

Apparent diffusion coefficient (ADC) measurements in normal fibroglandular breast tissue for women at high risk of developing breast cancer compared to normal individuals.

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INTRODUCTION:

Women at high risk of developing breast cancer because they carry a mutation in the BRCA1 or BRCA2 gene or because they have had mantle radiotherapy for Hodgkin's lymphoma have a lifetime risk of developing breast cancer approaching 80% [1]. Annual screening MRI is recommended to these women because of its greatly improved sensitivity compared to mammography for detecting cancers [2,3]. In addition, diffusion-weighted techniques (DWI) in the breast have potential to increase specificity of tumour detection compared to dynamic contrast-enhanced MRI alone from 72% [4] to 85% [5]. However, as apparent diffusion coefficient (ADC) values derived from DWI are sensitive to changes in cell density, composition and volume of the extracellular matrix and high risk women may have an increase in proliferative breast disorders such as microglandular adenosis (up to 23% of women with BRCA 1 mutations) [6], it is essential to document ADC values of non-malignant fibroglandular breast tissue in these women to aid the use in tumour diagnosis. This study therefore compares ADC values in the normal fibroglandular breast tissue of premenopausal women at high risk of developing breast cancer with those obtained from premenopausal normal risk women (without a family history of breast cancer or previous chest irradiation).

METHODS:

24 women at high risk of developing breast cancer (15 BRCA carriers, 9 mantle radiotherapy, median age 43 years) underwent breast MRI (in the proliferative phase of the menstrual cycle (days 6-16)) at our institution between August 2008 and August 2011 with DWI on a Siemens Avanto 1.5T system. A bilateral single shot echoplanar inversion recovery sequence was performed with 4 b values (0, 100, 700, 1150mm²/s) (TR/TE=7500/94ms, 340mm field of view (FOV), 4mm slice thickness with 0 slice gap, 2 excitations and a 2.7x2.7x4mm acquisition voxel). 12 age-matched normal risk premenopausal volunteers (median age 37 years) without a family history of breast cancer or previous breast irradiation underwent DWI also during the proliferative phase of the menstrual cycle with a reference T1W sequence on a 3.0T Philips Achieva MRI scanner (Best, Netherlands). A sagittal single shot echoplanar sequence, with SPAIR and a slice-selection gradient reversal (SSGR) method for fat suppression was performed with 7 b values (0, 100, 150, 200, 350, 700, 1200mm²/s (TR/TE=1220/67 ms, flip angle 90°, 180 mm FOV, 2.5 mm slice thickness with 0 slice gap, one excitation and a 1.96x2.02x2.5mm acquisition voxel)) in 7 women; and 4 b values (0, 100, 700, 1150mm²/s (TR/TE=3771/67ms, flip angle 90°, 180 mm FOV, 3 mm slice thickness with 0 slice gap, 3 excitations and a 1.96x2.02x3mm acquisition voxel)) in 5 women. A region of interest (ROI) of 200mm² was drawn on the axial slice located at the level of the nipple in the most visually homogeneous breast parenchyma in the centre of the breast to minimise partial volume effects. In-house software Adept was used to extract pixel-by-pixel ADCs computed from mono-exponential fitting of the data without the b=0 value (ADC_{high}). An independent samples t-test was used to compare differences in the mean and centile ADC_{high} values (C10, C25, C50, C75, C90) and in the skewness of the distribution between high risk individuals and volunteers. A p value<0.05 determined significance.

RESULTS:

Mean ADC_{high} values (x10⁻⁶mm²/s) for high risk women (1893+/-251) were significantly higher than for normal risk women (1689+/-237)(p=0.036) (figure 1), ADC_{high} centiles in high risk women were also significantly higher than in normal risk women. Histogram skewness was similar for the two groups (p=0.165) (table 1, figure 2)

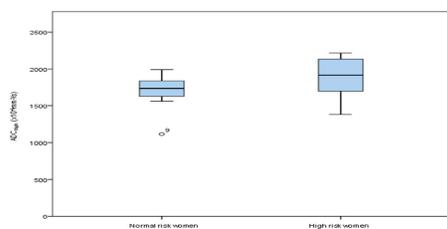


Figure 1: Box and Whisker plot showing the difference in ADC_{high} values between high risk and normal risk women in the same phase of the menstrual cycle (p=0.036).

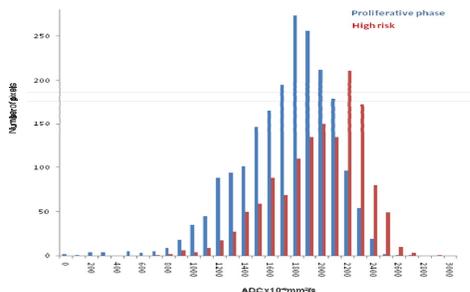


Figure 2: ADC_{high} histograms for all high risk and normal risk women in the proliferative phase of the menstrual cycle

parameter	Proliferative phase volunteers (n=10)	High risk women (n=24)	P value
C10	958 +/-253	1255 +/-174	<0.001
C25	1335 +/-84	1579 +/-77	<0.001
C50	1719 +/-128	1976 +/-138	<0.001
C75	1954 +/-68	2250 +/-34	<0.001
C90	2190 +/-90	2400 +/-86	<0.001
Skew	-0.850 +/-0.06	-0.664 +/-0.07	0.165

Table 1: ADC_{high} histogram parameters (mean+/-standard deviation) by centile with p value comparison. ADC_{high} units x10⁻⁶mm²/s, skew has no units.

DISCUSSION:

Differences in ADC of non-malignant breast tissue exist between women at high-risk compared to those at normal risk of developing breast cancer with right shift of the histogram in the former group. Differences are unlikely to be due to effects of hormones on the breast as both groups were scanned in the same phase of the menstrual cycle and are unlikely to be field strength dependent. Proliferative epithelial and glandular changes and associated alterations in the composition of the extracellular matrix are likely to contribute to the higher ADC_{high} values in high risk women. Higher ADC values in the fibroglandular parenchyma of high risk women than normal risk women should improve diffusion-weighted contrast between tumours and breast parenchyma in this group

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Acknowledgements : Dr James D'arcy for Adept in house software.