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

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Purpose/Introduction
T₁-dispersion curves of different glioma models were obtained by FFC-NMR relaxometry. Here parameters derived from mathematical models applied to T₁-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/invasion¹ and invasion models, respectively. Human glioma cells (5.10⁵ 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 T₁ relaxation occurs during tE (at 30 variable Bₑ in [0.2mT-0.5T]). For each Bₑ, 12 tₑ values were used to describe T₁ relaxation. Quadrupolar peaks (QPs) that result from ¹⁴N-¹H interactions were acquired around 58.7mT (n=30). Relaxation rate R₁ =1/T₁ versus ¹H Larmor frequency ν₀=γ/2πB₀ were plotted. Power model² (Eq.1) and Lorentzian model³ (Eq.2) were fitted T₁-dispersion curves. QP peak were modeled according to⁴(Eq.2). All the models and statistics (Kruskal–Wallis test) were achieved under MATLAB

Results
In Fig.1 the mean R₁-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 tₛ, tᵣ, tᵣ (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
¹Gimenez U and al. NMR in Biomed 2016.

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