Fast Field-Cycling NMR of human glioma resections: characterization of heterogeneity

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Synopsis

Fast-Field-cycling NMR (FFC-NMR) is a unique tool for the measurements of molecular dynamics in the range of nano- to microsecond. With the development of FFC-NMR scanner, it is now possible to investigate new contrasts using field-dependent variations of T1 over a wide range of magnetic fields, typically from 1 T down to earth field or even below. Contrary to standard NMR, which operates at strong and fixed magnetic field, FFC-NMR allows switching main magnetic field quickly compared to the system precession frequencies, from nanoseconds to hundreds of microseconds. It also shows Quadrupolar Peaks (QP) due to proton-nitrogen coupling that are invisible to conventional NMR. Several works demonstrated the usefulness of the T1-NMRD profiles to characterize biological tissues and diseases by exploiting either the T1 dispersion profiles or the QP. In this work we present the first results of FFC-NMR measurements on a variety of human glioma obtained from surgery. Our goal is to highlight the advantages of FFC-NMR over existing diagnostic techniques and specifically to show how FFC-NMR provides pertinent and complementary information on glioma disease mechanisms, which are still challenging to characterise non-invasively.

Purpose

Fast-field-cycling NMR (FFC-NMR) is an NMR method that allows measuring the variations of the longitudinal relaxation time T1 over a wide range of magnetic fields, typically from 1 T down to earth field or even below. Contrary to standard NMR, which operates at strong and fixed magnetic field, FFC-NMR allows switching main magnetic field quickly compared to the system precession frequencies, from nanoseconds to hundreds of microseconds. It also shows Quadrupolar Peaks (QP) due to proton-nitrogen coupling that are invisible to conventional NMR. Several works demonstrated the usefulness of the T1-NMRD profiles to characterize biological tissues and diseases by exploiting either the T1 dispersion profiles or the QP. In this work we present the first results of FFC-NMR measurements on a variety of human glioma obtained from surgery. Our goal is to highlight the advantages of FFC-NMR over existing diagnostic techniques and specifically to show how FFC-NMR provides pertinent and complementary information on glioma disease mechanisms, which are still challenging to characterize non-invasively.

Subjects and Methods

5 samples of human brain glioma and 3 reference samples of human epileptic brain were obtained frozen from a tissue bank (Grenoble centre for biological resources). Histological analysis were performed to target homogeneous regions. The target regions were cut while frozen. FFC-NMR acquisitions were performed at 37°C using a SpinMaster relaxometer (Steele, s.r.i., Italy) using an inversion recovery CPMAG sequence using Fortinl (Sigma-Aldrich) to prevent sample drying. The T1 dispersion profiles were acquired from 10 mT to 1 T and fitted using standard models obtained from the literature. Mass spectroscopy (MALDI-MS) was also acquired to define the range of tumor protein mass.

Results

The tumour dispersion curves showed power-law shapes, suggesting relaxation by protein matrix. The low-frequency region showed large differences between glioma and epileptic tissues, correlating with the mass distribution provided by MALDI-MS, possibly indicating variations in protein interactions. Altered tissue microstructures showed large QPs and distinct T1-NMRD profiles: glioma and epileptic samples showed a higher overall relaxation rate (Figure 1). One glioma sample presented regions of infiltrated brain tissues and others of solid tumour, which showed contrasting the NMRD profiles: we observed a very significant change in the slope of the dispersion at low field, indicating differences at slow motions. This may be used to characterize the peritumoral region of the glioma.

Discussion and conclusions

Contrast between tumour grades was more pronounced at low magnetic field for several samples, such as infiltrated tumour against solid tumour, and QP appeared as a potential source of contrast (Figure 4). High QP were found in certain glioma samples, but not all. Epileptic brain tissues showed lower QP amplitudes, and also different slopes.

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References

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