# Potential of diffusion MRI as a biomarker of low-risk DCIS

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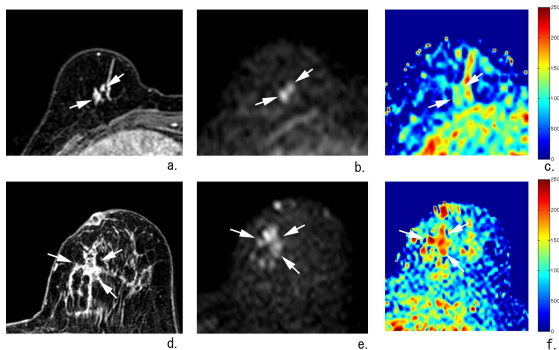
Fig.1 .Top row: **high grade DCIS**, bottom row: **low grade DCIS**. (a,d): Early phase of dynamic contrast-enhanced image; (b,e): DWI (b=1000); (c,f): ADC colored maps (c,f). While the low grade DCIS appears only with orange-red colors (high ADC), the high grade DCIS presents areas with light blue colors, corresponding to low ADC values.
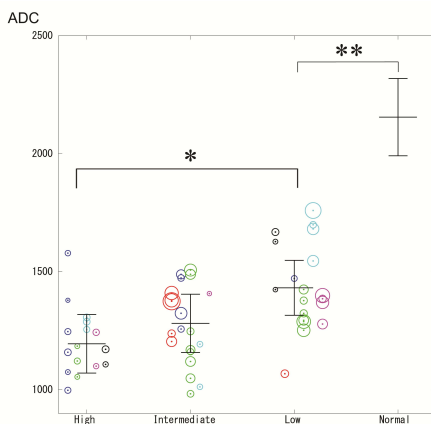
Fig.2 Mean ADC for each ROIs (all patients). Vertical axis: ranges of ADC values. Each patient is identified by a column and a color. Each ROI is shown as a circle, the area of which reflects the lesion size. Mean and standard-deviation are shown for each grade, and for the normal breast tissues (* $p < 0.05$, ** $p < 0.01$).
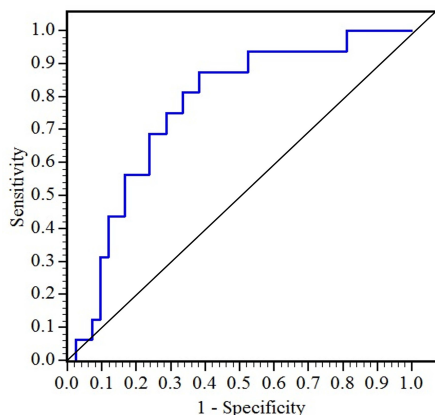
Fig.3 Receiver operating characteristic (ROC) curve for differentiating high from non-high grade DCIS lesions based on an ADC value of 1.3×10^{-3} mm²/s. The AUC was found to be 0.77, indicating a good discriminatory power.

Introduction: With the advent of widespread mammography screening the incidence of ductal carcinoma *in situ* (DCIS) has remarkably increased worldwide. However, all DCIS lesions are usually treated as invasive breast cancer, although some low grade DCIS have very good prognosis and may be considered a nonlethal type of tumor (1,2). Hence, there is an urgent need for more accurate DCIS grading at time of initial diagnosis. Diffusion MRI has already been proposed to differentiate benign and malignant breast lesions (3,4). We have specifically investigated the value of quantitative diffusion MRI (Apparent Diffusion Coefficient, ADC) to identify low-grade, low-risk DCIS.

Material and Methods: 18 patients diagnosed with DCIS underwent surgical resection and received pathological diagnosis. Breast MR imaging was performed at 1.5T (Intera and Achieva, Philips Medical Systems, Best, Netherlands) with a dedicated four-channel breast array coil. The following images were acquired: 1. bilateral sagittal fat-suppressed T2-weighted images (TR/TE: 49370/90 ms, FOV:20cm, matrix, 256², thickness: 4 mm); 2. Diffusion-weighted images (spin-echo SENSE EPI, TR/TE:8000/96 ms, FOV:40 cm; matrix: 128×104 interpolated to 256², i.e. 1.56²mm² resolution, parallel acquisition factor: 2.0, slice thickness: 5mm, diffusion gradient pulses were applied along the x, y, and z directions, b values: 0 and 1,000 s/mm²). Spectrally adiabatic inversion recovery was used for fat suppression. Quantitative diffusion (ADC) images were calculated on a voxel-by-voxel basis as: $ADC = (1/b) \times \ln(S_0/S)$ where S_0 and S are the signal intensities of each voxel obtained with the b values of 0, 1000, respectively; 3.dynamic contrast-enhanced MRI (3D fat-suppressed T1-weighted gradient-echo sequence, TR/TE: 6.1/3.5 ms, FA: 15°; FOV:40 cm, matrix: 400², slice thickness: 2 mm; reconstructed to $0.78 \times 0.78 \times 1$ mm³ resolution). Images were acquired before, immediately after and 9 minutes after contrast agent infusion of Gadoteridol (Gd) (0.2mL/kg, ProHance®, Braco-Eisai, Tokyo, Japan). Central k-space data were acquired first to catch early contrast enhancement.

Data post-processing: Regions of interest (ROIs) were manually placed in regions with high signal on the DWI images (b = 1000) by two radiologists blinded to the pathological results under the guidance of contrast-enhanced and T2-weighted images. As DCIS is usually a multi-focal disease several ROIs were taken for each lesion, and the number of ROIs varied from one to eight per patient. Normal tissue ROIs were drawn in homogeneous breast parenchyma in the center of the contra-lateral breast, avoiding contamination by fatty tissue. Areas with necrotic or cystic tissue were avoided by examining morphologic and contrast-enhanced images. The identified ROIs were then copied and pasted onto the corresponding ADC map for quantitative analysis. For each ROI, we extracted the mean ADC, standard deviation and the ROI size (surface area).

Results: Typical appearance on contrast-enhanced T1w images, DWI (b=1000s/mm²) and ADC maps are shown for low and high grade tumors (Fig.1). The mean apparent diffusion coefficient (ADC) values were 1.43+/-0.23 x 10^{-3} mm²/s, 1.28+/-0.12 x 10^{-3} mm²/s and 1.20+/-0.12 x 10^{-3} mm²/s for low, intermediate and high grades, respectively, and 2.10+/-0.25 x 10^{-3} mm²/s in normal breast. The ADC value of high grade DCIS was significantly lower than that of low grade DCIS ($p =0.01$), and there was a significant positive linear trend between ADC and tumor grade ($p < 0.01$) (Fig.2). A Receiver Operating Characteristic (ROC) analysis gave an ADC threshold of 1.3 x 10^{-3} mm²/s for the diagnosis of high grade DCIS with 81% sensitivity and 62% specificity. More importantly all patients with no lesion ROI below the ADC threshold value were identified as low grade (100% specificity).

Discussion and conclusion: The ADC appears as a good potential biomarker to identify with very high specificity low-grade DCIS lesions. The ability to screen lesions in their entirety is clearly a strong advantage for DWI (and MRI at large) over the necessarily limited sampling permitted by biopsies. Only patients with no part of the lesion above a given ADC threshold would be considered as low risk DCIS patients. Some patients with low grade DCIS may not satisfy this criteria and undergo some more invasive management, but overall a significant fraction of women might be spared from unnecessary invasive approaches, such as lumpectomy or mastectomy. In particular, those patients may not need axillary lymph node dissection, the morbidity of which is not negligible. This approach would decrease the economic and social burden associated with breast cancer and also potentially contribute to decrease the anxiety of women diagnosed with low risk (5).

References:

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