Correcting for perfusion and isotropic free diffusion in diffusion weighted imaging and DTI and CSD analysis

Martijn Froeling[1], Peter R Luijten[1], and Alexander Leemans[2]
[1]Radiology, UMC Utrecht, Utrecht, Netherlands, [2]Image Sciences Institute, UMC Utrecht, Utrecht, Netherlands

Introduction: In diffusion-weighted (DW) imaging, perfusion and partial volume effects with isotropic free diffusion compartments, such as CSF, are often ignored or seen as a limitation [1] and, in general the signal contribution of CSF and blood in large white matter tracts can be considered to be negligible. However, this is not true if white matter structures are small compared to the imaging resolution or in regions with high perfusion (e.g., tumors) and/or isotropic diffusion (e.g., CSF or inflammation). Therefore it can become a confound in diffusion analysis and may hamper fiber tractography. In this study, we have investigated the use of Intra voxel incoherent motion (IVIM) modeling in combination with moment nulled diffusion gradients [3] to correct DW imaging data for perfusion and partial volume effects and have tested this method using diffusion tensor imaging (DTI) and constrained spherical deconvolution (CSD) analysis [4,5].

Theory: Free isotropic diffusion on top of the anisotropic hindered diffusion can be modeled using a bi-exponential model. Perfusion can also be modeled using a bi-exponential model under the assumption that blood flowing through the microvasculature often changes direction during the diffusion experiment [2]. If this assumption is not met, blood flow will still cause intra voxel de-phasing, but cannot be described by an exponential decay [2]. However de-phasing due to intra voxel velocity gradients can be averted using a moment nulled gradient sequence [3]. If the DWI data is acquired with multiple b-values and fitted to a bi-exponential IVIM model, the relative signal contribution of each compartment can be calculated. The DWI signal can then be corrected by subtracting the signal fraction from perfusion and isotropic diffusion from the original data which results in signal that only originates from restricted anisotropic compartments. The resulting corrected data can then be used in any type of diffusion analysis e.g. DTI or CSD, free of signal contributions from perfusion and isotropic free diffusion.

Methods: DW data was acquired on a 3 T system (Philips Achieva) with a Stejskal-Tanner (ST) and an asymmetric bipolar (ASB) 2nd order moment nulled diffusion gradients (***fig. 1A***) using the following parameters; FOV: 240x240 mm^2; TE/TR: 133/9472ms; matrix size: 96x96; no. of slices: 60; voxel size: 2.5x2.5x2.5 mm^3; SENSE: 2.5; Fat suppression: SPIR. In total 80 DWI volumes were acquired; 6x b=0 s/mm^2; 3x b=5, 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400 ,500 and 750 s/mm^2; 30x b=1000 s/mm^2. The IVIM model was fitted using Bayesian modeling [4]. Next, the signal contribution of the pseudo diffusion component was subtracted from the original data, resulting in a corrected data set (***fig2 B-C***). Finally, DTI and CSD analysis using the b=0 and 1000 s/mm^2 volumes of the normal and corrected data was performed using iterative weighted least squares [4] and recursive calibration of fiber response function [5], respectively.

Results: For data acquired using the ASB gradients the diffusion the pseudo diffusion constant was higher and the pseudo diffusion fraction lower compared to data acquired using the ST gradient . After signal correction, the diffusion constant using both methods became similar (***fig. 1B***). DTI residuals for both acquisition methods were similar (***fig. 1C***). **Fig 2 A-C** shows the IVIM fit results and signal correction for the ASB data. After IVIM correction, the DTI residuals (***fig. 1C***) as well as the MD (***fig. 2D***) decreased for both acquisition methods. The FA increased (***fig. 2E***) resulting in almost twice the number of voxels above the common FA tractography threshold of 0.25 and roughly four times the number of voxels with a FA above 0.75 (***table 1***). This meant that DTI based tractography with the same thresholds resulted in a greater number of tracts (**fig. 3A-B**). Furthermore the increased FA resulted in a sharper estimated response function for the CSD analysis leading to more coherent fiber tractography (**fig. 3C-D**).

Table 1: *# of voxels above a certain FA threshold*

FA	*Norm.*	*Cor.*
>0.25	*25224*	*40325*
>0.35	15213	26587
>0.45	8294	17495
>0.55	3942	10685
>0.65	1675	5531
>0.75	*569*	*2271*

Conclusion: Typically for neurological applications diffusion b-values greater than 1000 s/mm^2 are used, in which signal contributions from perfusion and isotropic free diffusion are gone. However, most models of diffusion also require a low b-value reference image in which there is a substantial contribution of signal originating from perfusion and isotropic free diffusion that can bias the diffusion analysis. In this study, we have shown that using ASB diffusion gradients in combination with IVIM correction this bias can be minimized. Furthermore, using 2nd order moment nulled DW sequences prevents signal attenuation due to intra voxel de-phasing originating from velocity and acceleration gradients within a voxel resulting in more reliable IVIM fits.

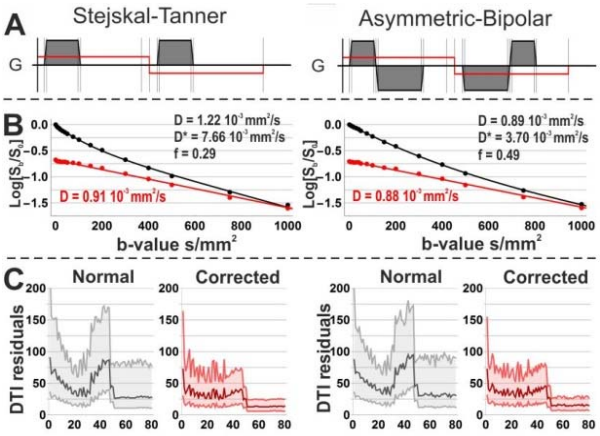

Figure 1: A) *Diffusion weighting gradients. The asymmetric-bipolar gradient is nulled for the first and second order moments (velocity and acceleration).* ***B)*** *Average whole brain signal decay (**black:** Normal data, **red:** data corrected for perfusion and isotropic diffusion) together with the fitted IVIM model (solid lines).* ***C)*** *Residuals of the DTI model as a function of DW volume for corrected data (**black**) and corrected data (**red**).*

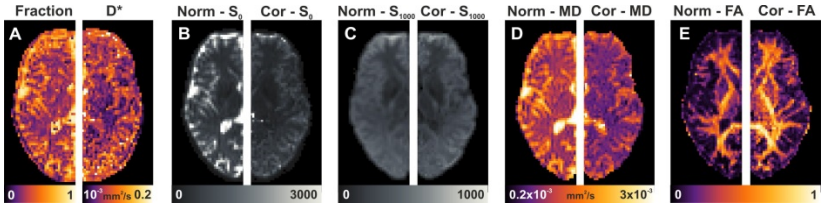

Figure 2: A) *Fraction and D* map of the IVIM fit for the ASB data.* ***B-C)*** *Normal data and data corrected for perfusion and isotropic diffusion with b = 0 s/mm^2* ***(B)*** *and b = 1000 s/mm^2* ***(C)****.* ***D-E)*** *MD and FA maps for normal data and corrected data.*

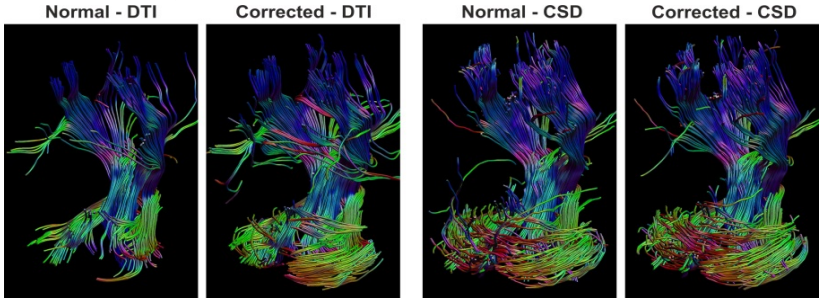

Figure 3: *Fiber tractography of the cerebellum and brain stem with DTI and CSD using normal data and data corrected for perfusion and isotropic diffusion, using only b = 0 and 1000 s/mm^2*

References: [1] S.B. Vos et al. Neuroimage 2011; 55:1566–1576. [2] D. Le Bihan et al. Radiology 1988; 168:497–505. [3] A. Wetscherek et al. Magn Reson Med 2014; M.R. Orton Magn Reson Med 2014; 71:411–20. [4] J. Veraart et al. Neuroimage 2013; 81:335–46. [5] C.M.W. Tax et al. Neuroimage 2014; 86:67–80.