4 YEAR LONGITUDINAL MRI FOLLOW-UP AND 1H SINGLE VOXEL MRS IN 22 PATIENTS WITH OLIGODENDROGLIAL TUMORS OR GLIOMATOSIS TREATED WITH TEMODAL

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Purpose: to better understand glial tumor metabolism and post-chemotherapy variation. To determine cerebral variation in MRS area, amplitude, and ratios of metabolites and spectral profiles during a 4 year longitudinal follow-up in 22 patients with oligodendroglial tumors (12; Fig 1a) or gliomatosis (10; Fig 1b) without initial hyperperfusion treated with Temodal and to detect differences in infiltration or proliferation. Gliomatosis Cerebri (GC) is a challenging tumor to treat, having a poor prognosis and poor response to treatment.

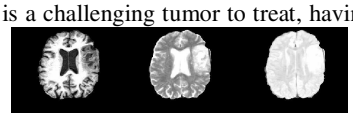

Fig1a :oligodendroglioma MRI

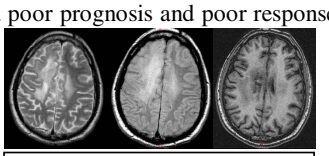

Fig1b gliomatosis MRI

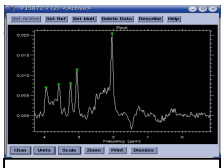

Fig 2a SAGE processing

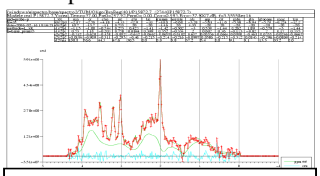

Fig 2 b : SCI-MRS LAB processing

Methods MRI: Sagittal T1, axial proton density, T2, FLAIR, diffusion, 3D T1 3 planes after gadolinium. MRS : 1H, single voxel (6 to 12 cm3), PRESS with multiple TEs on a 1.5 T (GEMS) MRI. Data processing : SA/GE (Fig 2a) software and home-written automated processing (SCI-MRS-LAB in Scilab cINRIA-ENPC open source code, Fig 2b) yielding amplitudes, areas, ratios, and relative concentrations. Statistical analysis of longitudinal spectroscopic data (every 3 months over 48 months).

Results : quantitative studies in MRI with multi-spectral segmentation and tissular classification are ongoing. Without chemotherapy spectroscopic profiles worsen with increases in Choline/N-Acetyl-Aspartate (Cho/NAA), Cho/Cr and Myoinositol/Creatine (mI/Cr) ratios, decreases in NAA/Cr and sometimes with increases in lactate. After chemotherapy, treated tumoral volumes, in MRI, change little between two exams while spectroscopic profiles and ratios (Fig 4) do change. MRS could, in fact, be more sensitive than MRI and could, in some cases, be predictive of worsening. Water and creatine are quite stable, which could justify using them for some other ratios to quickly detect spectroscopic variations. Cho concentration could be predictive in 7 out of 15 cases and more sensitive than ratios (5/15). Cho concentration increased in 3 patients with aggravation later in 2 gliomatosis and one oligodendroglioma. There was also a decreased Cho concentration in 3 patients before clinical improvement.

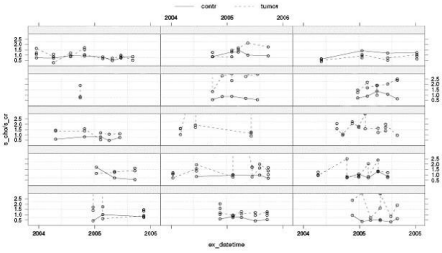

Fig 3 18 months Cho/Cr Follow-up

Effect of TE on measurements: Concentration of Naa always has a higher estimation on the short TE while lactate often has a higher estimation on the 288 ms TE.

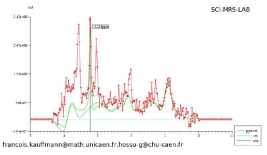

Fig 4a Cho/Cr ratio before chemotherapy

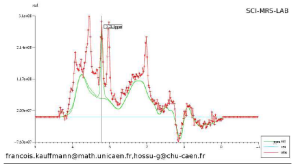

Fig 4b Cho/Cr ratio after chemotherapy

Spectroscopic and metabolic changes often occur well before clinical deterioration and sometimes before improvement. Therefore, MRS could be more sensitive and detect changes earlier than MRI and sometimes is predictive.

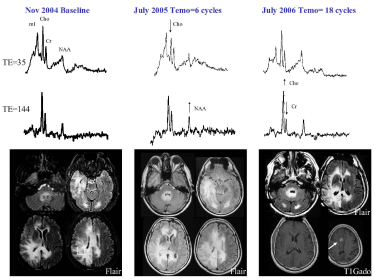

Fig 5 MRI and MRS follow-up of a gliomatosis patient

The patient (Fig. 5) had initial clinical and MRS improvement and a stable MRI. After 18 cycles MRS showed an increase in the Cho/Cr ratio and a nodular contrast enhancement (arrow). Four cycles later, the patient had clinical deterioration and radiotherapy was started.

Discussion and Conclusion :

Temozolomide was well tolerated. MRI remained stable for all patients, except for two late partial responses.

MRS showed variable ratios of mI/Cr, Cho/Cr and NAA/Cr at baseline. We observed a decrease in ratio in patients whose clinical condition improved and opposite results for those whose conditions deteriorated.

These spectroscopic and metabolic changes occurred well before clinical deterioration and just before improvement. MRS allows non-invasive follow-up of treated cerebral tumors. There is a large variability, but repetition and modelization of spectroscopic measurements during longitudinal follow-up could allow us to decrease this and to improve prognostic evaluation.

Studying the relationship between MRS measurements, methionine PET, segmentation and perfusion parameters could lead to a better understanding of therapeutic response, especially with regard to chemotherapy, and in the future hypoxia modulators and antiangiogenic molecules could also be monitored in the same way.

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