Correlation between estrogen receptor positive (ER+) and estrogen receptor negative (ER-) status with tCho concentration and tumor volume in breast cancer patients.

N. R. Jagannathan[1], R. G. Sah[1], U. Sharma[1], and R. Parshad[2]

[1]Department of NMR & MRI Facility, All India Institute of Medical Sciences, New Delhi, Delhi, India, [2]Department of Surgery, All India Institute of Medical Sciences, New Delhi, Delhi, India

Objective: The purpose of this study is to investigate the correlation of tCho concentration and tumor volume determined prior to therapy in invasive ductal carcinoma (IDC) patients with Estrogen positive and negative receptor status.

Introduction: Breast cancer is the most common cause of morbidity and mortality in women worldwide with heterogeneity in its clinical behaviour (1). Research to find out newer prognostic factors and predictors of response to therapy are constantly being explored. Molecular markers such as estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2/neu) are important for guiding treatment choices and to decide on the management protocol of breast cancer patients. Around 70% of breast cancers in women are ER positive. ER+/PR+ cancer is the most common type, followed by ER−/PR− and ER+ /PR− (2,3). It was reported that ER- cancer (30%) patients, have unfavorable prognosis and fewer treatment options compared to ER+ group (4). Patients with ER+ tumors tend to develop osseous, whereas those with ER−/PR− tumors tend to develop brain metastases (5). Further, compared with ER+/PR+ cancers, ER−/PR− cancers have poorer clinical outcome and shorter medium survival (6). Several MR studies characterizing various MR parameters such as tCho concentration, signal-to-noise ratio of tCho, water-fat ratio, contrast enhancement and apparent diffusion coefficient have been used with an aim to differentiate malignant and benign breast lesions and to monitor response to therapy. However, only few reports are available correlating MR features with molecular biomarkers in breast cancer. The objective of the present study was to investigate the correlation of tCho concentration and tumor volume determined prior to therapy with the ER expression status in 46 breast cancer patients.

Materials and methods: A total of 46 women with invasive ductal carcinoma (IDC) with known ER status were selected for this study: 22 women were ER+ (47.0±10yrs) while 19 were ER- (44.68± 10.4 yrs). Written informed consent was obtained and Institutional ethical committee approved the study. Patients were evaluated clinically and tumor size was measured using Vernier calipers. MR was performed using a phased array breast matrix coil at 1.5 T (Siemens, Avanto). Following the scout image, T2-weighted coronal images were obtained using standard SE sequence and fat suppressed MR images in the transverse and sagittal planes. Contrast-enhanced MRI was carried out using a fat-saturated 3D FLASH where-ever indicated for appropriate localization of the lesion. The in-vivo proton MRS was carried out prior to therapy using a single voxel PRESS sequence. Typical water peak line width ranged from 8 to 22 Hz and water+lipid suppression was achieved using MEGA pulse. The parameters used were: TR=1500 ms, TE=100 ms, averages=128, total acquisition time was 3:18 minutes. An additional spectrum from the same voxel without water and lipid suppression was obtained for the concentration calculation using the water signal as internal reference. tCho concentration was calculated using the equation reported by Baik et al for 1.5 T (7), while volume was measured from MR images using perimeter method using formula: volume=ST[A1+A2...An] (8). All statistical analyses were carried out in SPSS software 11.5 using non parametric test (Mann Whitney).

Table-1: Comparison of tCho and tumor volume associated with ER+ and ER- breast cancer patients.

	ER+ (n=27)			ER- (n=19)			
	Mean ±SD	Median	Range	Mean ±SD	Median	Range	P-value
Volume (cm^3)	33.6±45.7	24.9	1.1-232	67.2±60.8	33.1	14.0-211.9	0.03
tCho(mmol/kg)	4.2±2.3	3.5	0.8-11.1	4.1±3.5	3.1	1.0 -17.7	0.36

Results and Discussion: Table-1 summarizes the comparative analysis of the tumor volume and the tCho concentration in ER positive and negative breast cancer patients, while Fig-1 shows the box plot. The tumor volume for the ER+ and ER- cases were 33.57 ± 45.7 and 67.2±60.8, respectively which was statistically significant (p=0.03). However, tCho concentration was similar in ER+ and ER- cases (p=0.36). The prognosis of breast cancer is related to a variety of clinical and pathological factors. It is well known that ER, PR and HER-2 neu status represent the most acceptable factors for predicting prognosis, evaluation of response or resistance to treatment and the potential target for newer therapeutic approaches. In this study, we observed that the tumor volume was significantly larger in ER negative than in ER+ group (p = 0.03). However, there was no significant difference in the concentration of tCho between the two groups of patients. These findings are in agreement with the earlier report, where in larger tumor volume with markedly higher microvessels density was reported in ER- cancers (9) but no difference in Cho levels. Koukourakis et al. reported an inverse association of microvascular density with ER expression (10). The higher proliferative activity associated with ER- cancers is probably be one of the reasons for larger tumor size observed in the patients in our study (11). ER+ breast cancer is considered as a favorable prognostic indicator compared to ER negative, the cells are more likely to be well-differentiated, less aggressive, and it has more therapeutic options such as ER blockers or aromatase inhibitors. The less aggressive phenotype of ER+ cancer was possibly mediated through lower grade and lower angiogenesis as compared to that of ER- cancer. Thus, our data suggests that aggressive behavior with higher angiogenesis leads to the larger size tumors and is related to the ER expression; however, tCho concentration is not related with the ER status in breast cancer patients. Further studies are required to confirm these interesting findings.

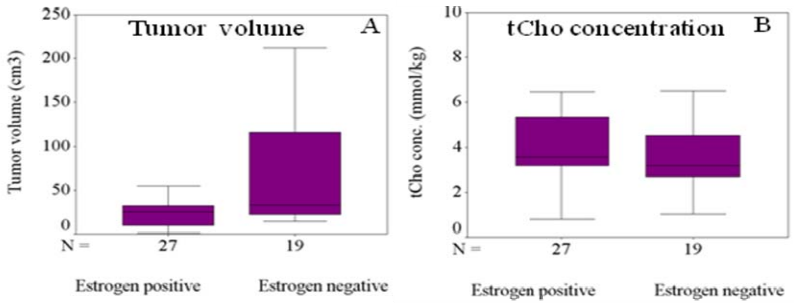

Fig-1: A box plot showing comparison of (A) tumor volume and (B) tCho with ER positive and negative breast cancer patients.

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