ALD DTI Data in 8 patients with Posterior-type ALD
Pre & Post BMT over 13-24 months
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Background:
Adrenoleukodystrophy is a rare X-linked disease. Defects in a gene involved in the breakdown of fatty acids lead to its accumulation in the nervous system and adrenal glands damages them and create an inflammatory response. The disease typically occurs between 4 to 10 years of age leading to severe disability and eventual death at the age of 10 to 12 years.

Hematopoietic stem cell transplantation can stop the progression of X-linked ALD. 9 Boys with evidence of demyelination have a likelihood of progression to dementia and death of about 80% to 90%, however, only 35 to 40% of boys under 10 with diagnoses will develop childhood onset cerebral disease. 12 Thus patients that demonstrate early MRI evidence without significant functional impairment or decrease in performance IQ measurement are good candidates for a BMT.

MRI evaluation typically includes a Loes score of 0 to 34 derived from location and extent of disease and the presence of focal and/or global atrophy. When used in conjunction with clinical parameters, this scoring method can help and monitor the disease progression or response.

DTI imaging with FA and ADC measurements can provide a quantitative measurement of white matter injury. In patients with X-linked ALD, DT MRI is an attractive method for interrogating the influence of the zonal pathologic features on molecular diffusivity and diffusion anisotropy in affected white matter. This study focuses on determining the isotropic apparent diffusion coefficient (ADC) and fractional anisotropy (FA) in the brain white matter in patients with X-linked ALD.

Purpose:

Preliminary studies of posterior-type X-linked adrenoleukodystrophy (ALD) have demonstrated significantly different diffusion tensor imaging (DTI) measurements such as fractional anisotropy (FA) and mean apparent diffusion coefficient (MADC) values in affected white matter (AWM) (1-3).

Our goal was to prospectively perform serial DTI measurements in multiple locations pre- and post-bone marrow transplantation (BMT), and to correlate such measurements with the MRI severity score (Loes score), and clinical outcome.

Materials and Methods:
Since late 2008 our 3.0T MRI protocol for ALD patients has included 3.0T 12-directional DTI along with routine FLAIR, T2WI, and pre- and postcontrast 3D MPGRAGE T1WI, performed at a time point <60 days prior to BMT (T0). After BMT if performed, MR imaging is optimally sought at time points approximately 30-60 days post-BMT (T1), 90-120 days post-BMT (T2), 180 days post-BMT (T3), and one year post-BMT (T4).

Of 38 ALD patients presenting for BMT evaluation, 8 were transplanted and underwent serial imaging. After IRB approval, staff neuroradiologists measured FA and MA values in 19 regions serially, and compared these with 8 control patients, while the corresponding Loes scores were obtained by consensus of two other staff neuroradiologists. Four clinical scores were measured at T0 and T4: Verbal IQ (VIQ), Visual-Motor IQ (VMIQ), Adaptive Function (AF), and Overall outcome (OO). DTI values in each tract were correlated with serial Loes scores and clinical scores, with statistical correction for multiple correlations.

Results:
There was no significant difference (p=0.05) between NAFWM when comparing MADC at most time points to controls, although PFWM was significantly different from controls at 3 time points (p=0.05). As compared to controls, FA values were significantly different at each time point pre- and post-BMT within the cerebellar white matter (CWM) lateral geniculate nucleus (LGN). Meyer’s loop (ML), optic radiations (OR), periaqueductal white matter (POWM), and callosal splenium (SPLCC) (all p<0.05); MADC values were only significantly different at most (not all) time points within the CWM, POWM, and SPLCC. Interestingly, anterior temporal white matter (ATWM) FA was significantly different from controls initially (p<0.05), but not at 1 year (p=0.13), raising the question of treatment response.

Regarding Loes scores, MADC in the optic radiations (OR) and POWM had the strongest correlations (r=0.699-0.762, p<0.05) with Loes scores initially and at 1 year, but with lower, non-significant correlations at intermediate time points (each p>0.05). FA values in the OR had a strong negative, and significant correlation (r=-0.721-0.905) at each time point, with posterior limb (PLIC) (r=-0.786), PFWM (r=0.862), and SPLCC (r=-0.905) correlating only at 1 year (for each, p<0.05).

Regarding clinical outcome, significant correlations existed between VIQ and the following: FA in the callosal genu (GCC, r=-0.852, p<0.031) and the PLIC (r=-0.897, p<0.015), and optic tracts (OT, p<0.043), and with MADC within the callosal body (BCB, r=-0.921, p<0.009) and NAFWM (r=-0.850, p<0.032). Significant correlation existed between VMIQ and only MADC within the decussation of the superior cerebellar peduncle (DSCP, r=-0.804, p<0.029). Regarding AF, there were significant correlations with MADC within the OR (r=-0.787, p<0.036) and the PLIC (r=-0.764, p<0.046), and with FA within the BCC (r=-0.860, p<0.010) and the trapezoid body/mid-pons (TB, r=-0.814, p<0.026). Overall, 6 patients stabilized, and 2 progressively worsened.

Conclusion:
To assess the effect of HCT we followed 8 patients who underwent bone marrow transplantation and post utilizing DT1 and MADC values utilizing a tract by tract basis and compared it to the Loes score and clinical score.

DTI and FA can be quantitative measurements of specific areas to monitor the progression of disease in areas that are on the edge of existing disease or otherwise normal appearing regions.

Several important findings were gleaned from this study, one being that FA is typically abnormal in CWM and NAFWM, structures which usually appear normal. Also improving FA with ATWM could relate to a treatment response. DTI values in HTC are dynamic. However, values within areas at the disease’s edge, such as PLIC and BCC may seriously correlate with clinical scores.