Apparent diffusion coefficient correlation with different clinico-pathological and molecular prognostic factors of breast cancer

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Background: The apparent diffusion coefficient (ADC) obtained from diffusion-weighted magnetic resonance imaging (DW-MRI) has been shown to be a useful tool for the evaluation of breast tumors. It has shown potential in differentiating between benign and malignant breast tumors, between different histological subtypes, between low grade and high grade tumors, as well as in monitoring and predicting response to therapy [1]. Various clinico-pathological and molecular prognostic factors are involved in breast cancer management in order to improve patient risk stratification. Prognostic factors include patient related factors such as age, menopausal status, and family history. Histologic prognostic factors include TNM status, grading and vascular invasion. Other established prognostic factors include estrogen receptor (ER), progesterone receptor (PR), and HER-2 status, as well as the proliferation index (Ki-67). Gene profiling has identified 4 molecularly distinct groups based on global gene expression profiles, characterized by different prognosis: Luminal A group (ER+ [>50%] or PR+ [>50%], Ki-67 <14% and HER-2 negative), Luminal B group (ER+ [>50%] or PR+ [>50%], Ki-67 >14% and HER-2 negative), HER-2 group, and triple receptor negative group (ER, PR, HER-2 negative) [2]. The aim of this study was to examine the correlation of ADC obtained from DW-MRI with clinico-pathological and molecular prognostic factors of breast cancer.

Materials and Methods: After approval by our Institutional Ethics Committee, written informed consent was obtained from each patient prior to entry into the study. Between May 2008 and May 2011 we prospectively enrolled patients with solid breast lesions of 10mm or more, with a histological diagnosis of breast cancer, who were candidates for surgery or neoadjuvant chemotherapy. We excluded patients who had had any previous therapy to their breasts. 91 female patients underwent conventional MRI (including T2-weighted Short-Tau Inversion Recovery, and dynamic T1 weighted Gradient Echo 3D sequences [one before and 5 after administration of paramagnetic contrast agent]) and DW-MRI (b-values 0, 250, 500 and 1000 s/mm^2) on a 1.5 T MR scanner (Avanto, Siemens Medical Systems, Erlangen, Germany) with a dedicated 7-channel coil. The ADC for the tumor volume, as defined manually on DW-MR images at b=1000 s/mm^2, was correlated with clinico-pathological and molecular prognostic factors. Gene profiling subtypes (Luminal A, Luminal B, HER-2, triple receptor negative), vascular invasion (present/absent), grading (G1/G2/G3), ER/PR/HER-2 expression (positive/negative), Ki-67 (<14% or >14%) and TNM staging were assessed for differences in ADC using analysis of variance (ANOVA). Spearman coefficient was used to assess correlation between ADC values and continuous variables (age, percentage of ER, PR, HER-2, Ki-67).

Results: Of the 91 eligible patients, 88 female patients (mean age 48.6, range 28-81 years) were suitable for ADC calculation. Two patients were excluded due to inability to visualise the tumour on the DW-MR images, one due to motion artefacts. The mean ADC of breast cancer was $1.216 \pm 0.21 \times 10^{-3}$ mm^2/sec. The mean ADC for T4 tumors was higher than that for T2 tumors (p<0.05). The mean ADC for lymph node positive tumors (N1/N2) was lower than that of lymph node negative tumors (p≤0.02). The mean ADC value for triple receptor negative tumors was higher compared to other genetic subtypes, however only reaching statistical significance when compared to Luminal B and HER-2 subtype (p≤0.035).

Conclusions: The higher mean ADC in T4 tumors compared to T2 tumors could be explained by the increasing likelihood of a larger tumor to undergo intratumoral necrosis. The lower mean ADC in node positive tumors could be due to a hypercellular architecture of breast cancer, thus having more aggressive tumors in this group. This reflects the potential of ADC as an additional non-invasive clinical prognostic factor in breast cancer. The small sample size may explain the lack of significant differences in ADC values between the four gene profiling subgroups; further experience is required to draw meaningful conclusions.

(a)

(b)
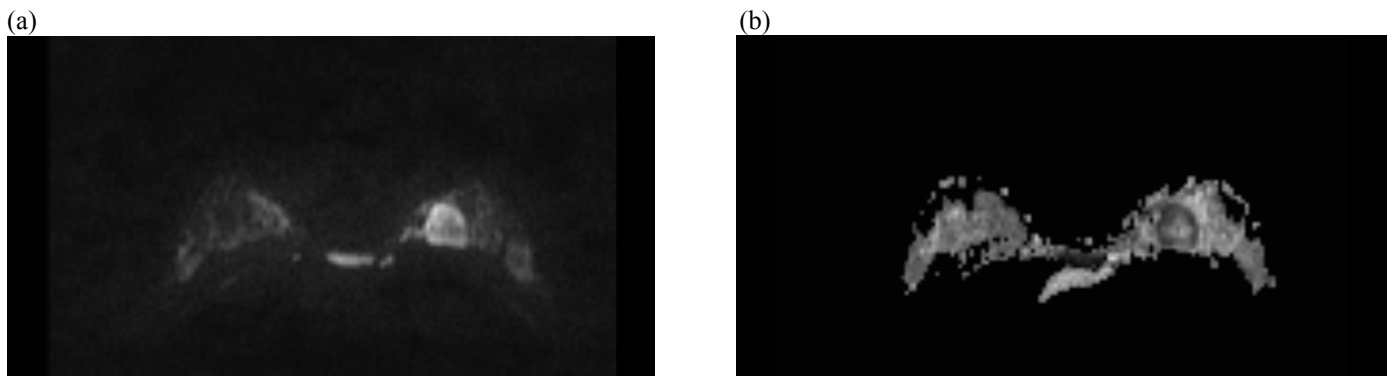
Axial high b-value (1000 s/mm^2) DW-MR image (a) showing a hyperintense lesion in the left breast, with a corresponding dark shade of gray on the ADC map (b), representing low ADC values (impeded diffusion).

References:
[1] Abdel Razek AA et al. Acad Radiol. 2010 Mar;17(3):382-6. [2] Perou CM et al. Nature. 2000;6797:747–752.