Non-metal electrodes for local field potential recordings in magnetic resonance scanners

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INTRODUCTION Magnetic resonance imaging (MRI) is a powerful technique to explore brain function and dysfunction *in vivo*, however it provides an indirect measure of neuronal activity. The addition of neuronal recordings in the MR scanner would provide valuable information about direct correlations between neuronal activity and functional MRI (fMRI) dynamics, particularly when looking at spontaneous activity during "resting state". However, neuronal recordings typically utilize metal electrodes, which create large MRI artifacts. To combat this problem, we have developed prototype electrodes for simultaneous neuronal recording and MRI using the non-metal materials carbon nanotubes (CNT) and graphene. CNT and graphene have been shown to be conductive, have low impedance, and are biocompatible with neurons.[1] Due to their non-metal nature and a magnetic susceptibility closer to that of human tissue, these materials produce minimal MR susceptibility artifacts even with the highly susceptibility sensitive EPI sequence.

METHODS *Electrode fabrication*: CNT (Timesnanoweb, China) and graphene oxide (GO; Graphene Laboratories Inc., Calverton, NY) were dispersed into water. The CNT and GO solution were coated onto two pretreated polyethylene terephthalate (PET) films using a layer-by-layer method and the films were dried on a 70°C hotplate overnight.[2] The CNT-coated PET was directly cut into desired electrode pattern by a laser. The GO-coated PET was first laser-engraved to achieve electrode patterns, and then the outline of the pattern was laser-cut to release the electrode from the rest of the film.[3] Photosensitive diazo polymer was applied as an insulation layer everywhere except for the recording tip and the layer was cured under ultraviolet light. Electrical connection to silver wire was made with silver conductive epoxy. *Phantoms*: Electrodes were embedded in 2% Agar for *in vitro* susceptibility testing. *Animal surgery*: Sprague-Dawley rats (n=8, including 4 MRI and 4 bench experiments) were intubated, an arterial line inserted, and physiology monitored. Animals were secured in an MRI compatible cradle with ear and bite bars. A small craniotomy over the rat S1F1 cortex was performed under 1.8-2.0% isoflurane for electrode implantation. The craniotomy was closed with agar or dental cement after electrode insertion, and a ground wire was placed in the nose. Anesthesia was then adjusted between 1.6-2.0% isoflurane to achieve a desired brain state characterized by a burst-suppression neuronal activity pattern.[4] *Electrode recording*: Continuous signal was referenced to ground or an insulated channel built into the electrode to reduce artifacts and recorded at 30kHz (Blackrock Microsystems, UT). A low-pass on-line filter was applied after calibration to determine the maximum filter cut-off frequency for which gradient artifacts would not max out the recording amplifier. Bandpass filters for 60Hz noise were applied during post-processing in MATLAB (MathWorks, MA). For verification, bench studies were performed to compare the non-metal electrode signal to that of commercial probes (NeuroNexus, MI) placed in the contralateral S1F1 cortex. *MRI/MRS*: Experiments were performed at a 9.4T/32cm animal MRI scanner (Agilent, CA) with a VNMRJ console (Varian, CA) using either a single-loop ^{1}H radiofrequency (RF) surface coil or double tuned butterfly ^{1}H and single loop ^{31}P radiofrequency (RF) surface coil. A gradient echo multislice imaging (GEMS; resolution: 78×78×500 μm^3) sequence and a multislice echo-planar imaging (EPI; resolution: 0.5×0.5×1 mm^3) sequence were used for anatomical and functional imaging, respectively.

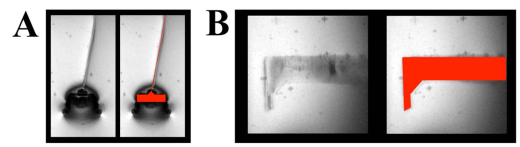

Figure 1: GEMS imaging of (A) a commercial Ag/AgCl EEG electrode and (B) a graphene electrode in agar. A graphic representation of each electrode's physical location is overlaid in red.

RESULTS & DISCUSSION Non-metal electrodes were first tested *in vitro* for susceptibility artifacts. The control image of a disk Ag/AgCl EEG electrode (Fig. 1A) displays large bipolar artifacts around both the contact and wire in the GEMS anatomical imaging. In contrast, the non-metal electrode has clean edges and does not affect signal outside of the physical electrode location (Figure 1B).

The same lack of susceptibility artifact is seen *in vivo* (Fig. 2). Smaller prototype electrodes, which cause less damage to the brain tissue, vanish from the anatomical images unless high resolution and thin slices are used. We believe the distorted brain-skull interface near the electrode is a physical distortion of the intracranial pressure pushing the tissue against the skull opening, as well as slight dehydration due to air exposure. However, small air bubbles may have been trapped in the craniotomy prior to closing it with agar or dental cement.

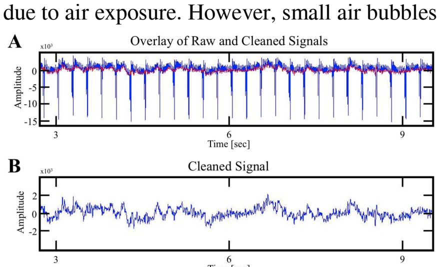

Figure 2: Non-metal electrode neuronal signal showing (A) EPI artifact (blue) with cleaned data (red) overlaid, and (B) cleaned data scaled for visualization of burst activity.

EPI is known to be highly sensitive to susceptibility artifacts. When closed with dental cement, neither the craniotomy nor the electrode affected the image quality (Fig. 2B). In the case shown, the electrode location cannot be determined from the EPI itself, although low signal voxels appear when larger electrodes are used due to the partial volume effect.

Local field potential (LFP) signal from the non-metal electrodes was verified as equivalent to commercial probes outside of the magnet. While moving into the MR scanner room added some noise, signals remained robust. During MRI scanning, gradient and radiofrequency pulse artifacts are induced in the non-metal electrode traces as expected, closely matching the sequence itself. Signal returned to baseline immediately following artifacts. Functional MRI (EPI) sequence artifacts were removable in post-processing to the level of LFP bursts (Fig. 3).

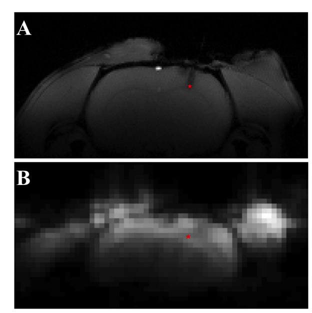

Figure 3: In vivo *(A) GEMS and (B) EPI imaging of a rat with graphene electrode. The electrode tip is indicated with a red star.*

CONCLUSION We have shown proof-of-concept for a working non-metal electrode in the MRI scanner. These electrodes have insignificant imaging artifacts, even when using an EPI sequence, presumably owning to the similar susceptibility properties of the non-metal material and brain tissue water. Additionally, we have shown that the neuronal recording is possible in the MRI scanner, that neuronal signal remains under gradient induced artifacts, and that the artifacts are removable. These novel electrodes should allow the simultaneous LFP/fMRI study of neuro-vascular coupling and the LFP/MRS study of neuro-metabolic coupling under normal and diseased conditions.

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