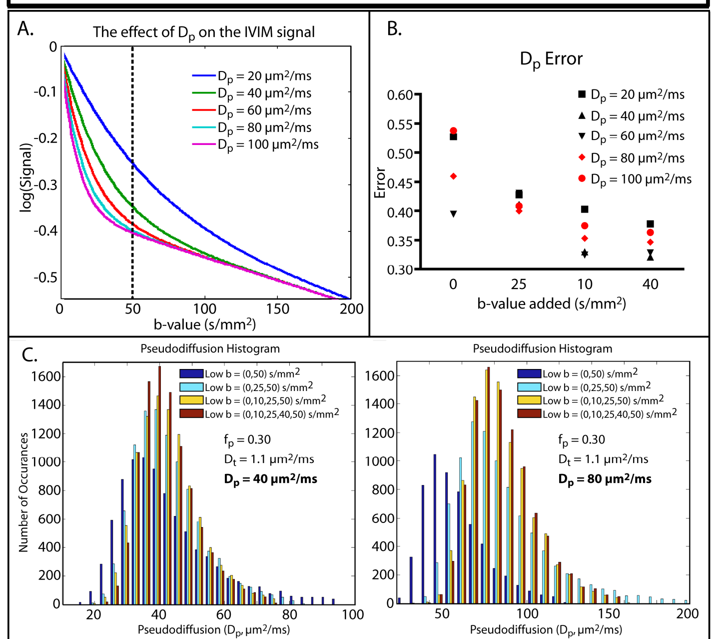

Figure 1. Simulation Results. A. The effect of increasing D_p on the IVIM signal. As D_p increases, the change in signal is driven by b-values less than 50 s/mm^2. **B.** Simulated D_p error for different D_p values and b-value distributions. Each b-value was added cumulatively to the original distribution of b = (0,50,100,150,200, 400,800) s/mm^2. **C.** Simulated D_p histograms for true D_p = 40 μm^2/ms (left) and 80 μm^2/ms (right). When the true D_p = 80 μm^2/ms, the distribution of simulated D_p values was pushed to the left when no b-values between 0 and 50 s/mm^2 were included in the distribution. As low b-values were added, the simulated D_p distribution became tighter and centered around the true D_p value.

Discussion The results of this simulation study show the importance of very low b-values when D_p becomes large. The simulated D_p underestimated the true D_p when the true D_p was larger than ~40 μm^2/ms. This is the case in the liver, where previous studies have shown D_p as high as 110 μm^2/ms[3]. Furthermore, even though the mean and median simulated D_p was similar to the true value for D_p < 60 μm^2/ms, the error and percentage of outliers substantially decreased with the addition of very low b-values. This indicates very low b-values are also important in voxels with lower true D_p.

Conclusion This study showed D_p tends to be underestimated when very low b-values (0<b<50 s/mm^2) are excluded from the distribution. Therefore it is recommended to include at least two very low b-values when performing IVIM studies in organs with high perfusion.

References 1. Luciani A et al. *Radiology*. 249(3):891-9, 2008. 2. Patel J et al. *JMRI*. 31:589-600, 2010. 3. Guiu B et al. *Radiology*. 265(1):96-103, 2012.