Brain tumour diagnosis and prognosis by in vivo 1H MRS and ex vivo metabolomic and genomic data. A prospective study as part of eTUMOUR (FP6-2002-LSH503094)

D. Monleon[1], C. Martinez-Bisbal[1], B. Martinez-Granados[1], V. Esteve[1], E. Piñero-Sagredo[1], R. Ferrer-Luna[1], M. Mata[2], J. Piquer[3], L. Marti-Bonmati[4], B. Celda[1]

[1]Depto. Quimica Fisica, Universitat de Valencia, Burjassot, Valencia, Spain, [2]Unidad central de Investigacion en Medicina, University of Valencia, Valencia, Valencia, Spain, [3]Neurocirugia, Hospital de la Ribera, Alzira, Valencia, Spain, [4]Radiologia, Clinica Quiron, Valencia, Valencia, Spain

Purpose:

. Although brain cancers are proportionately less common than other cancers, it is a devastating disease with high mortality. In addition, *Brain cancer is the leading cause of death in children under 15.* There is a great need to improve our understanding of brain tumour biology to improve diagnosis and prognosis to develop new treatments. ^{1}H-MRS is currently the only non-invasive method that can de used to investigate the molecular profile of brain tumours and also provides molecular images. New methods of studying the detailed biochemistry of tumour biopsies are ^{1}H-HRMAS and DNA microarrays. The purpose of this communication is to check the complementarities between in vivo ^{1}H-MRS and ex vivo metabolomic and transcriptomic data for a better diagnosis and clinical management of brain tumour, using the multi-center protocols provided in the LSH-FP6 European project eTUMOUR.

Subjects and Methods:

Spectroscopy and genetic microarrays studies were done in 20 patients with histopathology diagnosis of GBM, astrocytoma, meningiomas, oligodendrogliomas, oligoastrocytomas and metastases. The amount of tumoral tissue analyzed for each patient ranged from 16 to 35 mg.

In vivo metabolomic data acquisition:

The MR study was performed in a 1.5T superconductive unit. MRS protocol included SV (TE 31 and 136 ms) in the lesion, with TR of 2000 ms. The voxel volume was fitted to the high cellularity region of the lesional mass using TSE CSI (TE 272 ms) Cho, NAA and Cr images. Signals coming from outer volume were suppressed with saturation slabs.

Ex vivo metabolomic data acquisition:

The whole HRMAS study was performed at 4 C and 4 KHz spinning rate in a 500 MHz Bruker AVANCE. One dimensional sequences with water presaturation were recorded.

Genomic data acquisition:

RNA was extracted and isolated for the 20 patients using standard methods. Quality of the sample was assessed by spectrometric analysis (A260/280 ratio between 1.6 and 2.1) and by the ratio 18/28 determined by the Agilent2100 bioanalyser (above 1.2). Expression analysis was performed using Genechip Human-Genome U133Plus2.0.

Results and discussion:

The analysis of metabolomic and genomic data for the brain tumours analyzed here allows classification among different types of brain cancer (Figures 1A, 1B and 1C). In addition, the combination of HRMAS and genetic microarrays data for brain tumour biopsies made possible some tumour grading (Figure 1B). The classification obtained with the different techniques used here shows a high degree of consistency. These results suggest the viability of an extensive characterization of brain tumour biopsies by spectroscopic and genomic tools. In addition, comparative analysis of in vivo ^{1}H-MRS and HRMAS data have been useful for a better identification of in vivo spectra and, therefore, for an improved brain tumour classification and grading (Figure 1D). Particular attention has been focused in the metabolomic and phenotypic differences between glioblastomas with different survival time, short as primary and longer as secondary glioblastoma.

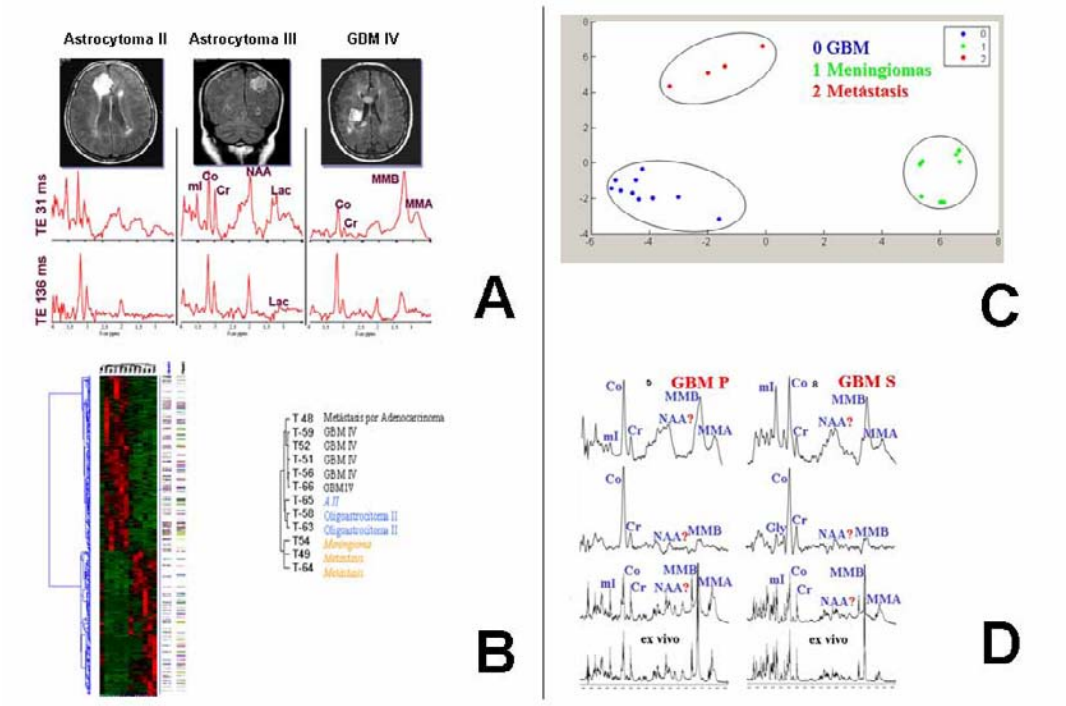

Figure 1. Example of A) comparison of 'in vivo' MRS assigned spectra at two different echo times for three different glial tumours, B) selected transcriptomic microarray data for 11 brain tumour biopsies classified by phylogenetic clusters, C) classification of the HR-MAS spectra of 20 brain tumour biopsies in three different groups and D) comparison between 'in vivo' and 'ex vivo' assigned NMR spectra.