The role of Diffusion Weighted Imaging (DWI) and Volumetric measurement in the early assessment of tumor response in patients with Locally Advanced Breast Cancer (LABC) undergoing Primary Chemotherapy (PCT).

L. Martincich[1], I. Bertotto[1], F. Montemurro[2], L. Cellini[1], I. Sarotto[3], and D. Regge[1]

[1]Diagnostic Unit, Institute for Cancer Research and Treatment, Candiolo, Turin, Italy, [2]Medical Oncology Unit, Institute for Cancer Research and Treatment, Candiolo, Turin, Italy, [3]Pathology Unit, Institute for Cancer Research and Treatment, Candiolo, Turin, Italy

PURPOSE: Diffusion Weighted Imaging (DWI) has a consolidate role in the evaluation of neurological diseases and more recently it has been applied to the breast. DWI provides a functional quantitative parameter, the Apparent Diffusion Coefficient (ADC) value, which is related to the tumor cellularity and the extracellular water content. Preclinical studies in animal breast cancer models have shown that DWI may detect early tissue changes during medical treatments, reflecting modifications in the tumoral microenvironment induced by chemotherapy, such as apoptosis and increase in water mobility. Preliminary clinical studies seem to confirm that ADC increase occurring during medical treatment may identify Responders subjects before macroscopic tumor size modifications, suggesting a potential role of DWI in early prediction of tumor response. Dynamic Contrast-Enhanced MRI (DCE-MRI) provides volumetric measurements of breast lesions; it has been reported that tumor volume reduction >65% after two cycles of Primary Chemotherapy (PCT) allows to identify tumors achieving a pathological complete response (pCR), which represents an important prognostic factor. In monitoring patients with locally advanced breast cancer (LABC) undergoing PCT, it is important to early define Non-Responders in order to both avoid unnecessary and potentially toxic therapy and shift from medical to surgical treatment. The purpose of the study was to assess if ADC value and volumetric changes during medical treatment are able to early evaluate tumor response in patients with LABC undergoing PCT.

METHODS AND MATERIALS: 17 patients with monolateral LABC (stage II with T>3cm or IIIA/B/C) undergoing taxane-based PCT were monitored by DWI and DCE-MRI (1.5T scanner and 8-channel coil) before and after two cycles of treatment. DWI was performed by axial EPI sequence (b-value 0 and 900 s/mm^2-slice thickness 4mm-acquisition time 80sec) and DCE-MRI was obtained by axial 3D high resolution sequence (slice thickness 2,6mm, matrix 416x416). For each LABC, the volume and the ADC value were assessed before and during PCT. The volume of enhancing portion of the lesion was obtained using a dedicated software while ADC value was calculated by tracing a region of interest within the tumor. Pathological tumor response was evaluated according to the five-point scheme described by Smith et al (JCO 2002): patients who achieved grade 5 (pathological complete response) or 4 (small cluster of residual cancer cells after PCT) were considered as Responders (R); those obtaining grade of response scored 1-3 were considered as Non-Responders (NR). Variation in ADC values (ADC during PCT-ADC before PCT) and the volume percentage reduction after two cycles of PCT were calculated for Responders and Non-Responders and univariate analysis was used to define cut off values. Accuracy of volumetric measurement and DWI in the early identification of Responders and Non-Responders was then evaluated.

RESULTS: At pathology 4 patients were classified as Responders (2 with grade 4 and 2 with grade 5) and 13 were the Non-Responders. A reduction of tumor volume ≥65% and an ADC value variation ≥0.3 were identified as cut off values.

Before PCT, mean ADC value was 1.08±0.12x10^{-3}mm^2/s (range 0.9-1.19) for the R and 1.02±0.33x10^{-3}mm^2/s (range 0.7-2.08) for the NR; after two cycles of PCT it was 1.45±0.05 x10^{-3}mm^2/s (range 1.4-1.5) and 1.12±0.3x10^{-3}mm^2/s (range 0.8-2.03) respectively. Mean variation in ADC value during PCT was 0.37±0.15 for Responders and 0.1±0.1 for Non-Responders, showing a significant difference in the two groups of patients (p=0.007); an ADC value variation ≥0.3 was observed in 3/4 Responders.

After two cycles of PCT, mean tumor volume changed from 17.44±6.45cm^3 (range 9.25-25) to 4.41±2.43cm^3 (range 1.68-7.56) in the R and from 18.37±13.54cm^3 (range 4.03-50.23) to 12.96±10.13cm^3 (range 0.33-35.6) in the NR. Mean reduction of volume percentage during PCT was significantly different between R and NR (76% vs 35%; p=0.01); a reduction of tumor volume ≥65% was observed in 3/4 Responders.

In the early discrimination between R and NR, the accuracy of both DWI and volumetric measurement was 96%; by combining the two methods the accuracy reached 100%.

CONCLUSION: Reduction of tumor volume associated to variation of ADC value after two cycles of PCT may accurately define patients who will benefit from PCT and Non-Responders. The results confirm the usefulness of volumetric measurements in the early assessment of tumor response and the capability of DWI in the early detection of tumor changes related to treatment effects. Moreover DWI shows some advantages for clinical application: it provides a quantitative parameter (ADC value), it does not require contrast media administration and it has short acquisition and post processing time.

References:

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