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

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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/mm^2) 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/mm^2) . 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), 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^{-3}mm^2/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.

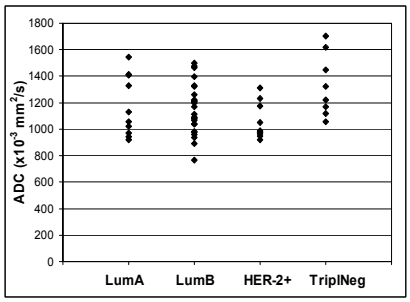

Figure 1. ADC values by gene profile group. The triple negative group tended to have values exceeding, and HER-2 positive group below the mean for the entire collection of tumours studied, leading to a significant difference only between these groups.

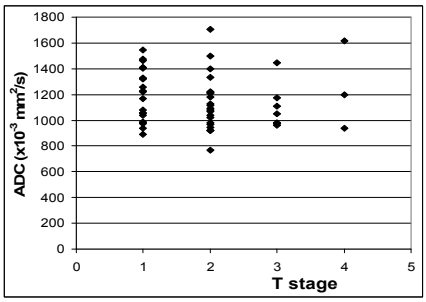

Figure 2. ADC values by T stage rating. The lower mean ADC seen in the T3 subgroup was significant only relative to that of the T1 subgroup (p<0.03).

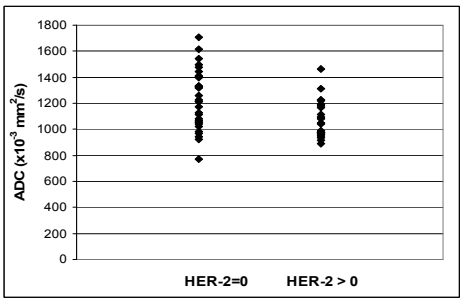

Figure 3. A significant difference was found between the mean ADCs of those patients without HER-2 expression and those with non-zero HER-2 (minimum non-zero level =20). This difference did not account for all of the weak negative correlation between ADC and level of HER-2 expression.

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:
[1] Aaltomaa S et al. Ann Med 1991. 23(6):643-8
[2] Sorlie T et al. Proc Natl Acad Sci USA 2001. 98:10869-10874.