Proton Chemical Shift Imaging for Monitoring Early Treatment Response of Breast Cancer to Neoadjuvant Chemotherapy

H-M. Baik[1], M-Y. Su[1], H. J. Yu[1], O. Nalcioglu[1]

[1]Tu & Yuen Center for Functional Onco-Imaging, University of California-Irvine, Irvine, CA, United States

Introduction

Single-voxel MR spectroscopy has been proven helpful in improving diagnosis and treatment monitoring of breast cancer [1, 2]. However, the low spatial resolution of single-voxel MRS technique is not optimal for studies of small lesions and large heterogeneous lesions, both in the setting of initial diagnosis and in detection of residual or recurrent tumor following therapy. The present study implemented a two-dimensional multi-voxel ^{1}H-CSI spectroscopy technique to improve the spatial resolution by a factor of two. This technique is particularly useful in patients with advanced disease that often covers a large region and presents with a high heterogeneity. The ^{1}H-CSI study was performed in patients before and after 1 cycle AC (doxorubicin and cyclophosphamide) treatment. The Cho-positive area, Cho level, and water-fat ratio were measured before and after therapy and compared to assess the therapy induced changes.

Methods

Six patients with advanced stage breast cancer who elected to receive neoadjuvant chemotherapy were included in this study. A baseline scan was done prior to the start of neoadjuvant chemotherapy. Patients were re-evaluated within 2~3 weeks after completion of the 1st cycle AC treatment. The examinations were performed on a Phillips Eclipse 1.5 T MR system, with the body coil as the transmitter and a dedicated bilateral breast coil as a receiver. ^{1}H-Chemical shift imaging was performed using a PRESS spin-echo sequence. The CSI was measured from the enhanced areas determined from DCE-MRI. The acquisition parameters were TR/TE 2000/270 ms, field of view (FOV) = 8×8 cm^2 , 8 x 8 phase-encoding steps, and 8 acquisitions. After the CSI grids have been placed, a set of fully relaxed, “unsuppressed” CSI data were acquired to measure the water and lipid peaks. The water-fat ratio was calculated using the respective peak areas. Then the dual water and fat suppression was implemented for detection of Choline. Water suppression was accomplished with “CHESS” pulses, and lipid suppression was achieved using an adjustable lipid saturation pulse. The spectrum from each voxel was analyzed, and if a Cho peak at 3.22 ppm was observed, this voxel was counted as a Cho-positive voxel. The Cho SNR was obtained for quantitative analysis, which was calculated as the Cho peak area at 3.22 ppm normalized to the background noise level measured between 7.0 and 9.0 ppm. Finally, the Cho levels from all voxels were reconstructed into the Cho map, as shown in Fig.1.

Results

Cho metabolite was detected in all patients before and after the 1st cycle AC treatment. Figure 1A and 1B show Cho metabolite maps from Patient #1 before and after chemotherapy. It can be noted that the area with positive Cho after chemo (in Fig. 1B) was substantially reduced compared to the size in the baseline study (in Fig. 1A), and a reduction in Cho intensity was also noted. The area with the highest Choline (coded in red) in the baseline study was no longer seen after 1 cycle AC. In each study the Choline-positive voxels were counted, and used as an indication of metabolically active area. The Cho-positive voxels reduced from 16 to 7 in this patient. Figure 1C and 1D show the Cho maps from patient #3 before and after 1cycle AC treatment. The Cho-positive voxels increased from 7 to 13, and the voxels with a high Cho peak (coded in red) increased. In every study the mean water-fat ratio and the mean Cho SNR values obtained from all Cho-positive voxels were calculated. The results for each patient before and after chemo are summarized in Table 1. The water-fat ratio after chemotherapy was reduced in 5 out of 6 patients, statistically significant ($p < 0.01$). However, the mean Cho SNR was reduced in only two patients (patient #1 and #6), and only patient #1 showed a reduced Cho-active area as indicated by the decreased Cho-positive voxel number.

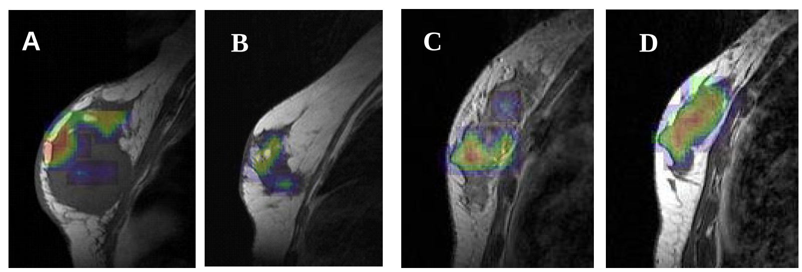

Figure 1. Patient #1: before (A) and after 1cycle AC treatment (B), and the Cho metabolite maps from Patient #3: before (C) and after 1cycle AC treatment (D). It can be noted that Patient #1 had smaller Cho-active area and lower intensity after treatment, but Patient #3 had a larger Cho-active area and higher Cho intensity after treatment.

Discussion

In this study, we demonstrated that ^{1}H-CSI is a suitable technique for monitoring the response of breast cancer to neoadjuvant chemotherapy. The multi-voxel localized ^{1}H-CSI can cover a large area, which was particularly important for cases with advanced stage diseases. The water-fat ratio has been reported as a useful index to monitor the response of breast cancer to neoadjuvant chemotherapy, and in our study the reduction of water-fat ratio was found in 5 out of 6 patients. In contrast, the reduction of Cho SNR was observed only in 2 patients, and only one patient showed a reduced Cho-active area (Cho-positive voxels). All patients included here are still undergoing chemotherapy, and the significance of our findings can be better interpreted when the final treatment outcome results become available. We will explore whether the early changes of Cho level (maximum or the mean), or the water-fat ratio, or combination of these measures, can be used to predict final therapy outcome.

Table 1. The Cho-positive voxels, Cho SNR, and water-fat ratio measured in 6 patients before and after 1 cycle AC neoadjuvant chemotherapy

	Patient #1		Patient #2		Patient #3		Patient #4		Patient #5		Patient #6	
	Pre (16)	Post (7)	Pre (3)	Post (4)	Pre (7)	Post (13)	Pre (4)	Post (5)	Pre (3)	Post (5)	Pre (8)	Post (8)
Cho SNR	3.5±1.7	1.7±0.5	1.2±0.4	1.8±0.6	1.8±0.5	1.9±0.7	1.3±0.3	1.6±0.7	1.3±0.7	1.4±0.3	1.1±0.4	0.9±0.5
W/Fratio	14±20	0.6±0.8	0.13±0.06	1.1±1.6	0.7±0.2	0.6±0.3	2.3±1.2	1.9±1.5	0.3±0.2	0.2±0.2	1.0±0.8	0.2±0.1

Pre (#) = Number of Cho-positive voxels before chemotherapy; Post (#) = Number of Cho-positive voxels after chemotherapy;

References

1. Jagannathan et al. NMR Biomedicine 11:414-422 (1998). 2. Jagannathan et al. British J Cancer 84(6):1016-1022 (2001).

Acknowledgement This work was supported in part by NIH/NCI R01 CA90437