Fast Field Cycling-NMR relaxometry: an emerging biomarkers of cancer invasion

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Purpose/Introduction

T_1-dispersion curves of different glioma models were obtained by FFC-NMR relaxometry. Here parameters derived from mathematical models applied to T_1-dispersion curves were compared to identify FFC-NMR biomarkers for glioma invasion diagnostic, which remains challenging in any medical imaging.

Subjects and Methods

Animal procedures were approved by French/European laws (C3818510003 license). 3 glioma mouse models were studied, the U87 a solid glioma model, and the Glio6 and Glio96 models of tumour cell migration/invasion, both derived from human stem cells, developed in our lab. The Glio6 and Glio96 were validated as migration/invasion[1] and invasion models, respectively. Human glioma cells (5.10^5 in 5µl PBS) were injected in nude mice in the right caudate nucleus. After, the tumor growth, brains were removed and glioma extracted (30-210mg) and stored at -80°C. FFC-NMR were performed at 37°C with a Stelar SpinMaster relaxometer. The magnetization polarization was built up at 0.8T and T_1 relaxation occurs during t^E (at 30 variable B_0^E in [0.2mT-0.5T]). For each B_0^E, 12 t^E values were used to describe T_1 relaxation. Quadrupolar peaks (QPs) that result from ^{14}N-^1H interactions were acquired around 58.7mT (n=30). Relaxation rate $R_1 = 1/T_1$ versus ^1H Larmor frequency $\nu_0 = \gamma/2\pi B_0^E$ were plotted.
Power model[2] (Eq.1) and Lorentzian model[3] (Eq.2) were fitted T_1-dispersion curves. QP peak were modeled according to[4](Eq.2). All the models and statistics (Kruskal–Wallis test) were achieved under MATLAB

Results

In Fig.1 the mean R_1-dispersion curves of Glio6, Glio96 and U87 glioma are presented. At low magnetic fields, invasive glioma is well separated from the solid one. In Fig.2, three biomarkers are selected: b (power model) and correlation times $\mathbf{t_s}, \mathbf{t_i}, \mathbf{t_f}$ (Lorentzian model) related to water dynamics, all found shorter in case of invasion, having therefore rapid dynamics. And the QP amplitude A, sensitive to immobilized proteins, found lower in invasion case. Clearly, these 3 parameters discriminate invasive glioma cells from solid tumor.

Discussion/Conclusion

Peritumoural regions invaded by infiltrative glioma cells are not adequately and sufficiently early diagnosed by MRI or any current medical imaging method. This study highlights the interest of low magnetic fields accessible by FFC NMR/MRI to discriminate tissue of infiltrative glioma cells from solid tumors. Similar results were observed in human resections highlighting the interest to develop FFC-MRI for clinical investigations which is under development at Aberdeen

References

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