# Comparison of Choline Concentration and Water-to-Fat ratio as Biomarkers for Discrimination of Mass/Non-Mass Malignant and Benign Breast Lesions

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**Introduction**

MRI contrast enhancement of breast lesions can usually be described as either mass or non-mass enhancement. Non-mass enhancement is defined as the "enhancement area that is not a mass", may extend over large or small regions, with internal enhancement being discrete from normal enhancing parenchyma (1). Although non-mass enhancement can be due to benign hormonal changes, it also occurs in malignancies (2). In recent years, several studies have demonstrated the potential of *in vivo* $^1$H MRS as an adjunct to breast MRI for improving specificity of breast cancer detection, using the resonance peak of choline-containing compounds (Cho) as the marker of malignancy (3-5). It has also been reported that water-to-fat (W/F) ratio can be used to differentiate malignant breast lesions from benign lesions and normal breast tissue (6) and to monitor the effects of cancer treatment with neoadjuvant chemotherapy (7). Our recent study (8) shows that based on signal to noise ratio, Cho is also a useful biomarker for diagnosis of non-mass malignant lesions *versus* benign lesions. In this study, we compare capabilities of absolute Cho concentration [Cho] and W/F ratio in differentiating mass and non-mass malignant breast lesions from benign lesions.

**Methods**

Informed consent was obtained from each patient for the $^1$H MRS examination. The MRS data were collected from 89 patients during their clinically scheduled MRI-guided preoperative needle localization or biopsy procedures, just before needle insertions. All MRS studies were conducted with a 1.5T GE LX or Excite systems with the body coil as the transmitter and a dedicated 4- or 7-channel phased array bilateral breast coil as the receiver. Post-contrast sagittal $T_1$-weighted scout images with fat saturation were used for placement of the 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 to 13 cc with the median of 3.5 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: fat was used as the measure of W/F ratio. Absolute lesion [Cho]s were calculated using the method introduced by Bolan et al. (5) with the water signal as the internal reference. To evaluate accuracy in differentiating mass and non-mass malignant lesions from benign lesions using [Cho] and W/F ratio, empirically estimated Receiver Operating Characteristic (ROC) curves were generated and the corresponding areas under the curve (AUCs) were compared for statistical significance (9).

**Results**

The pathology results showed that 57 of the 89 lesions were malignant [39 invasive ductal carcinomas (IDC), 10 invasive lobular carcinomas (ILC), 6 ductal carcinoma *in* situ (DCIS), 2 IDC/ILC mixtures and the other thirty two were benign]. Among these malignant and benign lesions, 12 malignant and 20 benign lesions had non-mass contrast enhancement, and the rest of the malignant and benign tumors had mass enhancement.

Fig. 1 shows the ROC curves of [Cho] (AUC = 0.96) and W/F ratio (AUC = 0.71) for discrimination of malignant and benign lesions. Comparison of the two AUCs ($p<0.0001$) suggests that [Cho] is a significantly more accurate biomarker than W/F ratio for breast cancer diagnosis. Fig. 2 shows the [Cho] and W/F ratio ROC curves (AUCs are 0.95 and 0.72, respectively) for differentiating the mass malignant lesion group from the benign group, while Fig. 3 demonstrates those (AUCs are 0.96 and 0.68 for [Cho] and W/F ratio, respectively) for differentiating the non-mass malignant lesion group from the benign group. Comparisons of AUCs in both figures give statistically significant p values of 0.0001 and 0.004, respectively, again indicating [Cho] as a better biomarker. For discrimination of mass and non-mass malignant lesions, the AUCs of [Cho] and W/F ratio ROC curves in Fig. 4 are 0.55 and 0.55, respectively, and not statistically different. This suggests that [Cho] and W/F ratio are equally poor biomarkers when used in this way.

**Discussion**

Though both [Cho] and W/F ratio are useful diagnostic biomarkers, the results of this study suggest that [Cho] performs the task significantly better than W/F ratio in differentiating malignant breast lesions, mass and non-mass, from benign lesions, with higher sensitivity and specificity. There is no significant difference in either [Cho] or W/F ratio between the mass and non-mass malignant lesions. This is consistent with our recent findings (8) that Cho peak signal to noise ratio is equally effective in discrimination of mass malignant *versus* benign lesions and non-mass malignant *versus* benign lesions. Incorporation of [Cho] measurement into clinical breast MRI protocol may reduce the number of possibly unnecessary (benign) biopsies in the future.

**References: 1.** ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas. In. Reston, VA: ACR, 2003. **2.** L. Bartella et al., AJR **186,** 865 (2006). **3.** L. Bartella *et al.,Radiology* **239**, 686 *(* 2006)**. 4.** D.K.W. Yeung *et al., Radiology* **225**, 190 (2002). **5.** P.J. Bolan *et al., Magn. Reson. Med.* **50**, 1134 (2003). **6.** S. Thakur et al., PISMRM 2874 (2006). **7.** N.R. Jagannathan *et al., NMR in BioMed.* **11**, 414 (1998). **8.** L. Bartella et al., *Radiology* 245,80 (2007). **9.** E.R. DeLong *et al., Biometrics* **44**, 837 (1988).