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Towards a microcoil for intracranial and intraductal MR microscopy

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Abstract

Implantable RF-coils have enabled sub-mm resolution magnetic resonance images (MRI) of deep structures. Scaling down the size of RF coils has similarly provided a gain in signal-to-noise ratio in nuclear-magnetic-resonance spectroscopy. By combining both approaches we designed, fabricated, and imaged with an implantable microcoil catheter. While typical implantable catheters use a transverse magnetization, the axial magnetization of the microcoil provides improved sensitivity and allows visualization of the tissue beyond the distal end of the catheter. The microcoil catheter was designed with a diameter of 1 mm for future integration with intracranial devices, and for intraductal use in breast oncology. We modified the NMR-microcoil design to allow implantation of the RF coil, by winding the microcoil on medical-grade silicone tubing and incorporating leads on the catheter to connect circuit components. In order to achieve proper turn spacing, we coated copper wire with 25 μm of biocompatible polymer (Parylene C). Tuning and matching circuitry insured that the impedance of the RF coil was approximately 50 Ω at the operating frequency for 3-T proton MR applications. A duplexer was used to enable use of the microcoil catheter as a transceiver. Experimental verification of the coil design was achieved through ex vivo imaging of neural tissue. As expected, the microcoil catheter provided microscale images with 20- μm in-plane-resolution and 170- μm -thick slices. While 3-T MRI typically provides 1 to 30 voxels per-cubic-millimeter, in this paper we report that the MRI microcoil can provide hundreds, and even thousands of voxels in the same volume.

I. Introduction

Implantable RF coils increase the signal-to-noise ratio (SNR) of magnetic resonance images (MRI) and spectroscopy by focusing in on the tissue of interest [1–8]. Similarly, nanoliter-volume and single-cell nuclear magnetic resonance (NMR) are possible using microcoils scaled to the sample size [9, 10]. The sensitivity of microcoils increases as the solenoid

diameter is reduced [11], making microcoils appealing for minimally invasive medical applications.

We have designed, fabricated, and tested an RF catheter coil that combines the SNR enhancements of implantable MRI coils and NMR microcoils. This catheter coil is a small solenoid at the tip of a catheter that can be integrated with existing catheter-based devices. Neurological applications of interest include intraoperative imaging during the implantation of deep-brain-stimulating (DBS) electrodes and recording electrodes for treatment planning in Temporal Lobe Epilepsy (TLE). Similar design criteria also allow intraductal use for breast oncology.

Most catheter coils use single-loop and opposed-solenoid configurations, which are optimized for imaging large-diameter blood vessels (>3 mm) oriented along the antero-posterior axis. Unfortunately, this approach sacrifices SNR to cover a long region of the vessel wall. Instead, high SNR is prioritized in our microcoil design to enable unprecedented spatial resolution of small regions at the tip of the catheter.

Microcoil designs can be leveraged to image typical biological cells [12, 13]. The physics group at the University of Ohio has designed gradient systems to allow high-spatial-resolution imaging employing microcoils and a 9 T, 10-cm diameter NMR system. While this group has achieved advances in spatial-gradient designs, the microcoil technology used is identical to that of NMR. Specifically, the probes exist as glass capillaries on silicon chips and cannot be used *in vivo*.

Others have used small solenoids to track interventional catheters by creating an intentional distortion in the magnetic field to produce an artifact in the MR image [14, 15]. One approach is to use fiber optics and photovoltaic transducers to transmit a dc current to a solenoid at the tip of the catheter [16]. An extension of such work is underway at Biophan Technologies, Inc. (West Henrietta, NY, USA), where optoelectrics are used for intraluminal and intra-parenchymal imaging. The advantage of using fiber optics in this situation is to reduce the risk of tissue heating for applications in which long catheters are inserted into the body. However, since the photovoltaic and transformer-based approaches degrade the signal, they are therefore less amenable to ultra high-resolution spatiotemporal imaging.

While typical implantable catheters require long leads to access longitudinal structures, the microcoil design is intended for implantation perpendicular to the main axis of the body. As such, our microcoil catheter is designed with short leads, minimizing signal attenuation, and MR-related heating.

In this paper we describe the catheter-coil design and fabrication, as well as verify the microscopic MRI capability of the microcoil catheter with images of butcher-grade neural tissue.

II. Methods and materials

The coil geometry was optimized for a diameter less than 2 mm and implantation of the catheter perpendicular to the static magnetic field of the MR scanner. The implantable microcoils are similar to hand-wound NMR microcoils, though modified to enable implantation. NMR microcoils typically consist of glass capillary tubes nested on a circuit board. In the work presented here, medical-grade silicone tubing was used in place of glass capillary tubing. The flexibility of silicone decreases the risk of tissue damage. A metal stylet fits inside the catheter to provide the necessary mechanical strength during

implantation, as is done for implanted depth electrodes. Parallel wires along the catheter connect tuning and matching capacitors at the non-implanted end of the catheter.

A. Fabrication

The centers of adjacent turns were separated by 3 wire-radii to maximize inductance while minimizing resistance [11]. This optimal turn spacing was achieved by coating 38-gauge bare copper wire (California Fine Wire, Co., Grover Beach, CA, USA) and Teflon-coated copper wire (Belden, Richmond, IN, USA) with Parylene C, using a vacuum-deposition process (2010 Labcoter®2, Specialty Coating Systems, Inc., Indianapolis, IN, USA). Wire was strung on a metal frame before placing it inside the vacuum chamber. To achieve the optimal turn spacing for a 100- μm -diameter wire, a 25- μm -thick layer of Parylene C was deposited, resulting in a final diameter of approximately 150 μm .

Coated wire was thread through a 2.5-cm-long segment of the 1-mm-diameter medical-grade silicone tubing (#806400 A-M Systems, inc. Carlsborg, WA, USA). An 800- μm -diameter metal style was inserted through the tubing to prevent the tube from deforming during subsequent steps. Gentle bending of the wire served to minimize the distance between the end of the tube and the first coil. Adjacent turns in the coil were placed in contact such that the wire insulation defined the turn spacing. After winding 4.5 turns, a drop of cyano-acrylate adhesive (HS-2, Satellite City Hot Stuff, Simi, CA, USA) was applied to anchor the coil windings. Next, the external wire was pulled along the length of the tubing and affixed with additional cyano-acrylate adhesive. After allowing the adhesive to dry, the stylet was removed from the finished coil. The Parylene C coating was scraped off the ends of the wire with a straight razor to allow soldering of the coil to connectors for characterization, and ultimately to capacitors for tuning and matching.

B. Characterization

Each coil was soldered to an SMA connector (Radiall, Paris, France) and characterized with an impedance analyzer (HP 8514A, Agilent Technologies, Inc., Palo Alto, CA, USA) or a network analyzer (HP 3495A, Agilent Technologies, Inc., Palo Alto, CA, USA). Impedance measurements at 123.3 MHz (i.e., the operating frequency of a Siemens 3-T proton MRI system) were obtained while the catheter was probing the tissue sample. Similarly, the Q of the coil was determined from S_{11} measurements using the network analyzer.

C. Circuitry

A parallel tank circuit enabled tuning of the coil to the Larmor frequency of 123.3 MHz. To minimize signal loss due to reflection, the impedance of the coil at the Larmor frequency was matched to approximately 50 Ω with a series capacitor.

An equivalent circuit of the coil was used to calculate the values of the parallel and series capacitors required to tune and match the coil. The coil was modeled from complex impedance measurements taken at the operating frequency. The magnitude of the impedance $|Z|$ and the phase of the impedance θ_Z determined the equivalent series resistance $R_{eq} = |Z| \cdot \sin\theta_Z$. Likewise, the impedance of the coil gave the equivalent inductance $L_{eq} = |Z| \cdot \cos\theta_Z / \omega$.

Appropriate values of the tuning capacitor C_T and matching capacitor C_M were determined from L_{eq} and R_{eq} using fundamental circuit theory. Equations for the overall resistance and reactance of the circuit were set to 50 Ω and zero respectively. MATLAB (The Mathworks, Natwick, MA, USA) was used to simultaneously solve for the required capacitor values to tune and match the coil.

Capacitors were soldered directly to the microcoil probes to minimize changes in the circuit. Non-magnetic capacitors were used to eliminate magnetic-susceptibility artifacts from the capacitor as well as a potential safety hazard. A non-magnetic variable capacitor (#5241, Johanson RF Division, Boonton, NJ, USA) in parallel to the tuning capacitor allowed fine-tuning adjustments.

Implemented as a transceiver, the microcoil was used with a crossed-diode duplexer. As the minimum voltage of the transmitter was greater than that necessary to drive a small coil, attenuators were employed (JFW Industries, Indianapolis, IN, USA). Seven small attenuators (up to 5 dB) combined for a total attenuation of 25 dB such that the maximum voltage drop across a given attenuator was not exceeded. The preamplifier had a 50-ohm output impedance and a gain of 25 dB (#1702, Advanced Receiver Research, Burlington, CT, USA).

D. Experimental Set-up

As a feasibility study, butcher-grade neural tissue (*Ovis aries*) was imaged with the microcoil catheter. The microcoil was implemented as a transceiver using a 3-T scanner at the Lewis Center for Neuroimaging, University of Oregon (Magnetom Allegra, Siemens AG, Berlin). In the magnet, the microcoil catheter was aligned perpendicular to the main magnetic field. Covering the microcoil and tissue with plastic-wrap prevented desiccation of the sample. Since the duplexer, attenuators, and preamplifier contained components with trace amounts of ferromagnetic material, all were placed outside of the magnet bore and anchored with tape to the scanner bed. The microcoil was then placed in the iso-center of the magnet bore. Transverse scout images were obtained by using a gradient-recalled-echo (GRE) pulse sequence. Transverse images were obtained with the following turbo spin-echo imaging sequence: 256×256 image matrix; 0.10 mm in-plane resolution; 0.4 mm slice thickness; TR/TE of 3000/22 ms; 7 echos with 21.6 ms spacing; an acquisition time of 0:05:29 (hr:min:s); 3 averages; 15 slices; fat saturation; and a bandwidth of 130 Hz/pixel. As well as with the following GRE sequence: 1024×1024 image matrix; 0.021 mm in-plane resolution; 0.17 mm slice thickness; TR/TE of 123/48 ms; an acquisition time of 3:56:10; 6 averages; 1 slab with 30 slices; fat saturation; and a bandwidth of 19 Hz/pixel.

III. Results

The implantable RF coil provided MR images of neural tissue at 3 T (Fig. 2 and Fig. 3). In saline, the impedance for the coil with Teflon coated wire was $39.29 \pm 0.035 \Omega$ with a phase angle of $88.43 \pm 0.03^\circ$, and thus used in favor of the coil that began with bare copper wire ($43.07 \pm 0.11 \Omega$ and $87.91 \pm 0.85^\circ$). As characterized with the network analyzer, the Q of the Teflon coil in the neural tissue was 36.6 ± 0.63 . Tuning and matching of the coil was achieved with a 4.7 pF capacitor in series and a 28 pF capacitor in parallel to the coil. Fine-tuning was achieved by a 1 to 10 pF variable capacitor in parallel with the static 28 pF capacitor.

IV. Discussion

Implantable MR coils pick-up more signal and less noise than conventional receive coils, providing small regions of enhanced SNR. While 3-T MRI typically provides 1 to 30 voxels per-cubic-mm, in this paper we report that the MRI microcoil can provide hundreds, and even thousands of voxels in the same volume.

We believe that performance can be improved through slight modifications to the microcoil design. In the present design, the conductor inside of the solenoid reduces the uniformity of the magnetic-flux density. Additionally, unwanted signal was probably received by the

parallel-lead configuration. With this in mind, we have completed the design, fabrication, and characterization of the next-generation MRI microcoil catheters. The new microcoils no longer have a central conductor inside the solenoid, and include twisted-pair leads.

While the short leads of the microcoil catheter minimize the risk of MR-related heating, we intend to integrate the coil catheter with other implanted structures, such as intracranial electrodes for TLE. The dangers of tissue heating must be addressed when any implant is combined with MRI studies. The body of literature addressing MR-related heating of recording depth electrodes for epilepsy is dominated by case studies and *in vitro* experimentation [17–21]. In a recent collaboration with Dr. Frank Shellock, the authors assessed three tightly bundled depth electrodes with microwire arrays at 3 T, combining conventional *in vitro* methods with network-analyzer measurements. Heating in excess of 6 °C (5 min of MRI) corresponded to network-analyzer measurements indicating microwire resonance at the MRI operating frequency (129 ± 6 MHz in saline, $n = 6$). Unsafe conditions were eliminated by removal of the implant resonant conditions (no resonance measured within 128 ± 12 MHz, $n = 4$). Our data strongly support the potential for safe use of depth electrodes at 3 T, but highlight the importance of considering self-resonance when assessing MRI compatibility of implanted structures.

In combining the microcoil catheter with existing intracranial devices, we aim to provide clinicians and researchers a new imaging modality with greatly improved imaging access and sensitivity. For example, implanting a receive coil along with an intracranial electrode can transform the areas of greatest interest in TLE into areas of enhanced SNR. In addition to the unprecedented microscopic MRI of human epileptogenic tissue, these images will be spatially correlated to electrophysiology data, and therefore of great value to clinicians and researchers exploring the underlying mechanisms of epilepsy. Additional intracranial applications include the potential use of this technology for ultra-precise implantation of DBS electrodes in small and complex brain structures. Aside from the MRI applications, microcoil MRS may be of value for studying cerebral metabolites [22].

The majority of breast cancers originate in the mammary ducts. As such many diagnostic techniques introduce mm-diameter devices into the ducts through the nipple. Established intraductal techniques suffer from low sensitivity and specificity. Magnetic resonance spectroscopy (MRS) is highly effective in distinguishing between benign and malignant tissue, however conventional methods require a cubic centimeter of tissue. Intraductal use of microcoils offer a potential for early detection of breast cancers. Micro-scale images of the lactiferous ducts may also facilitate treatment planning by allowing three-dimensional *in-vivo* microscopy of epithelial cells, and high-precision localization of tumors and tumor margins. We designed our microcoils for possible integration with fiber-optic endoscopes to facilitate localization of suspect tissue for analysis and imaging.

V. Conclusion

We successfully designed, fabricated, and imaged with an implantable MRI microcoil designed for integration with 1-mm-diameter catheters. The first-generation implantable microcoil has yielded microscopic MR images (i.e., in-plane resolution of 20 μm in 170- μm -thick slices). This work represents a 1 to 2 order-of-magnitude improvement in the achievable spatial resolution of 3-T MRI. Clinical applications of the improved resolution include early virtual-biopsies of breast cancer, as well as imaging changes in cell-layer organization of cortex and deep structures (e.g., hippocampus). The second-generation implantable micro-coils incorporate design changes to enhance performance. Safety experiments, assessing and reducing MR-related heating of depth electrodes at 3 T, indicate both the potential for safe use and the importance of quantifying the resonant frequencies of

implants. Future work includes quantification of SNR and development of an artifact-free electrode for electro-physiological recording or stimulation. While we have investigated the safety of the depth electrodes, we have not yet quantified the MR-related heating of the microcoils. In addition to furthering imaging capabilities we will also explore microcoil spectroscopy.

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Fig. 1. Microcoil-catheter design is optimal for integration with intracranial depth electrodes and for intraductal use in breast oncology.

Fig. 2.
Image obtained of *ex vivo* neural tissue with the microcoil. 100- μ m in-plane resolution with 400- μ m-thick slices. See text for imaging protocol.

Fig. 3.
In-plane resolution of 20 μm and a slice thickness of 170 μm . See text for imaging protocol.