Potential of choline SNR, tumor volume and diameter in the assessment of response of locally advanced breast cancer patients using sequential MRSI and MRI

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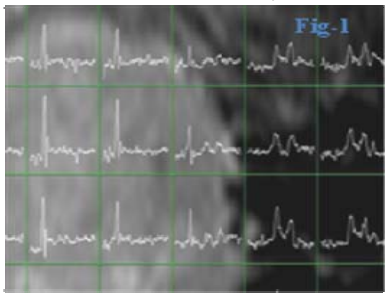
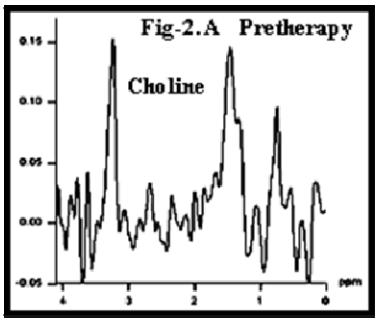
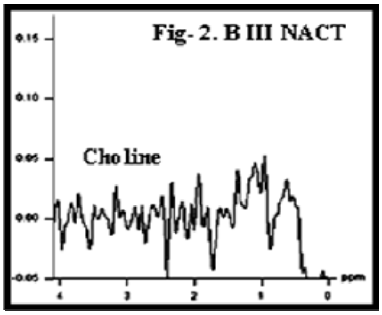
OBJECTIVE: To evaluate the clinical potential of signal-to-noise ratio (SNR) of total choline (Cho) peak calculated from multiple voxels obtained from MRSI together with tumor volume and diameter in predicting the tumor response of breast cancer patients undergoing neo-adjuvant chemotherapy.

INTRODUCTION: Single-voxel MRS was demonstrated to be useful in monitoring tumor response of breast cancer patients (1-3). However, its low spatial resolution is not optimal for small and large heterogeneous lesions. MRSI provides metabolite information from multiple voxels simultaneously and provides spatial variation of heterogeneous breast lesion or multiple lesions (4). Additionally, MRSI may be useful to monitor the viability of tumor cells on margins of the tumor as well on necrotic or apoptosis of tumor cells. Further, the changes in ChoSNR from tumor as well as from normal portion of the breast can be evaluated simultaneously (5). In this study we investigate: (a) the systematic changes of ChoSNR and the anatomical tumor parameters (volume and diameter) in locally advanced breast cancer (LABC) patients, and (b) to determine the clinical utility of these parameters in assessment of tumor response during the various stages of neo-adjuvant chemotherapy (NACT).

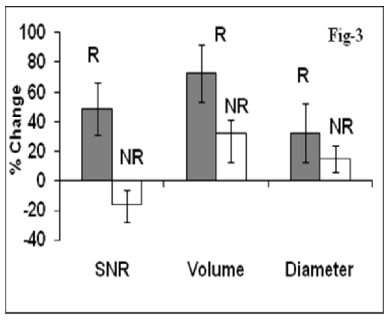


MATERIALS AND METHODOLOGY: Thirty LABC patients (age 47±12 yrs) with cyotologically proven malignancy were investigated at 1.5 T (Sonata/Avanto, Siemens) using a dedicated bilateral breast coil with the body coil as transmitter. Institutional ethical committee approved the study and written informed consent was obtained. Clinical evaluation was carried out according to TNM classification. Following MR image acquisition (T1 and T2 weighted), 2D MRSI was carried out using PRESS sequence, sequentially at four time points, prior to NACT (Tp0) and after one week of completion of I (Tp1), II (Tp2), and III NACT (Tp3). The acquisition parameters for MRSI were: TR =2000 ms, TE = 135 ms, number of scans = 4, FOV = 80 x 80 mm with scan resolution of 16 x 16 (acquisition time 9 mins). Out of 30, sequential monitoring was performed on 28 patients. Of 28 patients, two were studied at 4 time periods. 19 were monitored at three time periods, (Tp0+Tp2+Tp3, n=13; Tp0+Tp1+Tp3, n=5; Tp0+Tp1+Tp2, n=1). While six patients were monitored at two time periods (Tp0 + Tp3, n=5; Tp0 + Tp1, n=1). Thus for the pooled analysis, data was available for 30 patients at Tp0, 9 at Tp1, 17 at Tp2 while 25 at Tp3. ChoSNR was calculated using the formula SNR = [amplitude of Cho resonance / RMS amplitude of noise], while volume and diameter was measured using MR images.





RESULTS: The spectral map from multiple voxels of a patient suffering from LABC obtained prior to therapy is shown in Fig 1. The MR spectral pattern of a responder acquired prior to therapy and after III NACT is shown in Figure 2. The pooled analysis of 30 patients showed that pre-therapy mean ChoSNR was 7.1 ± 3.9, which reduced following I, II and III NACT ($p < 0.05$). Sequential data of 25 patients were retrospectively analyzed after classifying them as responders (R) and non-responders (NR) using clinical evaluation. In 14 responders, the pre-therapy ChoSNR was 7.8 ± 5.1. In 10/14 responders, no choline was observed after III NACT while in the remaining four patients the ChoSNR reduced to 3.6 ± 1.1 ($p = 0.0001$). A value of SNR of 2 and above was considered consistent with malignancy (6)**.** Non-responders showed no significant change in ChoSNR following NACT. Tumor volume and diameter reduced by 84.0 ± 14.8% and 46.6± 24.8%, respectively in responders after III NACT. Using receiver operating curve analysis, a cut-off value of 53% for ChoSNR, 47.5% for volume and 27.6% for diameter was obtained to differentiate between responders from non-responders. The comparison of the percentage reduction in SNR, volume and diameter in responders and non-responders after III NACT compared to the pre-therapy value is shown as histogram distribution in Fig. 3.



DISCUSSION: Identification of non-responders is essential in treatment planning since the decision of change of therapy regimens or early surgery may be taken accordingly. Our results indicate that all patients had elevated level of Cho prior to therapy that characterizes rapid growth rate of malignant tumors. The pooled analysis showed that significant decrease in ChoSNR occur as early as I NACT compared to pre-therapy. The retrospective analysis of sequential data of 25 patients revealed that responders showed significant decrease in ChoSNR after first cycle followed by II and III NACT. Tumor volume and the diameter also showed decrease in these patients. However, non-responders did not show any significant reduction in ChoSNR even after the completion of three cycles. In responders, an average of 19 (range 4 – 45) voxels was positive for choline before therapy. Cho was not detected 10/14 patients after III NACT. In remaining 4 patients, two to three voxels were choline positive. In non-responders, an average of 23 voxels (range 9 – 61) was choline positive prior to therapy, while 22 (range 2 – 52) voxels were choline positive after II and III NACT, respectively. The sensitivity of ChoSNR was 85.7% to differentiate responders from non-responders with 91% specificity. Volume and diameter showed 100% sensitivity but with reduced specificity of 73% for volume and 81.8% for diameter. Combined approach using all the three parameters provided 100% sensitivity, 82% specificity with 87.5% PPV and 100% NPV suggesting that the use of combination of parameters based on biochemical and anatomical alterations are better to predict the tumor response.

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