Can Proton MR Spectroscopy Provide Useful Information for Characterizing Estrogen Receptor Status in Breast Cancer?

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Introduction

Estrogen receptor (ER) status has been used in the clinical management of breast cancer both as a predictive factor for treatment and as a prognostic factor for survival. Compared with ER-positive cancer, ER-negative cancer has a poorer clinical outcome and shorter median survival [1, 2]. ER-negative cancer was more aggressive, with bigger tumor size, more prominent tumor infiltration showing non-mass-type enhancements on magnetic resonance imaging (MRI) features [3]. ER-negative tumors showed higher intratumoral microvessel density than did ER-positive tumors [4]. ER-negative breast carcinoma was also associated with an increased choline kinase (ChoK) activity [5]. The ChoK and its product, phosphocholine (PCho), have been implicated in human carcinogenesis. Elevated level of choline-containing compounds (tCho) is a tissue proliferative marker for malignant tumor [6]. In this study we reported a quantitative proton MR spectroscopy (^{1}H-MRS) study to further investigate if the tCho level shows difference between ER-positive and -negative breast cancers. The aim of our study was to determine whether in vivo ^{1}H-MRS can provide useful information for characterizing ER status in breast cancer.

Methods

Forty-seven breast cancer patients, who were scanned with the MRI/MRS protocol, were included in this study. The inclusion criteria were patients with biopsy confirmed diagnosis of malignant lesions that measured 1.8 cm or larger on MR images. All 47 patients had histopathologically an invasive ductal carcinoma. The ER status was examined by pathologists at hospital and was considered negative if immunoperoxidase staining of tumor cell nuclei in the biopsy specimen was less than 5%. The MRI/MRS study was performed using a 1.5 T MR scanner with a standard bilateral breast coil (Philips Medical Systems, Cleveland, Ohio). After the MRI study was completed, single-voxel ^{1}H-MRS was performed using a point-resolved spin-echo sequence (PRESS). The spectroscopic voxel was carefully positioned to maximize the coverage of the contrast-enhanced lesions while minimizing the inclusion of adipose tissue. The voxel size was from 2.4 to 8.0 mL. The jMRUI software package (http://sermn02.uab.es/mrui/) was used for time-domain analysis. AMARES [7], a widely used quantitation tool for MRS data, was employed to fit spectra. In this study, a Gaussian lineshape model was chosen to quantify the tCho peak (Figure 1). The Cramer-Rao lower bound (CRB) was used as a measure of fitting accuracy. Absolute quantification of tCho concentration was obtained using the water peak from the unsuppressed spectrum, fit at 4.7 ppm, as an internal reference. The tCho concentration was calculated using measured T1 and T2 values for intensity correction [8].

Results

Of 47 patients, 27 (57%) had ER-positive cancers and 20 (43%) had ER-negative cancers. The progesterone receptor (PR) status was available for 42 patients, including 22 ER-positive patients (20 PR-positive and two PR-negative) and 20 ER-negative patients (19 PR-negative and one PR-positive). The mean age was 51 years (range, 31 to 68 years) for ER-positive patients and 47 years (range, 31 to 68 years) for ER-negative patients (P = 0.264). The mean tumor size was 3.4 cm (range, 1.8 to 7.1 cm) for the ER-positive group and 4.2 cm (range, 1.8 to 8.6 cm) for the ER-negative group (P = 0.146) (Figure 2A). On the basis of the criterion (i.e., CRB < 100%), tCho detection rate was higher in ER-negative group (16/20, 80%) than in ER-positive group (15/27, 56%), but not reaching significant level (P = 0.083). For these 31 lesions with tCho detection, the measured tCho levels ranged from 0.19 to 7.84 mmol/kg (mean ± SD, 2.13 ± 1.96 mmol/kg), which are well within the previously published in vivo tCho concentration. The ER-positive group had a lower mean tCho concentration than the ER-negative group, as shown in Figure 2B, but no significant difference was observed (2.01 vs. 2.24 mmol/kg, P = 0.677).

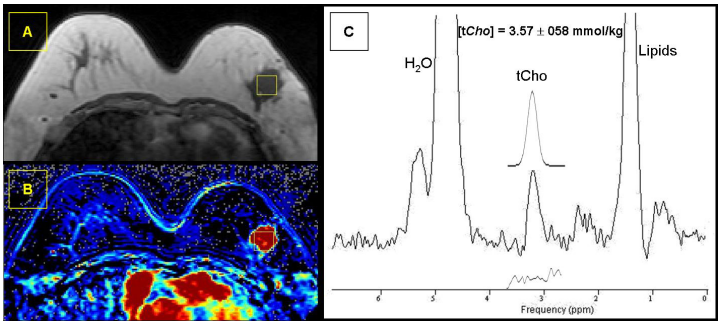

Fig. 1 MRI/MRS of a 52-year-old patient with an ER-positive invasive ductal carcinoma. The lesion was 2.6 cm and the spectroscopic voxel (size, 2×2×2 cm^3) was on the pre-contrast axial image (A) and on the color-coded subtraction image (B). An elevated tCho peak is clearly visible at 3.20 ppm in the spectrum (C).

Discussion

In our study, the tCho detection rate of in vivo ^{1}H-MRS in ER-negative group, although higher, wan not significantly different from that of ER-positive group, and also the absolute tCho levels did not appear to be related to ER status. The reason why our finding was not significant might be due to the heterogeneity of the breast cancer tissue. As shown in Figure 2B, the large range in tCho concentration may reflect the heterogeneous nature of breast lesions. Gribbestad et al. [9] reported that phosphatidylcholine, a precursor of tCho-derived phospholipids, also showed a large variation even among the same tumor types. In addition to the intrinsic heterogeneous nature of breast tumors, the limitation of in vivo ^{1}H-MRS detection may also contribute to a complicated tCho distribution pattern. tCho detection may be difficult in diffuse-enhancement-type cancers because of the intermingling of tumor cells with adipose tissues. Diffusive-enhancement type cancer showed a much lower overall tCho level than mass-type cancer [8]. From our present study, it was therefore suggested that that in vivo quantitative ^{1}H-MR spectroscopy can not provide useful information for characterizing ER status in carcinoma of the breast.

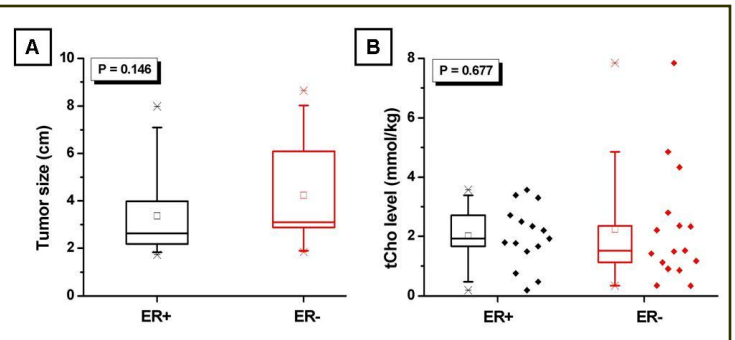

Fig. 2 Comparison of tumor size and tCho in ER-positive and negative groups. There was no significant difference in tumor size (Figure 2A) and tCho level (Figure 2B) between these two groups.

References

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