# Incoherent Motion analysis of Crohn's ileitis DW-MRI reveals group differences in both fast and slow diffusion

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**Introduction:** Crohn's disease (CD) is a chronic inflammatory bowel disease of unknown etiology which affects between 400,000 and 600,000 people in North America (1). CD can involve any part of the gastrointestinal tract, and has a chronic, relapsing, and remitting clinical course. Long-standing inflammation can result in bowel obstruction, stricture, fistula, and/or abscess. In addition, there is an increased risk for small and large bowel malignancy in areas of chronic inflammation (2). Assessment of inflammatory activity plays a crucial role in the individualized management of patients with CD. Therefore, the need for a reliable, non-invasive imaging evaluation for inflammatory activity is crucial for the effective management of CD. Diffusion weighted MR imaging (DW-MRI) has shown restricted diffusion in inflamed bowel segments (3, 4). These studies, however, were limited to overall diffusivity analysis with the apparent diffusion coefficient (ADC) as the quantitative parameter. Recently, Freiman et al. used the Intra-Voxel Incoherent Motion (IVIM) analysis to show that the restricted diffusion reflected by the ADC analysis is caused by decreased fast-diffusion component rather than to decreased slow-diffusion component associated with tissue cellularity (5).
However, the Incoherent Motion (IM) is a property of the tissue, not of the voxels, and does not stop at voxel boundaries. In homogeneous regions, it extends beyond voxel boundaries, and these properties change at changes in tissue microstructure and macrostructure, not at the voxel boundaries. We recently introduced a new model that drops the dependency on the voxel structure, and refer to the Incoherent Motion generating the signal arising from multiple connected voxels (IM-MRI). In particular, the IM-MRI model introduce a dependency between the parameters of the two exponential decays at one voxel and the parameters of the two exponential decay model at all of the adjacent voxels by introducing a spatial homogeneity prior. Our new IM model is therefore extending the original Intra Voxel Incoherent Motion (IVIM) model by considering the same model of Incoherent Motion but not limited to voxel boundaries (6). As a result, we increase the reliability of the incoherent motion parameter estimates from the DW-MRI data without acquiring additional data or losing spatial sensitivity. The goal of this work was to compare Incoherent Motion group differences between enhanced and non-enhanced ileum segments of Crohn's ileitis patients obtained using the spatially constrained IM model and the independent voxel-wise IVIM model.

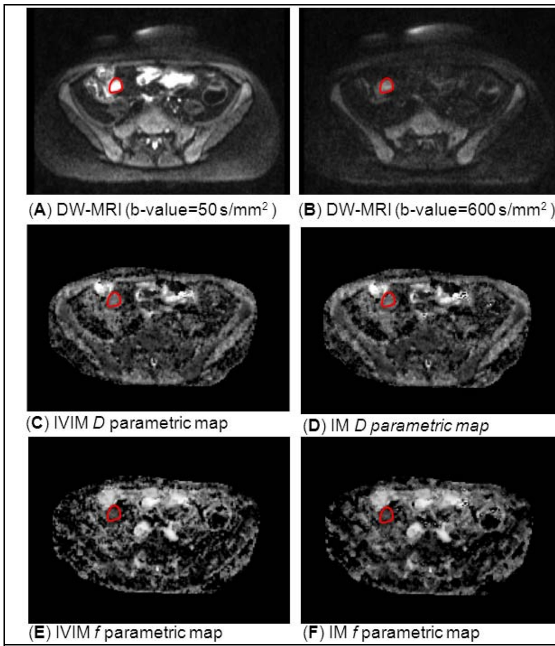


**Fig. 1:** DW-MRI of inflamed ileum with the computed maps

**Materials and Methods:** We acquired DW-MRI and MR enterography (MRE) data from 24 consecutive patients with confirmed Crohn's disease (15 males, 9 females; mean age 14.7 years; range: 5-24 years), who underwent a clinically indicated MRI study between January 1, 2011 and October 31, 2011 in our outpatient MRI department. We carried out MRI imaging studies of the abdomen and the pelvic using a 1.5-T unit (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) and a body-matrix coil and spine array coil for signal reception. We performed free-breathing single-shot echo-planar imaging using the following parameters: repetition time/echo time (TR/TE) = 6800/59 ms; SPAIR fat suppression; matrix size = 192×156; field of view = 300×260 mm; slice thickness/gap = 5 mm/0.5 mm; 40 axial slices; 8 b-values = 5,50,100,200,270,400,600,800 s/mm$^2$ with 1 average. We used a tetrahedral gradient scheme to acquire 4 images at each b-value with an overall scan acquisition time of 4 min. We generated diffusion trace-weighted images at each b-value using geometric averages of the images acquired in each diffusion sensitization direction. MR enterography (MRE) protocol included polyethylene glycol administration for bowel distention and gadolinium-enhanced, dynamic 3D VIBE (volume-interpolated breath hold exam) in the coronal plane. We calculated IVIM model parameter values with the non-linear least-squares method. We calculated IM model parameter values using the "fusion bootstrap moves" solver presented by Freiman et al. (6). We calculated mean values for the slow diffusion (*D*); the fast diffusion (*D**); and the fractional contribution (*f*) of the micro-capillary component for regions of interest in the ileum as defined by a board certified radiologist. We examined the statistical significance of the difference in the the parameter values for the IVIM and IM models using a two-tailed paired Student's t-test with $p<.05$ as indicating a significant difference. We performed the statistical analyses with standard statistical software (Matlab® R2010b; The MathWorks, Natick, MA, USA). We evaluated the capacity of each model to separate between enhanced and non-enhanced segments by constructing generalized linear models for the IVIM and IM parameter values. We calculated optimal sensitivity and specificity for each model using Receiver Operating Characteristics (ROC) analysis.

**Results:** Fig. 1 depicts the original DW-MRI data (A,B) parametric maps calculated with the IVIM model (C,E) and the IM (D,F) model. Visually, the IM maps were of higher quality with less noise. Table 1 summarizes the measured values in the enhanced and non-enhanced segments. The IM model was sensitive to the differences in both the slow-diffusion (*D*) and fractional contribution of the fast-diffusion component (*f*), while the IVIM model was not sensitive to the differences in tissue cellularity. The GLM classifier with IM model parameter values approach yield a sensitivity/specificity of 91%/92% while the GLM classifier with IVIM model parameter values yield only sensitivity/specificity of 81%/85%.

**Table 1:** Quantitative analysis of incoherent motion parameters for the non-enhancing and enhancing ileal segments. All values are in mean (std). *D* and *D** values are in µm$^2$/ms. Significant differences (two-tailed Student's t-test, $n1=11$, $n2=13$, $p<0.05$) are in bold.

| | IVIM | | | IM | | |
|---|---|---|---|---|---|---|
| | Enhanced | Non-Enhanced | p-value | Enhanced | Non-Enhanced | p-value |
| ***f*** | 0.28(0.16) | 0.55(0.24) | **0.004** | 0.32(0.15) | 0.66(0.43) | **0.02** |
| ***D**** | 36.1(20.6) | 24.2(16.3) | 0.13 | 42.5(32.7) | 28.7(22.9) | 0.24 |
| ***D*** | 1.3(0.4) | 1.6(0.6) | 0.17 | 1.2(0.3) | 1.7(0.4) | **0.002** |

**Discussion:** Inflammation processes in the ileum are associated with narrowing extra-cellular space due to lamina propria and submucosa of the small bowel and lymphoid aggregates, and vascular dilation and changes in blood supply (8). Both phenomena may alter the quantitative measurements derived from DW-MRI using the IVIM model. Our study revealed that the spatially constrained IM model analysis shows significant differences in both the slow-diffusion parameter (*D*), associated with narrowing extra-cellular space, and in the fractional contribution of the fast-diffusion parameter (*f*) associated with changes in microcirculation. However, the independent voxel-wise IVIM model analysis shows a significant difference only in the fractional contribution of the fast-diffusion parameter (*f*). The spatially constrained IM model may provide a more precise insight into the physiological causes of the DW-MRI signal decay in Crohn's ileitis patients. We are planning to evaluate the clinical advantage achieved by using this new model in analyzing inflammatory activity in Crohn's disease patients.

**Bibliography:**
1. Loftus EV, Jr., Schoenfeld P, Sandborn WJ. Aliment Pharmacol Ther. 2002 Jan;16(1):51-60.
2. Kirk GR, Clements WD. Int J Clin Pract. 1999 Jun;53(4):314-5.
3. Kiryu S, Dodanuki K, Takao H, Watanabe M, Inoue Y, Takazoe M, et al. J Magn Reson Imaging. 2009 Apr;29(4):880-6.
4. Oto A, Zhu F, Kulkarni K, Karczmar GS, Turner JR, Rubin D. Acad Radiol. 2009 May;16(5):597-603.
5. Freiman M, Perez-Rossello JM, Bittman M, Callahan MJ, Mulkern RV, Bousvaros A, et al. J Magn Reson Imaging. 2012;In press.
6. Freiman M, Perez-Rossello JM, Callahan MJ, Voss SD, Mulkern RV, Warfield SK. Med Image Comput Comput Assist Interv. 2012;15(1):1-9.
7. Targan SR, Shanahan F, Karp LC. Inflammatory bowel disease: from bench to bedside: Springer; 2005.