Comparisons of Water-to-Fat Ratios in Malignant, Benign Breast Lesions, and Normal Breast Parenchyma: An In Vivo Proton MRS Study

S. B. Thakur[1], L. Bartella[2], N. M. Ishill[3], E. A. Morris[2], L. Liberman[2], D. D. Dershaw[2], H. Hricak[2], J. A. Koutcher[1], W. Huang[1]

[1]Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [2]Radiology, Memorial Sloan Kettering Cancer Center, New York, NY, United States, [3]Epidemiology-Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, United States

Introduction

In recent years, several studies have demonstrated the potential of *in vivo* ^{1}H MRS for improving specificity of breast cancer detection, using the resonance peak of choline-containing compounds (Cho) as the marker of malignancy (1-4). In a few other proton MRS studies (5, 6), it was reported that the water-to-fat (W/F) ratio was higher in malignant invasive ductal carcinomas (IDCs) compared to normal breast tissue.

As part of our ongoing proton MRS study of suspicious breast lesions focused on improving specificity of breast cancer diagnosis(7). We compared the W/F ratios of malignant and benign breast lesions, as well as normal breast parenchyma, which were calculated from the reference MRS scans without water suppression. The goal was to examine if W/F ratio is a useful measure for distinguishing malignant lesions from benign lesions and normal breast tissue. A separate abstract comparing absolute Cho concentration and W/F ratio between subtypes of malignant lesions was also submitted.

Methods

Informed consent was obtained from each patient for the ^{1}H MRS examination. The MRS data from the lesions were collected from 73 patients before they underwent their scheduled MRI-guided preoperative needle localization or biopsy procedures. The pathology results showed that 33 of them had IDCs, 9 had invasive lobular carcinomas (ILCs), and 31 had benign lesions. The MRS data from normal breast parenchyma where there was no post-contrast enhancement were collected from 21 patients who underwent their clinical breast MRI screening tests. We assumed the breast tissue to be "normal" at the time of MRS acquisition based on the fact that the 6-month and 1-year follow-up MRIs of the same tissue area showed no contrast-enhancement.

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 MR spectra of the suspicious lesions were collected immediately before the MRI-guided interventional procedures. Post-contrast sagittal T_1-weighted scout images were used for placement of the MRS voxel which encompassed the enhanced lesion. Proton MR spectra of the normal breast parenchyma were acquired following the completion of the clinical MRI protocol using T_1-weighted images without fat-saturation as scouts after confirmation of no contrast enhancement. Single-voxel proton spectra were collected with a PRESS sequence, TE = 135 ms, TR = 2 s, and 128 scan averages in addition to 16 reference scans without water suppression. The size of the MRS voxel was in the range of 1.6 to 12.9 cc. The raw spectral data were processed off-line with GE's SAGE/IDL software; using 5 Hz exponential line broadening, zero filling, Fourier transformation, and phase and baseline corrections. From the reference MRS scans, the water and fat resonance peaks were identified and their peak areas were calculated using manual peak fitting routines. The line shapes of the resonances were assumed to be gaussian for area measurement.

The peak area ratio of water over fat was used as the measure of W/F ratio. Due to the highly skewed nature of the data, for statistical analysis, natural log transformations of the W/F ratios were used to normalize their distributions. Wilcoxon rank sum test was used to evaluate differences in medians between the groups. To evaluate accuracy in differentiating malignant, benign lesions, and normal tissues using W/F ratio, empirically estimated Receiver Operating Characteristic (ROC) curves were used, and the corresponding areas under the curve (AUCs) were compared (8).

Results

Fig. 1 shows the representative proton spectra obtained from reference scans without water suppression from an IDC lesion (top), a benign lesion (center), and normal breast parenchyma (bottom), revealing much higher W/F ratio of the malignant lesion compared to those of the benign lesion and normal tissue which were similar to each other. There was no significant difference ($p > 0.05$) in W/F ratio between the benign lesions (median = -0.11, range: -2.30 to 1.79) and the normal breast tissue (median = -0.69, range: -2.81 to 0.69). The AUC of the ROC curve (not shown here) for discrimination of benign masses from normal tissue was 0.28 (95% C.I. [0.14, 0.43]), indicating that W/F ratio could not be used to differentiate the two groups. Therefore, the data from these two groups were combined for comparison with the malignant group. The plots in Fig. 2 illustrate the distributions of log-transformed W/F ratios for the cancer and non-cancer (benign/normal) groups. The box gives the interquartile range (middle 50% of patients) and the line through it is the median. The difference in W/F ratio between the benign/normal group (median = -0.36, range: -2.81 to 1.79) and the malignant group (median = 1.05, range: -2.81 to 4.04) was significant ($p < 0.001$).

The AUC of the ROC curve for discrimination of the malignant group from the benign/normal group, as shown in Fig. 3, was 0.80 (95% C.I. [0.71, 0.89]) suggesting that W/F ratio may be useful in differentiating these two groups. When the W/F ratios of the malignant group were further divided into the IDC and ILC groups, it was found that the AUCs of the IDC and ILC ROC curves were 0.89 (95% C.I. [0.82, 0.97]) versus 0.46 (95% C.I. [0.31, 0.63]), indicating that W/F ratio is significantly ($p<0.001$) more accurate in detection of cancer when the cancer is IDC.

Discussion

To the best of our knowledge, this is the first *in vivo* breast MRS study comparing W/F ratios of subtypes of malignant lesions, benign lesions and normal breast parenchyma. The ROC curve analyses of the data suggest that W/F ratio alone may be useful for discrimination of malignant lesions from benign lesions/normal breast tissue. In particular, with significantly higher W/F ratios compared to ILCs, IDCs can be differentiated from benign lesions/normal tissue with high sensitivity and specificity. This is consistent with the previous MRS studies (5, 6). In the concurrent study of Cho peak detection (7), no Cho signal was detected in two IDC lesions, resulting in false-negative findings. When the W/F ratios were taken into consideration, these two lesions were easily classified as malignant. Therefore it may be feasible to combine Cho signal detection with W/F ratio measurement to further improve the sensitivity of Cho-detection-based MRS method in breast cancer detection, which suffers significantly when the lesion size drops below two cm in diameter (9). Further investigation is needed.

References: 1. W. Huang *et al., Radiology* **232**, 585 (2004). 2. P.J. Bolan *et al., Magn. Reson. Med.* **50**, 1134(2003). 3. M.A. Jacobs *et al., JMRI* **19**, 68 (2004). 4. D.K.W. Yeung *et al., Radiology* **225**, 190 (2002). 5. N.R. Jagannathan *et al., NMR in BioMed.* **11**, 414 (1998). 6. M.A. Thomas *et al., JMRI* **14**, 181 (2001). 7. W. Huang *et al., PISMRM* 133 (2005). 8. E.R. DeLong *et al., Biometrics* **44**, 837 (1988). 9. R. Katz-*Brull et al., J. Natl. Cancer Inst*. **94**, 1197 (2002).

Fig. 1

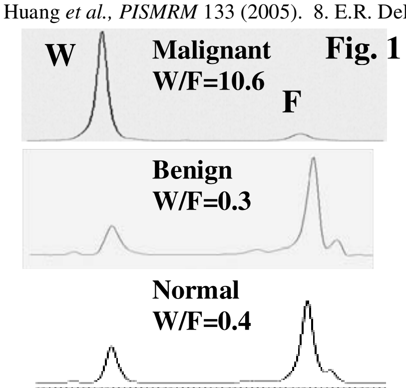

Fig.2

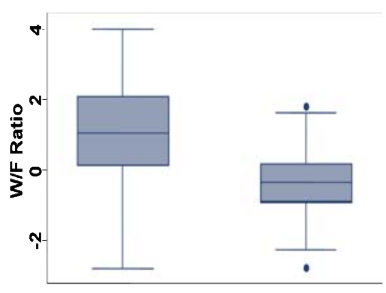

Fig.3