Quantification of Choline-Containing Compounds in Malignant Breast Cancer by ^{1}H Single-Voxel MR Spectroscopy at 1.5T

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Introduction

Recently, proton magnetic resonance spectroscopy (^{1}H-MRS) has been increasingly applied for the detection of breast cancer. Several studies have shown that total choline-containing compounds (Cho) can be detected in breast tumors using ^{1}H-MRS techniques (1-2). All of these studies used qualitative methods (i.e., detectibility or Cho signal to noise ratio (SNR)) for the differentiation of malignant and benign lesions. However, because the sensitivity of the MRS measurement may vary with variations in voxel size, adipose tissue content, and receiver coil efficiency, a quantitative analysis method is necessary to improve diagnostic accuracy. The purpose of this study was two fold, firstly to demonstrate the feasibility of using internal reference method for quantifying the Cho concentrations in patients with malignant breast tumors using a clinical 1.5T scanner, and secondly to compare the Cho concentration range measured with the current method with previously published results.

Methods

Thirty-two patients with histologically proven breast cancer were included in this study. The examinations were performed using a Philips Eclipse 1.5 T MR system with the dedicated bilateral breast coil. A dynamic contrast-enhanced (DCE) MRI study was first performed from bilateral breasts using a 3D SPGR (RF-FAST) pulse sequence. After the enhanced lesion was identified, single-voxel MRS was performed using a PRESS sequence. The spectroscopic voxel was carefully positioned to cover the entire enhanced lesion with minimal inclusion of surrounding normal tissues. The voxel size was 2×2×2 (or, 1.8×1.8×1.8) cm^3. After shimming procedure water suppression was accomplished with "CHESS" pulses, and lipid suppression was independently attenuated by using inversion recovery (STIR)-based fat signal nulling. The acquisition parameters were TR/TE= 2000/270 ms, and 128 acquisitions for averaging. A fully relaxed, unsuppressed spectrum was also acquired to measure the water peak (24 averages). The absolute Cho concentration of in vivo Cho in malignant breast tumors was calculated with Eq. [1], and was expressed as a concentration in units of mmol/kg. Where S_{cho} is the signal amplitude of choline; S_{H2O} is the signal amplitude of the unsuppressed water; n_{Cho} and n_{H2O} are the numbers of ^{1}H nuclei for each molecule, respectively; MW_{H2O}, is the molecular weight of the solvent. T_1 and T_2 values for Cho and water signals were measured from 4 patients with malignant cancer. T_1 values were estimated using a fixed TE (270 ms) and three TR values ranging from 1.5 – 8.0 s. T_2 values were estimated using a fixed TR (2 s) and three different TEs (150, 350, and 450 ms). The f_{T1} and f_{T2} are the relaxation correction factors expressed in Eqs [2] and [3].

$$[Cho] = \frac{n_{H_2O}}{n_{Cho}\,MW_{H_2O}} \times \frac{S_{Cho}}{S_{H_2O}} \times \frac{f_{T_1 H_2O}}{f_{T_1 Cho}} \times \frac{f_{T_2 H_2O}}{f_{T_2 Cho}} \qquad [1],$$

$$f_{T_1} = 1 - \exp(-TR/T_1) \qquad [2],$$

$$f_{T_2} = \exp(-TE/T_2) \qquad [3]$$

Results

34 MR spectra were acquired from 32 patients. The mean size of these tumors was 3.3 cm (range 1.0 – 8.5 cm, measured as the longest dimension of the enhanced lesions on the MIPs of subtraction images). The spectroscopic voxel size was either 5.8 mL or 8.0 mL. The Cho resonance peak was detected around 3.22 ppm (range; 3.17 – 3.26 ppm in the 34 breast spectra). The fitted Cho peak had Gaussian linewidth of 1.5 Hz and 7Hz, and the fitted water peak had a Lorentzian linewidth of 7 Hz and 24 Hz; the 1.32 ppm lipid peak had 11Hz and 46Hz at 1.5T. The T_2 relaxation times (mean ± SD, n = 4) were 269 ± 61 ms for Cho, and 97 ± 10 ms for water. The T_1 relaxation time were 1513 ± 156 ms for Cho, and 746 ± 118 ms for water. The absolute Cho levels measured from 34 malignant breast spectra ranged from 0.76 – 21.20 mmol/kg. Figure 1 provides an example of a patient with invasive ductal carcinoma. The spectroscopic voxel was carefully positioned to maximize the coverage of the hypointense lesion on the pre-contrast images and contrast-enhanced lesion on the axial subtraction images. The Cho peak at 3.23 ppm is clearly visible in the water-fat suppressed spectrum. The measured [*Cho*] = 19.24 ± 0.07 mmol/kg.

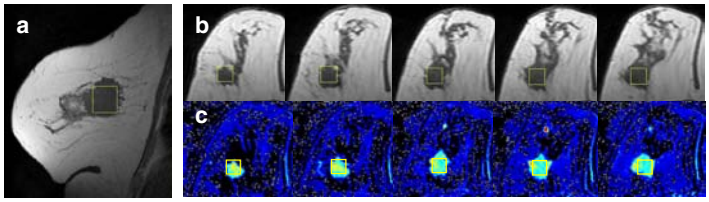
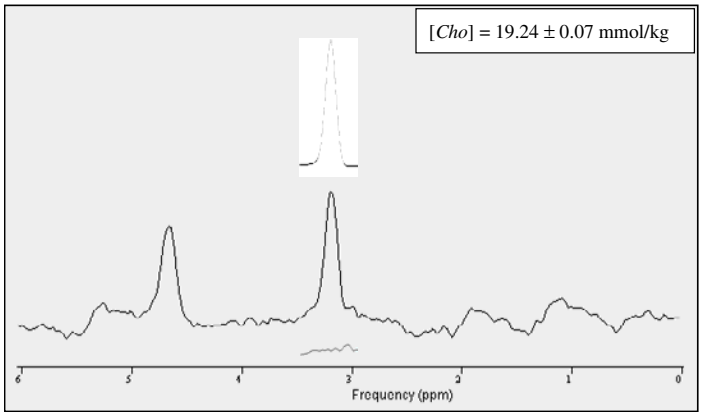


Figure 1 shows the MRI and MRS measurement of a patient with invasive ductal carcinoma. **a:** Sagittal view pre-contrast image, one hypointense lesion was clearly noted. **b:** Axial pre-contrast images. **c:** Contrast enhancement maps. The spectroscopic voxel (2 × 2 × 2 cm^3) is overlaid.



d: The MR spectrum measured from the selected voxel. The Gaussian model fitting yields [*Cho*] = 19.24 ± 0.07 mmol/kg. The estimated model fit is shown above the full spectrum and the residue is shown underneath.

Discussion

The quantification of Cho in breast tumors by ^{1}H-MRS is of great interest for lesion characterization. Qualitative assessment of presence or absence of Cho has not proven to be reliable for improving diagnostic accuracy. Additionally, quantification of Cho is also needed to allow comparison of Cho levels in longitudinal F/U studies for monitoring or predicting neoadjuvant chemotherapy response. In this study, an internal reference method for the absolute quantification of Cho metabolite in malignant breast tumors was demonstrated. After T_1 and T_2 relaxation times were corrected, the Cho levels from 28 spectra (82 %) were in a range of 0.76 – 10.22 mmol/kg, which seems to be consistent with previously published value (i.e., 0 – 10 mmol/kg) by Bolan et al (3). The remaining 6 spectra (18 %) showed higher Cho levels (12.19 - 21.20 mmol/kg). We conclude that the internal method using the fully relaxed water as a reference could be used for quantifying Cho metabolite concentration in breast cancer using a clinical 1.5T scanner. Further investigations are required to determine whether the absolute Cho values are reproducible in repeated MRS measurements.

References 1. Yeung et al. Radiology 220:40-60 (2001). 2. Huang et al. Radiology 232:585-591 (2004). 3. Bolan et al., MRM 50: 1134-1143 (2003).

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