2D MRSI in locally advanced breast cancer: Assessment of tumor response in patients undergoing neo-adjuvant chemotherapy

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Objective

The objective of the study was to assess the response of tumor to chemotherapy and to differentiate responders and non-responders using the signal-to-noise ratio (SNR) of choline resonance obtained using 2D MRSI.

Introduction

Multi-voxel MR spectroscopy has the ability to map spectra simultaneously from different areas of breast lesions. MR spectroscopy can also be used as a tool to assess the response of the tumor to chemotherapy. Changes in water-to-fat ratio or choline resonance are used for this purpose[1, 2]. Recently, quantitative measurement of the change in choline concentration was used to predict the response of the tumor after twenty four hours of the administration of the first cycle of chemotherapy[3]. Multi-voxel spectroscopy is more advantageous than single voxel spectroscopy in assessing the response of the tumor in terms of wide area of coverage, higher spatial resolution, simultaneous sampling of tumor and necrotic areas and mapping the distribution of metabolites in tumor. In this study, the SNR of choline in the tumor was measured using multi-voxel spectroscopy during various stages of neo-adjuvant chemotherapy (NACT) to assess the therapeutic response of tumor.

Methods

Sixteen LABC patients with proven malignancy, scheduled for NACT were recruited for the study. Eleven patients were given a combination of cyclophosphamide, adriamycine and 5-fluorouracil; four patients were given cyclophosphamide, epirubicin and 5-fluorouracil while one patient received paclitaxel and epirubicine. Out of sixteen patients, eleven were sequentially monitored at three time periods i.e., prior to NACT, also after II and III NACT. Five patients were monitored prior to therapy and after III NACT. Response status of patients was assessed three weeks after the completion of III NACT. Patients with 50% or more reduction in tumor size were classified as clinical responders while those with less than 50% size reduction or increment in size were considered as non-responders. All MR examinations were carried out at 1.5 T using Sonata/Avanto (Siemens, Germany) whole body MR scanners. After routine imaging, volume localized, 2D multi voxel spectroscopy was carried out using PRESS sequence (TR =2000 ms, TE = 135 ms, number of scans = 4, FOV = 80 x 80 and scan resolution =16 x 16 and voxel size = 5 mm x 5 mm x 10 mm). Simultaneous and water and fat suppression was achieved using MEGA pulses. Proper care was taken to ensure that the 2D multi-voxel slab was placed on the same region of the breast in pre- and post-therapy measurements in each patient. Spectral noise was measured from signal free region (-1 to -2 ppm) in the spectrum and choline SNR was calculated using the formula SNR_{Cho} = amplitude of Cho resonance / RMS amplitude of noise.

Results

Out of sixteen patients nine were clinical responders, while seven were non-responders. Choline SNR in responders measured prior to therapy was 7.8 ± 5, which decreased to 4.0 ± 2 after II NACT. Choline SNR obtained after the completion of III NACT in these patients was 1.6 ± 1. In clinical non-responders, choline SNR obtained prior to therapy, after II NACT and after III NACT were 6.1 ± 2, 5.6 ± 2 and 5 ± 2, respectively. In responders, mean choline SNR showed 48% decrease after II NACT and 60% decrease after III NACT compared to pre-therapy value, while in non-responders; the decrease was 8% and 17% after II NACT and III NACT, respectively. In responders, the mean choline positive voxels prior to therapy was eighteen which reduced to eleven and to zero after II NACT and III NACT, respectively. In seven out of nine responders, choline resonance was completely absent after III NACT. In non-responders there were sixteen voxels prior to therapy, which in most cases increased to seventeen and fifteen after II NACT and III NACT, respectively.

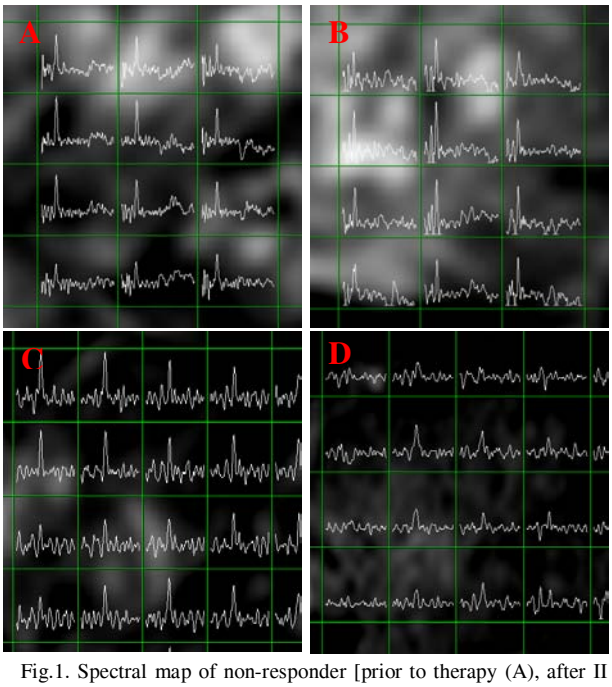

Fig.1. Spectral map of non-responder [prior to therapy (A), after II NACT (B)] and responder [prior to therapy (C), after II NACT (D)]

Discussion

Mean choline SNR reduced by 48% and 8% in clinical responders and non-responders, respectively, after II NACT. After the full course of therapy, choline SNR reduced significantly (60%) in responders while, there was only a marginal decrease (17%) in non-responders reduction. Significant decrease in choline SNR after NACT in responders is due to the inhibition of the proliferative activity and membrane synthesis in tumor by cytotoxic drugs in the chemotherapy regimen. In non-responders, choline SNR increased or showed only marginal decrease due to the resistance of the tumor to the therapeutic agents used. The study proved that SNR can be used to assess as well as to clearly differentiate responders and non-responders.

References

1. Jagannathan NR et al., Br J Cancer. 2001; 84:1016-22.
2. Jagannathan NR et al., NMR Biomed. 1998; 11:414-22.
3. Meisamy S et al., Radiology. 2004; 233:424-31.