High-Speed MR Spectroscopic Imaging of Total Choline in Breast Cancer and Healthy Controls at 3T: A Feasibility Study

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INTRODUCTION Mapping tCho in breast cancer using MR spectroscopic imaging (MRSI) was reported to improve lesion characterization, thus improving the limited specificity of dynamic contrast enhanced (DCE) MRI [1]. MRSI was also used for treatment monitoring in patients undergoing neoadjuvant chemotherapy to predict outcome [2]. However, a major limitation of conventional chemical shift imaging (CSI) is the long acquisition time due to time consuming phase encoding along the spatial dimensions, which introduces motion sensitivity. Here we demonstrate feasibility of tCho measurement using high-speed Proton-Echo-Planar-Spectroscopic-Imaging (PEPSI) [3]. We used whole slice PEPSI to map total Choline (tCho) in a breast cancer patient and compared with PRESS-CSI and single voxel spectroscopy (SVS) using PRESS. We also measured tCho in a control group of 29 healthy subjects.

METHOD Measurements on 1 breast cancer patient (age: 65) and 29 healthy female subjects (mean age: 22±2) were performed with informed consent using 3T MR scanners (Siemens Trio, Erlangen, Germany) equipped with array breast coils. The patient was a 65 year old female diagnosed with a locally advanced infiltrating ductal carcinoma, moderately differentiated, ER positive, HER2 negative, and treated with several rounds of chemotherapy. The extent of the cancer was irregular with small satellite lesions noted. The dimensions of the largest mass were approximately 5.8×5.6×6.4 cm. Both PEPSI and CSI scans were performed in the same oblique slice orientation and position. The PEPSI scans performed using long TR to reduce T1-weighting for both the WS and the NWS scans: TE/TR = 50/4000ms, matrix size = 16×32, voxel size = 1×1×2mm^3, total acquisition time (TA) = 9.7min. The CSI scan was performed using much shorter TR to obtain acceptable scan time: used TE/TR=125/2000ms for WS scan and TE/TR=125/800ms for NWS scan, matrix size = 16×16, TA = 7min.

For the healthy control subjects, 2D MRSI data of an entire oblique slice were collected using PEPSI [1]. Water suppressed (WS) metabolite scans were performed with WET water suppression and MEGA lipid suppression, TE/TR=125/1500ms, matrix size=32×32, voxel size=2×2×2mm^3, TA =7 minutes. PRESS SVS data were acquired with the same voxel size using identical TE/TR and acquisition time.

We developed a hybrid quantification method using LCModel and a customized basis set with singlet peaks at 3.2ppm for tCho and at 2.8±0.1ppm and 2.3±0.1ppm to account for residual lipids. We calculated tCho:water area ratio, tCho concentration and residual noise level. On the fitted WS spectra, the tCho peak was identified by detecting the local maximum in the vicinity of 3.2ppm. Then, two samples with local minimum values in the fitted spectra to the right and left side of the tCho peak within the range of 3.2±0.15ppm were identified to determine the baseline. The tCho baseline was generated by linear interpolation using these two samples. The tCho areas were computed by integrating the area enclosed between the tCho peak and baseline. The molal concentration of tCho was calculated by compensating the relaxation times [4].

RESULTS Fig1a demonstrates the slice position of the PEPSI and CSI. In a 3×3 neighborhood which is marked by a red square in Fig1a, tCho and water spectral arrays obtained from the PEPSI and CSI scans are shown in Fig1b and c, respectively. Across the 9 voxels, the tCho concentration measured using PEPSI was 14.6±5.4mmol/kg, vs 12.7±8.0mmol/kg using CSI, and the tCho SNRs were 46.2±31.2 and 41.9±17.2, respectively.

In the healthy control group, 10 of 29 subjects demonstrated tCho peaks with signal noise ratio (SNR) larger than 3.0 at 3.22ppm on at least one of the MRS scans, i.e, SVS, PEPSI or CSI. In most of these subjects tCho was detectable with all methods. The absolute tCho concentrations measured in these subject are 0.48±0.2mmol/kg using PEPSI, 0.69±0.60mmol/kg using SVS and 0.56±0.44mmol/kg using CSI. The tCho levels measured using the three techniques are presented in Table 1.

DISCUSSION AND CONCLUSION Despite the less favorable shimming and lipid suppression conditions compared to SVS, it is feasible to quantitatively map tCho in healthy breast tissue using PEPSI, with the resultant concentration values being consistent with those from SVS and CSI. PEPSI studies using phantom and in vivo demonstrated comparable spectral quality to conventional CSI studies, similar water line-width, and metabolite SNR, indicating that the eddy current effect accompanying the EPI readout are negligible. The fast acquisition time of PEPSI offers more flexibility in choosing the scan time, for example, to shorten the total acquisition time to reduce the motion artifacts which have limited spectral quality in this study. Spectral contamination from the lipid area due to the point spread function (PSF) potentially decreases spectral quality. We are in the process of implementing lipid deconvolution in post-processing to reduce lipid contamination [5]. Furthermore, the large SNR of tCho in the lesion indicates that spatial resolution may be increased in future studies to reduce lipid contamination due to the PSF.

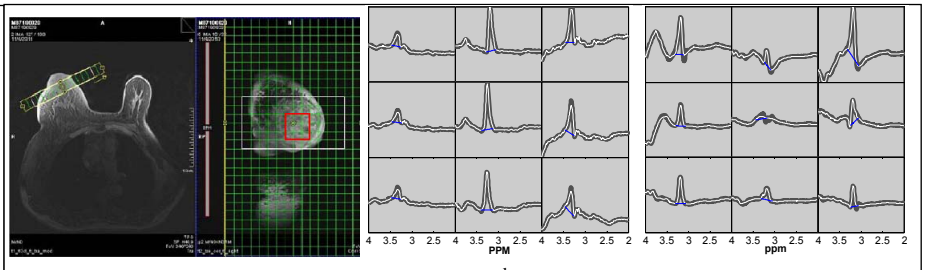
The major challenge of breast spectral quantification is the tCho baseline distortion due to the contamination of unsuppressed lipids at 2.8ppm and line broadening because of tissue heterogeneity of the breast. The commonly used polynomial baseline is not sufficient to solve this problem. Therefore a hybrid tCho quantification method was developed to use singlet peaks to compensate for the spurious residual lipid peaks at around 2.3 and 2.8ppms. It allows the fitting over a larger spectral range of 2ppm than the standard LCModel fitting, which only works well over a 0.5ppm range around the tCho peak on the WS spectra. In addition, the customized basis set offers more robustness in spectral quantification, which is suitable for automated spectral array data processing.

Subject 9 in the healthy group exhibited higher tCho level than documented values which may be due to the higher lipid contamination in this subject. We are currently acquiring data in breast cancer patients using PEPSI on a weekly basis. A comprehensive analysis of these data will be presented.

Table1. tCho concentration in healthy control subjects.

Coil Channels	Subject #	Age	tCho Concentration (mmol/kg) SVS	PEPSI	CSI
4-Channel	1	20	0.17	0.65±0.16(n*=11)	n/a
	2	20	0.71	0.62±0.19(n=5)	n/a
	3	25	0.25	0.68±0.08(n=2)	n/a
	4	22	0.26	0.23±0.19(n=4)	n/a
	5	21	0.18	0.32±0(n=1)	n/a
	6	26	0.98	0.56±0.23(n=4)	n/a
8-Channel	7	20	0.37	0.68±0.33(n=6)	0.53±0.37(n=4)
	8	22	0.96	n/a	1.02±0.22(n=3)
	9	20	2.12	0.44±0.38(n=11)	n/a
	10	26	0.91	0.15±0.04(n=4)	0.15±0.02(n=4)
Mean		22.20	0.69±0.60(n=10)	0.48±0.20(n=9)	0.56±0.44(n=3)

* n is the number of voxels.



a b c

Fig1. PEPSI and CSI spectral array in the tumor. a. Slice positioning. Across the 3×3 pixels in the red square marked in a, tCho spectral arrays over the [4.0 2.0] ppm range from PEPSI and CSI scans are shown in b and c. In each cell, the fitted spectrum is shown in thin white curve, which is overlaid on the raw spectrum in bold gray. TCho baseline under each tCho peak is shown as a short blue line segment.

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