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Recent Developments in Field-Cycling MRI – Free Radicals and Quadrupole Dips

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As indicated by the title of this conference, and discussed in several of the presented papers, field-cycling has found its main application in relaxometry. Nevertheless, field-cycling has also been used by a small number of groups in MR imaging, either to improve its sensitivity or to provide novel contrast mechanisms. This lecture will describe two aspects of field-cycling MRI, namely its use together with the Overhauser effect to image free radicals, and its application to the study of quadrupole dips in biological samples.

PEDRI (proton-electron double-resonance imaging, also known as Overhauser Imaging) is a method for imaging free radical distributions *in vivo*. It involves the irradiation of an EPR resonance of a free radical of interest during the collection of an NMR image [1]. In regions containing the free radical the Overhauser effect causes a transfer of polarisation from electron to nuclear spins, resulting in an enhancement of the NMR signal, which in turn reveals the distribution of the free radical in the image. PEDRI is normally implemented at low field (~10 mT) with EPR irradiation at ~250 MHz, but even under these conditions non-resonant absorption of the EPR irradiation is a significant problem, particularly in *in vivo* experiments. In field-cycled PEDRI (FC-PEDRI) the EPR irradiation is applied at lower field (2-5 mT) with correspondingly lower frequency and lower absorbed power, while the NMR signal is observed at a higher field to improve the signal-to-noise ratio (SNR) [2]. We have used FC-PEDRI to study the distribution of stable free radical contrast agents *in vivo*. FC-PEDRI can provide information on organ function and, by making use of the EPR spectral properties of these agents, to measure local pH [3] and oxygen concentration [4]. Figure 1 shows FC-PEDRI images of an anaesthetised rat following the intravenous administration of a dose of triarylmethyl (TAM) free radical. Organ structures and blood vessels are clearly visible in the image obtained with the EPR irradiation switched on.

FC-PEDRI experiments were carried out using a whole-body sized field-cycling MR imager constructed in our laboratory [5]. It uses a whole-body permanent magnet with a vertical field of 59 mT which provides the detection magnetic field. Field cycling is accomplished by the field-compensation method: a resistive, whole-body sized, saddle-shaped magnet is fitted into the bore of the permanent magnet, and the field from this secondary magnet can add to or subtract from the field of the permanent magnet. A field change of 59 mT can be achieved in 40 ms. There are no problems with eddy currents because the permanent magnet is made of ferrite, and the support structures are also non-conducting. The imager is controlled by a commercial MRI console.

It is well known that proton relaxation in proteins and other bio-polymers can be strongly affected by interactions with the quadrupolar nucleus ^{14}N, where ^{14}N–^{1}H groups act as "relaxation sinks". This gives rise to "quadrupole dips", reductions in the proton spin-lattice relaxation time which occur at the three NMR frequencies corresponding to the ^{14}N nuclear quadrupole transitions. This effect was studied extensively in the early to mid 1980s, and quadrupole dips were measured in hydrated proteins and various biological samples [6]. In the early 1990s Carlson *et al*. performed human relaxometry measurements using a small field-cycling coil inside a whole-body permanent-magnet MRI system [7]. We have implemented field-cycling inversion-recovery relaxometry and imaging pulse sequences on our whole-body field-cycling imager, and have studied quadrupole dips in human muscle *in vivo*. Inversion-recovery images obtained on and off the quadrupole dips exhibit significant differences, giving a novel contrast mechanism. Another biological system which exhibits quadrupole dips is illustrated in Figure 2 – the boiled egg! The measurement of quadrupole dips offers the possibility of non-invasive measurement of protein concentration [8], so may be of use in the characterisation of muscle-wasting diseases.

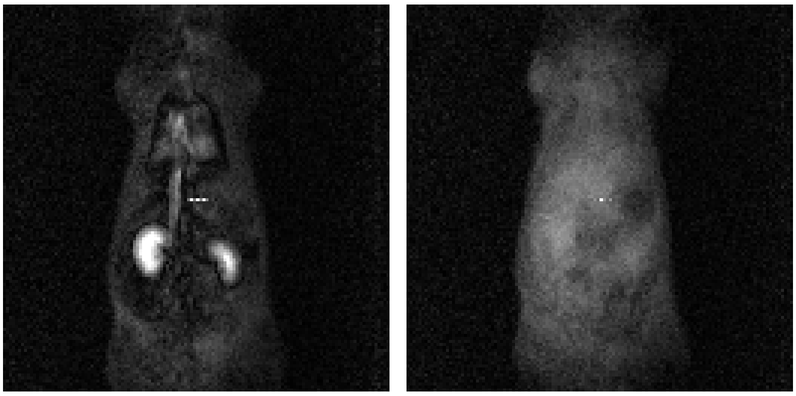

Figure 1: FC-PEDRI images of anaesthetised rat given 0.57 mmol/kg dose of TAM free radical (kindly donated by Nycomed Innovation, Malmö, Sweden). Detection field: 59 mT; Evolution field 4.25 mT. Left: image with EPR irradiation at 120.7 MHz. Right: image without EPR irradiation.

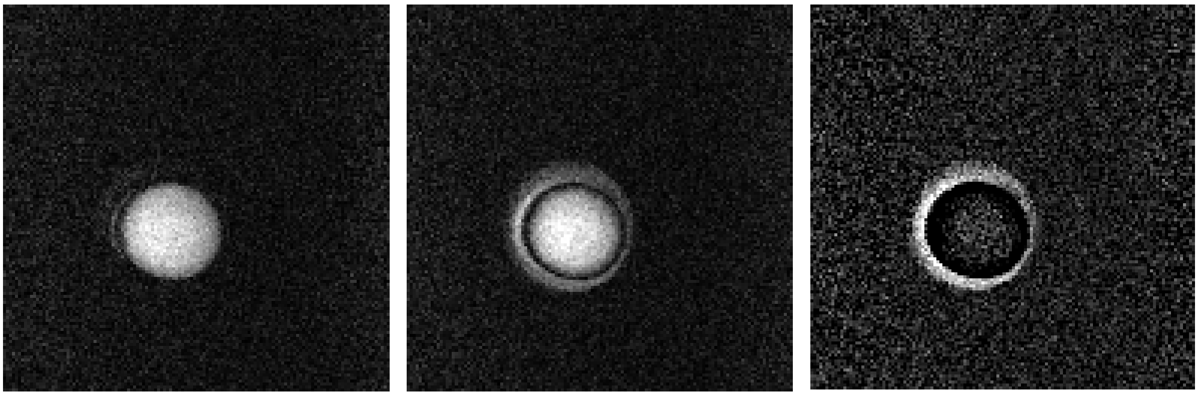

Figure 2: Field-Cycled Inversion-Recovery images of a freshly-boiled chicken egg. Detection field: 59 mT; detection frequency: 2.49 MHz. TR: 1500 ms; TI: 160 ms. Left image: evolution field 65 mT (on quadrupole dip). Middle image: evolution field 75 mT (away from quadrupole dip). Right-hand image shows difference between previous images, showing the egg white where the quadrupole dip effect is observed.

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