High resolution MRI and high sensitive 31P MRS of axillary lymph nodes at 7T

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Target Audience: Oncologists, radiologists, biochemists developing oncology therapeutics, and ultra-high-field RF engineers and MR spectroscopists.

Purpose: There is a need for a technology capable of evaluating the presence of macroscopic tumors in the lymph nodes of patients prior to, during, and after chemotherapy. Patients with a complete pathological response in breast and lymph nodes have a 5-year survival rate of 87%, as compared to 51% for patients in which lymph nodes have residual macro-metastases.[1] Existing noninvasive methods for staging axillary lymph nodes have poor *sensitivity* (CT/PET 63%[2]; DCE-MRI 72%[3]), and therefore sentinel node biopsy remains the standard method for evaluation. However, the false detection rate falls to 50% after chemotherapy and a previously obtained sentinel node biopsy.[4] Phospholipid metabolism indicates malignant transformation in cancer.[5] Preliminary clinical studies in small breast tumors at 7T indicate that the ratio of phosphomonoesters (PME) and phosphodiesters (PDE) as indicated by ^{31}P correlate more to neoadjuvant response than ^{1}H spectra.[6] In concert with investigations into tracking chemotherapy response in breast cancer, we have developed a coil system that targets the axillary lymph node for metabolic imaging at 7T.

Fig. 1 *Quadrature coil used for ^{31}P transmit/receive of and ^{1}H receive* ***(a)****. Radiative element on back* ***(b)*** *provides majority of 1H excitation held in place by custom fabric housing.[7]* ***(c)*** *Each loop element contains a modified dual-resonant unit to detune resonance at 300 MHz during transmit (* indicates choke inductor).*

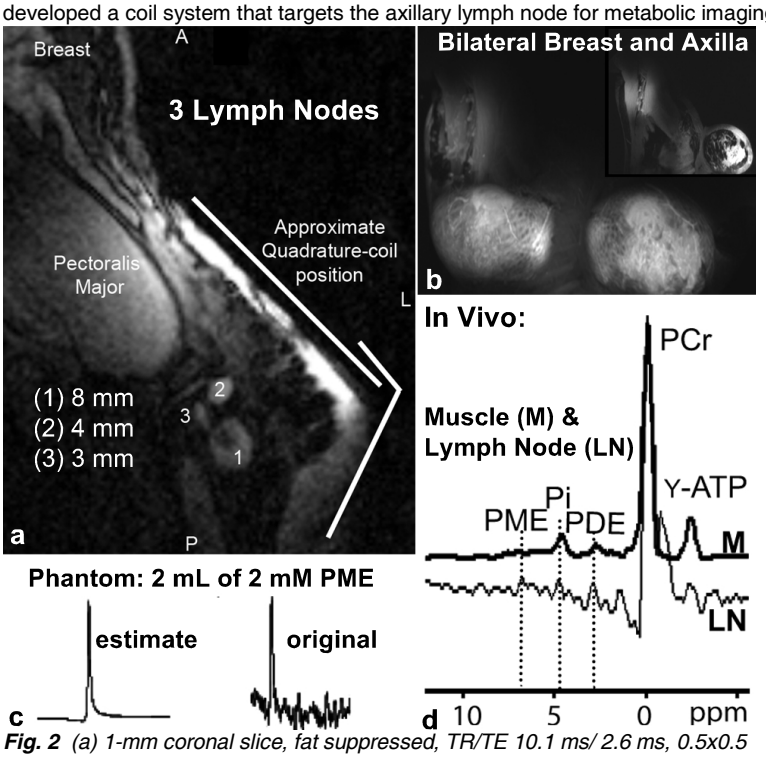

Fig. 2 *(a) 1-mm coronal slice, fat suppressed, TR/TE 10.1 ms/ 2.6 ms, 0.5x0.5 mm resolution, no averages, <4 min. (b) simultaneous imaging of breast and axilla: 1.5-mm-isotropic, fat suppressed, 3 min scan. (c) 2 mL spherical phantom. (d) In vivo spectra,1.25-cm isotropic voxels of muscle and lymph node (AMESING: < 10 W/Kg; <26 min).*

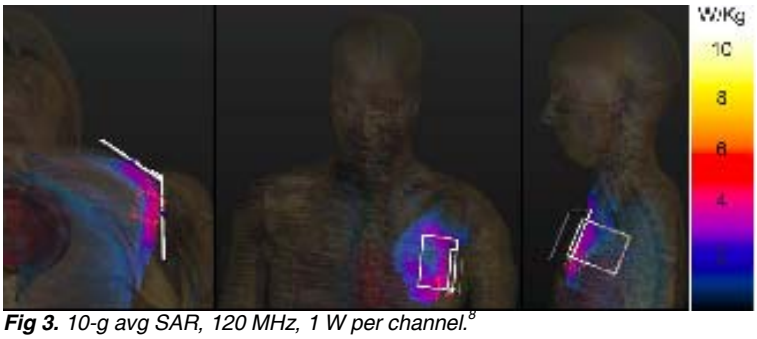

Fig 3. *10-g avg SAR, 120 MHz, 1 W per channel.*[8]

Methods: The lymph node coil system combines near-field and far-field approaches. A quadrature coil is dual tuned for transmit and receive or ^{31}P signal and receive-only of ^{1}H signal (Fig. 1a). Excitation of ^{1}H nuclei is achieved with a fractionated-dipole antenna,[7] placed on the back of the patient (Fig. 1b). Using a novel circuit in the loop elements, the resonance frequency is shifted away from ^{1}H (298 MHz to 290 MHz) without altering the resonance at ^{31}P (120 MHz) by forward biasing 1 pin diode during transmit (Fig. 1c). Local quadrature transceivers were used for ^{31}P and ^{1}H MRI and MRS for the human breast (MRcoils BV, Drunen, The Netherlands), and the dedicated lymph node coil was used for the axillary nodes (Fig. 1). Safety was assessed by simulation and experimental validation. Second order B_0 shimming was applied on the region of interest using B_0 maps. ^{31}P MRS sequence: fully adiabatic multi echo spectroscopic imaging (AMESING) with 1 FID and 5 echoes, 8x8x8 voxels of 1.25 cm isotropic resolution, TR = 6 s, delta TE = 45 ms, spherical k-space sampling.[9] Subjects: Written informed consent was obtained from the healthy volunteers and the local ethical committee approved the study.

Results: Healthy lymph nodes (<1 cm) can be imaged deep within the axilla (Fig. 2a). The axillary lymph node coil system is compatible with the bilateral breast coil array (Fig. 2b). The set up can resolve spectra from a spherical 2 mL phantom with 2 mM of PME metabolites (Fig. 2c). In vivo spectra from 1.25 cm isotropic voxels of muscle (M) and lymph node (LN), scaled to phosphocreatine (PCr) demonstrate that the peak between 6.2 and 8 ppm observed in the lymph node cannot be attributed to voxel bleeding from neighboring muscle tissue, hence suggesting detection of very low levels of PME originating from the lymph node (Fig. 2d). The coil is safe for use, as verified by simulation (Fig. 3), and corroborated with phantom measurements.

Conclusion: We demonstrate the first *in vivo* ^{31}P spectra of an axillary lymph node. Compatible with the bilateral breast coil, the axillary lymph node system allows simultaneous investigation of the axilla and the breasts.

Discussion: Healthy lymph nodes are both smaller and contain lower levels of PME,[10] therefore resolving peaks just above the noise floor in healthy lymph nodes indicates, it may be possible to provide MR spectra from enlarged axillary lymph nodes with macro-metastases of breast cancer patients.

References: *1. Kuerer HM, et al. Clinical course of breast cancer patients with complete pathologic primary tumor and axillary lymph node response to doxorubicin-based neoadjuvant chemotherapy. J Clin Oncol 1999;17(2):460-469. 2. Kooper KL, et al. Positron emission tomography (PET) and magnetic resonance imaging (MRI) for the assessment of axillary lymph node metastases in early breast cancer: systematic review and economic evaluation. Health Technol Assess. 2011;15(4): iii-iv,1-134. 3. Klerkx WM, et al. Detection of lymph node metastases by gadolinium-enhanced magnetic resonance imaging: systematic review and meta-analysis. J Natl Cancer Inst. 2010;102(4): 244-53. 4. Kuehn T, et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. Lancet Oncol 2013;14(7):609-618. 5. Aboagye EO, Bhujwalla ZM. Malignant transformation alters membrane choline phospholipid metabolism of human mammary epithelial cells. Cancer Res 1999;59(1):80-84. 6.Klomp DW et al. 31P MRSI and 1H MRS at 7 T: initial results in human breast cancer. NMR Biomed 2011;24(10):1337-1342. 7.Raaijmakers A, et al. Prostate Imaging at 7 Tesla with Fractionated Dipole Antennas: A New Type of Radiative Coil Array Element with Lower SAR Levels. 2013; Salt Lake City, Utah, USA. p 3401. 8. Christ A, et al. The Virtual Family--development of surface-based anatomical models of two adults and two children for dosimetric simulations. Phys Med Biol 2010;55(2):N23-38. 9. van der Kemp et al. Adiabatic multi-echo 31P spectroscopic imaging (AMESING) at 7 T for the measurement of transverse relaxation times and regaining of sensitivity in tissues with short T2* values. NMR Biomed 2013. 2013;26(10):1299-307. Wijnen JP et al. 31P magnetic resonance spectroscopy of the human breast at 7 T. Magn Reson Med 2012;68(2):339-348.*