Correlation between Choline and Contrast Enhancement in Human Breast Cancer Measured by Quantitative 1H Single-Voxel MR Spectroscopy and Dynamic Contrast-Enhanced MRI

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Purpose

High resolution dynamic contrast-enhanced MR imaging (DCE-MRI) has evolved into a standard approach for detection and diagnosis of breast lesions. Recently, in vivo proton MR spectroscopy (^{1}H-MRS) has been shown to improve cancer diagnosis based on elevated choline-containing compounds (Cho). Huang et al [1] and Meisamy [2] have demonstrated that the addition of ^{1}H-MRS can improve the specificity of DCE-MRI in the diagnosis of breast cancer. However, despite the wide application of DCE-MRI and ^{1}H-MRS in breast cancer, the correlation between the obtained vascular and metabolic information was rarely investigated. The quantitative measurements of ^{1}H-MRS and DCE-MRI from corresponding tissues were performed in patients with Cho-positive (signal-to-noise ratio > 2) breast cancer at 1.5T. The purpose of this study was to investigate the correlation between Cho on ^{1}H-MRS and contrast enhancement parameters (maximum enhancement percentage- Max%, K^{trans}, and k_{ep}) measured by DCE-MRI in malignant breast lesions.

Methods

Seventeen patients with 21 histological-proven breast cancer were included in this MR study. The examinations were performed on a Philips Eclipse 1.5 T MR system with the dedicated bilateral breast coil. After DCE-MRI scan, single-voxel MRS was performed using a PRESS sequence with water and fat suppressions. 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 in malignant breast tumors was calculated with Eq. (1) and was expressed as a concentration in units of mmol/kg. The used T_2 relaxation times were 269 ms for Cho, and 97 ms for water. The T_1 relaxation times were 1513 ms for Cho, and 746 ms for water [4]. For each MRS voxel, DCE-MRI enhancement kinetics was measured from tissues covered within that voxel (Fig. 1). A maximum enhancement (Max%) at 2 minutes after contrast injection (Fig.2) was calculated with Eq. (2). The obtained percent enhancement was assumed to be proportional to the total contrast concentration in tissue C_t, and was fitted using the standard Tofts model [3] to obtained two fitting parameters K^{tran} (%/min) and k_{ep} (1/min) in Eq. (3).

$$[Cho] = \frac{n_{H_2O}}{n_{Cho}\,MW_{H_2O}} \times \left(\frac{S_{Cho}}{S_{H_2O}} \times \frac{\sqrt{NS_{H_2O}}}{\sqrt{NS_{Cho}}} \right) \times \left(\frac{f_{T_1 H_2O}}{f_{T_1 Cho}} \times \frac{f_{T_2 H_2O}}{f_{T_2 Cho}} \right) \quad (1),$$

$$SE(t) = \frac{SI(t) - SI(0)}{SI(0)} \times 100\% \quad (2),$$

$$\frac{dC_e}{dt} = K^{trans}(C_p - C_e / v_e) = K^{trans} C_p - k_{ep} C_e \quad (3)$$

Results

After the T_1 and T_2 corrections, the Cho levels from 21 MR spectra ranged from 0.73 – 11.47 mmol/kg (mean ± SD, 4.65 ± 3.25). Figure 1 shows 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 (Fig. 1; Left). The Cho peak at 3.23 ppm is clearly visible in the water-fat suppressed spectrum (Fig. 1; Right). The measured [*Cho*] = 3.97 ± 0.19 mmol/kg. The corresponding DCE-MRI kinetics from the selected MRS voxel marked on Fig. 1(Left) is shown in Fig. 2 (Left). The symbol is the experimentally measured enhancement percentage, and the line is the best fitting results using the 2-compartmental pharmacokinetic model [3]. The association between Cho level and DCE-MRI parameters (Max%, K^{trans} and k_{ep}) was investigated among all 21 cases. Figure 2 (Right) shows the scattered plot between Cho level and kinetic parameter k_{ep}. There was a significant trend that a higher Cho level was associated with a higher wash-out rate (r = 0.045, p = 0.035). However, no relationship was found between the Cho level and the Max% value (r = -0.11, p = 0.623), or K^{trans} value (r = 0.05, p = 0.844).

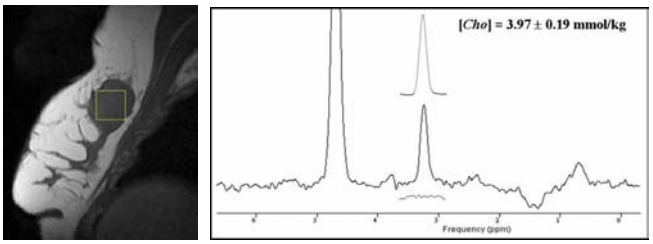

Figure 1: Sagittal view pre-contrast image, one hypointense lesion was clearly noted (Left). The elevated Cho concentration was measured from the selected voxel (Right).

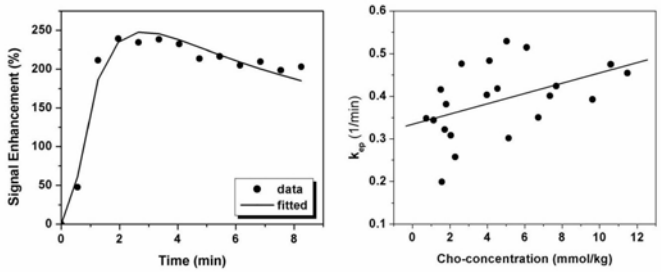

Figure 2: (Left) shows the corresponding kinetic enhancement from MRS voxel labeled in Fig. 1 (Left). The correlation between Cho level and parameter k_{ep} was measured among 21 patients with Cho-positive (Right).

Discussion

The combined use of ^{1}H-MRS and DCE-MRI can provide metabolic and vascular functional information, which can be acquired during the same MR imaging session. The measured Cho levels in this work were within a range of 0.73 – 11.47 mmol/kg, which was consistent with previously published value (i.e., 1.38 – 10 mmol/kg) by Bolan et al [5]. A significant correlation was found between the Cho level and k_{ep}, indicating that in tissues with a higher Cho level there was a higher wash-out in DCE-MRI. The result suggested that despite the heterogeneous nature of breast tumors, there was a positive correlation between Cho metabolism and vascular permeability due to angiogenesis activity. Since Cho seen on MRS is thought to derive from the cell membrane and thus to reflect cell proliferation and a higher vascular permeability is required to support the newly formed tumor vessels, this might explain the correlation between these two measures if cautiously interpreted. The wash-out phase in enhancement kinetics was very important in making differential diagnosis. However, it was common for a malignant tumor to show a plateau phase in enhancement kinetics not the wash-out phase, and as such a enhancement kinetic showing fast wash-in then reached to a plateau is also considered as suspicious of malignancy. In this situation the addition information of Cho concentrations may be of value for improving the specificity. We believe that the quantitatively combined ^{1}H-MRS and DCE-MRI (which can be completed in one imaging session) may have a potential clinical application in breast cancer diagnosis.

References [1]. Huang et al. Radiology 232(2):585-91 (2004). [2]. Meisamy et al. Radiology 236(2):465-75 (2005). [3]. Tofts et al., JMRI 7(1):91-101 (1997). [4]. Baik et al., MAGMA 19:96-104 (2006). [5]. Bolan et al., MRM 50: 1134-1143 (2003).

Acknowledgement This work was supported in part by NIH/NCI R01 CA90437 and CA BCRP #12FB-0031.