Characterization of high grade gliomas using TE-averaged PRESS at 3 T

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Introduction

Proton MR Spectroscopy (MRS) is a powerful noninvasive tool that has been used for the assessment of metabolites in patients with brain tumors. In short echo spectra, spectral overlap makes it difficult to isolate peaks, even at higher field strength, 3 T. A recently developed method, called TE-averaged PRESS, offers unobstructed detection of Glutamate (Glu) which is well separated from NAA and Glutamine (Gln) at 2.35 ppm, resulting in more reliable quantification of Glu [1]. Since data are acquired at multiple echo times, TE-averaged PRESS also enables measurement of T_2 relaxation times of singlets, such as Cho, Cr and NAA. The purpose of this study was to use single voxel TE-averaged PRESS acquisition, a) to acquire the relaxation times of Cho, Cr and NAA in tumors to compare with white matter (WM) in controls and NAWM in patients, and b) to obtain quantitative metabolite concentrations which were then related to tumor malignancy.

Methods

All data were acquired using an 8-channel phased array coil on a 3 T GE Signa scanner running Excite software (GE Healthcare Technologies, Waukesha, WI). TE-averaged PRESS data were obtained using 64 steps with an increment time of 2.5 ms starting at TE of 35 ms [1]. With a TR of 2 s, the total acquisition time was ~5 minutes. The 8-cc single voxel was located within regions indicated in **Table 1**. The tumors regions were defined by T_2 hyperintersity from T_2-FLAIR images and positioned to cover as much of the tumor as possible. Eight healthy volunteers and seven patients with high grade gliomas were recruited for the study. Tumors were graded by histological examination of the tissue samples from biopsy or surgery. Post-processing was applied on a Sun workstation using the SAGE software package™. 8-channel data were combined in the time-domain using the internal water signal [2]. T_2 relaxation times were obtained using a single exponential fit to the peak heights of Cho, Cr and NAA. To obtain metabolite concentrations, spectra were averaged in the t1 domain before zero filling and then quantified using LCModel with fitting performed between 3.85 ppm and 1.8 ppm to minimize spectral artifacts from lipid and improper water suppression [3]. Only metabolite concentrations with SD < 6% for Cho, Cr and NAA and 20% for mI and Glu were considered. T_2 correction was applied for levels of Cho, Cr and NAA by multiplying LCModel parameter estimates by a factor $f_{TE} = \exp[TE*(1/T_{2vivo}-1/T_{2vitro})]$. Nonparametric Wilcoxon rank sum tests were used for statistical studies with a significance cutoff level of $p<0.05$.

Results

The T_2 relaxation values of Cho, Cr and NAA are shown in **Table 2**. Since no statistically significant difference was found in the T_2 values between WM in controls and NAWM in patients, normal regions included WM and NAWM for comparison. The T_2 relaxation time of Cho in tumors was statistically significantly longer than normal regions (P=0.012), while the T_2 value of NAA was significantly shorter (P=0.010). **Figure 1** illustrates a TE-averaged PRESS spectrum and metabolite quantification by LCModel from a tumor lesion in a grade 3 glioma patient. The metabolite levels after T_2 relaxation correction were given in **Table 3**. The differences in levels of NAA and Glu were statistically significant between normal and lesions with P<0.001 and P<0.05, respectively. Compared to normal regions, the level of mI was statistically significantly increased in grade 3 lesions with P=0.018, and Cho was higher without any significance (P=0.079). Both metabolites were slightly decreased in grade 4 lesions but the differences between grades were not statistically significant.

		Numbers	Location
Controls		N = 8	WM
Gliomas	Grade 3	N = 3	NAWM + Tumor
		N = 1	Tumor only
	Grade 4	N = 3	NAWM + Tumor

Table 1 Study group profile.

	Cho	Cr	NAA
WM in controls	160±15	138±25	227±26
NAWM in patients	151±20	120±9	191±28
Normal (N = 14)	156±17	130±21	211±31
Tumor (N = 7)	188±27	143±28	158±43
P-value	**0.012**		**0.010**

Table 2 T_2 relaxation times of metabolites (ms).

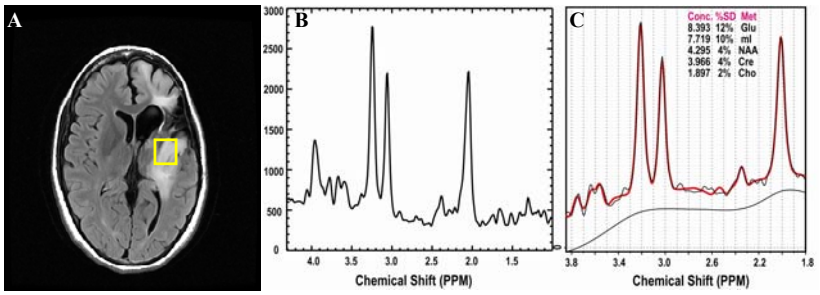

Figure 1 TE-averaged PRESS spectrum (B) corresponding to the location of tumor in the image (A) and quantified by LCModel with metabolites concentration shown in (C). The values of Cho, Cr and NAA shown here were not corrected for T_2 relaxation times.

Discussion

Gliomas are the most common primary brain tumor. High grade gliomas have more densely cellular regions and sometimes exhibit necrosis and vascular or endothelial cell proliferation. This study demonstrated that the T_2 relaxation values in lesions of high grade gliomas were different from normal white matter, which is indicative of the cellular environments in tumors. Due to the difference of T_2 in normal and tumor, corrections for relaxation times are important for metabolite quantification. A general marker of gliomas is the elevation of Cho peak and the reduction of neuronal marker NAA. The level of Cho was not statistically significant between normal and high grade tumor after T_2 correction. Cho was observed to be higher in grade 3 gliomas and decreased in grade 4. These indicated that the increase in Cho height is partially caused by T_2 effect and the difference was mainly seen in grade 3 gliomas. NAA levels were also reduced in the lesion, presumably indicating loss of neuronal function. mI is specific to glial cells and the spectrum could be contaminated by Glycine (Gly) at 3.56 ppm. mI+Gly is expected to be high in grade 2 astrocytomas but decreased in grade 4 [4], which are consistent with our findings. Glu showed a statistically significant increase in gliomas (P=0.044) but the number of voxels analyzed was only 2. These results are encouraging but further studies are required to see whether the finding holds up in a larger patient population. Previous studies have showed that a significant increase in Glx was found in oligodendrogliomas and also used to discriminate against low-grade astrocytomas [5]. Our results suggest that the elevation in Glx may be due to an elevation of Glu. Higher Glu in lesions could result in neuronal toxicity, which would aggravate neuron death in these lesions.

	Cho	Cr	NAA	mI	Glu
Normal (N = 14)	1.7±0.4	7.0±1.2	10.5±1.7	6.6±1.7 (N = 11)	5.6±0.7 (N = 8)
Tumor (N=7)	1.9±0.4	6.1±1.9	5.6±1.7	8.7±1.2 (N = 6)	7.8±0.9 (N = 2)
P-value			**<0.001**		**0.044**

Table 3 Metabolite levels with T_2 corrections were applied.

Reference:

1. Hurd R. et al., Magn Reson Med. 2004;51:435-440
2. Wright SM. et al. NMR Biomed. 1997;10:394-410
3. Provencher SW. et al. Magn Reson Med 1993;30:672-679
4. Howe FA. et al. Magn Reson Med. 2003;49:223-232
5. Rijpkema M. et al. NMR Biomed. 2003;16:12-18

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