Characterization of two high grade human oligodendroglioma mouse models using ^{1}H MRSI

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Introduction

Oligodendrogliomas represent 5-18% of all intracranial gliomas. They arise in the cortex and white matter of cerebral hemispheres. The majority of oligodendrogliomas are low grade tumors. Based on their clinical representation oligodendrogliomas can not be easily distinguished from other brain tumors especially astrocytomas. As the treatment is different in between oligodendrogliomas and astrocytomas correct characterization is clinically important. In general brain tumors are pathologically diagnosed by analysis of tumor tissue obtained by biopsies. MRI is well established for anatomical localization of tumors, however it is limited in the diagnosis of brain tumor type nor can it be used for reliable grading. Low grade oligodendrogliomas may show contrast enhancement while lack of contrast does not directly correspond with low grade malignancy. Here we characterize two human oligodendroglioma xenograft models by their metabolic profile using ^{1}H MRSI and compare the findings to previously published human oligodendroglioma data[1,5]

Material and methods

Two intracranial xenograft lines (E434, E478) were established by direct intracerebral inoculation of freshly obtained surgical human oligodendrogliama tissue and were serially serial passaged in female nude Balb/c mice (6-8 weeks old, weighing 18-25 g)[2]. Upon showing discomfort or weight loss, animals (n = 5 per group) were selected for investigations on a 7T MR spectrometer. Anatomical images in three directions were acquired using a T2w sequence (TSE, TR 3880 ms, TE 43 ms). Subsequently short and long echo time 3D chemical shift ^{1}H images were acquired (semi-LASER[3], TR 1500 ms, TE 24 or 144 ms, OVS, WET, voxel size 0.92 × 0.92 × 1.00 mm, 16 × 16 × 16). For phase correction and metabolic quantification an additional non-water suppressed data set was acquired (semi-LASER[3], same settings, no WET). After MR investigations the mice were sacrificed and their brains harvested for histological analysis. The spectroscopic data were quantified using LCModel 6.2-1G[4]. A molecular basis set for LCModel was simulated and a metabolic base line was estimated via an inversion recovery experiment (IRsemiLASER, same settings, TI 570 ms) in age matched non-tumour bearing healthy control mice (n = 2).

Results

MR imaging was used to delineate the tumor. Figure 1 shows an example of an MR image of an E478 oligodendroglioma. The grid indicating the MRSI voxels is plotted on these images. The corresponding LCModel fit of a single E478 tumor voxel (figure 1 blue box) is shown in figure 2. All spectra from within the volume of interest (white box in figure 1) where analyzed using LCModel and metabolite values compared between the two oligodendroglioma lines and healthy controls (table 1).

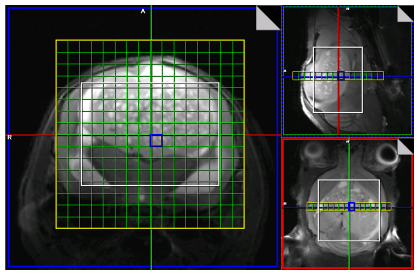

Figure 1: T2w MR image of E478 oligodendroglioma. Plotted on top are the MRSI grid (green), VOI (white) and single voxel (blue).

	E434	%	**E478**	%	**Control**	%
NAA	2.897	6	3.115	8	7.577	4
GPC	2.463	11	6.012	7	1.472	6
mI	7.377	9	3.383	18	8.432	5
Tau	7.665	6	10.079	6	5.581	6
Glu	4.69	10	3.666	18	3.93	13
Gln	2.262	18	4.594	11	3.387	12
MM	43.104	4	68.268	6	43.173	4
Cho+GPC+PCh	3.649	17	12.681	5	2.06	4
NAA+NAAG	2.897	6	4.286	7	9.2989	2
mI+Gly	8.199	4	6.43	7	8.559	3
Cre+PCr	5.334	4	6.953	4	8.271	3
Glu+Gln	*6.952*	*7*	***8.259***	*10*	*7.317*	*8*

Table 1: Metabolite concentrations for oligodendrogliomas and control

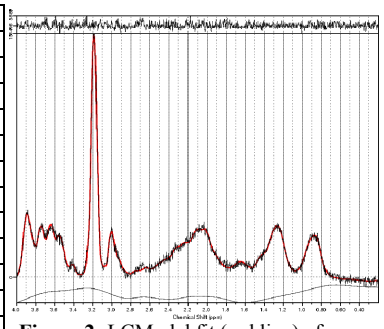

Figure 2: LCModel fit (red line) of a single E478 tumor voxel.

Besides the metabolic profile generally observed in brain tumors (increase of choline and decrease of N-acetylaspartate (NAA) signals) an increase in Glu+Gln was observed in the E478 oligodendroglioma line. In addition this line showed higher MM and total Cho than the other line. Furthermore we observe increased mI+Gly/Cr + PCr in E434 but not E478.

Discussion

As in the human MRSI oligodendroglioma study[1] increased levels of Glu+Gln were observed in the E478 oligodendroglioma line. In the human study Glu + Gln was particularly increased in the higher grade olidendrogliomas. The E434 did not show an increase in Glu+Gln. Several other metabolic characteristics (increased MM, Cho/Cr, lower mI/Cr) also observed in human oligodendriogliomas [1,5] identify E478 as high grade and E434 as low grade oligodendrioglioma. .

Conclusion

MRSI might be used to characterize high grade oligodendroglioma from other brain tumors by looking at Glu+Gln levels and is able to differentiate metabolic signatures for low and high grade oligodendrioglioma models.

References

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[4] S.W. Provencher, Magn Reson Med. 30(6):672-679 (1993) [5] M Jenkinson et al Neurology 2005, 64, 2085