

Fast-Field-Cycling Nuclear Magnetic Resonance:

A non-invasive method allowing detection of an intracellular biomarker of glioma cell invasion

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Nowadays, there is no way to detect invasive glioma cells either by MRI or by other medical imaging. Challenging methods are needed to discriminate peri-tumoral region characterized by glioma infiltration (invasion and migration) from the glioma mass.

By using Fast-Field-Cycling Nuclear Magnetic Resonance (FFC-NMR) technology, which measures longitudinal relaxation times (T_1) in function of magnetic fields (B_0) at low magnetic fields ($1\mu\text{T} < B_0 < 1\text{T}$), we have demonstrated the potential of FFC-NMR to differentiate solid glioma mass from infiltrative glioma cells. In fact, comparing R_1 -dispersion curves ($R_1=1/T_1$ vs B_0) of 3 human glioma mouse models U87 (solid standard model) and Glioblastoma and Glioblastoma (cell migration/invasion models developed in our lab), we have (using mathematical models and statistical analysis) identified 3 FFC-NMR biomarkers of cell invasion: the offset and the slope parameters which correspond to R_1 difference and dispersion curve slope, at low magnetic fields respectively, and the amplitude of the QP peak which appears in R_1 -dispersion curves.

In our study, we focused on the QP peaks which result from quadrupolar interactions between water protons and nitrogen 14 of amino acids from large and immobilized proteins. Our aim is to determine if proteins involved on the formation of QP peaks are extra or intracellular

Two experiments were performed comparing QP between : (i) glioma tissue (composed of extra and intracellular compartments) to their corresponding glioma cells and (ii) cell pellets with and without trypsin, a serine protease which does not cross cell membranes and hydrolyzes extracellular proteins.

From both experiments, QP amplitudes were found unchanged confirming that proteins at the origin of the QP peaks are intracellular. FFC-NMR, a non-invasive method, show an intracellular biomarker of glioma invasion that can lead to a better understanding of glioma cell metabolism.