Specificity of Choline Metabolites for *In Vivo* MRS Diagnosis of Breast Cancer at 1.5T

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Objective: Determine if *in vivo* proton (^{1}H) MRS at 1.5T can provide diagnostic pathology with accuracies suitable for clinical application.

Introduction Pre-surgical assessment of the pathology, spatial location and extent of breast malignancy would improve management. Proton MRS at field strength of 8.5T of fine needle aspirate biopsies (FNAB) from breast lesions provides the pathology, lymph node involvement and lympho-vascular invasion with accuracies approaching 100% (*1*). *In vivo* ^{1}H MRS assessment of the cellular chemistry of breast cancer has been undertaken (See Katz-Brull for review (*2*)), but the accuracies quoted, based on the presence of the single broad composite resonance at 3.2ppm, were not appropriate for clinical management.

Materials and Methods: Forty-three asymptomatic volunteers including three lactating mothers were examined and compared with 21 breast cancer patients. None of the volunteers had a palpable lesion or history of breast disease. The cancer diagnosis was substantiated by surgical excision and histopathology. Examinations were undertaken at 1.5 Tesla using a purpose-built transmit-receive single breast coil (*3*). Localizing scans were undertaken to identify the lesion/s. Single voxel spectroscopy was undertaken using echo times of 135ms and 350ms. Following spectroscopy the location of the volume of interest was confirmed by performing a multi-phase contrast-enhanced MR mammography (gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany)). For the volunteer cohort the spectroscopy volume of interest was defined within the glandular tissue and placed to minimize the contribution from fatty breast tissue. Spectra were acquired with 256 signal averages per data frame with an eight-phase cycling scheme (2048 data points per spectroscopy frame with a spectral band width of 2500Hz). Chemical shifts were relative to the water signal at 4.74ppm. Post processing was undertaken with 2048 data points, zero filled to 8192 data points and a Gaussian function of 1.5Hz applied with a 15% echo offset.

Results and Discussion: The composite resonance at 3.2ppm, which includes contributions from choline, phosphocholine (PC), and glycerophosphocholine (GPC) and taurine, was found not to be a unique marker for malignancy providing a sensitivity and specificity of 80.0% and 86.0%, respectively. In post processed spectra, volunteers previously classified as false positives had a resonance centered at 3.28ppm consistent with GPC while malignant breast lesions had a resonance centered at 3.22ppm consistent with PC. The spectra from lactating mothers also had a resonance centered at 3.28ppm consistent with GPC (Figure1). Thus, post acquisition processing of the spectra resolved the 3.22ppm resonance improving the specificity of the test to 100%. This is consistent with the literature with Aboagye and Bhujwalla having demonstrated a GPC to PC switch with cell immortalisation in oncogene-transformed and human breast tumour cell lines. An increase in PC levels was also reported (*4*).

^{1}H MRS *in vivo* distinguished volunteers from breast cancer patients with 100% specificity but only when the spectra were accurately referenced and subjected to post acquisitional processing. Spectra from lactating women and healthy women that contained a resonance in the choline region ceased to be false positives when the spectra were post processed and the broad composite choline resonance was identified as containing mostly GPC at a chemical shift of 3.28ppm. Sixteen of the 20 breast cancer patients recorded a resonance centered at 3.22ppm consistent with PC. The sensitivity remained at 80% since the post processing method failed to record additional information in the 3.2-3.3ppm region for 4 of the 20 breast cancer patients. This sensitivity is similar to reports by the other groups (See Katz-Brull for review (*2*)).

Conclusion: Post acquisitional processing of *in* vivo ^{1}H MR spectra from human breast tissue allows the distinction of patients with malignant disease from volunteers with a sensitivity of 80% and specificity of 100%. Resolution of the composite choline into its constituent components improves the specificity of the *in vivo* proton MRS method but does not overcome the problem of 20% false-negatives.

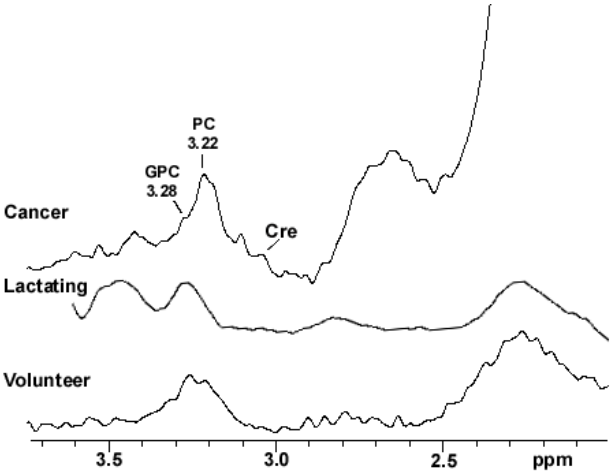

Figure 1. Typical proton single voxel spectrum (135/2000, 256 signal averages) from a patient with histologically confirmed invasive ductal carcinoma is compared with a typical spectrum from one of the 3 lactating volunteers and one of the false-positive volunteers. Spectra were processed by zerofilling the 2048 data points to 8192 data points, applying a Gaussian apodization function of 1.5Hz with a 15% echo offset before fast Fourier transformation.

References:

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