# Multi-slice spectroscopic imaging of late infantile metachromatic leukodystrophy (MLD)

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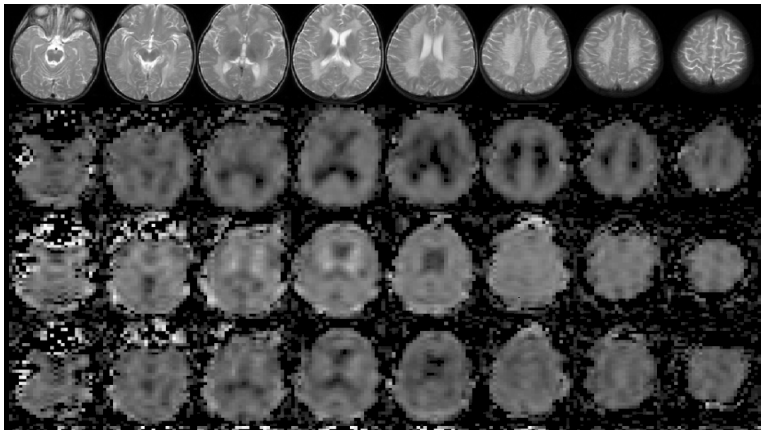
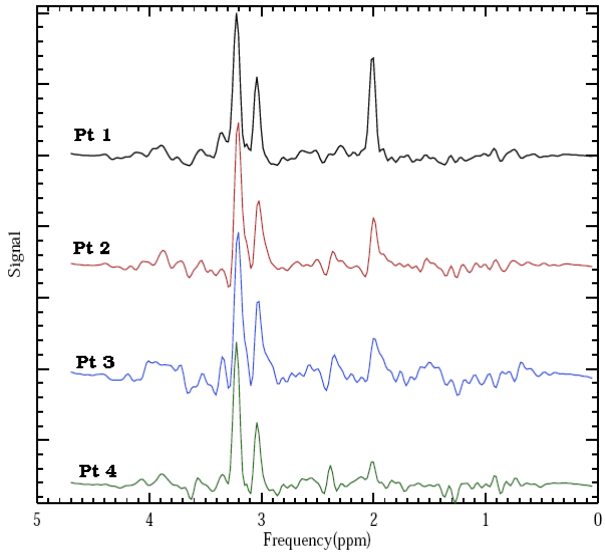
**Introduction:** Metachromatic Leukodystrophy (MLD) is an autosomal recessive disorder caused by deficiency of the Arylsulfatase A enzyme, resulting in an accumulation of galactosyl sulfatide, a major constituent of myelin. Accumulation of sulfatide leads to a progressive degeneration of white matter in the brain and also demyelination in peripheral nervous system. In the late infantile form that affects 60% of the patients, the initial symptoms appear at the second year of life. They are dominated by sensory-motor dysfunctions with muscle rigidity and later loss of mental abilities. The disease is rapidly progressive and fatal normally before the age of 10 (1). As treatment options are now being explored (1) there is increased focus on the disease that is relatively easy to diagnose, once suspected. But since it is rare, with an incidence of 1:50000 the children are often diagnosed one year after the symptoms show.

Spectroscopy studies of MLD are sparse. Two localized studies (2,3 reviewed in 4) conducted at short echo time showed a reduction of N-acetyl-aspartate (NAA) in grey and white matter, elevated lactate and increased levels of brain myo-inositol compared to age matched controls. A case study found decreased levels of choline (Cho), but this finding is questionable due to missing baseline correction (4). The spatial variation of metabolite concentrations is hitherto unexplored. We present multi-slice spectroscopic imaging of late infantile MLD showing drastic spectral changes at long echo time and pronounced tissue specific variation.

**Methods:** Four clinically different MLD patients were anesthetized and scanned. Pt 1 (age 2.6 y) was able to walk independently, pt 2 (age 3.4y) was talking holding hands and able to sit by herself, both children appeared cognitively normal for their age. Pt 3 (2.8 y) and pt 4 (2.10 y) both had severe spasticity in arms and legs. They were without expressive language but with preserved normal perception. Echo-planar spectroscopic imaging was performed on a 1.5T Siemens Vision as described in (5) with the following parameters: 8 axial slices covering most of the cerebrum, matrix: 32x32, isotropic $(1cm)^3$ resolution, TE/TR=144/4300 ms. Lipid suppression was achieved via inversion (TI=165ms). A water-reference acquisition provided voxelwise frequency correction and phasing. The spectroscopic measurement duration was 20 minutes. Spectra were evaluated for individual voxels and for regions of interest using software developed in house. Corresponding T2-weighted anatomical images with high in-plane resolution (matrix 256x256) were measured with a spin echo sequence with echo train length 11, TE/TR=99/5400ms.

**Results:** The structural images show diffuse changes in white matter. These were visible for all patients and pronounced for Pt 2, 3 and 4. The spectroscopic images show an almost complete loss of NAA signal in white matter in the later stages of the disease. In contrast, there is high, yet abnormal, signal from NAA, Cho and Creatine (Cr) in grey matter. Spectra from white matter in the superior slices are shown for the 4 patients (right figure). The spectra are scaled to normalize Cho peak heights, which amounts to nearly similar amplitude of the Cr peaks, also. The NAA signal vanishes as the disease progress. Minor lactate peaks appearing as inverted doublets at 1.3 ppm are seen to varying extent.






**Figures:** Structural images and corresponding metabolite maps for pt 4. Top to bottom: T2-weighted water, NAA, Cho, and Cr images. Right: White matter spectra measured in the upper 4 slices. An undersampling artefact appear at 2.4 ppm (5).

**Discussion:** Multi-slice spectroscopic imaging provides high quality metabolite maps in clinically relevant measurement times. The technique could potentially aid early diagnosis and monitoring of MLD. For the severely affected patients, the superior NAA images are virtually indistinguishable from grey matter masks as the signal loss from NAA in white matter is nearly complete. Since the spectroscopic images are both T1- and T2-weighted and since relaxation times may change with disease progression, it cannot be concluded that NAA is absent though an NAA loss is expected.

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