Differentiation of malignant, benign and normal breast tissues in a large cohort using ADC determined by DW MRI

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Introduction: Contrast enhanced magnetic resonance imaging MRI of the breast is known for high sensitivities of 71% -100% but simultaneously it suffers from low/variable specificity (20%-98%) (1). The limitation of low specificity of (MRI) in breast cancer diagnosis initiates the use new technique like diffusion weighted imaging (DWI). DWI measures the diffusivity of water molecules by means of the application of motion probing gradients. This imaging property is unique and provides a different contrast mechanism than that observed on conventional T1 and T2 weighted MR images. It provides potentially unique information on the viability of various tissue that is dependent on the molecular motion of water, which may be altered by disease processes which in turn help to compare the diagnostic capability among malignant, benign and normal breast tissues. A significant advantage of DWI over conventional MRI and contrast enhanced MR imaging is its high sensitivity to changes in the microscopic cellular environment without the need for intravenous contrast material. Therefore, in the present investigation, we examined the utility of DWI in the differentiation of normal, benign and malignant breast tissues and to determine a cut-off value for ADC for their discrimination.

Materials and Methodology: A total of 203 subjects were recruited for this study. Among them 141 (45.3 ± 10.2), were infiltrating ductal carcinoma (IDC). 34 were with benign breast pathology (mean ± SD age, 31.8 ± 9.7, range 15-61) and 28 were normal volunteers with mean ± SD age, 33.6 ± 8.9, range 21-59; who did not have any breast abnormalities based on clinical evaluation and MRI examination. DWI of 8 women (4 malignant, 2 benign and 2 control) could not be used due to motion and other artefacts. Written informed consent was obtained from each patient the study was approved by Institutional ethical committee. The DWI was carried out women using a phased array breast matrix coil at 1.5 T (AVANTO, Siemens). Prior to study in humans, DWI was acquired on phantoms containing water and acetone at 25ºC for calibration of the sequence. DW images were acquired in the transverse plane using a single-shot echo planar imaging sequence with TR = 5000 ms; TE= 87 ms; FOV = 250 – 350 mm; NS = 1; EPI factor =128; acquisition matrix = 128 x 128; and slice thickness = 4 to 5 mm, without any inter slice gap. Three b values of 0, 500 and 1000 s/mm^2 were used; Mean ADC were calculated from the ADC map by drawing contiguous circular ROIs of five pixels (size = 0.31 cm^2) from the each group (malignant, benign lesion and normal tissue). Statistical analyses were carried out using software SPSS 16.0.

Results: The ADC values for water and acetone were calculated to be 2.22 x 10^{-3} mm^2/s and 4.4 x 10^{-3} mm^2/s, respectively, which were in agreement with the value reported in literature (2). Figure 1 shows the ADC map of malignant, benign and normal breast tissue. The mean ADC of malignant lesion was significantly lower (1.03 ± 0.18) compared to benign (1.63 ± 0.28) and normal (1.80 ± 0.12) breast tissues (Figure 2). An ROC analysis was used to determine the cut-off values of mean ADC among malignant, benign and controls. Accordingly, a cut-off value of 1.19 (x10^{-3} mm^2/s) with sensitivity 93.8%; specificity 89.8% and area under the curve (AUC = 0.96) for ADC was obtained to differentiate malignant from benign diseases. Similarly, a cut-off value of 1.46 (x10^{-3} mm^2/s) with sensitivity 100%; specificity 97.8% (AUC = 0.99) was obtained to differentiate malignant and normal breast tissue. A cut-off value of 1.74 (x10^{-3} mm^2/s) with sensitivity of 73.1%; specificity of 75% (AUC = 0.77) for ADC was obtained to differentiate benign from normal tissues.

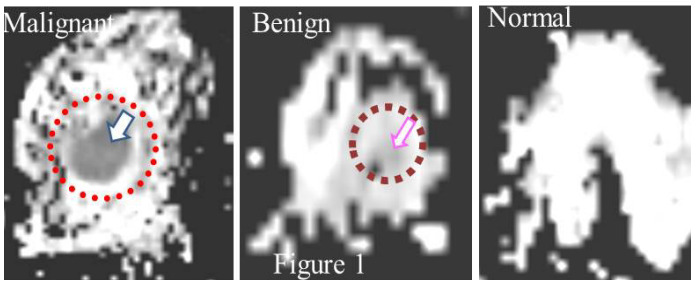

Figure 1

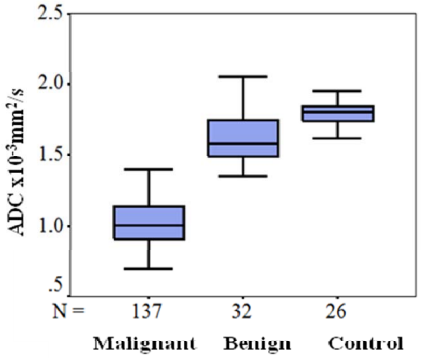

Figure 2: Box plot showing the mean ADC in malignant, benign and control (normal volunteers).

Discussion: We present here the ADC values in a large cohort of IDC patients. Our results indicated that ADC of IDC patients were significantly lower compared to benign patients and controls. The decreased ADC reflects the underlying histological pattern of densely packed randomly organized tumor cells, which inhibit effective motion of water molecules and restricted diffusion results into lower ADC values (3). The high cell proliferation in malignancy increases the cellular density, which decreases the extra-cellular volume water fraction and thereby decreases the ADC. An inverse relation between ADC and tumor cellularity has been also reported (4). Further, mean ADC of normal tissue (control) was higher compared to the benign tissue, indicating the potential of ADC in discriminating normal versus benign tissues. The present findings are in agreement with the previous studies (5, 6). We also reported a cut-off value of ADC to differentiate malignancy from the benign and normal breast tissues. The results suggest that quantitative diffusion-weighted MR imaging could be used to identify different type of breast tissues and addition of ADC values may help increase the sensitivity and specificity of MRI in the breast cancer diagnosis.

Conclusion: In conclusion, the present study on a large cohort revealed that low ADC value is an indicative of malignancy. The properties like permeability, cellularity etc varies in normal, malignant and benign tumors, diffusion coefficient of water in these tissues has the potential to provide useful information that could be of diagnostic importance in discrimination of various breast tissues value.

References: (1). Kuhl CK et al. 2006. *Radiology*; 239: 666-76; (2). Guo et al. 2002. *J Magn Reson Imaging*; 16: 172-78; (3) Guo et al. 2002a. Radiology; 224: 177-83.; (4) Nonomura et al. 2001. J. Magn. Reson. Imaging; 13: 757-60; (5). Sharma et al. NMR Biomed; 22: 104-13. (6). Woodhams et al. 2005. Magn. Reson. Med. Sci; 4: 35-42.