Rapid Imaging of Free Radicals *In Vivo* using Hybrid Fast Field Cycled PEDRI

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Introduction

Proton electron double resonance imaging (PEDRI) is a powerful technique for imaging free radicals in biological samples and small animals [1,2,3]. PEDRI is based on the Overhauser effect: a proton NMR image is collected after the EPR resonance of a free radical solute is irradiated. In parts of the sample containing free radical the NMR signal is enhanced and these regions appear with greater intensity in the final image. In order to reduce the EPR power deposition for *in vivo* experiments, the technique of field-cycled PEDRI (FC-PEDRI) was developed [4]. First, the magnetisation is built up at "high" field (the polarisation field, Bo^P, 59 mT in our case). The EPR irradiation is then applied at low field (the evolution field, Bo^E ~5 mT) at correspondingly low EPR frequency and power, then the NMR signal is collected at "high" field (the detection field, Bo^D, 59 mT). Conventional FC-PEDRI requires N EPR irradiation periods for an N x N image. Snapshot FC-PEDRI was introduced recently in order to reduce both the SAR and the acquisition time [5]. A high-power EPR irradiation is applied during a single period at field Bo^E, followed by rapid acquisition of all the NMR signals for the image at field Bo^D. Although the technique worked it was found to be difficult to implement *in vivo* due to the rapid decay of the Overhauser enhanced magnetisation after the EPR irradiation.

In this work we have implemented a hybrid fast imaging method which lies between snapshot imaging and conventional FC-PEDRI. The number of EPR irradiation periods per image can be selected to generate enough detail of the free radical distribution in the final image, while giving a significant reduction in acquisition time and SAR. Pulse sequences and post-processing algorithms have been developed to address the problem of magnetisation decay during image acquisition. This hybrid fast FC-PEDRI technique has been used successfully to obtain images of exogeneous free radicals in the living rat.

Methods

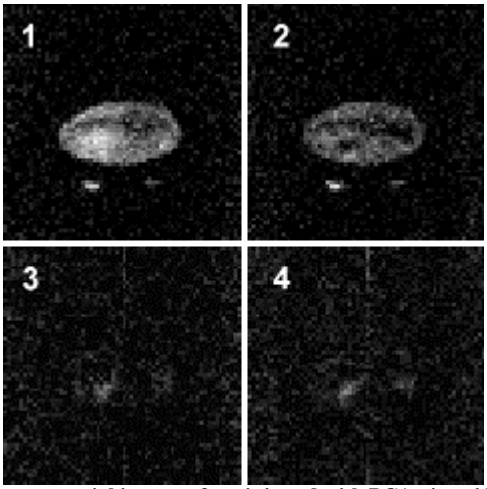
The hybrid fast FC-PEDRI pulse sequence is based on a FAST pulse sequence [6] with a short repetition time. The magnetic field is switched to a low value (Bo^E) for the period of EPR irradiation, then the field is returned to Bo^D and the fast pulse sequence is used to collect the data for M phase encoding views. Centric reordering of the phase encoding gradients [7] is used so that the most significant data at the centre of k-space is collected as soon as possible after the end of EPR irradiation. For the case of 4 EPR irradiation periods per 64 x 64 image, for example, M is equal to 16. Then the field is reduced once again to Bo^E for a second period of EPR irradiation, followed by acquisition of the next M lines of k-space, and so on. Typically, two data sets are collected, one without and one with EPR irradiation. Subtracting the data sets yields a "Difference" image which shows the free radical distribution in the sample.

Because the Overhauser-enhanced magnetisation decays after EPR irradiation, it is necessary to start data acquisition as soon as possible after ramping the magnetic field from Bo^E up to Bo^D. Any instability of the magnetic field after ramping up will cause a phase-shift of the signal resulting in severe ghost artefacts. To address this problem, two extra data sets are collected in the usual way but without the phase encoding and readout gradients being applied. These two data sets are then used to retrieve the phase of each view number, k. A phase difference ($\Delta\varphi_k$) is obtained by subtraction of the phase of each view (φ_k) from the asymptotic phase value. The complex data obtained from the full imaging pulse sequence is then corrected by multiplying each gradient echo signal by $\exp(i\Delta\varphi_k)$ to shift the phase to the asymptotic value.

Experiments were carried out using a whole-body FC-PEDRI imager [8]. The polarisation field and the detection field were both 59 mT while the evolution field in this case was 5.7 mT. A split-solenoid NMR transmit/receive coil was used at 2.5 MHz and a coaxial Alderman-Grant resonator was used for EPR irradiation at 120 MHz. *In vivo* experiments were carried out using adult male Sprague-Dawley rats of approximately 210 g body weight (b.w.). The proxyl carboxylic acid (PCA) free radical contrast agent used in these studies was administered at a dose of 4 mmol/kg b.w. by injecting ~1.1 ml of 300 mM PCA solution in bicarbonate buffer via a jugular cannula. Animals were maintained under Ketamine/Xylazine anaesthesia throughout the imaging procedure.

Results

In vivo images using the hybrid fast FC-PEDRI pulse sequence were obtained. Images were collected on a 64 x 64 matrix transaxial through the abdomen of the rat with a field of view of 107 x 107 mm and a slice thickness of 20 mm. The repetition time was 25 ms, the EPR irradiation time was 500 ms and the applied EPR power was 50 Watts. The number of EPR irradiation periods was varied for each imaging experiment from 1 to 8 periods. The figure shows typical images obtained without and with EPR irradiation, together with "Difference" images obtained using 4 and 8 periods of EPR irradiation. In both cases the animal's kidneys are clearly visible, as expected from previous work [2,3].



***In vivo* transaxial images of rat injected with PCA nitroxide. 1: without EPR; 2: with EPR irradiation; 3: hybrid fast FC-PEDRI "difference" image obtained with 4 EPR irradiation periods; 4: as image 3 but with 8 EPR irradiation periods.**

Discussion

A hybrid fast FC-PEDRI method for rapid imaging of free radicals *in vivo* has been implemented. With four EPR irradiation periods per image, the image quality is acceptable. The EPR power deposition in the samples is reduced by 16 fold compared to conventional FC-PEDRI. The other advantage of the hybrid fast imaging technique is that the acquisition time is reduced five-fold compared to the conventional technique.

References

[1] Lurie D.J. *et.al.*, J. Magn. Reson. **76**, 366-370 (1988).
[2] Lurie D.J. *et.al.*, Phil. Trans. R. Soc. **A 333**, 453-456 (1990).
[3] Seimenis I. *et.al.*, Magn. Reson. Med. **37**, 552-558 (1997).
[4] Lurie D.J. *et.al.*, J. Magn. Reson. **84**, 431-437 (1989).
[5] Puwanich P. *et.al.*, Phys. Med. Biol. **44**, 2867-2877 (1999).
[6] Hawkes R.C. and Patz S., Magn. Reson. Med. **4**, 9-23 (1987).
[7] Norris D.G. *et.al.*, Magn. Reson. Med. **15**, 483-490 (1990).
[8] Lurie D.J. *et.al.*, Phys. Med. Biol. **43**, 1877-1886 (1998).