Quantitative Diffusion Weighted MRI biomarkers for the evaluation of Crohn's ileitis

Moti Freiman[1], Jeannette M Perez-Rossello[1], Michael J Callahan[1], Mark Bittman[1], Robert V Mulkern[1], Athos Bousvaros[2], and Simon K Warfield[1]

[1]*Radiology, Children's Hospital Boston/Harvard Medical School, Boston, MA, United States,* [2]*Inflammatory Bowel Disease Center, Children's Hospital Boston/Harvard Medical School, Boston, MA, United States*

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. Recently, diffusion weighted MR imaging (DW-MRI) has been shown to reflect inflammatory activity (3,4). These studies utilized a mono-exponential function associated with the so-called, apparent diffusion coefficient (ADC) as the decay rate parameter, expressed conveniently in units of $\mu m^2/ms$ to quantify changes in pure diffusive motion of the water molecules (1). While it is unclear why intestinal inflammatory lesions have restricted diffusion that is translated into a hyperintense signal on DW-MRI and decreased ADC values relative to normal segments (5), it is well known that the inflammation process involves vascular dilation and changes in blood flow (6) which can alter the ADC measurements depending on the acquisition parameters (2). The intra-voxel incoherent motion bi-exponential model (IVIM) (7,8), attempts to separate intra- and extracellular water diffusion from the incoherent motion of water molecules within randomly oriented blood capillaries. It is the goal of this work to investigate mono-exponential ADC and IVIM model parameters as quantitative biomarkers for the detection of Crohn's ileitis in comparison with MR enterography radiological evaluation.

Materials and Methods: DW-MRI data was acquired from 29 patients with histologically proven Crohn's disease (17 males, 12 females; mean age is 14.6 years; age range between 5 and 24 years) who underwent an MRI study between Jan. and Oct. 2011. MR imaging studies of the abdominal organs were carried out 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 4 averages. The clinical algorithm included Polyethylene glycol administration for bowel distention and gadolinium enhanced dynamic 3D VIBE (volume interpolated breath hold exam) in the coronal plane. Disease activity was defined as abnormal bowel wall thickening and enhancement in the gadolinium enhanced images. Mono-exponential ADC maps were computed using b-values=0,600 s/mm^2 ($ADC_{0\text{-}600}$) (4) and 0,50,800 s/mm^2 ($ADC_{0\text{-}50\text{-}800}$) (3). The IVIM model was fitted to the data for each voxel in the ROI with a maximum likelihood estimator that account for the Rician noise in the DW-MRI data as proposed by Freiman et al (9). Mean ADC and IVIM values were calculated over regions of interest in the ileum as defined by a board certified radiologist. Two-sample Kolmogorov–Smirnov test was used to evaluate the statistical significance of the difference of ADC and IVIM values between the normal and abnormal ileum segments. Logistic regression model was used to evaluate the joint power of the IVIM parameters in classification of normal/abnormal ileum segments. Receiver operating characteristic (ROC) curves were used to assess the sensitivity and specificity of the ADC and the IVIM logistic regression model.

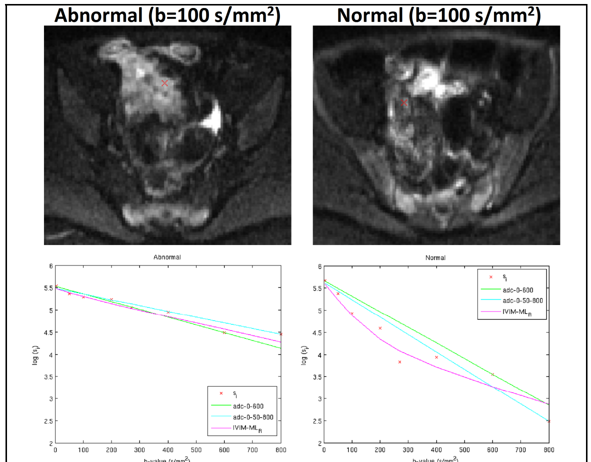

Fig. 1: Representative example of the observed signal and the fitted curves of the $ADC_{0\text{-}600}$, $ADC_{0\text{-}50\text{-}800}$ and the IVIM models for one voxel (red x) in abnormal and normal ileum segments.

Results: Fig. 1 presents representative examples of the fitted curves using the different models ($ADC_{0\text{-}600}$, $ADC_{0\text{-}50\text{-}800}$, IVIM) to two representative samples from normal and abnormal ileum segments. The major difference is the elimination of the fast-diffusion decay in low b-values (0-200 s/mm^2) associated with the perfusive motion of the water molecules. Table 1 depicts average ADC and IVIM model parameters values for the normal and abnormal ileum segments. The difference between the ADC values was significant for both $ADC_{0\text{-}600}$ and $ADC_{0\text{-}50\text{-}800}$, while only the difference in the values of the *f* parameter from the IVIM model was significant. The best ratio between specificity and sensitivity expressed by the Area under the curve of the ROC curves was obtained by the $ADC_{0\text{-}50\text{-}800}$.

Discussion: Inflammation processes in the ileum are associated with vascular dilation and changes in blood supply which may alter the quantitative measurements derived from DW-MRI. Our investigation show that there is no significant difference in the pure diffusion compartment as expressed by the *D* parameter from the IVIM model, while the changes in blood supply are reflected in the significant difference in the *f* parameter from the IVIM model. The changes in blood supply also make the ADC highly sensitive to the acquisition parameters, in particular to the choice of b-values used for ADC calculations. In practice the $ADC_{0\text{-}50\text{-}800}$ biomarker obtained the best sensitivity-specificity ratio for the separation between abnormal and normal ileum segments in the study cohort. Quantitative IVIM model parameters evaluation derived from DW-MRI provides better insight to the specific processes involved in the inflamed segments. Optimization of the acquisition parameters and model selection has substantial role in utilizing quantitative DWMRI biomarkers for effective Crohn's ileitis assessment.

Table 1	Normal	Abnormal	p-value	Area under the curve (AUC)
ADC_{0_600} ($\mu m^2/ms$)	3.2 (0.9)	1.8 (0.5)	$6.49*10^{-4}$*	0.9
$ADC_{0\_50\_800}$ ($\mu m^2/ms$)	2.5 (0.5)	1.6 (0.3)	$2.68*10^{-5}$*	0.95
f	0.53 (0.23)	0.29 (0.17)	0.02*	0.91
D (µm^2/ms)	1.6 (0.6)	1.3 (0.4)	0.09	
D* (µm^2/ms)	22.3 (14.4)	29.1 (19.3)	0.48	

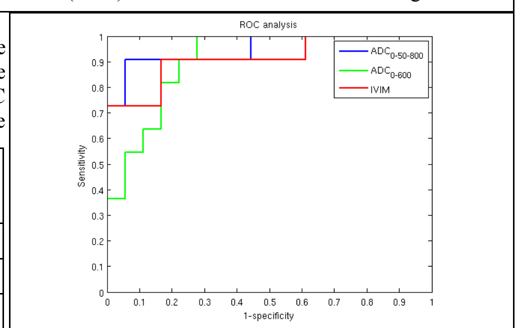

Fig. 2: ROC analysis of the sensitivity-specificity ratio of the DW-MRI biomarkers for the separation of abnormal and normal ileum segments.

Bibliography:

1. Loftus EV, Jr., Schoenfeld P, Sandborn WJ. Aliment Pharmacol Ther 2002;16(1):51-60.
2. Kirk GR, Clements WD. Int J Clin Pract 1999;53(4):314-315.
3. Kiryu S, et al. J Magn Reson Imaging 2009;29(4):880-886.
4. Oto A, et al. Journal of Magnetic Resonance Imaging 2011;33(3):615-624.
5. Panes J, Ricart E, Rimola J. Gut 2010;59(10):1308-1309.
6. Targan SR, Shanahan F, Karp LC. Inflammatory bowel disease: from bench to bedside: Springer: 2005.
7. Le Bihan D. Radiology 2008;249(3):748-752.
8. Le Bihan D, et al. Radiology 1988;168(2):497-505.
9. Freiman M, et al. Med Image Comput Comput Assist Interv 2011;14(Pt 2):74-81.