Sequential MRSI and DWI Study for Early Assessment of Response of Breast Cancer to Neo-adjuvant Chemotherapy: A Pilot Study

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Objective: To study the neo-adjuvant chemotherapy (NACT) induced early response of tumor using 2D magnetic resonance spectroscopic imaging (MRSI) and diffusion weighted imaging (DWI) in breast cancer patients.

Introduction: Magnetic resonance spectroscopy (MRS) is a promising method providing biochemical and physiological information of tissues and has wide variety of applications in oncology while apparent diffusion coefficient (ADC) values can be used quantitatively to assess cellularity, a functional property of the tumor which correlates with its histological grade. In breast cancer an elevated presence of choline containing compounds (total choline, tCho) signal at 3.2 ppm in the MR spectra is associated with malignancy. Both MRS and DWI have shown to have the potential in assessing the tumor response to NACT in breast cancer patients.

Methods: Five clinically proven locally advanced breast cancer patients (mean age = 50 ± 9 years) scheduled to undergo NACT were recruited. MR studies were carried out on patients positioned prone in a 1.5 T MRI scanner (Siemens, Avanto/Sonata) with their breasts placed in a double breast array coil prior to NACT and after the completion of the first and third cycle of NACT. Following the routine imaging in three planes, DW images were obtained from both the breasts in transverse plane using an echo planar imaging sequence (EPI). Diffusion gradients were applied simultaneously in three directions with b = 0, 500 and 1000; TR = 5000 ms; TE= 87 ms; FOV = 250 - 350 mm; NS = 1-2; acquisition matrix = 128 x 128; and slice thickness = 5 mm. Mean ADC values were calculated from the ADC map by selecting circular ROIs of five pixels for all the measurements. Volume-selective, 2D ^{1}H-MRSI was performed using PRESS sequence with MEGA pulse for the simultaneous suppression of water and fat resonances (TR = 2000 ms TE = 270 ms Average = 4) on a 10 mm thick slab (FOV = 120 x 120 mm). It was ensured that the 2D CSI slab was placed on the same region of the breast in pre- and post-therapy measurements on the same patient. Spectral noise was measured from signal free region (-1 to -2 ppm) in the spectrum and tCho SNR was calculated using the formula SNR = Amplitude of tCho resonance / RMS amplitude of noise. Largest diameter was measured from MR image. Clinical response was assessed in patients after third cycle of NACT.

Results and Discussion: tCho SNR decreased significantly (~60 %) in responders (No. 4 & 5, Table 1) after first NACT, while in non-responders (No. 2 & 3, Table 1) an increase (10 %) or a marginal decrease (18 %) was observed. Patient No. 1 is under treatment. ADC values remained same in non-responders while a statistically significant increase was observed in responders after I and III NACT. The largest diameter of the tumor showed a reduction of 75 % in responders, while less than 50 % reduction was observed in non-responders.

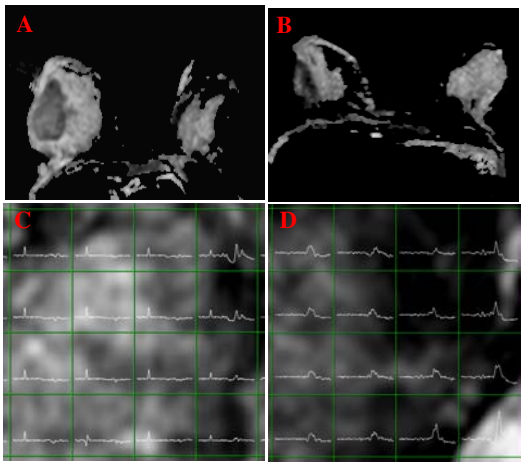

Fig.1: ADC map (a) pre-therapy (b) after III NACT and spectral map (c) pre-therapy (d) after III NACT of a responder

Lower ADC value in tumor compared to normal tissues is due to the restricted diffusion of water caused by the dense architecture and high cellularity of tissues, while high tCho SNR in tumor is attributed to the increased cell membrane synthesis. The interesting finding of this pilot study is the 60 % reduction of tCho SNR after I NACT compared to the pre-therapy value. In patients 4 and 5 no choline was detected after III NACT. This decrease in tCho SNR after NACT is due to the inhibition of the proliferative activity of tumor by cytotoxic drugs in chemotherapy regimen and in these patients. In non-responders, tCho SNR increased or remained same due to the resistance of the tumor to the therapeutic regimen used. This observation is in concordance with the change in ADC values and tumor size observed. In responders, ADC values were found to increase due to NACT induced apoptosis and cell damage which increases the extra-cellular space, thus an increase in water diffusion and higher ADC values. In non-responders, the therapeutic regimen may not cause any of these changes in tumors due to its resistance to chemotherapy. Recently Meisamy et al. have reported the early response of the tumor to therapy using MRS[1].

Table 1

Patient No.	tCholine SNR			Largest diameter of tumor (cm)			ADC (x 10^{-3} mm^2/s)			Clinical response
	Pre therapy	I NACT	III NACT	Pre therapy	I NACT	III NACT	Pre therapy	I NACT	III NACT	
1	7.7 ± 3.6	8.5 ± 2.7	UT*	5.0	5.8	UT*	0.88	0.89	UT*	UT*
2	9.7 ± 4.3	7.9 ± 1.5	5.4 ± 1.8	3.4	2.7	1.9	0.99	1	1.2	Non responder
3	5.4 ± 2.1	3.0 ± 1.1	3.0 ± 0.7	8.4	5.3	4.5	1.07	1.26	1.2	Non responder
4	16.1 ± 7.2	6.5 ± 5.3	No choline	4.7	2.6	1.5	0.76	0.86	1.11	Responder
5	21.1 ± 3.5	8.3 ± 2.1	No choline	6.2	5.7	1.1	0.9	1.1	1.15	Responder

* Under treatment

Conclusion: Our pilot study indicates that using tCho SNR it is possible to assess the early response of the tumor to NACT. The ADC values detected from these patients also corroborated the MRSI findings.

References

1. Meisamy S et al., Radiology 2004; 233(2):424-31.