5 YEAR LONGITUDINAL MRI FOLLOW-UP AND 1H SINGLE VOXEL MRS IN 13 PATIENTS WITH GLIOMATOSIS TREATED WITH TEMODAL, RADIOTHERAPY AND ANTIANGIOGENIC THERAPY.

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Purpose: to better understand glial tumor metabolism and post chemotherapy, radiotherapy and antiangiogenic variations in a longitudinal study. To determine cerebral variation in MRS area, amplitude, and ratios of metabolites and spectral profiles during a 5 year longitudinal follow-up in 13 patients with gliomatosis without hyperperfusion initially and treated with Temodal and to detect changes in infiltration proliferation or lipids.

Gliomatosis Cerebri (GC) is a challenging tumor, considered to have a poor prognosis and poor response to treatments.

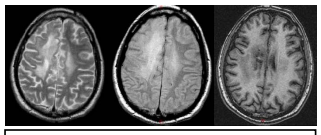


Fig1b gliomatosis MRI

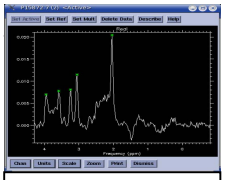


Fig 2a SAGE processing

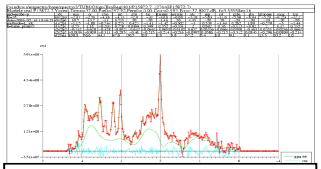


Fig 2 b : SCI-MRS LAB processing

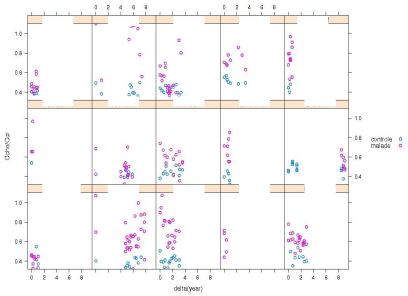
Methods : MRI: Sagittal T1, axial proton density, T2, FLAIR, diffusion, 3D T1 3 planes after gadolinium. MRS : 1H, single voxel (6 to 12 cm3), PRESS with MRI. multiple TEs on a 1.5 T (GEMS) Over 13 patients, 9 underwent radiotherapy and 4 antiangiogenic therapy.

Data processing : SA/GE software and home-written automatic processing (SCI-MRS-LAB in Scilab cINRIA-ENPC open source code) yielding amplitudes, areas, ratios, and relative concentrations. Statistical analysis of longitudinal spectroscopic data (every 3 months over 60 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 do change. MRS could, in fact, be more sensitive than MRI and could, in some cases, be predictive of worsening.The 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 5 out of 13 cases and more sensitive than ratios (3/13). Cho concentration increased in 2 patients with aggravation later. There is also decrease Cho concentration in 2 patients before clinical improvement.

Fig 3
48 months
Cho/Cr
Follow-up



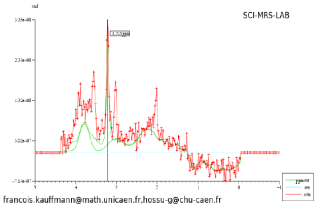


Fig 4a Cho/Cr and mI/Cr ratio before chemotherapy

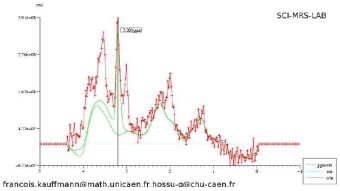


Fig 4b Cho/Cr and mI/Cr ratio after chemotherapy

Effect of TE on measurements: Concentration of Naa always has higher estimation on the short TE while lactate has higher estimation on long TE.

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

The patient (Fig 5) had initial clinical and MRS improvement and stable MRI. After 18 cycles MRS showed an increase of Cho/Cr ratio and a nodular contrast enhancement (arrow). Four cycles later, the patient had clinical deterioration and radiotherapy was started. Later in the evolution for 2 patients with hyperperfusion this one disappears but proliferationstayed very important.

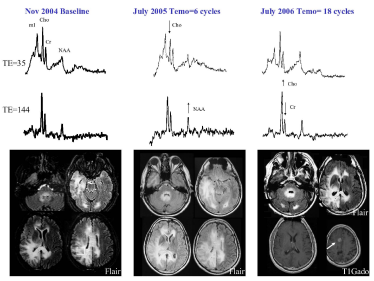


Fig 5 MRI and MRS follow-up of a gliomatosis patient

Discussion and Conclusion :

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

MRS showed variable ratio of mI/Cr, Cho/Cr and NAA/Cr at baseline. We observed a decrease in Cho/Cr ratio and mI/Cr (at a lesser extent) and an increase in NAA/Cr ratio for patients whose clinical condition improved and inverse 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 modelisation of spectroscopic measurements during longitudinal follow-up could allow us to diminish it and to improve prognostic evaluation especially in some cases under antiangiogenic therapy.

Studying the relationship between MRS measures, methionine PET, segmentation and perfusion parameters could lead to better understanding of therapeutic response, especially with regard to chemotherapy and antiangiogenic molecules and in the future hypoxia modulators.

References:

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