Before the tumour shrinks: apparent diffusion coefficient in early assessment of breast cancer response to neoadjuvant chemotherapy

Poster No.: B-0016
Congress: ECR 2015
Type: Scientific Paper
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Keywords: Breast, Oncology, MR, Diagnostic procedure, Cancer
DOI: 10.1594/ecr2015/B-0016

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Purpose

The purpose of this paper was to assess tumor response after the 2nd cycle of neoadjuvant chemotherapy (NACT) according to:

1.) **Standardized assessment tool - RECIST**, based on purely morphologic changes - tumor diameter change, with the response assessment categorization assigned according to the percentage of the change in the sum of the target diameters [1].

2.) **Apparent diffusion coefficient (ADC)**, based on the diffusion-weighted imaging (DWI), i.e., the change in ADC value initially and upon the completion of the 2nd cycle of the standardized NACT regimen (anthracycline based) [2-6].

NACT is the standardized therapeutic approach for pre-surgical treatment of the locally advanced breast cancer (LABC) and the initially operable breast cancer - aiming to downstage the large tumors in order to improve surgical options: breast-conserving surgery, taking into account the fact that the pathological complete response (pCR) is defined as the specific surrogate endpoint for survival outcome [4-8].

The "early tumor response" defined on breast DCE-MRI after the 2nd cycle of NACT based on morphologic (RECIST) and functional (ADC) criteria may contribute to the identification of the responders to the standardized anthracycline-based NACT [6-8]. According to RECIST, the complete response (CR) considers the disappearance of all target lesions, while the partial response (PR) represents the decrease of at least 30% in the sum of diameters of target lesions compared to the initial values [1]. The change in ADC value, as the measure of tumor response to NACT has not been standardized, neither from the technical point of view (e.g. selection of the gradients - b-values...), nor from the clinically relevant predefined cut-off values based on the large trials and set as the standard through the relevant guidelines. Certain cut-off values were however suggested, based on the limited number of trials: the increase in ADC value of at least 14% after the 1st cycle and/or 27% after 2nd cycle of NACT in responders (R) [8].
Methods and materials

Fifty patients (N=50) with histologically confirmed invasive ductal carcinoma (IDC) were analyzed on MRI (1.5 T Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany; Standardized diagnostic protocol: T2W STIR, T2W-TSE, T1W-TSE, DWI, dynamic 3D-FLASH enhanced; Contrast medium: Gd-DTPA, Magnevist, Bayer Schering Pharma, Berlin, Germany):

- Before the initial course of NACT
- After the 2nd cycle of NACT

According to the predefined endpoints:

1.) **RECIST** - Response evaluation criteria in solid tumors, version 1.1 (RECIST 1.1): the unidimensional measuring tool, defining and further evaluating the largest tumor diameter (cm) or the sum of the target lesions largest diameters (cm), with the follow-up response evaluated according to the response categories: CR, PR, stable disease (SD) and progression of the disease (PD) [1, 6].

2.) **Apparent diffusion coefficient (ADC)** - DWI and ADC maps were acquired using b-values of 0 and 800 mm2/s. ADC maps were calculated / created using image processing software - DICOM viewer OsiriX with plug-ins (OsiriX, Pixmeo, Geneva, Switzerland). ADC values were calculated according to the following model:

\[
ADC = \ln \left( \frac{s_0}{s_1} \right) / (b_1 - b_0)
\]

\( \ln \) - the natural log;
\( b_0 = 0 \) mm2/s;
\( b_1 = 800 \) mm2/s;
\( s_0, s_1 \) - signal intensities of the lesion per each b-value [4].

The selected MRI parameters (RECIST and ADC) were tested against the histopathological findings. Based on the histopathological findings, the two subgroups were created [6, 7]: a.) Responders (R, N1=25; patients with pathologic complete response (pCR) and near-pCR) b.) Nonresponders (NR, N2=25)
The nonparametric two-tailed Mann-Whitney U test was performed for the comparison of R and NR [9]. The P value of 0.05 or less, or when possible 0.01 or 0.001, was considered significant. The Spearman's rank correlation coefficient was also calculated [9]. Wilcoxon's test was chosen to test the differences within the subgroup R or NR [9].
Results

The average tumor size initially in R and NR (as shown in Table 1), was not significantly different: 2.99 +/- 0.57 cm vs. 3.33 +/- 0.49 cm; p>0.05

The difference in ADC between R and NR, was considered highly statistically significant initially: 1.004 +/- 0.009 mm²/s x 10^-3 vs. 0.840 +/- 0.134 mm²/s x 10^-3; p=0.0001

RESPONDERS:

After the 2nd cycle of NACT, ADC value increased significantly in R: 1.004 +/- 0.009 vs. 1.284 +/- 0.005; p=0.05 and the change was +27.89% (Fig. 1, 2).

Although the change in tumor size according to RECIST in R was considered significant after the 2nd cycle (2.99 +/- 0.57 cm vs. 2.59 +/- 0.53 cm; p<0.0001), the assigned response category according to RECIST was SD (-15.44%) (Fig. 1, 2).

In R, only moderate correlation between ADC and RECIST was noted after the 2nd cycle of NACT (r=0.49).

NONRESPONDERS:

After the 2nd cycle of NACT, ADC value was not significantly different in NR: 0.840 +/- 0.147 mm²/s x 10^-3 vs. 0.872 +/- 0.134 mm²/s x 10^-3; p>0.05 and the change was 3.81% (Fig. 3).

Although the change in tumor size according to RECIST in R was considered significant after the 2nd cycle (3.33 +/- 0.49 cm vs. 3.18 +/- 0.49 cm; p<0.001), the assigned response category according to RECIST was SD (-4.50%) (Fig. 3).

The difference in ADC value between R and NR after the 2nd cycle of NACT was considered highly statistically significant: 1.284 +/- 0.005 mm²/s x 10^-3 vs. 0.872 +/- 0.134 mm²/s x 10^-3; p<0.0001.
Table 1: Morphologic and functional predefined parameters (RECIST; ADC b0,800) in R (N1=25) and NR (N2=25), initially and upon the completion of 2nd cycle of NACT.

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Fig. 1: Initial MRI in R. According to RECIST - the largest Tu diameter measures 2.5 cm. ADC (b 0,800): 1.0 mm²/s x 10-3.
**Fig. 2:** MRI after 2nd cycle of NACT in R. According to RECIST - the largest Tu diameter measures 2.2 cm, the response is defined as SD. ADC (b 0,800): 1.3 mm²/s x 10^-3. The change in ADC value is higher than the cut-off value of 27% upon the completion of 2nd cycle of NACT.
Fig. 3: Initial MRI and MRI after 2nd cycle of NACT in NR. According to RECIST - the response is defined as SD. ADC (b 0,800) 0.8 remained unchanged initially and after 2nd cycle of NACT.

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Conclusion

In the two subgroups: R and NR - the initial tumor size was not considered statistically significant (p>0.05), therefore the comparison of the morphologic criteria, was performed in the two subgroups of patients with the tumors of similar size. The initial ADC value differed significantly between the two subgroups: R vs. NR (p=0.0001).

It was noted that the ADC value changed in R after the 2nd cycle of NACT and the change was slightly higher than the predefined cut-off value of 27% for R, based on the previously published limited number of trials (p=0.05; +27.89%), while the tumor response was categorized as SD according to RECIST (-15.44%). The predefined parameter of functional imaging - ADC based on DWI, changed as early as after 2\textsuperscript{nd} cycle, before the morphologic tumor change eventually became apparent in R. However, only modest correlation in parameters (RECIST, ADC) was noted in R, which was not considered significant.

In NR, neither parameter changed significantly.

Our results confirmed the previously published cut-off value of 27% increase in ADC value upon the completion of 2\textsuperscript{nd} cycle of NACT in R. It is worth mentioning that the DWI and ADC value change in NACT have not been standardized and recommended in the guidelines for standardized breast MRI.

Should larger trials confirm these results, ADC may have predictive value in early tumor response assessment to NACT, before the apparent morphologic changes based on the recommended standardized measuring tools, which could contribute to the standardization of the method.

The practical aspects of the early identification of R and NR - after the completion of 2\textsuperscript{nd} cycle - may contribute to the adequate selection of patients and the avoidance of toxic effects of the otherwise inefficient treatment in NR and the selection of the appropriate regimen.
Personal information

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References


