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Letter to the Editor Open Access

# *In Vivo* $^{1}$H-MRS Lipid Signal: Is it Useful for Tumor Response to Neoadjuvant Chemotherapy?

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## Letter to the Editor

Early change of tumor size measured on magnetic resonance imaging (MRI) is a good predictor of final response after neoadjuvant chemotherapy. However, even if the cells respond to treatment, it takes some time for the tumor to shrink. Substantial research effort has been spent on investigating whether other information provided by MRI may serve as earlier response indicators than size change. *In vivo* proton MR spectroscopy ($^{1}$H-MRS) has been proven helpful for the detection and therapy response monitoring of breast cancer based on choline-containing compounds (tCho) [1-3]. However, the usefulness of $^{1}$H-MRS lipid signal for therapy response prediction is less established. The purpose of our study was to compare changes in $^{1}$H-MRS lipids and in tumor size at early times after neoadjuvant chemotherapy between who achieved pathological complete response (pCR) and those who did not.

This study is a retrospective analysis of a prospective enrollment study. Twenty-one patients with biopsy-confirmed breast cancer who elected to receive neoadjuvant chemotherapy were included in this study. The age of the patients was from 31 to 77 years old (mean ± SD, 50 ± 13 years). The examinations were performed on a Philips Eclipse 1.5 T MR system with the dedicated bilateral breast coil. In all patients, MRI and 1H-MRS were performed prior to treatment as the baseline, then at least 2 follow-up (F/U) times, F/U-1 after 1-2 cycles AC, and F/U-2 after 4 cycles AC or 2 cycles AC followed by first cycle of taxane regimen. A radiologist determined the tumor size based on the maximum intensity projection (MIP) of the subtraction images. After completing the treatment protocol, patients received surgery. Based on the pathological examination results, they were categorized into two groups: pCR (pathological complete response, no presence of invasive tumors, N=12) and non-pCR (with minimal or bulk invasive residual disease, N=9). Single-voxel 1H-MRS was performed using a point-resolved spin-echo sequence (PRESS). The spectroscopic voxel was carefully positioned to maximize coverage of the contrast-enhanced lesions and minimize the inclusion of adipose tissue. The spectroscopic voxel size was either 5.8 mL or 8.0 mL. The acquisition parameters were TR/TE=2000/270 ms, and 16 acquisitions for averaging. The jMRUI software package was used for time-domain analysis [4]. AMARES [5], a widely used quantitation tool for MRS data, was employed to fit spectra. A priori knowledge was incorporated in the AMARES fitting routines to reduce the number of model parameters and thus to enhance the robustness and speed of the fit. The spectrum shows resonances form the fatty-acid chains of lipid with methyl (-$CH_3$) at 0.92 ppm, methylene (-$CH_2$-) at 1.33 ppm, allylic methylene ($CH_2CH_2$*CH=) at 2.06 ppm, diallylic methylene (-CH-$CH_2$*CH) at 2.79 ppm, and olefinic (-CH*=CH*) at 5.34 ppm.

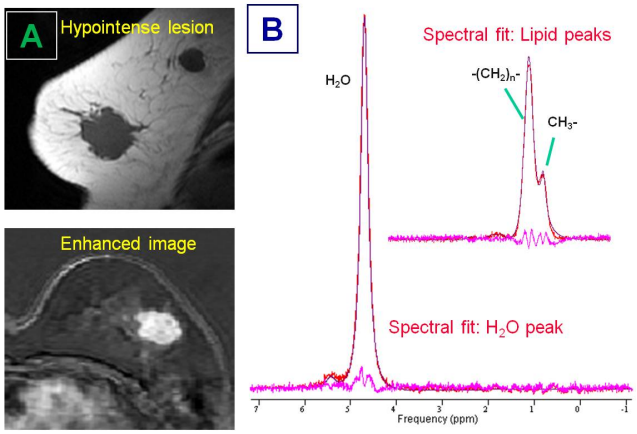


**Figure 1:** Shows a representative MR imaging and 1H-MRS measurement from a patient who received chemo-follow up treatment. Free-hand core biopsy revealed an invasive ductal carcinoma. A radiologist determined the size measurement based on the maximum intensity projection (MIP) of the subtraction images. Before treatment, the lesion was 3.0 cm and showed a heterogeneous enhancing pattern (Figure 1A). Lipids peaks (e.g., methyl (-$CH_3$) at 0.92 ppm, methylene (-$CH_2$-) at 1.33 ppm) were clearly visible in the spectrum without water-fat suppression and fitted by using a Lorentzian model (Figure 1B).

Figure 1 shows a representative MR imaging and $^{1}$H-MRS measurement from a patient who received chemo-follow up treatment. One large hypointense lesion was shown on the pre-contrast sagittal image (Figure 1A, top) showing heterogeneous enhancements on the contrast-enhanced subtraction image (Figure 1A, bottom). The spectroscopic voxel (2×2×2 $cm^3$) was positioned over the enhanced lesion noted on the subtraction image. Lipid peaks at 0.92 and 1.33 ppm were observed in the water-fat unsuppressed spectrum (Figure 1B). The estimated model fit and residue are shown on the full spectrum. Baseline tumor size was not significantly different between pCR and non-pCR groups (P>0.05). The change at first follow-up compared with baseline also did not show significant difference (-20.5% vs. -19.6%, P>0.05). To assess the effects of varying water content during chemotherapy, the percentage change of the water spectra was calculated. Although the change of water peak area showed reduction in the non-pCR group, there was no significant

difference compared to that of the pCR group (-41.5% vs. 15.3%, P>0.05). The mean percentage change in methylene lipid peak at 1.33 ppm after 1-2 cycles AC was +71% in pCR group, while that of the lipid peak was +117.2% in non-pCR group. The mean percentage change in methyl lipid peak at 0.92 ppm after 1-2 cycles AC was +87.1% in pCR group, while that of the lipid peak was +139.5% in non-pCR group. However, no significant change was observed between pCR and non-pCR groups (P>0.05, P>0.05).

As the therapeutic agents become more effective, more patients can achieve the pathological complete response which is expected to lead to a better prognosis. Our study performed on breast cancer treated with chemotherapy showed that in non-pCR group the change in lipids peak signals at the first follow-up (F/U-1, 1-2 cycles AC) was higher, but not significant compared to that of pCR group (P>0.05). The result suggests that the change of lipid peak signals maybe not serve as an early indicator for predicting later clinical response or pathological complete response [6]. However, in previous studies [1-3], tCho level has showed significant reduction in the response group but not in non-response group, suggesting an early response predictor.

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## References

1. Jagannathan NR, Kumar M, Seenu V, Coshic O, Dwivedi SN, et al. (2001) Evaluation of total choline from in-vivo volume localized proton MR spectroscopy and its response to neoadjuvant chemotherapy in locally advanced breast cancer. Br J Cancer 84: 1016-1022.
2. Meisamy S, Bolan PJ, Baker EH, Bliss RL, Gulbahce E, et al. (2004) Neoadjuvant chemotherapy of locally advanced breast cancer: predicting response with in vivo (1)H MR spectroscopy--a pilot study at 4 T. Radiology 233: 424-431.
3. Baek HM, Chen JH, Nie K, Yu HJ, Bahri S, et al. (2009) Predicting pathologic response to neoadjuvant chemotherapy in breast cancer by using MR imaging and quantitative 1H MR spectroscopy. Radiology 251: 653-662.
4. Naressi A, Couturier C, Devos JM, Janssen M, Mangeat C, et al. (2001) Java-based graphical user interface for the MRUI quantitation package. MAGMA 12: 141-152.
5. Vanhamme L, van den Boogaart A, Van Huffel S (1997) Improved method for accurate and efficient quantification of MRS data with use of prior knowledge J Magn Reson 129: 35-43.
6. Cerussi A, Hsiang D, Shah N, Mehta R, Durkin A, et al. (2007) Predicting response to breast cancer neoadjuvant chemotherapy using diffuse optical spectroscopy. Proc Natl Acad Sci U S A 104: 4014-4019.