Towards a Microspectroscopy Catheter for Early-Stage Breast Cancer Detection

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Introduction: Although more than 95% of breast cancers originate in the mammary ducts,[1] clinicians cannot reliably diagnose cancers at this early intraductal stage. Magnetic resonance spectroscopy (MRS) can distinguish between benign and malignant tissue with specificity and sensitivity upwards of 80%.[2] Unfortunately, conventional methods are limited to late-stage diagnosis, as cm^3 of malignant tissue is needed.[3] We propose a miniature radio frequency (RF) coil for intraductal spectroscopy, as a potential method for early detection of breast cancers (Figure 1). Here we present the prototype.

Methods: We designed a prototype for proton MR at 3 T with a 1-mm-diameter solenoid and 5-cm-long twisted-pair leads. We selected a 50 Ω reactance, corresponding to 10-turns, such that the inductance of the coil and the tuning capacitance would be 10-fold greater than the inductance of the leads and the stray capacitances. Turns were crowded near the catheter tip to create a forward-looking probe. A moisture barrier minimized dielectric losses, and prevented contact of copper (toxic) with the body.

Fabrication: We hand-wound microcoils on silicone tubing (806400, A-M Systems, Inc., USA) under a stereo-microscope. A lathe-like set-up with a metal stylet set in an alligator-clip stand facilitated winding. We taped wire (38 gauge, 8058, Belden, USA) onto the tubing, and taped 1-g of weight to the hanging end of the wire to maintain uniform tension. We twisted the leads by rolling a pin-vice on a flat surface to achieve uniform twists with a minimum of 1 per mm. We added heat-shrink tubing and trimmed the excess tubing to within 0.1 mm of the coil tip. We sealed the interface of the concentric tubes with a single dip-coat of polydimethylsiloxane (PDMS) to inhibit water penetration between the layers.

Soak Test: We monitored the impedance over time of 5 devices immersed in body-temperature saline (0.9%) with a network analyzer.

Circuitry: We incorporated tuning and matching circuitry onto an SMA connector. A series tuning capacitor (9402-6, Johanson Manufacturing, USA) with parallel-inductance matching (looped brass foil 18 pF) reduced the interdependence of tuning and matching. Fine tuning was done with the coil in the sample. We implemented the microcoil as a transceiver (Figure 2). We fabricated a duplexer with two pairs of anti-parallel Schottky diodes (5082-2810, Agilent Technologies, USA), leveraged with a quarter-wave transformer. In transmit mode our microcoil is connected to the signal generator of the scanner via a 20-dB-attenuator (RFS30G04/20dB, RF Lambda, Plano, USA). During receive mode signal flows from the microcoil to a preamplifier (123GNST, Angle Linear, Lomita, USA).

Spectra: Spectra of mayonnaise were acquired with a 3-T Scanner (Tim Trio, Siemens AG, Germany) using the microcoil (0.0015 mL sample; STEAM; 10 Hz; 25 V) and for comparison a matrix-head coil (7.5 mL sample; STEAM; 10 Hz; 300 V).

MR-related heating: We assessed MR-related heating of the tuned microcoil in a vial containing 40 mL of poly-Acrylic-Acid (5.8 g/L), with fluoroptic temperature probes using the body coil for excitation (steady-state free precession sequence: 1.69/3.37 msec; flip angle of 40 degrees; scanner reported SAR of 1.9 W/kg; for 60 s).

Results: The microcoil is capable of providing microliter spectroscopy. Impedance measurements during soak tests indicate that the feasible period for use of this prototype is within 4 h of implantation. Spectra of 1.5 µL of mayonnaise show distinct fat and water peaks. Figure 3 compares the spectra from a 7.5-mL sample of mayonnaise to that obtained by the microcoil of a sample that is three-orders of magnitude smaller. Observed temperature changes for a tuned-and-matched microcoil were within the standard error of the fluoroptic temperature probes. Heating of the microcoil due to coupling with the transmit pulse of the bodycoil can be made insignificant, though this requires attention to resonant length coaxial cables.

Discussion: The need for early-stage diagnosis of breast cancer is more pressing than ever due to the development of localized intraductal chemotherapy, demonstrated in animals[1] and in phase-1 clinical trials.[4] Conventional approaches for identifying ductal carcinomas during the in situ phase suffer poor sensitivity (dynamic contrast enhanced (DCE)-MRI: 40–89%, mammography: 37–55%, ultrasound: 47%).[5,6] Direct imaging of the ducts is possible through mammary ductoscopy, however ductoscopic cytology is insufficient for diagnosing malignancies.[7] The proposed microcoil can be used at any field strength and with reduced diameters. It may be combined with ductoscopy to enhance sensitivity, or with DCE-MRI to confirm whether there is a true or false positive, currently overestimated in 21% of patients.[5] In a multicenter review of over 2000 patients, MRI findings led to an increase in resection, including mastectomy, with half of the decisions based on histologically identified false positives.[8]

Conclusions: We propose a new technique and present a prototype for intraductal microspectroscopy, reducing the spectroscopic voxel size by approximately three orders of magnitude. Our device has the potential to leverage the high sensitivity and specificity of MRS at the early stage of disease, and to reduce the number of false-positives in DCE-MRI.

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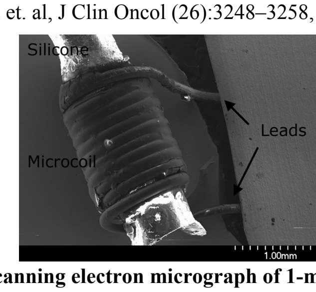

Figure 1 Scanning electron micrograph of 1-mm-diameter microcoil prior to twisting leads, adding dielectric layer, and trim.

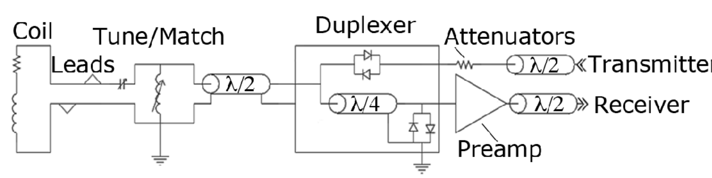

Figure 2 System schematic for microcoil as a transceiver.

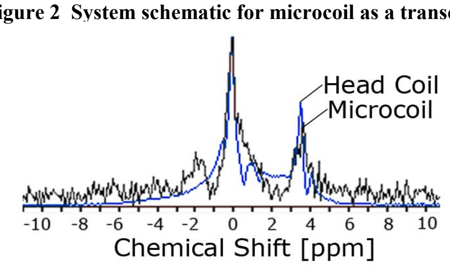

Figure 3 Proton spectrum of mayonnaise using a standard head coil (blue) and our novel microcoil (black) showing distinct fat and water components.