Quantitative DWI for differentiation of benign and malignant breast lesions: the influence of the choice of b-values

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Introduction

Dynamic contrast enhanced (DCE) MRI of the breast has obtained a prominent role in clinical practice because of its high sensitivity for detecting invasive breast tumors. The specificity of DCE MRI of the breast is lower. A promising adjunct MRI technique is Diffusion Weighted Imaging (DWI), which indirectly assesses the cellularity of a lesion. The rationale is that in malignant lesions, the cells are more densely packed in a certain volume than in benign lesions and normal tissue, leading to less intra- and extracellular space for Brownian motion of the water molecules. This results in a lower Apparent Diffusion Coefficient (*ADC* [mm^2/s]) in malignant lesions. However, perfusion effects can also contribute to the *ADC* value [1, 2]. Perfusion effects cause a substantial signal attenuation already at low *b*-values, which explains the contribution of mainly perfusion effects to the *ADC* when only low *b*-values are used. Since in well-perfused tumor tissue, perfusion effects are expected to be larger than diffusion effects, the *ADC* found using only low *b*-values is higher than the *ADC* obtained with higher *b*-values. At higher *b*-values, the signal loss due to perfusion effects is already complete, so only diffusion effects remain, leading to a relatively low *ADC* which is mainly attributed to diffusion. It was shown by Le Bihan et al. and Thoeny et al. that omitting low *b*-value scans from the fit procedure used to calculate the *ADC* considerably decreases the contribution of perfusion effects to the diffusion measurement [1, 2]. Since both perfusion and diffusion are thought to be different in benign and malignant lesions, it is unclear which combination of *b*-values allows optimal differentiation between benign and malignant breast lesions. In this study, we evaluated which combination of *b*-values is optimal for the differentiation of benign and malignant breast lesions.

Materials & Methods

Seventy-one patients with 88 nonpalpable suspicious breast lesions detected on x-ray mammography were included in this study. All patients underwent biopsy after MRI to confirm the diagnosis histologically. Written informed consent was obtained from all patients and the study was approved by the ethics board of our institution. Images were acquired on a 3-T whole body system (Intera Achieva, Philips, Best, The Netherlands). Patients were placed in prone position. Signals were acquired using a 4-channel bilateral open breast coil (MRI devices, Würzburg, Germany). From our MR breast tumor scan protocol, the 3D post-contrast fat-suppressed T1-weighted gradient-echo sequence totally covering both breasts was used to depict the lesions. The DWI series was a fat-suppressed single-shot EPI sequence with four *b*-values: 0, 150, 499 and 1500 s/mm^2. An ROI was placed inside the lesion on the *b*=0 s/mm^2 diffusion weighted images which were shown adjacent to the T1-weighted images at the same anatomic location. The signal intensity was averaged over the ROI for each *b*-value to calculate the *ADC* of the lesion. This was done by applying a non-linear least squares method (Marquardt–Levenberg) to fit the following function $S(b) = S_0 \cdot e^{-b \cdot ADC}$ to the data, with S_0 and *ADC* as fit parameters. To evaluate which combination of *b*-values used in the fit procedure is best to differentiate benign from malignant breast lesions, the *ADC* was calculated using 5 different combinations of *b*-values: method 1: measuring mainly diffusion effects: using the highest three *b*-values (150, 499, 1500 s/mm^2); method 2: using all available information: all four *b*-values (0, 150, 499, 1500 s/mm^2); method 3: measuring primarily perfusion effects: using the lowest two *b*-values (0, 150 s/mm^2); method 4: comparable to commonly used method in literature: using the lowest and the highest *b*-value (0,1500 s/mm^2) and method 5: measuring diffusion effects: using the highest two *b*-values (499, 1500 s/mm^2). Receiver operating characteristic (ROC) curves were constructed and the area under the ROC curve of the five methods was compared.

Results

Eighty-eight lesions in 71 patients were analyzed. Size of the lesions ranged from 4 mm to 40 mm (median 11 mm). Histology of the lesions showed 36 benign lesions (7 fibroadenomas, 7 fibrocystic change, 10 hyperplasia/adenosis, 3 metaplasia, 1 abscess, 3 papilloma, 4 normal breast tissue, 1 intramammary lymph node), 14 non-invasive carcinomas and 38 invasive carcinomas. A typical example of the acquired images is shown in figure 1. The distribution of the *ADC* values for benign, non-invasive carcinomas and invasive carcinomas using different combinations of *b*-values is shown in figure 2. The median *ADC* value was highest in benign lesions, intermediate in non-invasive carcinomas and lowest in invasive carcinomas for all methods. Calculating the *ADC* with only the lowest 2 *b*-values (0 and 150 s/mm^2, measuring primarily perfusion effects) resulted in the highest *ADC* values for all lesions types. Using the highest 2 *b*-values (499 and 1500 s/mm^2 measuring diffusion effects) resulted in the lowest *ADC*. The area under ROC curve was 0.71, 0.72, 0.70, 0.72 and 0.69 respectively for the 5 methods (figure 3).

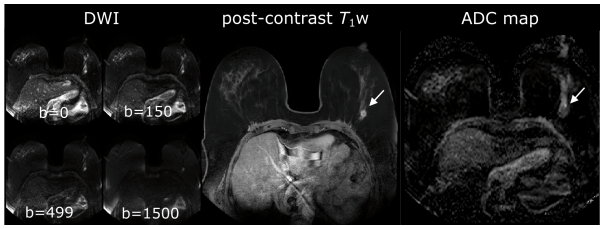


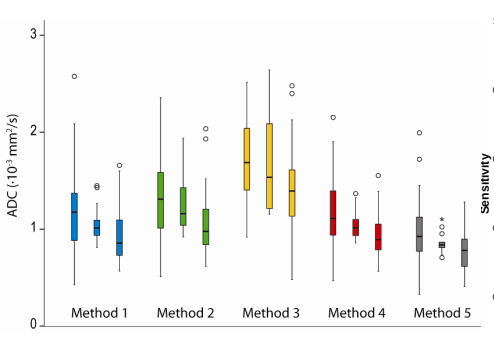
Figure 1. DWI (b=0, 150, 499 and 1500 s/mm2), post-contrast T1 weighted image and *ADC* map of a patient with an invasive carcinoma (arrow)

Conclusion

The *ADC* varies with the choice of different *b*-values. The diagnostic performance is not affected by the choice of the *b*-values. The results imply that to differentiate benign from malignant breast lesions, the choice of *b*-values is not relevant. However, when the *ADC* value is compared to reported *ADC* threshold values in literature, the *b*-values used to calculate the *ADC* should be taken into account.

References

[1] Le Bihan et al. Radiology 1988;168(2):497-505. [2] Thoeny et al. J Magn Reson Imaging 2004;20(5):786-90.



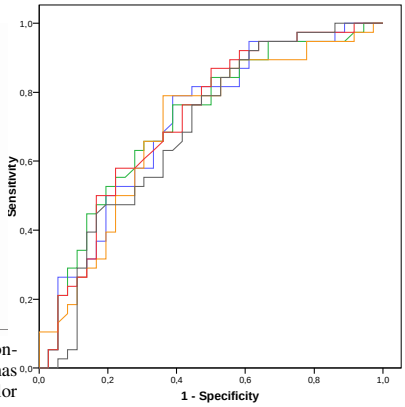


Figure 2. Distribution of *ADC* values of benign (left box), non-invasive carcinomas (middle box) and invasive carcinomas (right box) for all five methods to calculate the *ADC* (color coding for the 5 methods is explained in the table). ° = outlier: cases that lie 1.5–3 times the interquartile range (IQR) from the box; * = extreme value: cases that lie >3 times the IQR from the box.

b-values used to calculate the *ADC*	AUC	95% Confidence Interval	
		Upper Limit	Lower Limit
150, 499, 1500	0.712	0.593	0.831
0, 150, 499, 1500	0.719	0.601	0.836
0, 150	0.697	0.575	0.819
0, 1500	0.720	0.602	0.837
499, 1500	0.689	0.565	0.812

Figure 3. ROC curve and AUCs of *ADC* values of benign and invasive carcinomas for all five methods to calculate the *ADC*. (the non-invasive carcinomas (n=14) were excluded from the ROC analysis)