Feasibility of Using MR Spectroscopy Without Water-Fat Suppression to Monitor Tumor Response to Chemotherapy

H-M. Baek1, J-H. Chen2, O. Nalcıoglu2, and M-Y. Su2

1Advanced Imaging Research Center, UT Southwestern Medical Center, Dallas, TX, United States, 2Tu & Yuen Center for Functional Onco-Imaging, UC Irvine, Irvine, CA, United States

Introduction

In vivo 1H-MRS acquired with water-fat suppression has been proven helpful for the detection and therapy response monitoring of breast cancer based on total choline-containing compounds (tCho) [1]. However, the technique with water-fat suppression has also several disadvantages: partial suppression of other metabolite signals, magnetization transfer effects, increased total RF power deposition, increased acoustic noise by spoiler gradient pulses [2-3]. Recently, it has been reported that the reduction of H2O/CH3 ratio in the water-fat unsuppressed spectrum can provide a response indicator to monitor the clinical outcome of breast cancer patients to neoadjuvant chemotherapy. However, the role of 1H-MRS acquired without water-fat suppression for therapy response monitoring is less established [4]. Of in vivo breast metabolites, tCho and lipids signals have shown great interest for in vivo cancer diagnosis and treatment monitoring [1]. In this study, we applied in vivo 1H-MRS without water-fat suppression for evaluating the tCho, H2O, and lipids (CH2 and CH3) signals in patients who received neoadjuvant chemotherapy. The aim of our study was to determine the feasibility of using quantitative 1H-MRS without water-fat suppression to monitor tumor response to neoadjuvant chemotherapy.

Methods

Eleven patients with biopsy-confirmed breast cancer who elected to receive neoadjuvant chemotherapy were included in this study. The examinations were performed on a Philips Eclipse 1.5 T MR system with the dedicated bilateral breast coil. In all patients, MRI and 1H-MRS were performed prior to treatment as the baseline (BL), then at least 2 follow-up (FU) times, FU-1 after 1-2 cycles AC, and FU-2 after 4 cycles AC or 2 cycles AC followed by first cycle of taxane regimen. A radiologist determined the tumor size based on the maximum intensity projection (MIP) of the subtraction images. Single-voxel 1H-MRS without water-fat suppression was performed using a point-resolved spin-echo sequence (PRESS). The spectroscopic voxel size was from 3.4 to 8.0 ml (1.5-2 cm cubic voxel). The acquisition parameters were TR/TE=2000/270 ms, and acquisition averages of 32. We quantified tCho, H2O, and lipids signals by fitting a voigt-lineshape model to the data. Metabolite basis set signals (e.g., tCho, H2O, and lipids) were simulated in SIMULNE software (e.g., \( S = S_0 \times \exp(\text{-}(t/T_1) \times \text{exp}(i(2\tau t + \varphi_0)) \text{ and quantified with QUEST [5]. The Cramer-Rao lower bounds (CRLB) were used as a measure of fitting accuracy. Uncertainty in the tCho concentration was presented as the standard deviation. For absolute quantification, the amplitude of the tCho metabolite estimated by the QUEST was converted to concentrations (mmol/kg) using water as an internal standard. The tCho concentration was calculated using measured \( T_1 \) and \( T_2 \) values for intensity correction [6].

Results

Figure 1 shows a representative MR imaging and MRS measurement from a patient who received chemo-follow-up treatment. Tumor size (Fig. 1A), H2O area (Fig. 1B), tCho area (Fig. 1C), and lipids areas (Fig. 1D) were measured at baseline and first, second, and third follow-up. The tCho peak at 3.22 ppm is clearly visible in the 1H-MRS acquired without water-fat suppression (Fig. 1C) at the FU-1 and FU-2. 9 (82%) of 11 patients had a positive tCho at the baseline. The mean percentage change in tCho, H2O, CH2, and CH3 after 1-2 cycle AC was -72.6%, -36.2%, 78.4%, and 69.2% (p = 0.003, p = 0.097, p = 0.073, and p = 0.180 in Figure 2), while the mean percentage change in lesion size in FU-1 study was -9.7% (+8.8% ~ -32.5%) (p = 0.042). There were no significant correlation between change in tCho in FU-1 and the change in lesion size in FU-2 (\( r^2 = 0.06, p = 0.536 \)). After completing the F/U-2 study, 3 (27%) of 11 patients did have positive tCho based on the criterion (i.e., tCho CRLB < 30%). The mean percentage change tCho, H2O, CH2, and CH3 after FU-2 study was -96.6%, -76.9%, 119.6%, and 119.5% (p = 0.004, p = 0.044, p = 0.008, and p = 0.005 in Figure 2), while the mean percentage change in lesion size in FU-2 study was -56.7% (-22.7% ~ -100%) (p = 0.007).

Discussion

The measured tCho levels at the baseline from 9 spectra were in a range of 0.19 – 5.29 (mean ± SD, 1.94 ± 1.76 mmol/kg). Our study showed the reduction in tCho at the first and second follow-up was significantly higher compared with the reduction in the tumor size (mean percentage change -72.6% vs. -9.7%, p < 0.0001; -96.6% vs. -56.7%, p < 0.003). The result demonstrates that the metabolic changes were greater than the tumor size changes, suggesting that they might have occurred before gross morphological changes. An early reduction of tCho can be interpreted as reflecting the inhibition of cellular proliferation and the cytotoxic effect of chemotherapy. In addition, the reduction in H2O and H2O/CH3 were also significantly higher than the reduction in tumor size at FU-1 (-36.2% vs. -9.7%, p = 0.028; -43.2% vs. -9.7%, p = 0.033), but not significant at FU-2 (-76.9% vs. -61.1%, p = 0.125, -82.3% vs. -61.1%, p = 0.120). Our finding suggests that a greater reduction in tCho and H2O/CH3 at the FU-1 may help to predict a final (or, pathological) complete response. Therefore, we demonstrates that in vivo quantitative 1H-MRS without water–fat suppression can be useful for the detection and therapy response monitoring of breast cancer.

References


Acknowledgement

This study was supported in part by NIH/NCI No. CA90437, CA127927, and the California BCRP No. 9WB-0020 and No. 12FB-003.