European Journal of Radiology 84 (2015) 1888–1893

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Comparison of contrast enhancement and diffusion-weighted magnetic resonance imaging in healthy and cancerous breast tissue

Gene Young Cho[a,b,c,*], Linda Moy[a,c,d], Sungheon G. Kim[a,c], Ana Paula Klautau Leite[e], Steven H. Baete[a,c], James S. Babb[a,c], Daniel K. Sodickson[a,c], Eric E. Sigmund[a,c]

[a] Bernard and Irene Schwartz Center for Biomedical Imaging, Department of Radiology, New York University School of Medicine, New York, NY 10016, USA
[b] Sackler Institute of Graduate Biomedical Sciences, New York University School of Medicine, New York, NY 10016, USA
[c] Center for Advanced Imaging Innovation and Research (CAI²R), Department of Radiology, New York University School of Medicine, New York, NY 10016, USA
[d] New York University Langone Medical Center – Cancer Institute, New York, NY 10016, USA
[e] Hospital das Clínicas, School of Medicine, University of São Paulo, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 8 January 2015
Accepted 22 June 2015

Keywords:
Breast MR
Dynamic contrast enhancement
Background parenchymal enhancement
3 Tesla
Diffusion-weighted imaging

ABSTRACT

Objective: To measure background parenchymal enhancement (BPE) and compare with other contrast enhancement values and diffusion-weighted MRI parameters in healthy and cancerous breast tissue at the clinical level.
Materials and methods: This HIPAA-compliant, IRB approved retrospective study enrolled 77 patients (38 patients with breast cancer – mean age 51.8 ± 10.0 years; 39 high-risk patients for screening evaluation – mean age 46.3 ± 11.7 years), who underwent contrast-enhanced 3T breast MRI. Contrast enhanced MRI and diffusion-weighted imaging were performed to quantify BPE, lesion contrast enhancement, and apparent diffusion coefficient (ADC) metrics in fibroglandular tissue (FGT) and lesions.
Results: BPE did not correlate with ADC values. Mean BPE for the lesion-bearing patients was higher (43.9%) compared to that of the high-risk screening patients (28.3%, $p = 0.004$). Significant correlation ($r = 0.37$, $p < 0.05$) was found between BPE and lesion contrast enhancement.
Conclusion: No significant association was observed between parenchymal or lesion enhancement with conventional apparent diffusion metrics, suggesting that proliferative processes are not co-regulated in cancerous and parenchymal tissue.

1. Introduction

First introduced in 1986 [1], contrast enhancement magnetic resonance imaging (CE-MRI) is a sensitive imaging tool for the detection of breast malignancy. It provides detailed information of the tumor microenvironment regarding the vasculature by providing biomarkers related to tumor perfusion and permeability [2]. The enhancement patterns help to recognize and differentiate lesion morphology and relate to aggressiveness of the breast tumor [3,4].

Recent studies have identified a potential CE-MRI biomarker, background parenchymal enhancement (BPE). BPE is the enhancement of normal fibroglandular tissue (FGT), often in a "stippled" pattern (tiny dots, separated by normal tissue, sometimes confluent), assessed on the first post-contrast breast MRI sequence. BPE correlates significantly with a higher odds ratio for developing breast cancer [5,6].

However, much is still unknown about the biophysical processes that are the source of such intriguing connections. The association of BPE with cancer risk motivates comparative studies with other imaging biomarkers such as apparent diffusion coefficient (ADC) from diffusion MRI to understand the precise biological mechanism of changes in BPE. The relationships between cancerous tissue, background parenchyma, and cancer risk are becoming increasingly important in understanding the heterogeneity found within the breast cancer patient population. Although BPE is believed to be secondary to hormone-induced physiologic changes seen with breast MRI, the variability of the volume and intensity of enhancement of normal fibroglandular tissue (FGT) after administration of a contrast agent is still poorly understood. Understanding the precise mechanism of fluctuations in BPE may lead to a better understand-

* Corresponding author at: Bernard and Irene Schwartz Center for Biomedical Imaging, 660 First Ave. 4th Floor, New York, NY 10016, USA. Fax: +1 212 263 7541.
E-mail address: Gene.Cho@nyumc.org (G.Y. Cho).

http://dx.doi.org/10.1016/j.ejrad.2015.06.023
0720-048X/

Table 1
Demographic make-up of the lesion-bearing patient population.

		# of patients
DCIS		6
Invasive	IDC	21
	ILC	2
Mixed	IDC with DCIS	8
	ILC with LCIS	1
Total		38
Post-menopausal	19 (50%)	
Premenopausal	19 (50%)	
Week 1	2 (10.5%)	
Week 2	11 (57.8%)	
Week 3	4 (21%)	
Week 4	2 (10.5%)	

ing of the different microstructural and microvascular influences on breast physiology.

In this study, we compare quantitative BPE between asymptomatic high-risk screening patients and lesion-bearing breast cancer patients. The primary focus of this study was to examine the relationship between BPE and ADC. Secondarily, we also explore potential associations between BPE, lesion contrast enhancement, and other clinical assessments (mammography, morphologic MRI). A better understanding of BPE's underpinnings may contribute to the utility of BPE as an imaging biomarker.

2. Materials and methods

2.1. Patient subjects

This HIPAA-compliant retrospective study, approved by the local institutional review board, evaluated 77 patients, 38 women with confirmed malignant lesions and 39 asymptomatic high-risk women who were not diagnosed with a malignant lesion. Twenty-four patients had been previously included in a breast cancer study focusing on diffusion metrics [7]. All patients underwent a breast CE-MRI examination between 1/7/2009 and 10/5/2012. The mean age for all subjects was 56.8 years, with a range of 27–85 years; for breast cancer patients the mean age was 51.8 ± 10.0 years while for high-risk patients for screening evaluation the mean age was 46.3 ± 11.7 years.

All patients with malignant lesions were diagnosed through stereotactic core biopsy ($n = 4$), US-guided fine needle aspirations ($n = 6$), or core biopsies ($n = 28$). Inclusion criteria for the high-risk screening group were analogous to a recent study by Hambly et al. [8] with asymptomatic women who had a normal mammogram within 6 months of their breast MRI. All high-risk women that were greater than 18 years of age were recruited. Clinical indication for the breast MRI in the high-risk group included: BRCA1/2 mutation carriers ($n = 7$), personal history of breast cancer ($n = 12$), strong family history ($n = 8$), and personal history of high-risk lesions ($n = 12$). At the time of exam, none of the high-risk screening patients showed high-risk or malignant lesions. Among the 12 patients with prior history of breast cancer, 2 were undergoing therapy at the time of exam. Of the 38 lesion-bearing patients, 38 lesions were observed in this study: 2 invasive lobular carcinoma (ILC), 6 ductal carcinoma in situ (DCIS), 21 invasive ductal carcinomas (IDC), 8 cases with mixed IDC and DCIS, and 1 case with mixed ILC and a foci of lobular carcinoma in situ (LCIS) (Table 1). Complete contrast enhancement data (described below) for BPE calculation was available for 34 of the 38 lesion-bearing patients and for all 39 high-risk screening subjects (4 lesion-bearing patients had differing contrast-enhancement data). Final histopathologic diagnosis was confirmed through surgery and clinical follow-up. All patients also underwent follow-up examination with imaging; the distribution of follow-up times was 2.6 ± 1.3 years for lesion-bearing breast cancer patients and 3.0 ± 0.9 years for high-risk screening patients. No new malignancies were found in either group within the follow-up periods. One patient, however, received treatment elsewhere after initial examinations; therefore, follow-up results were not recorded for that patient. Menstrual cycle data was collected for all patients.

2.2. MRI scans

Patients underwent a bilateral MRI breast examination in a full body Siemens Trio 3T MRI scanner (Siemens Medical Solutions, Erlangen, Germany) using a 7-channel breast coil (Invivo Corp., Gainesville, FL, USA). Anatomical imaging was performed with pre-contrast fat-saturated and non-fat-saturated T1-weighted volume interpolated breath hold examinations (VIBE) (resolution $1.2 \times 0.9 \times 1.5\,mm^3$ and scan time 1:10 each).

The diffusion weighted imaging (DWI) protocol was carried out using a twice refocused, bipolar gradient single-shot turbo-spin echo (TSE) sequence (repetition time/echo time = 2000/103 ms, 108×128 matrix, echo train duration 110×4.5 msec = 495 msec, 18 matrix axial slices, $2.7 \times 2.7 \times 4$ mm voxel). Axial TSE–DWI images with bilateral breast coverage were collected with frequency-selective fat suppression and diffusion sensitization in the anterior–posterior direction applied with weighting factors (b values) of 0, 30, 70, 100, 150, 200, 300, 400, 500, 800 s/mm^2. A full set of b values was sampled in order to calculate an ADC value ($ADC_{200-800}$) that was free from any possible intravoxel incoherent motion effects as observed in other diffusion MR studies for breast cancer patients [7,9–12]. A TSE sequence was used for readout, instead of echo planar imaging (EPI), to avoid susceptibility artifacts and distortion [13,14]. Total scan time for the TSE–DWI scan was 4 min.

The patients also underwent contrast enhanced (CE)-MRI. Contrast enhanced scans consisting of 3D T1-weighted sagittal fat saturated VIBE images with resolution of $1.4 \times 0.9 \times 1.5\,mm^3$ were performed four times after an injection of gadopentetate dimeglumine (Gd-DTPA, Magnevist, Berlex 0.1 mM/kg body weight) at 2 mL/s, followed by saline flush with a power injector (Spectris Solaris, Medrad, Indianola, PA). It should be noted that four lesion-bearing patients had contrast enhanced scans only three times after injection of Gd-DTPA, and therefore, they were excluded from the analysis. The acquisition time for each post-contrast scan was 1:20. The total duration of the dynamic study was approximately 7 min.

2.3. Image analysis

For this retrospective review, two readers (breast radiologists with 4 and 12 years of experience - APKL and LM) identified lesions on anatomical images based on the morphologic and kinetic features of the enhancing mass on the post-contrast axial and sagittal T1 VIBE images. Using a combination of pre- and post-contrast fat-suppressed T1-weighted and subtraction images, qualitative BPE and MRI FGT were visually assessed by radiologists who examined the entire breast parenchyma. Both the volume and the intensity of enhancement were considered in this global assessment [5,8,15]. The degree of parenchymal enhancement was categorized into the following descriptive modifiers: minimal (<25% volumetric enhancement), mild (25–50% volumetric enhancement), moderate (51–75% volumetric enhancement), or marked (>75% volumetric enhancement) [5,8,15]. The categories are based on the proposed Breast Imaging Reporting and Data Systems (BI-RADS criteria). Mammographic density data was also obtained from mammographic reports and confirmed by breast radiologists, while the amount of MR imaging-depicted FGT (non-fatty non-cystic breast parenchyma) was visually assessed by using a combination of T2-weighted and T1-weighted non-fat suppressed and fat-suppressed