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Original Article

Applicability and discriminative value of a semiautomatic three-dimensional spherical volume for the assessment of the apparent diffusion coefficient in suspicious breast lesions—feasibility study☆

Jan Hering [f], Frederik Bernd Laun [b], Wolfgang Lederer [c], Heidi Daniel [d], Tristan Anselm Kuder [b], Anne Stieber [e], Stefan Delorme [a], Klaus H. Maier-Hein [f], Heinz-Peter Schlemmer [a], Sebastian Bickelhaupt [a,*]

[a] German Cancer Research Center (dkfz), Department of Radiology, Im Neuenheimer Feld 280, 69120 Heidelberg
[b] German Cancer Research Center (dkfz), Medical Physics in Radiology, Heidelberg Im Neuenheimer Feld 280, 69120 Heidelberg
[c] Radiological Practice at the ATOS Clinic Heidelberg, Heidelberg, Bismarckplatz 9-15, 69123 Heidelberg
[d] Radiology Center Mannheim (RZM), Mannheim, Rosengartenplatz 7, 61818 Mannheim
[e] University Hospital Heidelberg, Department of Clinical and Interventional Radiology, Heidelberg, Im Neuenheimer Feld 400, 69120 Heidelberg
[f] German Cancer Research Center (dkfz), Junior Group Medical Image Computing, Heidelberg, Im Neuenheimer Feld 280, 69120 Heidelberg

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ABSTRACT

Introduction: To evaluate the feasibility and accuracy of a semiautomatic, three-dimensional volume of interest (3D sphere) for measuring the apparent diffusion coefficient (ADC) in suspicious breast lesions compared to conventional single-slice two-dimensional regions of interest (2D ROIs).
Method: This institutional-review-board-approved study included 56 participants with Breast Imaging Reporting and Data System 4/5 lesion. All received diffusion-weighted imaging magnetic resonance imaging prior to biopsy (b=0–1500 s/mm^2). ADC values were measured in the lesions with both methods. Reproducibility and accuracies were compared.
Results: Area under the curve was 0.93 [95% confidence interval (CI) 0.86–0.99] for the 3D sphere and 0.91 (95% CI 0.84–0.98) for the 2D ROIs without significantly differing reproducibility (P=.45).
Conclusion: A semiautomatic 3D sphere could reliably estimate ADC values in suspicious breast lesions without significant difference compared to conventional 2D ROIs.

1. Introduction

Diffusion-weighted magnetic resonance imaging (DW-MRI) can be used to display the random motion of water molecules within a voxel [1]. Since this motion is thought to be closely related to the cellular density of the underlying tissue, DW-MRI has gained increasing interest in diagnostic imaging over the past years [2]. Since malignant tumors are commonly characterized by densely packed cells with restricted diffusion, DW-MRI may help to find and characterize suspicious lesions, which is of interest especially in oncologic imaging [2].

The apparent diffusion coefficient (ADC) is a measure for the magnitude of the diffusion and is commonly computed for the whole image and provided as a parameter map. Such maps are extracted from multiple DWI measurements. High ADC values are more commonly found in benign lesions, whereas low ADC values are more common in malignant lesions [3].

In magnetic resonance mammography (MRM), additional DWI sequences with ADC maps and locally calculated ADC values can increase the specificity of MRM, as several publications suggest [3–8]. Yet, a manual segmentation for obtaining a mean ADC of an entire breast lesion is time consuming. Therefore, the ADC is commonly obtained from two-dimensional regions of interest (2D ROIs) in a single slice, potentially excluding relevant information from parts of the lesion outside this slice [9]. A semiautomatic three-dimensional (3D) sphere tool would be a possible remedy. Indeed, many lesions are almost spherically shaped, and so a spherical region may be used to include large parts of the lesion volume.

We therefore investigated the applicability and reliability of ADC metrics computed in a semiautomatically defined 3D spherical volume of interest as compared to a representative 2D ROI for characterization of suspicious breast lesions found in X-ray mammograms prior to biopsy.

2. Method

2.1. Participants

Fifty-six female participants of the national mammography screening program were included in this retrospective analysis within a

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* Corresponding author. Im Neuenheimer Feld 280, 69126 Heidelberg, Germany. Tel.: +49 6221 422603; fax: +49 6221 422615.
E-mail address: S.Bickelhaupt@dkfz.de (S. Bickelhaupt).

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prospective study that received institutional and governmental review board approval. Written informed consent was obtained prior to inclusion in the study. All participants were scheduled for biopsy for suspicious screening results (October 2014–February 2015). Mean age of the participants was 57 years (SD ±7.4 years). This manuscript addresses a retrospective methodological evaluation of a prospective study on DWI in screening-detected breast lesions, of which the principles of the methods as described in following and preliminary results have been reported previously [10].

2.2. MRI technique and image analysis

Prior to breast biopsy, the participants underwent breast MRI examinations using a 1.5-T MR scanner (Ingenia, Philips) with a two-channel breast coil as previously described [10]. All participants were placed in prone position with the breasts slightly fixed in the dedicated breast coil using foamed material.

The MRI protocol consisted of a full diagnostic standard breast MRI protocol including DWI with four different *b*-values (0, 100, 750, and 1500 s/mm^2). The diagnostic protocol included nonenhanced T1-weighted and T2-weighted MR sequences, DWI sequences, and a contrast-enhanced (gadobenate dimeglumine, 0.1 mmol/kg, Multihance; Bracco, Milan, Italy) sequence. All sequences and parameters are listed in Table 1.

2.3. Image preparation

All images were transferred to a dedicated PACS workstation (OsiriX Imaging Software V.6.0; Pixmeo, Bernex, Switzerland). ADC maps were calculated using the OsiriX open-source ADC map plugin, and the ADC maps were then transferred to the in-house software MITK Diffusion [11]. ADC maps were generated using all *b*-value images as a fit to SI = exp($-b_i$*D) with SI = images at *b*-values b_i and D representing the ADC. The fit used was a least-squares fit to log(SI) against ($-b_i$*D).

2.4. Image analysis

The following two methods were evaluated in calculating a representative ADC of a suspicious lesion:

1. Conventional analysis of the lesion using 2D ROIs: The respective lesions were retrieved on the ADC map in knowledge of all diagnostic series, and a single circular 2D ROI per lesion was manually drawn covering the tumor area with the lowest ADC values as depicted within the lesion and avoiding apparent vessels or necrotic areas (Fig. 1) as previously reported [9].
2. Analysis of the lesions using the semiautomatic 3D spherical metric tool: After locating the lesion on the ADC map as described above, a 3D sphere was placed over the lesion covering the whole lesion. For this, the user interactively placed a circular ROI in the axial slice with the largest diameter of the lesion with the software tool automatically extending the 3D shape extension of the ROI into the cranial and caudal slices, ultimately forming a 3D sphere with the same radius as the placed ROI. In order to avoid the inclusion of benign glandular or fatty tissue, the 3D sphere was carefully adjusted along the inner, not the outer, borders of the suspicious lesion. For this purpose, the multiplanar localizer showed the intersection of the 3D sphere overlaid on the ADC map. In more longitudinal than circular lesions, the 3D sphere was so placed that it covered the lesion at its shortest diameter, without including extralesionary tissue and knowingly excluding parts of the lesion itself (Fig. 2).

One experienced reader (S.B., >5 years of experience including substantial MRI experience) evaluated both methods two times at a 2-week distance using an integrated virtual multiplanar reconstruction mode provided by the MITK software in order to ensure an accurate placement of the 3D spheres inside the suspicious lesions and the correct placement of the 2D ROI. Reading time was measured using an electronic stopwatch.

2.5. Biopsy

Following MRI, the participants of the study underwent a breast biopsy in concordance to the regular mammography screening procedures, with the histopathologic diagnosis serving as the standard of reference for validation of the ADC value analysis [10]. Breast biopsy was performed by either ultrasound or conventional X-ray guidance.

2.6. Data analysis

Variables are expressed as means±standard deviations if not declared otherwise. Normality testing was performed using the Shapiro–Wilk test. Receiver operating curves of the ADC value calculation were computed to assess the optimal accuracy and cutoff ADC values for differentiating between malignant and benign lesions.

Differences between measured ADC values of both methods for benign and malignant lesions were evaluated using the two-sided Student's *t* test after normality testing with the Shapiro–Wilk test. Differences between the ADC values in identical lesions calculated with the different methods were quantified using one-way repeated-measures analysis of variance (ANOVA) after normality testing. Measurement time was evaluated using the Mann–Whitney *U* test after normality test using the Shapiro–Wilk test failed. Reproducibility of repeated measures of ADC value calculation for both methods was assessed using Friedman's repeated-measure ANOVA after normality testing using the Shapiro–Wilk test failed for 3D sphere data and with the one-way repeated-measure ANOVA for the 2D ROI after normality testing using the Shapiro–Wilk test.

Data analysis was performed using commercially available software Sigma Plot (Version 12.5). A *P* value of less than .05 was considered significant.

Table 1
Breast MRI protocol

	Orientation	TE (ms)	TR (ms)	Slice thickness (mm)	FOV (mm × mm)	Acquisition matrix	Averages	Additional features
General preparations: MRI coil: dedicated 7-channel breast coil; patients placed prone; breast not compressed but fixed using foamed material.								
Localizer								
T1w TSE	Coronal	8	512	3	280×360	280×282	2	Turbo factor: 5; parallel imaging: SENSE ×2
T2w TSE	Transverse	120	3800	3	340×280	280×272	2	Turbo factor: 20; parallel imaging: SENSE ×2
T2w SPAIR	Transverse	70	3800	3	340×280	224×219	2	Fat suppression: SPAIR; turbo factor: 18
DWI	Transverse	99	10,530	3	400×340	136×156	1	*b*1=0, 100, 750, 1500 s/mm^2; parallel imaging: SENSE ×2.5
T1w DCE	Transverse	4.6	7.3	1	340×280	328×402	1	6 dynamic pre-/postcontrast series, each 1.23 min; parallel imaging: SENSE ×3
T1w TSE	Coronal	8	512	3	280×360	280×282	2	Turbo factor: 5; parallel imaging: SENSE ×2

TE = echo time, TR = repetition time, FOV = field of view; TSE = turbo spin echo, DCE = dynamic contrast enhanced, SPAIR = spectral adiabatic inversion recovery, SENSE = sensitivity encoding.