Analysis of 1H metabolite ratios using image segmentation at 7T in adult patients with X-linked adrenoleukodystrophy

T. Kok[1], E-M. Ratai[2,3], F. Eichler[3,4], and E. Adalsteinsson[1]

[1]Department of Electrical Engineering and Computer Science, Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA, United States, [2]Department of Radiology, A.A. Martinos Center for Biomedical Imaging, Cambridge, MA, United States, [3]Harvard Medical School, Boston, MA, United States, [4]Department of Neurology, Massachusetts General Hospital, A.A. Martinos Center for Biomedical Imaging, Cambridge, MA, United States

Introduction: The combination of segmented structural data with low-SNR spectroscopy has been used to provide brain metabolite estimates in separate tissue compartments [1-3]. Inhomogeneities of B0 and B1 at high fields poses a challenge for absolute metabolite quantification, and to correct for comparison across subjects under different scanning conditions, expressing metabolite signals as ratios to the sum of the metabolite signals from Cr and PCR (Cr') is a common technique. We extend compartmental analysis of absolute metabolite measures to ratio measures, and demonstrate its use in a study of NAA+NAAG (NAA') changes in X-linked adrenoleukodystrophy (X-ALD) at 7T.

Methods: We obtained a model shown in Eq. 1 for the metabolite ratio observed in a particular voxel r_i for the metabolite M. We aim to determine the optimal values of the global quantities M_g/Cr'_g and M_w/Cr'_w for each subject, which are the gray and white matter contributions to the metabolite M expressed as ratios to the gray and white matter contributions to the metabolite Cr'. M_g/Cr'_g, and M_w/Cr'_w indicates the value of the metabolite signal ratio r_i for particular g_i'' and w_i'' in a certain voxel by Eq. 1. This model is derived from Eq. 2 of reference [3] where y_i is the measured metabolite signal, g_i and w_i are the structural representations of the gray and white matter and n_i is additive noise. First, Cr'_g and Cr'_w were obtained by estimating $r_{gw} = Cr'_g / Cr'_w$ using the absolute metabolite data of Cr' from each voxel of the subject. This estimate of r_{gw} was then used to determine g_i'' and w_i''. With g_i'' and w_i'' expressed as shown, the procedure for finding the optimal values of M_g/Cr'_g and M_w/Cr'_w is equivalent to finding the optimal M_g and M_w of Eq. 2 where g_i is substituted by g_i'' and w_i is substituted by w_i''.

$$r_i = g_i'' \cdot \left(\frac{M_g}{Cr'_g}\right) + w_i'' \cdot \left(\frac{M_w}{Cr'_w}\right) \qquad (1)$$

$$y_i = g_i \cdot M_g + w_i \cdot M_w + n_i \qquad (2)$$

$$g_i'' = \frac{g_i}{g_i + w_i \cdot \frac{Cr'_w}{Cr'_g}} \qquad w_i'' = \frac{w_i}{w_i + g_i \cdot \frac{Cr'_g}{Cr'_w}}$$

We demonstrate the use of this model in data obtained from twelve ALD patients and nine healthy subjects. The spectroscopic VOI was selectively excited with PRESS at TE = 35ms and TR = 2s with CHESS water suppression and six spatial outer-volume suppression pulse for fat suppression. A spectroscopic voxel size of 2.3cm^3 resulted from partitioning the FOV of 20cm with 16x16 phase encoding steps. The structural image was acquired with MPRAGE at TE = 3.6ms, TR = 2.5s, TI = 1.1s with voxel size of 0.31mm^3. The gray and white matter composition of each of the subject's structural image was determined by a combination of automated segmentation using Freesurfer [4-5] and manual segmentation, and registered to the spectroscopic data. We assumed an idealized rectangular point spread function for the structural acquisition and for the spectroscopy. In a previous analysis [6], only spectroscopic voxels manually assigned as containing 100% white matter (predominantly white) or 100% gray matter (predominantly gray) were used. Here, we incorporate segmented structural data into this analysis of metabolic ratios for the same set of spectroscopic voxels. Correct metabolic segmentation has relevance to the monitoring of demyelination and axonal degeneration in X-ALD.

Results and Discussion: Fig. 1 is an example of the analysis applied to NAA' of ALD patients. The z-axis shows values of the metabolic ratio r_i and the x and y-axis shows values of g_i'' and w_i''. The red crosses ('x') in the figure are obtained by manually assigning spectroscopic voxels as either 100% gray or 100% white. The averages of r_i for both the 100% gray-matter and 100% white-matter voxels are shown in purple ('●'). Based on the segmentation, most of these spectroscopic voxels contain mixed-volume tissue and their composition is represented by the black triangles in the figure ('▽'). Using these mixed-volume data and applying our model, we obtained an estimate of M_g/Cr'_g and M_w/Cr'_w for each ALD patient and averaged these values across the patients. With the averaged metabolite ratio r_i is expressed as a function of g_i'' and w_i'' as Eq. 1 and represented by the blue line ('—') in Fig. 1. The green lines ('—') of Fig. 1 indicate one standard deviation of the averaged values. The same procedure in obtaining Fig. 1 is repeated for the control subjects. The anatomy of the selected VOI is such that fully-volumed gray-matter voxels are less common than fully-volume white matter voxels. The M_g/Cr'_g and M_w/Cr'_w obtained from this analysis offers a comparison metric for changes in metabolite ratio levels between ALD patients and healthy subjects and we demonstrate its use as such a metric in Fig. 2 where we did an ANOVA test and see a significant decrease of NAA'/Cr' in both the gray and white matter of ALD patients.

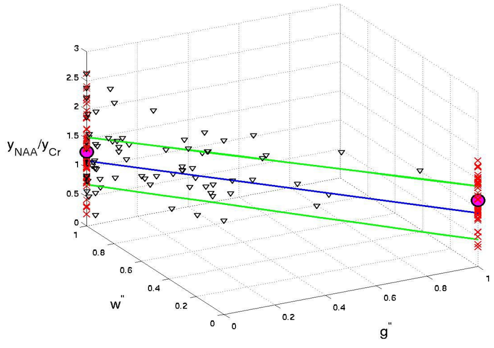

Fig. 1

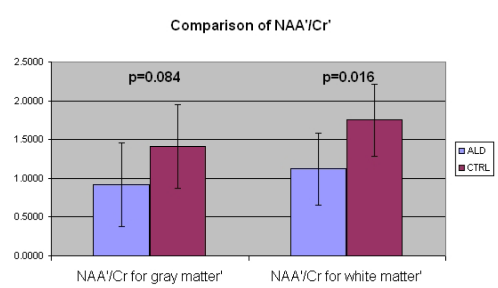

Fig. 2

References: [1] Hetherington et al. MRM 1996;36:21. [2] Lim et al. MRM 1997;37:372. [3] Pfefferbaum et al MRM 1999;41:276. [4] Fischl et al NeuroImage (in press). [5] Fischl et al Neuron. 2002; 33:341. [6] Ratai et al Proc. ISMRM, Berlin, 2007 p.769.