Molecular biomarkers in human pathologies from fast field-cycling MRI

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Fast Field-Cycling (FFC) is an NMR technique that involves changing the main magnetic field during the pulse sequence, which provides an extra dimension to the experimenter. It is a rich technique that is well known to characterise molecular dynamics with various applications already demonstrated in polymer matrices, porous media, liquid crystals and many other systems [1]. However, much work remains to be been done on the applications of FFC NMR in medical applications.

Our research group is working on translating FFC techniques to MRI [2]. We have developed three innovative FFC MRI scanners with that aim, two of which are whole-body scanners. This presentation exposes how FFC MRI may be used to find molecular biomarkers of clinical relevance through the results obtained from several research projects using FFC MRI on human tissues, mainly on cancer, osteoarthritis [3], muscle damage and thrombosis.

The table below summarises the studies done so far by our team. Preliminary analyses were made on a benchtop FFC NMR relaxometer (SMATracer, Stelar s.r.l., Italy) when possible using field-cycled inversion recovery sequences and were followed by FFC MRI using mainly FC-PRESS, field-cycled spin echo and field cycled gradient echo. All the work performed here has been reviewed by ethics committees (CERB and NoSREC).

Study	Sample size	Type of tissues	State
Osteoarthritis	90 resections	Femoral heads and knee joints	Normal and grade 3
Breast cancer	10 mastectomies	Ductal and lobular carcinomas	Low to high grades
Musculoskeletal sarcomas	10 resections	Sarcomas	Low to high grades
Muscle damage	10 volunteers	Gastrocnemius	Healthy volunteers
Thrombosis	10 in vitro preparations	Fibrin clots	

Several biomarkers appeared from our studies: the shape of the dispersion curve, which varies dramatically in breast tissues around carcinomas, the presence of the so-called quadrupolar signal [4], which was shown to quantify the amount of fibrin and to characterise the state of the collagen matrix in osteoarthritis, and the offset of the dispersion curve, which is closely related to tumour grade.

FFC MRI shows a general trend to detect protein modifications quantitatively and in particular variations of collagen content. Several biomarkers have been extracted so far that are closely linked to biologically relevant information. More work is ongoing in order to explore other pathologies and to better explain the pathways that connect the biomarkers and the diseases.

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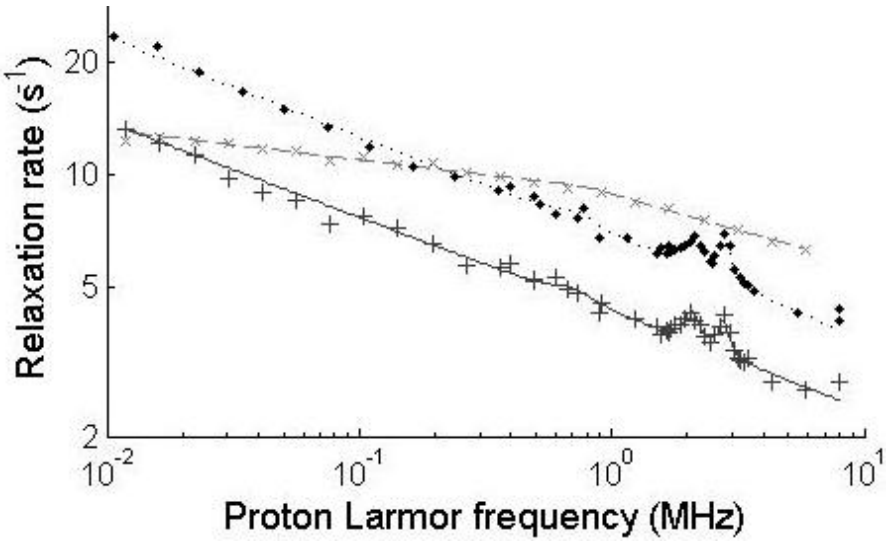

Figure 1: R_1 Dispersion curves of healthy breast tissue (light crosses), peritumoral breast tissue (dark dots) and carcinoma (dark crosses) from the same patient. The shape of the dispersion curve changes markedly between healthy tissues and tumour, but also in the peritumoral region even though that region appeared normal on visual inspection. The similarity between tumour and peritumoral shapes suggests the presence of specific proteins that invade the peritumoral region. This is an illustration of FFC MRI biomarkers of clinical relevance.