High Performance Probe for in vivo Overhauser MRI

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Purpose: Overhauser-enhanced MRI (OMRI) is an electron-proton double resonance imaging technique of much interest due to its ability to detect the concentration and distribution of free radicals. Tracking of exogenous free radicals with OMRI *in vivo* has enabled the development of oxymetry probes [1] and the imaging of redox reactions [2]. The large gyromagnetic ratio of electrons (28 GHz/T) demands that *in vivo* OMRI is performed at very low magnetic fields (~10 mT) in order to minimize RF heating and penetration depth issues. Operation at low magnetic field causes a drastic reduction in NMR sensitivity despite the signal enhancement that comes from the Overhauser effect, and emphasizes the need for high S/N probes. OMRI probe design is still relatively unexplored, despite its importance, and presents challenges unique to the frequencies of operation (f_H = 276 kHz and f_e = 140.8 MHz in our experiments at 6.5 mT). Here, we report the development of a high performance OMRI probe built to image free radical probes of the blood brain barrier following ischemic stroke in a rat model [3].

Methods: Our OMRI probe, consisting of an NMR solenoid inside a modified Alderman-Grant Resonator (Figure 1), was designed for use with a custom built, very low-field MRI scanner operating at 6.5 mT (f_H = 276 kHz) [4]. Images were acquired using a recently developed, fast, high-resolution b-SSFP based OMRI methodology [5]. NMR probe design in the low-field regime is fundamentally different to that at conventional MRI fields as thermal noise due to the intrinsic resistance of the pickup coil dominates over sample noise. This leads to a compromise where S/N improvements come at the expense of imaging bandwidth S/N $\sim\sqrt{Q} \sim 1/\sqrt{BW}$. An 85 turn solenoid was wound, using low AC resistance 5/39/42 litz wire, on a 3D printed polycarbonate former. This high filling factor coil has a bandwidth of 3 kHz.

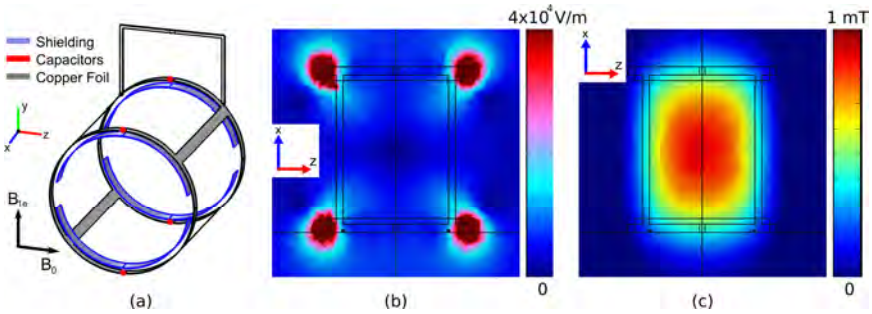

Figure 2: COMSOL Multiphysics simulations (a) Our modified Alderman-Grant Resonator. (b) Plot of |E| showing that the electric field is strongly suppressed inside the resonator. (c) B_{1e} shows high homogeneity in the imaging volume – less than 10% variation across the imaging region.

TEMPOL (4-hydroxy-TEMPO) a stable radical, is detected by OMRI with high sensitivity, and because of its small size may facilitate imaging blood brain barrier leakage in cases of oxidative stress [3]. Simulations were validated in 2mM TEMPOL solutions (not shown) using simple spectroscopic measurements as well as fast imaging strategies [5]. The ESR resonator was tuned to 141 MHz, the lowest frequency of the TEMPOL triplet state at 6.5 mT, to minimize RF heating during ESR irradiation.

Results: Previously we reported the development of an OMRI probe for a rat head model utilizing an NMR solenoid and ESR surface coil [3]. Testing of our new OMRI probe shows that it has 3x the S/N of the probe reported in [3] and rectifies problems with B_{1e} homogeneity, yielding homogeneous enhancement of –6.7 in 2mM TEMPO when 10 W of RF power is applied.

In vivo OMRI signal enhancement is clearly visible in the rat brain after TEMPOL injection, as shown in Figure 3. As the Overhauser-enhanced signal has a phase opposite to that of the thermal signal, the phase image in Figure 3 provides sensitive contrast in regions of low TEMPOL concentration.

Discussion and Conclusion: We have implemented a high performance probe for high temporal and spatial resolution OMRI in a rat brain. The S/N of this probe may be further improved, whilst maintaining imaging bandwidth, by using an active feedback circuit [7]. Higher S/N could also be realized through supercooling of the NMR solenoid or by using a free radical with a longer T_{1e} such as triphenylmethyl [1]. This probe may allow the *in vivo* detection of rapid redox changes in pathologic tissues, specifically in the context of brain trauma or stroke.

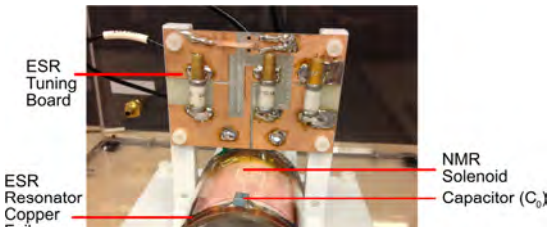

Figure 1: NMR/ESR rat head probe for operation at 6.5 mT. The ESR resonator is tuned to 140.8 MHz. The litz wire NMR solenoid coil (276 kHz) resonator board is not shown.

A modified Alderman-Grant ESR resonator was built using copper foil on Pyrex tubing. All metal placed in close proximity to the NMR solenoid strongly couples, reducing the NMR sensitivity. We therefore minimized amount of copper in the ESR resonator. Windows were removed from the panels on the sides of an Alderman-Grant resonator, a region of low current flow [6], in an attempt to reduce coupling whilst maintaining B_1 homogeneity. Shielding at the ends of the resonator prevents high electric fields at the capacitors penetrating the imaging volume, important because $P_{RF\text{-}absorbed} \sim E^2$. Slits in the shielding prevent the formation of closed loops that couple to the solenoid. Figure 2 demonstrates the high B_1 homogeneity and strong E suppression in our ESR resonator.

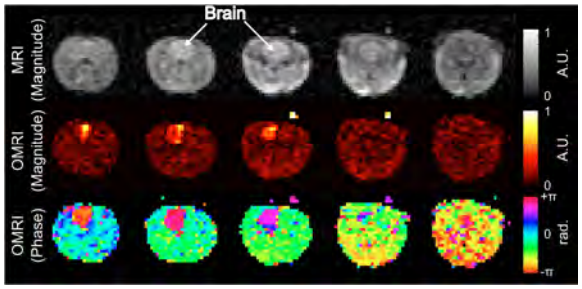

Figure 3: OMRI images acquired from a rat at 6.5 mT following injection of 1mL of 150 mM TEMPOL. Five slices from an 11 slice data set shown. OMRI (NA=1) imaging time was 9 seconds. Anatomical MRI (NA=30) was acquired in the OMRI scanner with ESR power disabled. All images, voxel size: 1.1 x 1.6 x 8 mm^3, Matrix: 128 x 35 x 11

References: [1] K. Golman *et al.*, J. Mag. Res. Im., 12, 929-938 (2000). [2] Utsumi *et al.*, PNAS, 103, 1463-1468 (2006). [3] M. Rosen *et al.*, ISMRM, 6461 (2014). [4] Tsai *et al.*, J. Mag. Res., 193, 274-285 (2008). [5] M. Sarracanie *et al.*, Magn Res. Med., 71, 735-745 (2014). [6] Mispelter *et al.* 'NMR Probeheads: For Biophysical and Biomedical Exeperiments', Imperial College (2006). [7] Baudin *et al.*, J. of Phys. Conf. Series, 294, 012009 (2011).

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