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Original

Proton (^{1}H) MR Spectroscopy of the Breast at 3.0T: Detectability of the Choline Peak of Breast Cancer in Comparison with a 1.5T Imager

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Abstract: ^{1}H-MR spectroscopy (MRS) of the breast demonstrated that choline could be detected in breast cancers. The purpose of this study was to evaluate the detectability of the choline peak (Tcho) in breast cancer using a 3.0T imager. A total of 52 female patients who underwent MR imaging were evaluated. Localization methods included the SVS and PRESS, with acquisition times of approximately 5 minutes. Correlations among tumor size, histological type, and the presence of Tcho were evaluated. Of 52 breast lesions that were pathologically diagnosed, 50 were malignant [45 invasive ductal carcinomas (IDC), five ductal carcinomas in situ (DCIS)] and 2 were benign. The presence of Tcho was evaluated in 50 cases. The average diameter of malignant tumors was 2.2 cm and that of benign tumors was 1.9 cm. Tcho was identified in 24 of 48 breast cancers (sensitivity 50%, specificity 100%). There was a significant difference between the identification in tumors according to tumor size. Tcho was identified in 76.9% of IDC cases with a diameter greater than the voxel size (1.5 cm), while it was identified in only 17.6% of tumors less than 1.5 cm in size. Tcho was identified in approximately 77% of breast cancer tumors overall with a diameter greater than the voxel size. The result was comparable with the detectability at 1.5T, although the acquisition times at 3.0T were much shorter than at 1.5T. The advantages at 3.0T include the ability to investigate smaller lesions within a shorter time frame.

Key words: breast, MR Spectroscopy, cancer, choline, 3.0 Tesla

Introduction

Magnetic resonance imaging is highly sensitive for detecting breast lesions in general. However, the specificity for malignant tissue is relatively low. The differentiation of malignant from benign breast lesion in contrast-enhanced MRI is determined by tumor morphology and kinetic analysis of dynamic studies. Breast proton magnetic resonance spectroscopy

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(^{1}H-MRS) can demonstrate molecular information of the breast lesions[1-3]. With the addition of the tissue metabolism analysis to morphologic and kinetic analysis, the differentiation of malignant from benign breast lesions will be improved. MRS of the breast demonstrates the presence of choline (Cho), which can be detected in breast cancers, where as it usually undetected in normal breast tissues[2, 5-10]. Breast MRS is proposed as an adjunct to MRI examinations to improve the specificity of detecting malignant breast lesions. Recently, several investigators reported the efficacy of MRS of the breast at 1.5T[6-12]. However, few studies have evaluated MRS of the breast at 3.0T. This study therefore assessed detection of the Cho peak in breast cancer using a 3.0T imager.

Materials and Methods

The study group comprised 52 female patients aged 37-83 years (mean : 59.7 years) who underwent diagnostic breast MR imaging from June 2008 to August 2009. Patients undergoing neo-adjuvant chemotherapy for breast cancer were excluded. All breast lesions were histopathologically diagnosed by surgical resection or biopsy. All MR imaging was performed with the patients in the prone position on a 3.0T magnet (MAGNETOM Trio A Tim System ; Siemens-Asahi Medical Technologies). All examinations were performed bilaterally using an open breast array coil. MRS localization methods used were a single-voxel system (SVS) and a PRESS (point-resolved spectroscopy) sequence. The following acquisition parameters were used : TR = 2000 msec, TE = 100 msec, average = 150, bandwidth = 1200 Hz, vector size = 1024, voxel size = 15 × 15 × 15 mm, acquisition time = 5 min and 8 sec. The selection of the voxel was non-contrast MRI, or contrast-enhanced MRI when necessary. Contrast material (gadodiamide hydrate, 15 ml ; Omniscan, Daiichi Sankyo, Japan) was intravenously injected followed by a saline flush. Detection of the Cho peak was evaluated visually by two radiologists in consensus. Presence of the Cho peak was correlated with tumor size and histological type.

Results

Of 52 breast lesions, 50 were pathologically diagnosed as malignant tumors, comprising 45 invasive ductal carcinomas (IDC) and 5 ductal carcinomas in situ (DCIS). There were 2 benign tumors, comprising cyst and normal breast tissue. In 2 of the 52 cases, the Cho peaks were uninterpretable due to signal contamination. The remaining fifty patients were evaluated for the presence of the Cho peak. The average diameter of malignant tumors was 2.2 cm and that of benign tumors was 1.9 cm.

Figs. 1-3 represent MRI and MRS images of patients with IDC with tumors of 2.2 × 1.0 cm, 1.2 × 1.0 cm, and 3.0 × 2.8 cm in diameter, respectively. Fig. 1 shows Cho peak detection (positive). Fig. 2 demonstrates the absence of a Cho peak (negative). Fig. 3 shows a case where it was not possible to interpret the Cho peak due to contamination by noise (uninterpretable).

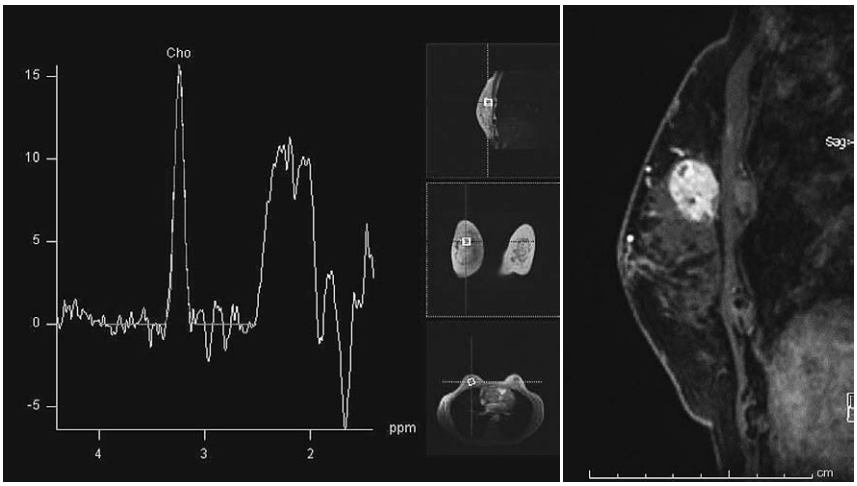


Fig. 1. A 64-year-old patient with an invasive ductal carcinoma (tumor size : 2.2 × 1.0 cm).
a : The MRS spectrum is positive for a choline peak.
b : Contrast-enhanced MRI showing a heterogeneous enhanced tumor.

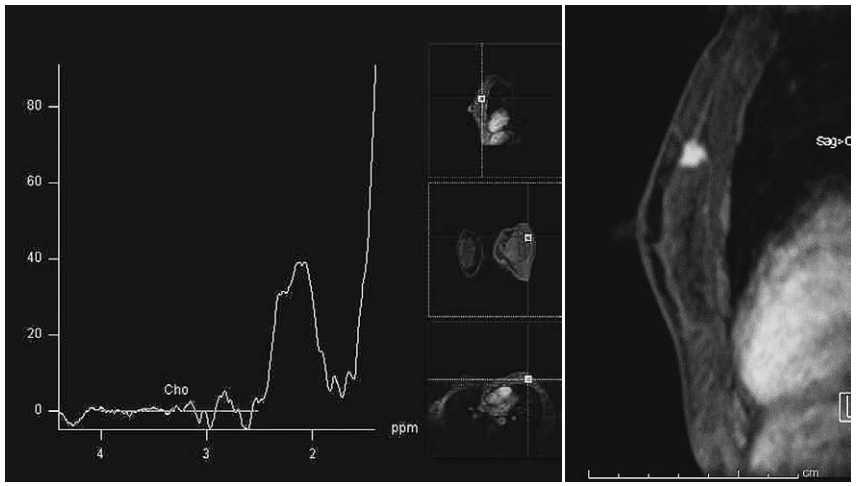
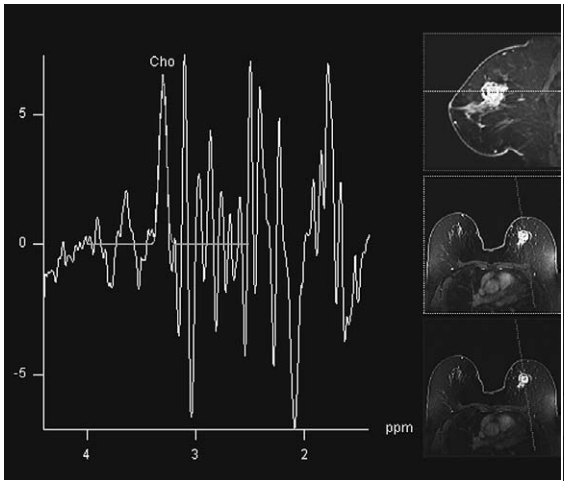
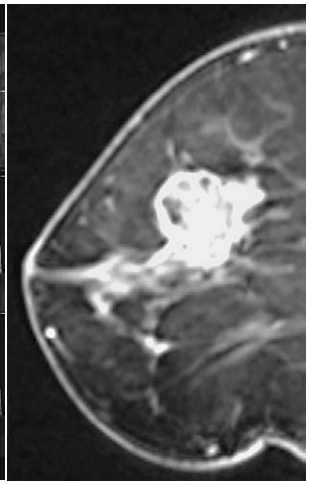


Fig. 2. A 45-year-old patient with an invasive ductal carcinoma (tumor size : 1.2 × 1.0 cm).
a : The MRS spectrum is negative for a choline peak.
b : Contrast-enhanced MRI showing a homogeneous enhanced tumor.

Table 1 details the relationship between the presence of the Cho peak and malignancy of the tumors. Cho peaks were detected in 50.0% of malignant lesions (24 / 48), making the sensitivity 50.0%. The specificity was 100%, and the positive predictive value was 50.0%. Benign lesions showed no Cho peak (0%). Table 2 indicates the relationship between the presence of the Cho peak and tumor size. Cho peaks were detected in 76.9% (20 / 26) of tumors with a size greater than the voxel size (≧1.5 cm), whereas Cho peaks were detected in only 17.6% of the tumors < 1.5 cm in diameter (3 / 17). There was a significant difference

a





b

Fig. 3. A 65-year-old patient with an invasive ductal carcinoma (tumor size : 3.0×2.8 cm).
a : The MRS spectrum could not be evaluated due to signal contamination. This is an uninterpretable finding.
b : Contrast-enhanced MRI showing a heterogeneous enhanced tumor.

Table 1. MRS results for the relationship between the detectability of the choline peak between malignant and benign tumors

	Benign (*n*=2)	*Malignant* (*n*=48)
Choline positive	0	24
Choline negative	2	24
Positive predictive value (%)	0	50.0
Sensitivity (%)	0	50.0
Specificity (%)	0	0

Table 2. The relationship between the detectability of the choline peak by MRS and tumor size

Tumors size	*Cho positive*	*Cho negative*	*total*	%
Tumor size > *1.5 cm*	20	6	26	76.9
Tumor size < *1.5 cm*	3	14	17	17.6
DCIS	1	4	5	25.0
Total	24	24	48	

Cho, choline peak ; DCIS, ductal carcinoma in situ

between the detectability of the Cho peak by voxel size ($P < .01$). In cases of DCIS, Cho peaks were detected in only 20.0% of cases (1 / 5).

Discussion

MRI signals come mainly from protons found in water and lipids. In MRS, proton

Table 3. Results of the MRS study of breast tumors compared with past studies that used a 1.5T imager

Study	*No. of malignant lesions*	*No. of benign lesions*	*Sensitivity* (%)	*Specificity* (%)	*Positive predictive value* (%)	*Voxel size* $(cm)^3$
Roebuck *et al* (1998) [8]	10	7	70	86	88	(0.9)-(2.1)
Kvistad *et al* (1999) [7]	11	11	82	82	82	(1.0)-(2.9)
Cecil *et al* (2001) [10]	23	15	83	87	90	(1.0)-(1.5)
Yeung *et al* (2001) [6]	24	6	92	83	97	(1.0)-(4.6)
Tse *et al* (2003) [11]	19	21	89	100	100	not described
Huang *et al* (2004) [12]	18	12	100	67	82	(1.2)-(3.0)

signals originating from hydrogen atoms attached to various metabolites of interest such as N-acetyl-aspartate (NAA) (2.02 ppm), choline (Cho) (3.2 ppm), creatine (Cr) (3.02 ppm), myo-inositol (mI) (3.57 ppm), and lactate (Lac) (1.32 ppm) are detectable[2, 3]. Proton magnetic resonance spectroscopy (^{1}H-MRS) can obtain molecular information in a non-invasive manner.

Breast ^{1}H-MRS can demonstrate molecular information about the breast lesions. There are increased composite choline metabolites (free choline, phosphocholine, and glycerol phosphocholine) in breast cancers, whereas choline is generally undetectable in normal breast tissue[2, 4-10]. Detection of the choline is therefore a useful criteria for differentiating between benign lesions and cancer, based on elevated levels of choline compounds being a marker of an active tumor. This is an especially useful method to complement tissue metabolism analysis with morphological and kinetic analysis.

Sensitivity and detectability of the choline peak on a 3.0T imager in comparison with a 1.5T imager.

Recently several investigators reported sensitivities of 70-100% for Cho peak detection in breast ^{1}H MRS of malignant lesions at 1.5T (Table 3). Yeung *et al*[6] reported that the sensitivity of ^{1}H MRS for detecting the Cho peak was 92%, with a specificity of 83% in all breast lesions (n = 30). In their study, the tumors were relatively large (≥1.5 cm), and they did not include tumors smaller than the voxel size[6]. In other studies, the number of tumors with a diameter greater than 1.5 cm was 73% (11 / 15) (Roebuck *et al*) and 94% (29 / 31) (Cecil *et al*)[8, 10]. In these studies, the average (largest dimension) tumor dimensions were 5.1 ± 2.6 cm (Yeung *et al*), 2.7 ± 1.0 cm (Cecil *et al*), and 2.2 ± 1.0 cm (Roubuck *et al*), which are all relatively large. In our study, 35% (17 / 48) of tumors were smaller than 1.5 cm, and the average diameter was 2.2 cm. The reason for the low detectability of the Cho peak in our study seems therefore related to the fact that we included many tumors smaller than the voxel size. On the other hand, the sensitivity in the tumors larger than the voxel diameter (1.5 cm) was 76.9% in our study, which is consistent with the prior reports using 1.5T imaging.

Of interest, the acquisition time for 3.0T MRS was about 5 minutes in our study. On the other hand, the acquisition took about 20 minutes in the study by Yeung *et al*[6], although the acquisition time at 1.5T is always much longer than is needed for 3.0T on the same tissue. Shorter acquisition times is a major advantage of using the 3.0T imager. If we made the voxel size smaller than that used in this study, the acquisition time would be slightly longer, however this slightly longer acquisition time would still likely be shorter than that of 1.5T MRS.

About 23% (6/26) of the tumors where the diameter was greater than the voxel diameter (≥1.5 cm) did not show a Cho peak. In 2 cases, the tumors had necrosis. The necrotic area of the tumor was chosen as a region of interest by the MRS spectra. In one case, the position of the tumor was close to the edge of the breast. Field inhomogeneity and chest wall motion on respiration may have been the reason for the lack of a Cho peak in this tumor. Only one of 5 DCIS cases showed a Cho peak on MRS. The prior reports suggest that DCIS may not always demonstrate a Cho peak[1, 8, 10, 11, 13], and our results supports these findings.

Tumors with a diameter less than the voxel size (<1.5 cm) showed a low sensitivity (16%). This result was attributed to the fact that small tumors contain normal breast adipose tissue around the tumor[1], decreasing the detectable composite choline signal. Although we failed to detect a Cho peak in small tumors, advances in 3.0T technology, including higher-field strength MR imagers and advances in the development of coil and sequence design may allow MRS investigation of smaller lesions within a short time frame, thereby resolving this sensitivity problem.

Conclusion

MRS demonstrated a Cho peak in 77% of breast cancers with diameters greater than the voxel size. In spite of the fact that our study included many tumors smaller than those examined in prior reports using a 1.5T imager, our results were comparable to these studies. In addition, the shorter acquisition time frame is a major advantage of the 3.0T imager. We therefore recommend the application of MRS in addition to routine MRI studies, to improve the differentiation of malignant from benign breast lesions.

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