Neoadjuvant chemotherapeutic response of breast cancer: evaluation by high spatial resolution MRI with adjusted 3-time point method

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Introduction: Neoadjuvant chemotherapy has been used in patients with local advanced breast cancer before surgery. However, the precise residual viable tumor volume is difficult to evaluate since breast tissue micro-environment has been altered after chemotherapy. This suggests a dedicated MRI analysis strategy might be needed for evaluation of breast cancer before and after chemotherapy, respectively. The aim of this study was to exam whether a high-spatial resolution, model-based method breast MRI method (1) can precisely predict the viable and non-viable parts of breast tumor after chemotherapy. We have been performing clinical trials of a high resolution, for breast MRI diagnosis with the promise of both high sensitivity and specificity for residual tumor after neoadjuvant chemotherapy.

Methods: Fifteen patients with locally advanced breast cancer (invasive ductal carcinoma) underwent twice 1.5-T MRI scan: (a). prior to and (b). following neoadjuvant chemotherapy (5-Fluorouracil, Epi-Adriamycin, Cyclophosphamide) with 4 - 6 cycles, before mastectomy. Dynamic contrast enhancement was measured using a 3-D SPGR sequence without fat suppression. Image analysis was done on images overlaid with a color map. One pre- (t0) and two post- contrast (t1 and t2) images were shown with thin section (1mm) bilateral breasts including tumor. Morphologic response was determined according to published criteria involving changes in tumor volume after chemotherapy (2). With adjusted 3TP analytic parameters, every coded color area within original tumor site was interpreted as suspicious residual tumor. Tumor volume was calculated on transverse MR images section by section. The largest diameter was measured in the transverse plane of the color-mapped images as well as calculated from the number of slices on which tumor was visible. The mastectomy specimens were sectioned at 5-mm increments perpendicular to cranial-caudal axis. The pathomorphological diameter, which was to be compared with tumor diameters measured on MR images, always included the scattered foci. The correlation between 2nd MRI and pathomorphological tumor size was determined by Pearson correlation test.

Results: Before treatment, the median of tumor volumes by MRI was 27cm^3(range 16-76cm^3). After treatment, the median of tumor volumes was 11 cm^3 (range 4-32cm^3). There were 12 partial responders and 3 stable cases. The correlation between tumor diameter measured by histopathology and 2nd MRI before mastectomy (Fig.1) was 0.88 ($p<0.001$). Tumors with chemotherapy response were associated with decease of distribution and intensity of red color area on 3TP color mapping. Two patterns of residual tumor were observed: (A). Solitary type: a response of tumor after chemotherapy was associated with decease of distribution and intensity of red color area (Fig.2) (N =6). (B.) Cluster type: Tumors with complex non-contiguous microscopic foci (<0.1cm) were coded in green or blue color on 3TP color mapping (Fig.3) (N = 9).

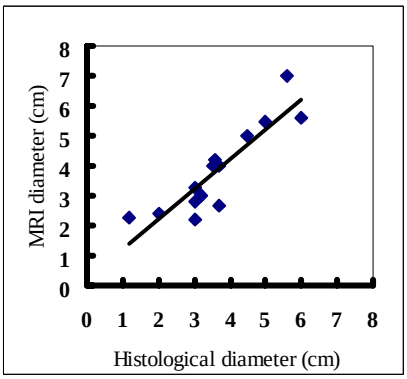

Fig1. Histological tumor diameter and corresponding tumor diameter obtained from MRI.

Discussion: Previous reported methods to monitor response to neoadjuvant chemotherapy showed to be suboptimal in some cases because of chemotherapy-induced fibrosis. More recently, dynamic information from MR contrast agent kinetic analysis appears to be useful in the assessment of tumor response to neoadjuvant chemotherapy. With high-spatial resolution, adjusted 3TP dynamic MRI, we found residual viable tumor and fibrosis can be reliably distinguished. However, the microvessels permeability and the extracellular volume fraction of the residual tumor might be altered as compared to status before chemotherapy. The significance of two patterns of tumor responses requires further clinical investigation.

Reference: 1. Degani et al (1997) Nature Medicine 3: 780-2 .
2. Therasse et al.. J Natl Cancer Inst. 2000 Feb 2;92 (3):205-16.

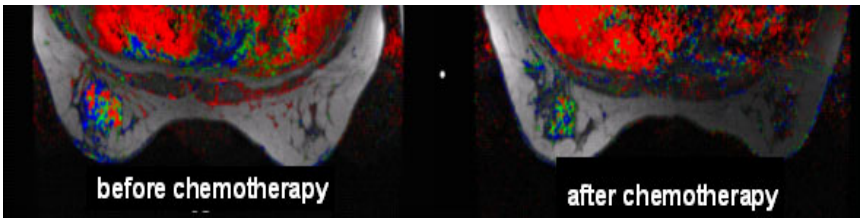

Fig2. Images show a breast tumor with partial response in the left breast before chemotherapy and after 4 cycles of chemotherapy. The distribution and intensity of red color in this solid residual tumor shows decrease

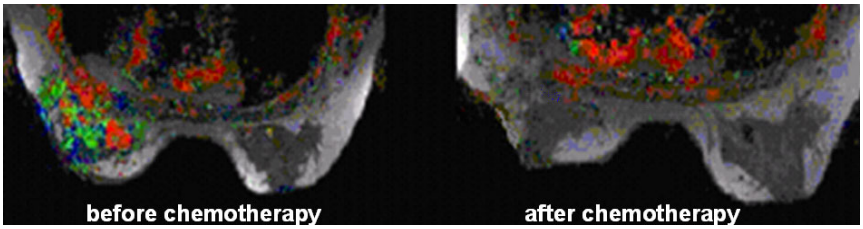

Fig3. Images show a lesion with partial response in the left breast before chemotherapy and after 6 cycles of chemotherapy. The distribution and intensity of red shows decrease, the blue and green color represents small foci of residual tumor.