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Original Article

Diagnostic interplay of proton magnetic resonance spectroscopy and diffusion weighted images with apparent diffusion coefficient values in suspicious breast lesions

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ABSTRACT

Aim of the work: To study the diagnostic performance of combined single voxel 1H-MRS and DW-MRI with ADC values as a non-contrast diagnostic tool, compared to the DCE-MRI, in suspicious breast lesions.
Materials and methods: 113 female patients (mean age 45.8 years) with suspicious breast lesions, categorized as BI-RADS 3 or 4 by sono-mammographic examinations, were subjected to bilateral breast imaging with non-contrast MRI including conventional MRI, DW-MRI with quantitative ADC values, and single voxel 1H-MRS, in addition to DCE-MRI. They had 132 pathologically proved lesions (74 benign and 58 malignant).
Results: DW-MRI with ADC values was 96.97% accurate with 94.92% sensitivity and 98.63% specificity, while DCE-MRI was 97.73% accurate with 98.29% sensitivity but with 97.29% specificity, and 1H-MRS was 98.48% accurate with the highest sensitivity (100%) and 97.33% specificity. Furthermore, the combined use of DW-MRI with ADC values and 1H-MRS improved the diagnostic capability than utilization of each sequence alone with the highest accuracy of 99.24%, 100% sensitivity and 98.65% specificity.
Conclusion: The combined use of DW-MRI with quantitative ADC data and single-voxel 1H-MRS is a reliable non-contrast tool that provides higher accuracy in characterizing suspicious breast, and can efficiently be used in the absence of DCE-MRI.

1. Introduction

Breast cancer is a disease that knows no boundaries and can strike women at any age [1]. Breast magnetic resonance imaging (MRI) becomes now an integral component of breast imaging protocols. Functional MRI techniques can provide non-invasive digital biomarkers of tissue properties that are highly relevant to the assessment of tumor progression [2]. The dynamic contrast-enhanced MRI (DCE-MRI) of the breast enables adequate assessment of the tumor angiogenesis, which is often too small to be proved by another imaging method [1,2]. Additionally, the time-signal intensity curve (TIC) from DCE-MRI reflects the hemodynamic features of a specific lesion; however, limited by its low specificity. Other functional MRI parameters as diffusion weighted magnetic resonance imaging (DW-MRI) with quantitative apparent diffusion coefficient (ADC) mapping and the proton magnetic resonance spectroscopy (1H-MRS) may provide additional specificity [2,3].

The DW-MRI has higher detection rates of breast cancers and can be an adjunct to standard imaging protocols [2]. It generates images that are sensitive to water displacement at the diffusion scale and quantifies such diffusion according to a quantitative index revealing the apparent freedom of diffusion by the ADC values and maps, which emit significantly lower values in malignant than in benign breast lesions or normal tissue [3].

The 1H-MRS is a unique imaging tool that non-invasively detects the relative concentration of biochemical components within tissues [4], which facilitates diagnosis and characterization of indeterminate breast lesions. The free choline, phosphocholine and glycerophosphocholine are the main choline metabolites detected by 1H-MRS, and are usually referred to as total choline (tCho). Elevated tCho metabolite peak and concentration can be considered as a reliable biomarker for breast cancer [5,6].

The aim of this study was to appraise the diagnostic performance of the combined use of 1H-MRS and DW-MRI with quantitative ADC values as unique non-contrast diagnostic tools in the suspicious breast

Abbreviations: 1H-MRS, proton magnetic resonance imaging; DW-MRI, diffusion weighted magnetic resonance imaging; ADC, apparent diffusion coefficient; DCE-MRI, dynamic contrast enhanced magnetic resonance imaging; BI-RADS, Breast Imaging Reporting and Data System

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Table 1
Parameters of the MR imaging sequences of breast used in the study.

MRI sequences	Non-contrast scans			Non-contrast fat suppressed scans		Contrast-enhanced fat suppressed scans
	T1WTSE	T2WTSE	3D T2WI	T2WTSE + SPAIR	DWI + STIR	DCE-MRI
Type of scan	TSE	TSE	VISTA	TSE + SPAIR	SENSE-SSh-EPI + SPAIR	3D dyn-eTHRIVE- SENSE + SPAIR
Imaging plane	Axial	Axial	Axial	Axial and sagittal	Axial	Axial and sagittal
TR/ TE (msec.)	450/10	9022/120	2.0/213	4264/70	14207/82	560/14
SPAIR inversion delay (msec.)	–	–	–	125	305	305
NEX	1	1	1	1	2	1
FOV (mm^3)	340 × 340 × 150	340 × 340 × 150	340 × 340 × 150	340 × 340 × 150	340 × 340 × 150	26 × 26
ST (mm)	3	3		3	3	4.0
Flip angle (°)	10	10	90	90	90	15
Intersection gap (mm)	0	0	0	0	0	0
Matrix	320 × 320	320 × 320	320 × 320	256 × 256	256 × 256	448 × 322
Acquired voxel size (mm^3)	1.00 × 1.26 × 3.0	1.00 × 1.42 × 3.0	1.00 × 1.42 × 3.0	1.25 × 1.52 × 3.0	1.49 × 1.50 × 3.0	0.99 × 1.03 × 1.0
Scan time (min)	3:20	2:28	2:28	2:28	3:33	7:42

T1WTSE: T1-weighted turbo spin-echo, **T2WTSE:** T2-weighted turbo spin-echo, **VISTA**: volumetric isotropic T2W acquisition, **SPAIR:** spectral attenuated inversion recovery, **SSh-EPI:** single shot-echo planar imaging, **SENSE:** sensitivity encoding, **STIR:** short tau inversion recovery; **3D dyn-eTHRIVE:** three dimensional dynamic enhanced T1WTSE high resolution isotropic volume excitation, **TR/TE:** repetition time/echo time, **mm^3:** cubic millimetres, **msec:** millisecond, **NEX:** number of excitations, **FOV:** field of view, **(°):** degrees, **mm:** millimetres, **ST:** slice thickness, **T1W:** T1-weighted, **T2W:** T2-weighted, **TSE:** turbo spin- echo, **FS:** fat suppressed, **min:** minutes.

Table 2
Distribution of the studied breast lesions (n = 132) according to histopathological diagnosis.

Histopathological diagnosis of breast lesions		Number	Percent
Benign breast lesions (n = 74; 56.06%)	Fibroadenoma	34	25.76%
	Fibrocystic disease	8	6.06%
	Lipomas	7	5.30%
	Intraductal papilloma	6	4.55%
	Fibroadenosis	4	3.02%
	Intramammary lymph node	4	3.02%
	Hamartoma	3	2.27%
	Fat necrosis	3	2.27%
	Benign phyllodes tumor	3	2.27%
	Breast abscess	2	1.52%
Malignant breast lesions (n = 58; 43.94%)	Invasive ductal carcinoma	30	22.73%
	Ductal carcinoma in situ	8	6.06%
	Invasive tubular carcinoma	6	4.55%
	Medullary carcinoma	5	3.79%
	Intracystic papillary carcinoma	3	2.27%
	Colloid carcinoma	2	1.52%
	Infiltrating lobular carcinoma	2	1.52%
	Malignant phyllodes tumor	2	1.52%
Total		132	100%

Table 3
Number and percent of benign and malignant breast lesions according to the results of MR-DWI, 1H-MRS and histopathology.

Differentiation of the breast masses	Imaging sequence				Histopathology	
	MR-DWI with ADC		1H-MRS			
	n	%	n	%	n	%
Benign	75	56.82	73	55.30	74	56.6
Malignant	57	43.18	59	44.70	58	43.4
Total	132	100	132	100	132	100
McNemar test	P = 0.298					
Likelihood ratio	P = 0.061					

MR-DWI: magnetic resonance diffusion weighted imaging, **ADC:** apparent diffusion coefficient, **1H-MRS:** proton magnetic resonance spectroscopy; **n:** number; **%**: percent.

lesions. Also, we aimed to estimate the optimal cut-off value of the tCho concentration, which is quantitatively assessed by single-voxel 1H-MRS, to provide adequate characterization and efficient discrimination between benign and malignant breast lesions with subsequent reduction in superfluous breast biopsies.

2. Materials and methods

2.1. Study participants

The current prospective study was carried out in the period from March 2016 to April 2017. One hundred and thirteen consecutive female patients, having 132 breast lesions (95 palpable and 37 non-palpable), constituted the subjects of the current study. Their ages ranged from 19 to 71 years and the mean age was 45.8 ± 9.51 years. They had indeterminate suspicious breast lesions; categorized according to the Breast Imaging Reporting and Data System (BI-RADS) [7], as BI-RADS 3 or 4, by sono-mammographic examinations; their images were available for review in all study participants. Their imaging results were verified by biopsy either fine needle, core needle or open surgical biopsies, and correlated with histopathological proven results, which considered as the golden standard reference.

The exclusion criteria were contraindications to MRI (claustrophobia, any metallic prosthesis), or contrast media (such as; elevated renal function tests, pregnancy, lactation), bad general condition, previous breast biopsy, prior treatment with chemotherapy or radiotherapy and small lesions with the largest diameter ≤1 cm, because of the voxel size [6]. An official permission to carry out this study was acquired from the local medical research ethics committee. An informed written consent to participate in the study was obtained from all studied patients.

2.2. Imaging procedures

All study participants underwent examination of both breasts using an imaging protocol with multiphase dynamic sequence and 1H-MRS on a closed MRI unit of 1.5 T (Multiva; Philips Medical Systems, Best, The Netherlands), which was equipped with a dedicated phased-array bilateral (four-channel) breast coil (Philips Healthcare, dStream Flex breast coil). They were imaged in prone position with both breasts were