Proton MRS at 1.5T Further Improves Specificity in Breast Cancer Detection Following Positive MRI Diagnosis

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Introduction Conventional mammography is known to have high false positive rate (60-80%) in detection of breast malignancy, resulting in unnecessary biopsies. Dynamic contrast enhanced (DCE) T_1-weighted breast MRI has been reported to have high sensitivity (88-100%), but also lower specificity (about 50%, a range of 37-97% was reported) (1). In recent years, several studies (2-4) have shown the potential of *in vivo* ^{1}H MRS for improving specificity of breast cancer detection, using the resonance of choline-containing compounds (Cho) as the marker of viable tumor.

In this ongoing study, single-voxel ^{1}H MRS examinations were performed on patients who had positive MRI findings of suspicious lesions, requiring MRI-guided interventional procedures. We sought to determine if addition of proton MRS examination is practical in a clinical setting and if proton MRS improves specificity in detection of breast malignancy, and thus may help to avoid unnecessary biopsies.

Methods 45 patients who had diagnostic breast MRI findings of suspicious lesions were recruited for this IRB-approved MRS study. The BIRADS (Breast Imaging Reporting and Data System) scores were 4 or higher. The diagnostic breast MRI protocol includes multi-slice FSE T_2-weighted MRI with fat saturation, pre-contrast 3D SPGR T_1-weighted MRI with and without fat saturation, and DCE MRI (3D SPGR) with fat saturation. The reading of MRI was based on morphology of contrast enhanced lesion and contrast wash-out kinetics (5). These patients were consented for the ^{1}H MRS examination before they underwent their scheduled MRI-guided preoperative needle localization or biopsy procedures. The pathological results were used as the reference standard for correlation analysis with the MRS data.

The MRS study was conducted with a 1.5T GE LX or a 1.5T GE Excite scanner with the body coil as the transmitter and a dedicated phased array breast coil as the receiver. Proton MRS spectra were collected following post-contrast 3D sagittal T_1-weighted MRI, but immediately before the MRI-guided interventional procedures to avoid any artifacts that might be introduced by the presence of surgical wires or bleeding. Post-contrast sagittal T_1-weighted images were used as scouts for the placement of MRS voxel which encompassed the enhanced lesion to be needle-localized or biopsied (Fig. 1). Single-voxel proton spectra were acquired with a PRESS sequence, TE = 135 ms, TR = 2 s, and 128 scan averages. The voxel size ranged from 1.6 to 11.2 cc. The total MRS scanning time, including pre-scan automatic and/or manual adjustment of shimming and water suppression, was less than 10 min.

The raw spectral data were processed off-line with GE's SAGE/IDL software, using 5 Hz line broadening, Fourier transformation, and phase and baseline corrections. The water resonance peak observed in the reference scan without water suppression was used as the reference to locate the Cho and lipid/lactate (Lip/Lac) resonance frequencies. The detection of an apparent Cho peak with S/N $\geq$ 2 at 3.23 ppm was defined as a positive finding for the MRS study, and a negative finding was defined otherwise.

Results Fig. 2a shows a representative magnified proton spectrum collected from an enhanced lesion which was later pathologically proven to be malignant invasive ductal carcinoma. An apparent Cho peak was detected with S/N > 2, indicating positive MRS finding. As an example of negative MRS findings, Fig. 2b depicts a magnified proton spectrum from a lesion that was later revealed by biopsy results to be benign fibrocystic changes. No apparent Cho peak was detected; there was only noise level signal intensity at 3.23 ppm. The positive and negative MRS findings were classified as true or false by comparison with the pathologic findings. The results of the correlation analysis were summarized in the Table.

Table Correlation Analysis of Proton MRS Results with Pathologic Findings (n = 45)

	True Positive	True Negative	False Positive	False Negative
Patient Number	27	16	2	0

There were no false negative MRS findings, showing 100% [27/(27 + 0)] sensitivity of this method in breast cancer detection; while there were two false positive findings, resulting in 89% [16/(16 + 2)] specificity. Among the 45 lesions examined, pathological analyses yielded cancer in 27 and benign findings in 18. Thus the positive predictive value of breast MRI was 60% (27/45). If biopsy had only been performed on those with positive MRS findings, the positive predictive value would have increased to 93% (27/29). Biopsy would have been spared in 36% (16/45) of the patients, and none of the cancers would have been missed.

Discussion Though more patients are still to be recruited for this ongoing study, the early results show that the specificity of proton MRS in detection of breast malignancy is significantly higher compared to that of breast MRI reported in the literature (1). The inclusion of a proton MRS scan in a clinical breast MR protocol may be potentially very valuable in disproving false positive breast MRI findings, thus sparing patients from undergoing unnecessary biopsies. As we have shown, breast MRS data acquisition can be easily implemented in a clinical setting on a 1.5T scanner. The total scanning time is short and the addition of an MRS scan to the existing MRI protocol is quite tolerable to most patients. One limitation of the study is that the lesion size was chosen to be larger than 1 cc to insure MRS sensitivity in detection of Cho peak. For smaller lesions, increasing scan averages to improve sensitivity may not be practical with consideration of patient comfort and time constraint in clinical environment. Higher field scanner, such as 3T, may be the answer for proton MRS study of sub-centimeter breast lesions.

References 1. Padhani, A.R. *JMRI* **16**, 407 (2002). 2. Huang, W. *et al., Radiology* **232**, 585 (2004). 3. Bolan, P.J. *et al., Magn. Reson. Med.* **50**, 1134 (2003). 4. Yeung, D.K.W. *et al., Radiology* **220**, 40 (2001). 5. Liberman, L. *et al., AJR* **179**, 171 (2002).

Acknowledgments DOD W81XWH-04-1-0568 for grant support.

Fig. 1

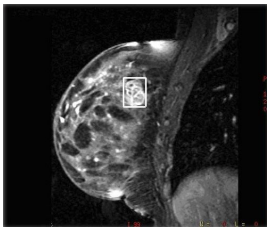

Fig. 2a

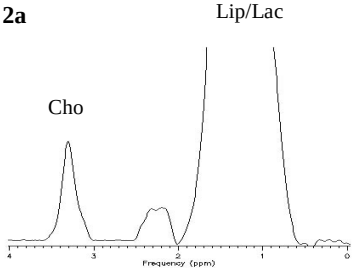

Fig. 2b