Evaluating brain metabolites in patients with glioma using short and long TE MRSI at 3T and 7T

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Target audience: MRS researchers, neurologists, neuro-oncologists, neuro-surgeons and any clinicians that are interested in brain tumors.

Introduction: Three-dimensional (3D) proton (H-1) magnetic resonance spectroscopic imaging (MRSI) is a powerful noninvasive tool to characterize metabolite profiles within a spatial extent for patients with glioma. A general marker to distinguish regions of tumor from normal brain is the elevation of choline-containing compounds (Cho), due to increased cell density and membrane turnover in neoplasms, and the reduction of the neural marker N-acetyl-aspartate (NAA). Other brain metabolites, such as glutamate (Glu), glutamine (Gln) and myo-inositol (mI), appear in the short echo time (SE) spectra, and have been shown alterations in *ex vivo* HRMAS from tissues samples that highlight the importance of using these metabolites in evaluating patients. At 3T it can be difficult to isolate their individual components without spectral editing and they are typically reported as combination indexes, such as Glx (Glu+Gln) and mIG (mI+glycine). The availability of ultra high field MR systems (7T) has the potential for more detailed analysis of such metabolites because it provides higher SNR and improved spectral resolution. The purpose of this study was to compare the metabolite profiles that were acquired with conventional long echo time (LE) MRSI at 3T, and SE MRSI at 3T and 7T in patients with glioma.

Methods: MR studies were obtained from 22 patients with glioma using either an 8-channel receive-only phased array on a 3T GE scanner or 32-channel receive-only phased array with a volume transmit head coil on a 7T GE scanner. Ten patients (6 G2, 1 G3 and 3 G4) had both LE and SE MRSI at 3T, 14 patients (6 G2, 4 G3 and 4 G4) had LE MRSI at 3T and SE MRSI at 7T. Two patients of 22 patients (G2) had all three acquistions (Figure 1). The 3T MRSI data were obtained using CHESS water suppression, VSS outer volume suppression and PRESS volume selection with an automatic prescription of both excitation regions and outer volume suppression (TE=35/144ms, spectral array=18x18x16, spatial resolution=1cm^3) [1,2], while the MRSI data-set at 7T were localized using spin echo and positioned to cover as much of the T2 hyperintensities (T2L) as possible with TE/TR=30/2000ms, spectral array=18-22x8 and spatial resolution=1cm^3 [3]. The spectral data were combined and processed as described previously, and then quantified by LCModel using simulated basis-sets. Only metabolite ratios with CRLB<10% for Cho, Cr and NAA, and <20% for other resonances were considered in the analysis. The T2L was defined from the 3T FLAIR images and then aligned to the 7T IRSPGR images followed by down-sampling to the spectral resolution of the MRSI data. Voxels overlapping by at least 25% with the T2L were considered as being abnormal. Signed-rank tests were utilized in making comparisons.

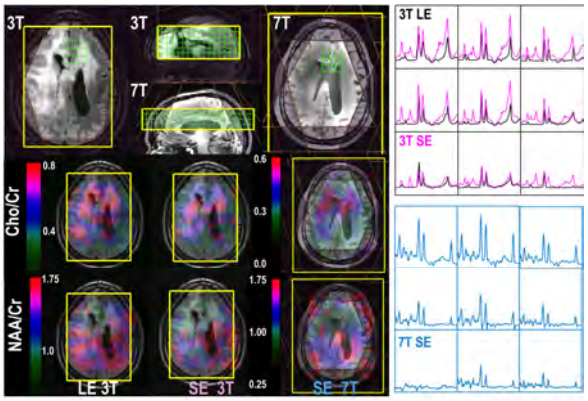

Figure 1. MRSI data (LE at 3T, SE at 3T and 7T) along with maps of Cho/Cr (left middle row) and NAA/tCr (left bottom row) quantified using LCModel acquired from a patient with grade 2 glioma.

Results: For the patients who had only 3T scans, the median T2L volume was 13.64 cc and the median voxel coverage over the T2L volume was 76.6%, while for patients who had both 3T and 7T scans they were 39.76 cc, 71.4% (3T) and 63.9% (7T), respectively. Figure 1 illustrates an example of MRSI data from a patient who had all three acquisitions. Voxel-by-voxel comparisons and box plots on Cho/Cr, NAA/Cr and Cho/NAA between acquisitions within the T2L are shown in Figure 2, and metabolite ratios are summarized in Table 1. The levels of Cho/tCr were significantly higher at LE MRSI compared to SE at 3T or 7T (P<0.001), but there was no difference in Cho/NAA between SE and LE MRSI at 3T, or NAA/Cr between SE MRST at 3T and 7T. The percent of quantifiable voxels at 7T for glutathione and GABA at 7T were 75% and 45%, respectively.

Table 1. Metabolite ratios (mean±std) and percentage of quantifiable voxels (%).

ROIs			Cho/Cr	NAA/Cr	Cho/NAA	mIG %	Glx %
T2	3T	LE	0.58±0.20	1.26±0.45	0.52±0.28		
	3T	SE	050±0.17	1.04±0.37	0.56±0.39	82%	44%
	3T	LE	0.52±0.13	1.21±0.49	0.53±0.36		
	7T	SE	0.31±0.08	1.09±0.31	0.32±0.21	84%	67%
Nor	3T	LE	0.40±0.12	1.64±0.44	0.25±0.09		
mal	3T	SE	0.32±0.10	1.31±0.34	0.25±0.10	82%	51%
	3T	LE	0.36±0.02	1.41±0.15	0.26±0.05		
	7T	SE	0.23±0.02	1.40±0.21	0.17±0.03	84%	79%

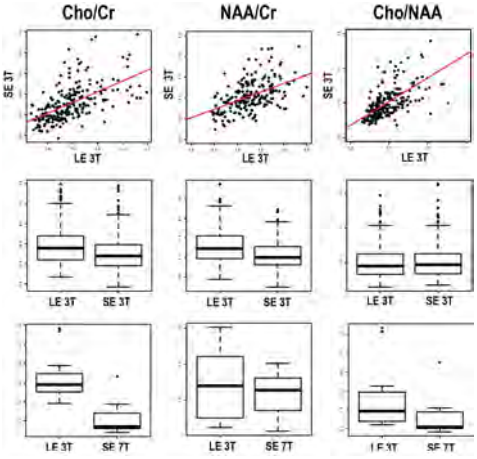

Figure 2. Scatter and box plots of Cho/Cr, NAA/Cr and Cho/NAA from the T2 lesions that were acquired with LE MRSI at 3T, SE MRSI at 3T and 7T. Cho/Cr was significant different within 3 acquisitions; NAA/Cr was different between SE MRSI at 3T and LE MRSI at 3T. Cho/NAA was significantly different between LE MRSI at 3T and SE MRSI at 7T.

Discussion/Conclusion: This study has evaluated metabolite profiles in patients with gliomas acquired with different TE and field strengths. The difference on Cho, Cr and NAA between acquisitions reflects the differences in relaxation times, which were consisted with the previous finding of a differential increase in T2 for Cho and Cr relative to NAA [4]. For Cho/NAA, the LE MRSI at 3T would be the best for differentiating T2 lesions from surrounding brain tissue. Although there was no difference on Cho/NAA between SE and LE MRSI at 3T, the tumor voxels with very low NAA were excluded from the analysis. With improved quantification and metabolite detection using SE MRSI at 7T, it would be possible to examine heterogeneity in T2 but tumor coverage is limited relative to MRSI at 3T. Future studies will perform a more detailed analysis on the changes of these metabolites in SE MRSI at both 3T and 7T.

Reference: [1] Ozhinsky E. et al. J Mag Res Imaging 2013;33:792-802; [2] Ozhinsky E. et al. Mag Res Med 2013;69:920-930; [3] Li Y. et al. J Mag Res Imaging 2014; [4] Li Y. et al. J Mag Res Imaging; 2008; 28:342-350. **Acknowledgements**: This research was supported by NIH R01CA127612 and GE healthcare.