Diffusion MR Breast Imaging: ADC values for differentiating of Malignant from Benign Breast Tumors

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Introduction

Diffusion MRI is a noninvasive technique which provides information about early changes in morphology and physiology of tissues by monitoring changes in the local apparent diffusion coefficient (ADC) of water molecules. These changes in ADC values are associated with different degrees of restriction to motion and are connected with pathological modifications such as those encountered in tumors. In recent years, diffusion imaging has demonstrated potential in discriminating malignant from benign breast tumors (1, 2) and in assessing progression of disease following therapy (3).

In this work we present the clinical usefulness of diffusion weighted imaging (DWI) and apparent diffusion coefficients (ADCs). Diffusion MRI examinations were performed on patients who had positive MRI findings and underwent MRI-guided interventional procedures. Our objective was to determine if the acquisition of quantitative ADC values can improve the detection efficiency of breast malignancy. Histopathology examination was used as the reference standard to discriminate conclusively between malignant and benign lesions.

Methods

The IRB approved this HIPAA-compliant study. 140 lesions from 126 patients with suspicious or biopsy-proved cancer lesions were studied between Sep'2008 and June'2009 (median age, 49 years; range, 25–84 years) who underwent 1.5-T MR imaging as part of their diagnostic MRI protocol.

The diagnostic breast MRI protocol includes multi-slice FSE T_2-weighted MRI with fat saturation, pre-contrast 3D SPGR T_1-weighted MRI with and without fat saturation, DWI with fat-saturation, and DCE MRI (3D SPGR) with fat saturation. The reading of MRI was based on morphology of contrast enhanced lesion and contrast wash-out kinetics (4). In addition, DWI images were obtained by using single-shot spin-echo EPI sequence with a pair of gradient pulses in all three orthogonal axes. The parameters were TR=6000 ms, TE=90-100 ms, FOV=26-32 cm, slice thickness is 4 or 5 mm with 0 mm spacing and matrix size of 192x128. The orientation and location of these images were prescribed similar to the sagittal T_1- weighted images for unilateral and axial T_1-weighted images for bilateral breast cases. The gradient *b* values were 0 and 1000 sec/mm^2. With 4 to 6 averages, and the duration of the DWI examination was about 2-3 minutes.

All studies were conducted with 1.5T GE Excite systems with the body coil as the transmitter and a sentinel coil or phase arrayed coil as the receiver. 140 lesions (77 malignant and 63 benign) were evaluated. Malignant lesions were further classified as invasive carcinomas(IC,n=63) and non-invasive carcinomas (NIC,n=14). 26 of 71 evaluated lesions were metastasized based on positive lymph nodes obtained from pathological exam. The lesion pathology was determined from a histological examination performed on biopsy or needle localization samples obtained after the MR scan. ADC maps were calculated with GE's FUNCTOOL software. Regions of interest (ROIs) were manually drawn well within the enhancing lesions on diffusion images. Quantitative ADC measures between malignant lesions and benign lesions were compared (Table.1). All statistical analyses were done within SAS® 9.2 and R 2.9.2.(5)

Table 1: Descriptive variables and lesion-type classification (Benign/Malignant/NIC/IC)

	Total n=140	Benign n=63	Malignant n=77	NIC n=14	IC n=63
Age	48.5 ± 10.7	47.5 ± 10.8	49.4 ± 10.7	46.0 ± 10.1	50.4 ± 10.8
Tumor Size	2.05 ± 1.66	1.53 ± 1.14	2.48 ± 1.89	2.25 ± 1.57	2.53 ± 1.96
Average ADC*1e3	1.35 ± 0.47	1.77 ± 0.33	1.00 ± 0.20	1.15 ± 0.25	0.97 ± 0.18
BIRADS, n(%)					
4	60 (43%)	52 (83%)	8 (10%)	3 (21%)	5 (8%)
5	8 (6%)	4 (6%)	4 (5%)	0 (0%)	4 (6%)

Results and Discussions

Fig. 1a and 1b shows the ADC parametric map and the matching post-contrast T_1-weighted MR image for a women with invasive ductal carcinoma that was confirmed with biopsy procedure. By drawing a region of interest (red circles on image) on hypointensity (mixed green and blue) lesion corresponding to enhanced lesion from post contrast images, we calculated the diffusion coefficient to be 0.00090±0.00022 mm^2/s (Mean±SD). SD represents the standard deviation. Fig. 2a and 2b show the ADC maps (mixed yellow and green) and matching T1-post image of benign fibroadenoma lesion. ADC coefficients were calculated as 0.0017±0.00011 mm^2/s. The pathology results showed that 77 of the 140 lesions were malignant and the other 63 were benign. Table 1 lists the average mean and standard deviations (Mean±SD) of diffusion coefficients calculated from group of benign, malignant lesions, sub-types of malignant lesions, metastasized and non-metastasized lesions along with MRI results for highly suspicious lesions (BIRADS=4 &5). Fig 3 represents the box plot showing difference between these groups and the average mean and standard deviations of diffusion coefficients calculated from group of malignant and benign lesions are (1.00±0.20) x 10^{-3} mm^2/sec and (1.77±0.33) x 10^{-3} mm^2/s respectively. Areas under the ROC curves were 0.98. Malignant lesions further classified as invasive carcinomas 'IC' (n=63) and non-invasive carcinomas 'NIC' (n=14); their mean and standard deviation are (0.97± 0.18) x 10^{-3} mm^2/s and (1.15± 0.25) x 10^{-3} mm2/s. ROC analysis done for groups of benign/IC (AUC=0.99), benign/NIC (AUC=0.95), and IC/NIC (AUC=0.72) (Fig.4). Since ADC values are approximately proportional to cellular density, they represent a valuable biomarker for detecting malignant lesions. There were no significant correlations between the ADC value and prognostic factors (Abstract2) . Our calculated mean ADC coefficients were in the range of values that have been previously reported for benign and malignant lesions (1, 2). Among BIRADS 4/5 patients, the sensitivity of detecting malignancy using MRI along is 33.3% (4/12), and the corresponding specificity is 92.9% (52/56).

Conclusion

ADC measurements are useful to differentiate malignant lesions from benign lesions yielding 98.4 % specificity and 90.9 % sensitivity with ADC cut-off value of 1.28x10^{-3} mm^2/s. ADC was less reliable for differentiating invasive and non-invasive carcinomas .Since ADC values are roughly proportional to cellular density (High density Low ADC, Low density High ADC) they represent a valuable biomarker for detecting malignant lesions (which are believed to have a higher cellular density). The findings suggest that cell density might play an important role in the different ADCs obtained from benign and malignant breast lesions and the measurement of extracellular water content is an additional feature that can improve MRI specificity and may help to understand treatment changes.

Fig.1a

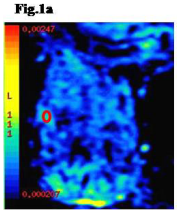


Fig.1b

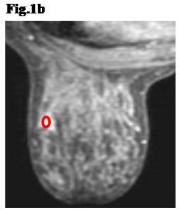


Fig.2a

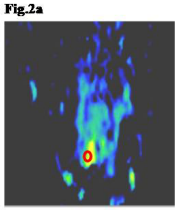


Fig.2b

Fig.3

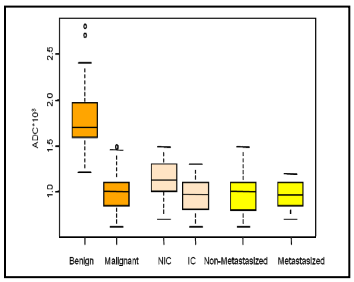
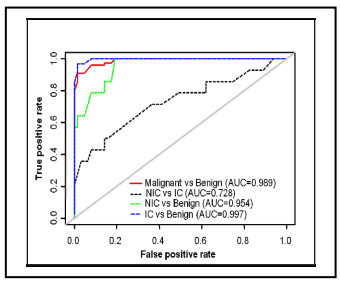


Fig.4



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