# Discrimination of Choline-Positive Invasive Breast Carcinomas Using Water-to-Fat Ratio: A Proton MRS Study

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**Introduction**

Breast MRI has been shown to have excellent sensitivity (88-100%), but rather unsatisfactory specificity (about 50%, a range of 37-97% was reported) (1). 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 (2-5). However, so far, no MRS studies have been stratified by different types of breast pathology.

As part of our ongoing proton MRS study of suspicious breast lesions focused on improving specificity of breast cancer diagnosis (5), we examined the Cho concentrations and water-to-fat (W/F) ratios of the malignant breast lesions. The goal was to determine if Cho concentration and/or W/F ratio can be used to discriminate invasive ductal carcinoma (IDC) from invasive lobular carcinoma (ILC). A separate abstract comparing W/F ratios between malignant, benign lesions, and normal breast parenchyma was also submitted.

**Methods**

All the patients were consented for $^1$H MRS examinations before they underwent their scheduled MRI-guided preoperative needle localization or biopsy procedures. MRS studies were 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 were collected following post-contrast 3D sagittal $T_1$-weighted MRI, but immediately before 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 scout images were used for the placement of MRS voxel which encompassed the enhanced lesion. 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.

42 patients with pathologically proven breast malignancies (33 IDCs and 9 ILCs) were Cho-positive (signal-to-noise ratio (S/N) >= 2 (2, 5)). The MRS data from these patients were further analyzed. 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 peak area ratio of water over fat was used as the measure of W/F ratio. Absolute lesion Cho concentrations [Cho] were calculated using the method introduced by Bolen et al. (3) with the water signal as the internal reference.

Due to the highly skewed nature of the data, for statistical analysis, natural log transformations were used on [Cho] and W/F ratio to normalize their distributions. Wilcoxon rank sum test was used to evaluate differences in medians between the groups. To evaluate accuracy in differentiating between ILC and IDC cancers using [Cho] and W/F ratio, empirically estimated Receiver Operating Characteristic (ROC) curves were used, and the corresponding areas under the curve (AUCs) were compared (6).

**Results**

Fig. 1 shows the proton spectra with water suppression (left panels) and without water suppression (right panels) from an IDC and an ILC, respectively. Cho peaks were clearly detected in both malignant lesions. The W/F ratio was much higher in the IDC than the ILC. The plots in Fig. 2 illustrate the distributions of log-transformed [Cho] (Fig. 2A) and W/F ratio (Fig. 2B) for the IDC and ILC groups. The box gives the interquartile range (middle 50% of patients) and the line through it is the median. There was no significant difference (p=0.51) in [Cho] between the IDCs (median = 1.57 mM, range: -2.04 to 3.85 mM) and the ILCs (median = 0.74 mM, range: -0.42 to 3.17 mM). However, the W/F ratio was significantly ($p < 0.001$) higher in the IDCs (median = 1.65, range: -2.81 to 4.04) compared to the ILCs (median = -0.54, range: -1.20 to 0.26).

The ROC curves in Fig. 3 show that the W/F ratio performs significantly ($p < 0.001$) better than [Cho] in differentiating the two types of malignancies, with the AUC of the former being 0.95 (95%C.I. [0.89, 1.0]) while that of the latter being 0.54 (95% C.I. [0.31, 0.76]). For example, IDCs can be discriminated from ILCs with 97% sensitivity and 89% specificity with a W/F ratio threshold of 1.1, or 82% sensitivity and 100% specificity with a W/F ratio threshold of 1.5.

**Discussion**

The results of this preliminary proton MRS study suggest that although the malignant breast lesions exhibit detectable Cho signal, which may improve the specificity of breast cancer diagnosis (2-5), there is no significant difference in Cho level between the two major invasive carcinomas: IDC and ILC. On the other hand, W/F ratio measured from MRS data can be used to differentiate these two malignancies with high sensitivity and specificity. Identification of breast cancer subtypes at radiological diagnostic stage may help in clinical management of the patients. This difference in W/F ratio between IDCs and ILCs may be attributed to the fact that in ILCs, the tumor cells from different lobules are connected as a single strand extending through fatty breast tissue; while in IDCs, tumor cells invade healthy tissues and form solid tumors (7). Measurement of W/F ratio can be easily achieved using the reference MRS scans, which take less than one minute of extra scanning time, and therefore is clinically practical. Furthermore, W/F ratio may be important in monitoring breast cancer treatment, as Cho signal may become undetectable following therapy (8, 9).

**References**

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**Fig.1**

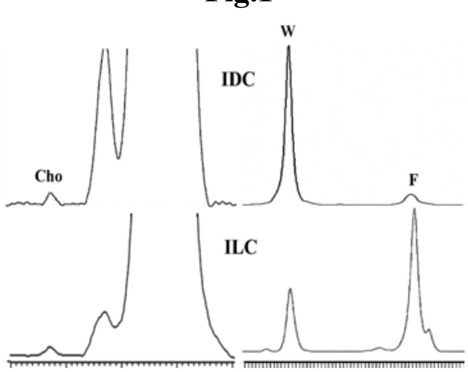


**Fig.2**

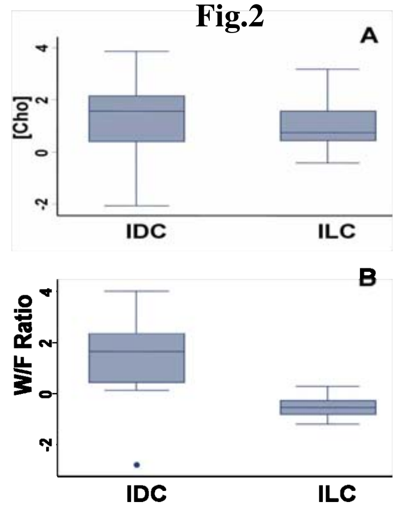


**Fig.3**