A Dual-Purpose 20 mT PEDRI and 0.38 T MR Imager based on a Resistive-Magnet Clinical MRI System

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Introduction

Proton electron double resonance imaging (PEDRI, also known as Overhauser Imaging), is a method of imaging free radicals *in vivo* which offers good sensitivity and high spatial resolution which is independent of the EPR linewidth of the free radical under study [1]. It is based on the Overhauser effect: the free radical's EPR resonance is irradiated during the acquisition of an MR image. An enhancement of the NMR signal occurs in regions of the sample containing free radical, revealing its spatial distribution. Although a number of research groups are now using PEDRI, its widespread use has been limited by a lack of commercially available equipment. In this work, we have adapted a resistive-magnet clinical MR imager to allow PEDRI imaging of free radicals. The system has been used to image stable free radicals injected intravenously into anesthetized mice. The imager can be easily and rapidly changed from PEDRI mode (20.1 mT) to MRI mode (0.38 T), allowing both PEDRI and high-resolution MR images to be obtained of the same animal.

Methods

The MR imager used in this work is a Resonex RX-5000/PARADIGM system. It uses an iron-core resistive magnet, generating a vertically-oriented field of up to 0.4 T. The console is operated by an HP 9000/380 workstation, running Resonex clinical MRI software. The imager normally operates at a field of 0.38 T, with a proton NMR frequency of 16.18 MHz; the console's narrow-band RF transmit/receive electronics are fixed at this frequency. If PEDRI were attempted at 0.38 T the EPR frequency would be approximately 10 GHz, much too high for whole-animal experiments. It was therefore necessary to reduce the magnetic field to 20.1 mT, with an EPR frequency of 564 MHz, to allow whole-body mouse imaging. The corresponding NMR frequency is 856 kHz.

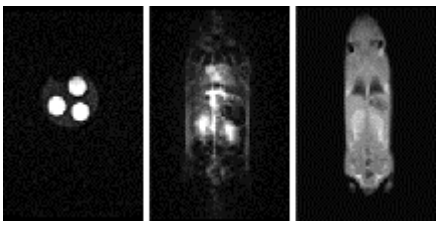
The console's 16.18 MHz RF pulses were down-converted to 856 kHz before transmission. Following amplification (63 dB) by a home-built pre-amplifier the 856 kHz NMR signals were up-converted to 16.18 MHz and fed into the console's NMR receiver. Frequency down- and up-conversion was implemented using two passive mixer modules (Mini-Circuits ZP-3) into which were fed reference signals at 15.324 MHz (the difference between 16.18 MHz and 856 kHz). The reference signals were generated by a synthesised signal generator (Fluke 6080A) which itself took its 10 MHz reference input from the MRI console, thus ensuring phase coherence during signal transmission and reception. The output of the down-converter mixer was low-pass filtered (Mini-Circuits BLP-15) to remove the sum-frequency signal prior to RF pulse amplification by a 10 W amplifier (ENI 300L).

PEDRI requires a dual-resonance coil assembly for NMR transmission (Tx) and reception (Rx) and for EPR Tx. For NMR at 856 kHz a solenoid (diameter 4 cm, length 6 cm) was used for both Tx and Rx. EPR irradiation was applied to the sample using an Alderman-Grant resonator [2] (diameter 7 cm, length 7 cm) made from 0.15 mm copper sheet on a Plexiglass former. The resonator was enclosed in a cylindrical shield (diameter 14 cm, length 26 cm) made of 40 µm self-adhesive copper foil on a Plexiglass former. An inductive coupling loop was placed between the shield and the resonator. The EPR irradiation signal at 564 MHz was supplied by a synthesised source (Fluke 6071A) which was amplified in two stages (Mini-Circuits ZHL-1010-75 and TIA-1000-4) to a maximum output of 10 W.

In *in vivo* PEDRI experiments care must be taken to avoid excessive non-resonant RF power deposition in the lossy sample. One way of reducing the SAR is to apply the EPR irradiation in long pulses (typically 3xT1, or about 500 ms) before each NMR detection pulse, thereby reducing the duty cycle. The best way to accomplish this would be via a control line from the MRI console's pulse programmer, however this would require changes to the system's hardware and software. An alternative solution, which was adopted here, was to make use of the clinical MRI system's cardiac gating unit. A signal generator provided a periodic rectangular waveform (400 ms on, 800 ms off) which was used to gate on and off the EPR irradiation source. A TTL output from the signal generator was used to trigger an arbitrary waveform generator which was programmed to generate a 20 ms bipolar triangular waveform, as a crude simulation of an ECG "R wave". This in turn was connected to the MRI console's "ECG" input and was used to synchronize the MRI acquisition with the EPR irradiation.

Results

PEDRI experiments were carried out using a triaryl-methyl (TAM) free radical [3] kindly donated by Nycomed Innovation of Malmö, Sweden. This is stable in solution, and exhibits a single, narrow EPR line, making it ideal for use in PEDRI due to its ease of saturation. A phantom was constructed from three 9 mm diameter sample tubes, filled with a 1 mM aqueous solution of TAM, mounted inside a 26 mm diameter tube filled with saline solution. A PEDRI image of this phantom is shown on the left; an enhancement factor of -10 can be seen in the tubes containing free radical. (FOV of original image 10x10 cm; slice 10 mm; TR 1200 ms; TEPR 400 ms; NEX 1; EPR 564 MHz, 5 W.) The middle image shows part of a projective coronal PEDRI image of a 30 g mouse which had been given an i/v administration of 0.66 mmol/kg TAM following pentabarbitone anesthesia. The image was obtained 3 min after injection of the free radical, and shows an enhancement of -5 in the kidneys and major blood vessels. (FOV 8x8 cm; TR 1200 ms; TEPR 400 ms; NEX 1; EPR @ 564 MHz, 10 W.) The imager was then converted back to "clinical" mode at 0.38 T and the mouse was imaged using a 16.18 MHz NMR coil; part of a 256x256 image (FOV 10x10 cm) can be seen on the right.



Sections from 128x128 20.1 mT PEDRI images of TAM in phantom (left) and anesthetized mouse (centre). Image on right shows section from 0.38 T MRI image of same animal, obtained using the same scanner.

Conclusions

A PEDRI imager operating at 20.1 mT has been constructed, based on a clinical MRI system. No permanent hardware modifications nor software changes were necessary, and the imager can be converted between PEDRI mode at 20.1 mT and "regular" MRI mode at 0.38 T in less than 15 minutes, allowing high-resolution MR images and PEDRI images of the same animal to be obtained. There are now a large number of "open" MR imagers in clinical use, most using resistive or iron-assisted resistive magnets, many of which could be used for PEDRI experiments by following a similar strategy.

References

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