Quantitative ^{1}H MRS of the Normal Human Breast

P. J. Bolan[1], and N. Lakkadi[1]
[1]Radiology/CMRR, University of Minnesota, Minneapolis, MN, United States

Introduction: The clinical utility of ^{1}H MRS measurements in breast cancer is well-established: cancers are more likely to have a detectable total choline (tCho) resonance than benign lesions. Quantitative MRS methods have also found higher concentrations of tCho in cancers than in benign lesions. The question of whether tCho can be detected in normal (non-lactating) fibroglandular tissue has not been answered consistently in the literature. It has been reported that normal glandular parenchyma does not consistently show a tCho resonance at 1.5T (*1*), whereas at 3T, a broad 3.2ppm resonance can be measured in some normal fibroglandular tissues (*2*). Understanding the detectability and concentration of tCho in normal breast tissue is important, as this impacts measurements in lesions due to the unavoidable inclusion of some fibroglandular tissues in most MRS voxels. Furthermore, if tCho can be measured in normal subjects, they can be used as model subjects for developing new MRS acquisition and analysis techniques. In this work we aimed to measure tCho in normal fibroglandular tissues, quantity the tCho levels, and determine what factors impact the tCho detectability. Furthermore, we used these normal subjects to compare the performance of two single voxel spectral editing methods, TE averaging (3) and MEGA lipid suppression (4).

Methods: Fourteen subjects with no history of breast disease, aged 20-40 yrs (median 25 yr), were recruited to this IRB-approved study. All scans were performed on a 3T Siemens TIM system (Siemens, Erlangen, Germany) using a 4-channel breast array coil. 3D fat-suppressed gradient-echo images were used to place the MRS voxel in the fibroglandular tissue. The voxel size was maximized (up to 30mm/side) while avoiding adipose tissue as much as possible. Prior to spectral acquisition, the transmit power and shim currents (*5*) were adjusted using prototype software provided by the manufacturer. All spectra were acquired using PRESS localization with no OVS. Water reference scans were acquired with TR=6s and TE=50, 75, 100, 125, 150 ms. Metabolite spectra were acquired from the same voxel, with weak water suppression enabled, and using either fixed TE (TE=125ms, 64-256 averages) with MEGA lipid suppression (0.53-2.08ppm) or with TE averaging (TE=50-200ms in 64-256 increments). All acquisitions used 1024 complex points and 2 kHz bandwidth.

Spectra were analyzed using semi-automated routines developed in Matlab (Mathworks, Natick, MA). Water T_2 reference scans were fit with a mono-exponential decay to estimate water T_2 and M_0. The aqueous % was calculated from the T_2-corrected water and fat signals (acq% = W/[W+F]). The single-shot water signal-to-noise (based on frequency-domain amplitude) was corrected to estimate the theoretical water SNR at TE=0ms (wSNR). Metabolite spectra were individually phased and frequency-corrected prior to averaging to reduce respiration artifacts. Frequency referencing was performed by setting the water peak to 4.67ppm, and manually co-registering the frequency-corrected metabolite scan with the water reference scan. SVD-based passband filtering was then used to remove resonances outside the 2.5-4ppm range and reduce baseline distortion. The choline region (3.03-3.43ppm) was then fit with a single Voigt lineshape and a linear baseline. Objective detection of tCho required SNR>2, Cramer-Rao estimated standard deviation < 200% of the peak amplitude, and total linewidth>4Hz. The choline:water ratio was then converted to a molal concentration (mmol tCho / kg-water) as described previously (*6*). After fitting, all spectra and fit results were qualitatively assessed to identify resonances other than tCho, and to assign a data quality score (good, fair, or poor) for each dataset.

Results: A total of 35 spectra were acquired from one or both breasts in 13 of the 14 subjects. One subject had no spectra acquired due to insufficient contiguous gland. Two spectra were rejected as poor quality. Using the objective detection criteria, a tCho resonance was found in 23/33 spectra, and in 9/14 (64%) subjects. An example is given in Fig.1, and summary of relevant parameters from the analysis is given in Table 1. A taurine peak was observed (but not fit) at 3.45ppm in spectra from four subjects. No distinct creatine resonances were observed. The ability to detect a tCho resonance was largely dependent on the single-shot water SNR. For voxels with wSNR>13,000, tCho was detected in 92% of spectra; for voxels with wSNR<13,000 the tCho detection rate was 13%.

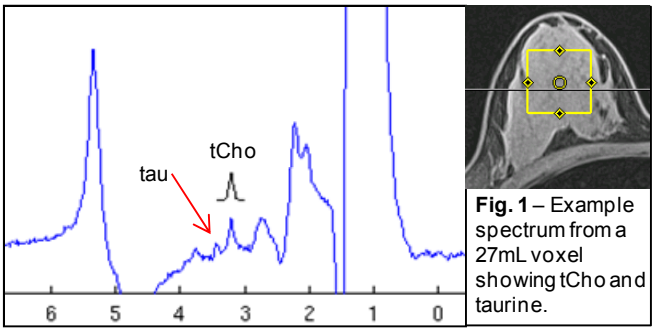

Fig. 1 – Example spectrum from a 27mL voxel showing tCho and taurine.

There were 11 cases in which both a TE-averaged spectrum and a MEGA spectrum were acquired from the same voxel. In one case no tCho was detected with either method, in two cases tCho was detected with TE averaging and not with MEGA, and in 8 cases tCho was detected in both. In the 8 comparable cases the tCho SNR was not different (p=0.30) but the concentration was lower with TE averaging than with MEGA (p=0.014).

Parameter (unit)	Range (median)
Voxel size (mL)	3.5 – 27 (9.2)
Aqueous (%)	69.7% – 96.8% (85.9%)
Water FWHM (Hz)	11.7 – 32.4 (20.0)
Water T_2 (ms)	39.5 – 63.9 (48.4)
1.3ppm Lipid T_2 (ms)	54.3 – 118.1 (83.5)
[tCho] (mmol/kg)	**0.15 – 1.47 (0.46)**
tCho frequency (ppm)	3.10 – 3.29, (3.20) std. dev. 0.05

Table 1 – Results from MRS Analysis.

Discussion: The ability to detect tCho was determined by the water SNR, which is largely a function of the voxel size. As the voxels were maximally sized within fibroglandular tissue, the ability to detect tCho is dependent on the fibroglandular structure, which varies greatly in form and homogeneity between subjects. The concentration found (~0.5 mmol/kg) is similar to that of benign lesions based on prior studies (7). The taurine resonance can interfere with the tCho fitting. Future work will focus on fitting taurine and tCho separately when possible. The comparison between TE averaging and MEGA shows that TE averaging better reduces artifacts, but also leads to a lower estimated concentration. This is likely due to an incorrect assumption of tCho T_2 (263ms) as the T_2 weighting is different between the sequences. Further data are needed to revise this tCho T_2 estimate.

Conclusions: A tCho resonance is regularly quantifiable in normal breast at 3T, provided a sufficiently large voxel can be placed in the fibroglandular tissue. Normal subjects can therefore be used to develop and compare MRS techniques.

References: 1) Bartella L and Huang W, Radiographics 2007; 2) Stanwell P and Mountford C, Radiographics 2007; 3) Bolan PJ et al., MRM 2002; 4) Mescher et al, JMR A 1998; 5) Shah S et al., Proc ISMRM, 2009:4202; 6) Bolan PJ et al., MRM 2003; 7) Meisamy S et al., Radiology 2005

Acknowledgements: NIH P41 RR08079, R01 CA120509