Estimation of Fat fractions in Different Subtypes of Breast Cancer using in-vivo 1H MRS Study

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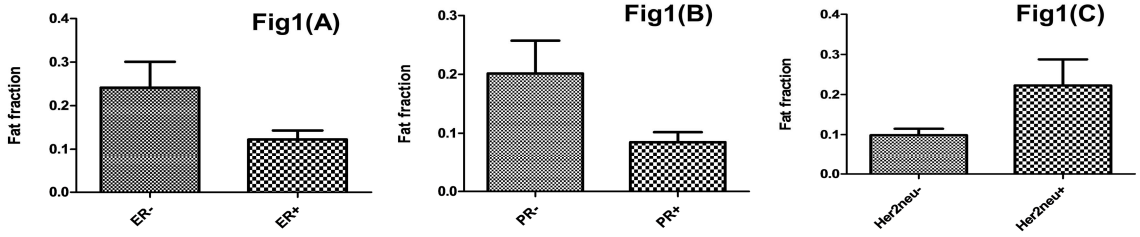
OBJECTIVE: To investigate the relation between fat fraction and different molecular subtypes (ER+/-, PR+/- and Her2neu+/-) of breast cancer patients using in vivo proton (^{1}H) MR spectroscopy (MRS) in

INTRODUCTION: Breast cancer is a heterogenous and complex disease and research is ongoing for an accurate classification of the disease to reduce patient risk and the outcomes of therapy. An important histopathological feature related to patient outcome is the tumor expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2neu); these receptor expression is the basis for treatment planning in breast cancer patients. Lipid metabolism has been a central feature of many cancers like breast cancer. There are two sources of lipids in human cells i.e., diet or de novo synthesis (1). Lipid serves as membrane building blocks as well as energy supply to support rapid cell proliferation during malignancy. The increased lipid synthesis has long been proposed to lead to the upregulation of phospholipid synthesis that fits the need for membrane biogenesis in highly proliferative cancer cells. The present study was aimed to find an association of fat fraction with ER, PR and Her2neu status of breast cancer patients.

PATIENTS AND METHODS: A total of 54 women (age 46.3 ± 10.4 yrs) with pathologically known hormone receptor status were included in the present study. MR investigations were performed using a four-channel phased array receive breast matrix coil at 1.5 T (Avanto, Siemens). Following the scout image, short inversion recovery coronal images were acquired (TR/TE = 6940/58 ms; slice thickness = 3 mm; and matrix size = 320 × 256). Also, fat-suppressed MR images were acquired in the transverse and sagittal planes with the following parameters: TR/TE = 6270/102 ms; slice thickness 3 mm with no gap; and matrix size = 512 × 440. A single voxel in-vivo ^{1}H MRS was carried out using point-resolved spin-echo (PRESS) sequence with TR/TE = 1500/100 ms); NSA = 2; spectral width = 1000 Hz; vector size = 1024. Using reference MR images, a voxel was positioned within the tumor varying in size ranging from 10 × 10 × 10 to 10 × 35 × 45 mm^3 depending on the tumor volume. Magnetic field shimming was carried out both globally and over the voxel prior to MRS. The linewidth at half maximum after voxel shimming corresponded typically 5-15 Hz for the water peak in spectra obtained from tumors. The fat fraction (fat/water + fat) was calculated using the unsuppressed spectra from the peak areas under the water peak at 4.7 ppm and the major lipid peak at 1.23 ppm.

RESULTS: Out of 54 breast cancer patients, 27 were ER+; 24 ER-; 18 PR+; 31 PR-; 26 Her2neu+ and 21 Her2neu-. A statistically significant increase in the fat fraction was observed in ER-/PR- (0.24 ± 0.31/0.20 ± 0.31) compared to ER+/PR+ (0.12 ± 0.11/0.08 ± 0.07) breast tumors with a p value of 0.03 [see Figures 1(A) & 1(B)]. Also, a significant increase (p=0.04) in the fat fraction was obtained in Her2neu+ (0.22 ± 0.33) compared to Her2neu- cases (0.10 ± 0.07) [see Figure 1(C)]. Statistical significance ($p \leq 0.05$) was evaluated using Student's t tests as part of PRISM Graphpad Software.



DISCUSSION: The present study demonstrated that the lipid content is associated with hormone receptor status of breast cancer patients. Our results showed a significant increase in fat fraction of ER-/PR- and Her2neu+ than ER+/PR+ and Her2neu- breast tumors. Several individual breast cancer markers have been established for target-specific pharmacologic intervention. The most clinically relevant subtypes proven for neoadjuvant chemotherapy are hormonal-positive ER, PR, Her2neu receptors. ER+/PR+ breast cancers have better prognosis compared to ER-/PR- breast cancers (2). Moreover Her2neu expressing breast cancers are very aggressive. Highly proliferating cancer cells need to synthesize fatty acids de novo to continually provide lipids for membrane production. Further, cancer cells seem to be highly dependent on de novo lipogenesis for their proliferation and survival (3). ER-/PR- breast tumors are one such type of highly proliferating cancers. The lipid metabolism is an attractive target for cancer therapy, as it differs between tumors and normal tissues, with the most dramatic changes observed in the most aggressive tumors. In a previous study from our laboratory (4) a significant decrease in w-to-f ratio was reported following NACT in breast cancer patients. Our results show that in-vivo ^{1}H MRS might be a useful technique in providing insight into lipid content in different subtypes of breast cancer and for therapeutic planning of breast cancer patients.

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