

## Preliminary experience with DTI and multi-exponential T2 relaxation imaging of myelin in children treated for ALL

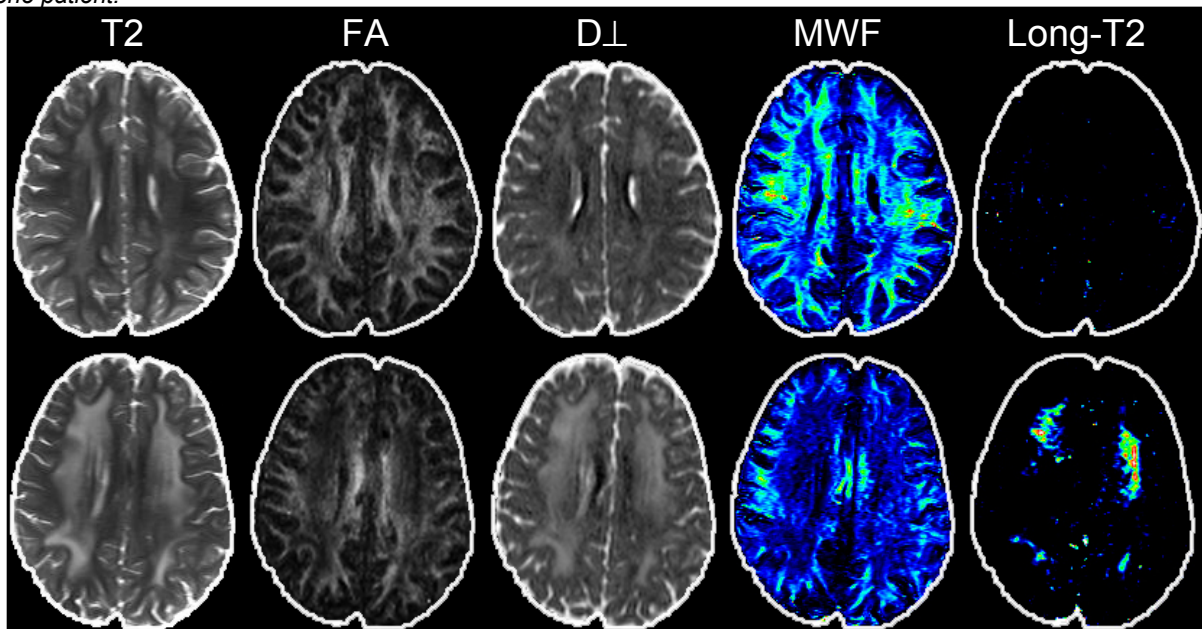
W. E. Reddick<sup>1</sup>, Q. Ji<sup>1</sup>, D. C. Carver<sup>1</sup>, J. O. Glass<sup>1</sup>, J.-Y. Guo<sup>1</sup>, and Z. Patay<sup>2</sup>

<sup>1</sup>Division of Translational Imaging Research, St. Jude Children's Research Hospital, Memphis, TN, United States, <sup>2</sup>Division of Diagnostic Imaging, St. Jude Children's Research Hospital, Memphis, TN, United States

**PURPOSE:** Acute Lymphoblastic Leukemia (ALL) is the most common form of childhood cancer, but with a 5-year survival exceeding 90%, there is a compelling need to improve the quality of life for survivors by minimizing the impact of therapy on the developing brain. It is believed that variable methotrexate toxicity related to genetic differences in methotrexate metabolism causes differing degrees of myelin disruption early in the course of therapy, which can be reliably quantified through multiple quantitative MR imaging methods. Diffusion tensor imaging (DTI) measures of fractional anisotropy (FA) and radial diffusivity (D<sub>⊥</sub>) have been shown to reliably reflect myelin integrity<sup>1</sup>. Multi-exponential T2 relaxation imaging of myelin water fraction (MWF) and long-T2 spectrum have also been shown to be reliable measures of myelin disruption in normal and MS patients<sup>2</sup>. In this preliminary study we sought to investigate the feasibility and utility of performing these measures in this vulnerable group of young patients with varying degrees of leukoencephalopathy (LE).

**PATIENTS & METHODS:** To investigate the feasibility and utility of performing these measures, we imaged two 4 year old children during treatment for ALL, both exhibiting conventional MR imaging evidence of LE following consolidation therapy as seen in the T2-weighted images in Fig. 1. DTI was acquired as forty 3 mm thick contiguous sections with whole-head coverage and a 3 mm square in plane matrix using a diffusion encoded spin echo EPI pulse sequence (TR/TE = 6500 / 120 ms; 12 directions b=1000 s/mm<sup>2</sup>; 4 averages). Once the tensors have been calculated, Eigen values were derived and used to calculate D<sub>⊥</sub> and FA maps for the whole brain. Multi-exponential T2 spectrum data were acquired as seven axial sections using a 2D spin echo pulse sequence with 32 multi-contrast echoes (50% partial Fourier phase encoding; TR/TE spacing = 3300/9 ms, receiver bandwidth = 300 Hz/pixel; GRAPPA reduction factor = 2). The multi-component T2 spectrum is estimated from the multi-contrast spin echo signals for each pixel using the spatially regularized non-negative least squares algorithm recently proposed<sup>3</sup>. MWF maps and long T2 component maps are generated from the ratio of the T2 components (MWF: 10-50 ms; long-T2: 150-800 ms) to the total spectrum.

**Fig 1.** Representative sections from two 4 year old patients during treatment for ALL. While both patients exhibit LE, one patient (bottom row) has more intense changes that may be indicative of more severe myelin disruption and possible axonal damage. DTI and quantitative multi-exponential T2 relaxation maps yield both complimentary and contrasting evidence of more severe damage in the one patient.



**RESULTS:** Both patients were successfully imaged with the quantitative imaging sequences for myelin assessment as part of routine imaging. On DTI imaging, relatively low FA and increased D<sub>⊥</sub> were evident in regions of the T2 hyperintensities. MWF maps demonstrated the anticipated, but never before shown, decrease in myelin integrity in these same regions. Additionally, the long-T2 component maps demonstrate that one patient (bottom row) has more severe myelin and axonal damage than the other patient. We would anticipate that this patient would likely have more severe neurocognitive deficits at completion of therapy.

**CONCLUSIONS:** While FA reductions have been demonstrated previously for survivors of ALL<sup>4-6</sup>, there has never been a published report of FA and D<sub>⊥</sub> during therapy immediately post high-dose methotrexate. Furthermore, there have been no studies of MWF or long-T2 components in this population. This study has demonstrated the feasibility and utility of conducting these quantitative MR measures and provided preliminary evidence to justify the need for a larger prospective study.

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