Correlation between apparent diffusion coefficient and molecular and histological prognostic factors in breast cancer: initial observations in 53 patients.

G. Petralia1, L. Bonello1, P. Summers1, L. Preda1, R. Di Filipp1, M. Pasin1, M. Locatelli1, G. Curigliano1 and M. Bellomi2-3

1Radiology, European Institute of Oncology, Milan, Milan, Italy, 2School of Radiology, University of Milan, Milan, Italy, 3Medical Oncology, European Institute of Oncology, Milan, Milan, Italy

BACKGROUND: The clinical course of breast cancer (BCa) is dependent on several factors including molecular and histological characteristics such as oestrogen and progesterone receptor (ER, PgR) expression, Ki-67 proliferation index, HER-2/ neu status. Other factors such as age, TNM staging and tumour grading are also important for their prognostic significance. Patients with endocrine responsive tumours usually have a better disease-free and overall survival when compared to tumours which are oestrogen and progesterone receptor negative for example [1]. Gene profiling has allowed clinicians to further classify breast carcinomas into four different molecular sub-types characterized by different prognoses and responses to therapy: Luminal A (ER+ (>50%) or PR+ (>50%), Ki-67: <14% and HER-2 negative), Luminal B (ER+ (>50%) or PR+ (>50%), Ki67: >14% and HER-2 negative), HER-2 positive, and triple receptor negative (ER, PR, HER-2 negative) [2]. The aim of this study was to correlate apparent diffusion coefficient (ADC) obtained from diffusion weighted (DW) MRI of the breast with molecular and histological prognostic factors.

METHODS AND MATERIALS: This study was approved by our Institutional Ethics Committee, and written informed consent was obtained from all patients prior to enrolment into the study. Fifty-three female patients (mean age 48.1, range 28-81 years) with histologically proven breast cancer greater than 10mm in diameter underwent conventional MRI and DW-MRI (b-values 0, 250, 500 and 1000 s/mm²) on a 1.5T scanner (Avanto, Siemens Medical Systems, Erlangen, Germany). The conventional sequences included T2-weighted Short-Tau Inversion Recovery (STIR), and dynamic T1 weighted Gradient Echo 3D sequences (one before and 6 after administration of paramagnetic contrast agent). The ROI for breast tumour volume was defined manually on the highest b-value images (b = 1000 s/mm²). The ADC for each ROI was then obtained and correlated with continuous molecular and histological prognostic variables (age, percentage of ER, PgR, HER-2, Ki-67). ADC values were assessed for difference between gene profiling subtypes (Luminal A, Luminal B, HER-2, triple receptor negative), vascular invasion (present/absent), grading (G1/G2/G3), ER / PgR / HER-2 expression (positive/negative), vascular invasion (present/absent), grading (G1/G2/G3), ER / PgR / HER-2 expression (positive/negative), Ki67 (<14% or >14%) and TNM staging.

RESULTS: The distribution of ADC values by molecular subtype can be seen in Figure 1. The mean ADC of breast cancer was 1.14±0.20 x 10⁻³mm²/sec. The mean ADC value of the HER-2 subtype was lower than other subtypes, however this difference approached statistical significance only when compared with the triple receptor negative group (p=0.055). The ADC for the small T3 subgroup (n=8) was lower than other T stages, however it was only statistically significant when compared to T1 subgroup (p=0.03). There was a marginally significant anti-correlation (Spearman r=-0.39, P<0.05) between ADC and HER-2 expression, with significantly higher (p=0.005) mean ADC values in patients with HER-2 expression rated 0 compared to those with non-zero HER-2 expression. For all individual parameters however, there was notable overlap in the ADC values between subgroups.

![Figure 1](image1.png)  
**Figure 1.** ADC values by gene profile group. The triple negative group tended to have values exceeding, and HER-2 positive group below the mean for the entire collection of tumours studied, leading to a significant difference only between these groups.

![Figure 2](image2.png)  
**Figure 2.** ADC values by T stage rating. The lower mean ADC seen in the T3 subgroup was significant only relative to that of the T1 subgroup (p=0.03).

CONCLUSIONS: The results of our study did not show any correlation between ADC values and the molecular and histological prognostic factors, showing only a possible exception for HER-2 expression. T3 tumours may also have a lower ADC value when compared to other T stage tumours; however the subject numbers are small for the T3 group herein, so further experience is needed to confirm this.

References: