

Application of high b value DWI in Adrenoleukodystrophy

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Introduction: Adrenoleukodystrophy (ALD) is an x-linked genetic disorder characterized by wide phenotypic variations, affecting central and peripheral white matter and adrenal function. Both age of onset and pattern of neurological involvement can vary. Early diagnosis plays an important role for clinical intervention. Magnetic resonance spectroscopy (MRS) and diffusion tensor imaging (DTI) were shown to be sensitive in early detection of the demyelination process in the normal appearing white matter (NAWM) areas of ALD patients (1,2). High-b value DWI is an advanced diffusion-based technique recently shown to be more sensitive to white matter maturation and to the demyelination process (3,4). However, to the best of our knowledge, this technique has not yet been applied in ALD patients. In this work we have applied MRS, DTI and high-b value DWI – using q-space analysis in symptomatic and pre-symptomatic patients.

Methods: Five subjects with ALD: three symptomatic and two pre-symptomatic were scanned. MRI protocols included: proton spectroscopy - single voxel PRESS sequence of both lesions and NAWM. The DWIs were acquired using single-shot spin-echo diffusion-weighted echo-planar imaging sequence (SSFSE DW-EPI), with 8 diffusion gradient steps reaching maximal b value of 6,000 s/mm². For each b value increment, the diffusion images were measured in 6 non-colinear gradient directions. Fractional anisotropy (FA), displacement and probability maps were analyzed from the same data set as previously reported (4,5).

Results and Discussion:

In symptomatic patients with extensive T₂ hyperintensity lesions, MRS revealed reduced NAA/Cr ratio, increased Cho/Cr ratio and the appearance of Lac peak within lesions. Abnormal metabolite distribution was also detected in some regions in the NAWM with reduced NAA/Cr ratio and increased Cho/Cr ratio. Figure 1 shows a: T₂ weighted, b: displacement and c: FA images of a 6 year-old symptomatic patient. Table 1 summarized the values measured in ROI placed in the anterior and posterior subcortical white matter of an aged matched control subject and values measured in ROIs placed in the lesions (Fig 1, ROIs - red color) and in the NAWM of the ALD patient (Fig 1, ROIs - yellow color). In lesions, reduction in the FA value and increase in the displacement value compared to the normal age-matched control were observed. However, in some regions of the NAWM, FA values were found to be similar to control values whereas displacement values were significantly increased. In the pre-symptomatic patients, MRS as well as DTI and high-b value DWI were normal in all measured cerebral regions. Based on our diffusion database, which includes high-b value and DTI from 36 normal subjects from 4 months to 23 years old, we can follow up development of the young pre-symptomatic ALD subjects.

Figure 1.

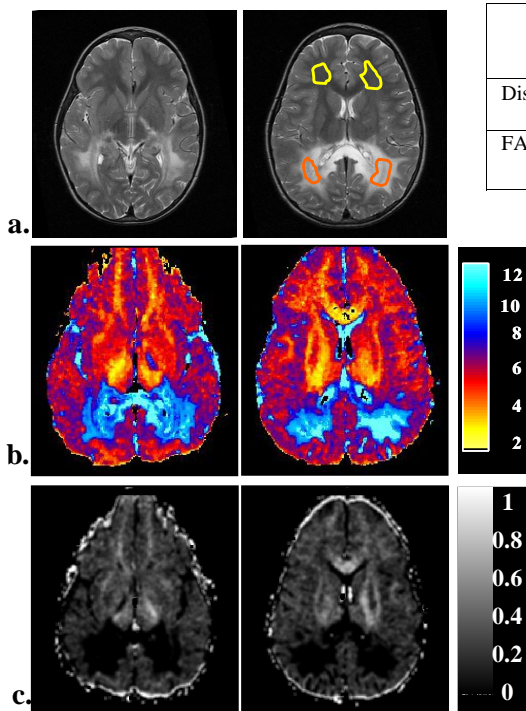


Table 1.

	Normal Posterior	Normal Anterior	ALD-Lesion Posterior	ALD-NAWM-Anterior left	ALD-NAWM-Anterior right
Disp μ m	5.6	6.7	17	8.0	7.2
FA	0.42	0.3	0.05	0.31	0.3

Conclusion: Advanced MR techniques (MRS, DTI and high b value DWI) are very important in early detection of the demyelination process, as well as in follow-up of normal development in young pre-symptomatic patients. High b values may be more sensitive in detection of changes in the white matter and thus may contribute additional important information for treatment decisions.

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