Anatomic distribution and extent of 1H MRSI metabolites in treatment-naïve grade III and IV gliomas

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Background and Purpose:

High-grade gliomas are among the most invasive and aggressive tumors and have defied many decades of therapeutic inroads and remain largely incurable. Necrosis and hypoxia are two important malignant phenotypes of high-grade gliomas that have been linked to their destructive behavior and florid angiogenesis. Proton magnetic resonance spectroscopy (1H MRS) has been used to analyze levels of such metabolites, including n-acetylasparate (NAA), choline (Cho), creatine (Cr), lactate (Lac) and lipid (Lip) within both normal and diseased specified areas of the brain for gliomas of different grades (Pirzkall et al, Pirzkall et al, Li et al). These data have shown that there are regions with elevated Cho and decreased NAA in the enhancing volume, in the non-enhancing T2 lesion and, in some cases, even beyond the anatomic lesion. The purpose of this study was to use 1H MRSI to separately quantify levels of Lac and Lip in grade III and grade IV glioma patients to assess differences in their distribution within anatomically defined regions and to compare these results with the spatial extent of the Cho to NAA (CNI) abnormality..

Methods:

Patient Population: The pre-operative MRI scans for thirty-eight newly diagnosed, high-grade glioma patients were studied for this project. Based upon the histopathologic analysis of resected tumor tissues, the patients were divided into grade III (n=16) and grade IV (n=22) gliomas, based upon World Heath Organization tumor grading system.

Data Acquisition and Processing: In addition to anatomic MR imaging, all patients underwent 3D J-difference lactate-edited MRSI using a PRESS (Point REsolved Spectral Selection) volume selection technique to separately quanify levels of Lac and Lip (Li et al). The spectroscopic data was analyzed using software developed in our group to yield values of Lip, Lac, and choline to NAA index ratio (CNI). The basis for quantification was the z-scores of a voxel within the MRSI, where z-score equals the number of standard deviations of the value of the parameter in the voxel from the control assuming a normal distribution. A z-score of 4 or more was considered abnormal or significant for Lip and Lac and a z-score of 2 or more was considered significant for CNI.

The number of voxels with significant metabolite levels (sigZ) was quantified for different subsets of tumor anatomy, including necrosis (Nec), contrast enhancing lesion (CEL), T2L region (T2L), and outside of the T2L region (oT2L). Voxels were considered to be in one of these respective regions if over 50% of the voxel was within the anatomic ROI. 1H MRSI voxels that were identified as being contaminated with lipid artifact by an experienced spectroscopist were excluded from analysis.

Results:

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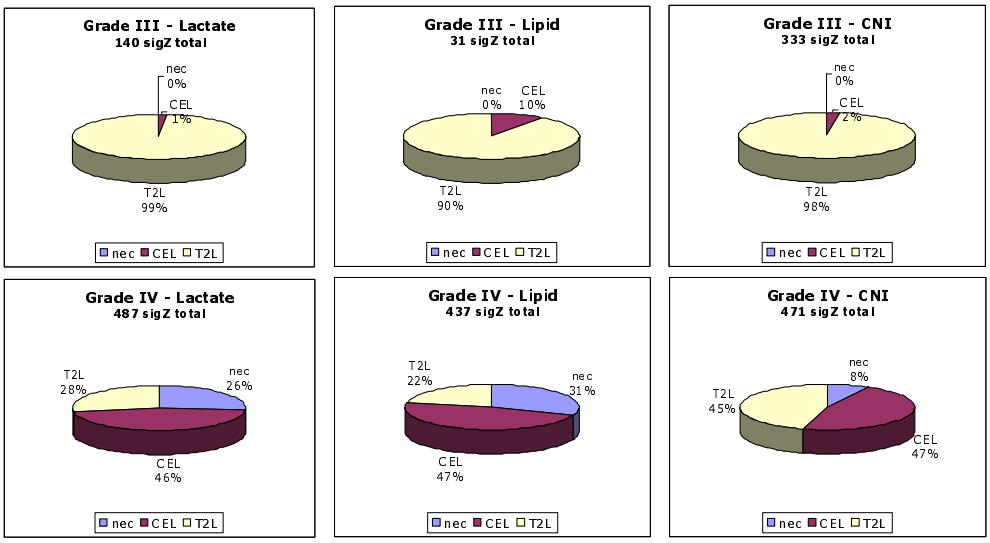
	Lactate				Lipid				CNI			
GRADE III	**nec**	**CEL**	***T2L***	**Total**	**nec**	**CEL**	**T2L**	**Total**	**nec**	**CEL**	**T2L**	**Total**
# of sigZ	0	2	*138*	140	0	3	28	31	0	8	325	333
% of total	0%	1.0%	*99%*	100%	0%	10%	90%	100%	0	2%	98%	100%
GRADE IV	**nec**	**CEL**	***T2L***	**Total**	**nec**	**CEL**	**T2L**	**Total**	**nec**	**CEL**	**T2L**	**Total**
# of sig Z	127	223	137	487	136	206	95	437	37	220	214	471
% of total	26%	45.8%	28.1%	100%	31%	47%	21.6%	100%	7.8%	46.7%	45.4%	100%

Lactate: Grade III – 99% of all lactate positive voxels were located within the T2L region and 1% was within the contrast enhancing region. Grade IV – 45.8% of all lactate positive voxels were located within the contrast enhancing region, 28.1% were located within the T2L region and 26% were located in the region of necrosis.

Lipid: Grade III - 90% of all lipid positive voxels were located in the T2L region and 10% were located in the contrast enhancing region. Grade IV - 47% of all lipid positive voxels were located in the contrast enhancing region, 31% were located in the necrotic regions and 21.6% were located in T2L regions.

CNI: Grade III – 98% of CNI positive voxels were located within the T2L region and 2% were located within the contrast enhancing region. Grade IV– 46.7% of CNI positive voxels were located within the contrast enhancing region, 45.4% were located in the T2L region, and 7.8% were located inside the necrotic region.



Note: Necrosis (Nec), contrast enhancing lesion (CEL), T2L region (T2L).

Discussion and Conclusions:

The results of our study suggest that lipid, lactate and CNI metabolic maps derived from 1H MRSI have distinct topographic distributions between grade III and grade IV gliomas. Both lipid and lactate were much more commonly seen in grade IV gliomas and displayed diverse anatomical presentation, but with specific prominence in the CEL region. Abnormal CNI was observed far less in necrotic regions and more in the T2L region than lactate and lipid for grade IV gliomas. The distribution of lactate and CNI in grade III gliomas was similar; meanwhile, the anatomical distribution of lipid was somewhat more concentrated in the CEL. The topographic distribution of spectroscopic abnormality may be related to the different biologic and molecular behaviors of these tumors, and further analysis may provide a noninvasive means of studying tumor heterogeneity.

Additional References:

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