International Journal of Chemical and Biochemical Sciences
(ISSN 2226-9614)
Journal Home page: www.iscientific.org/Journal.html

Comparison of Contrast-Enhanced Mammography and Contrast-Enhanced Breast MR Imaging in Evaluation of Breast Lesions

Doaa Mohamed Fouad, Alaa Mohamed Aly Sayed*, Marwa Makboul, Amr F. Mourad

Radiology Department, South Egypt Cancer Institute- Assiut University

Abstract

Invasive lobular carcinoma is the second most prevalent histological subtype of breast cancer after invasive duct carcinoma, with a reported increased incidence in the last two decades. It often presents challenging imaging characteristics that lower the sensitivity of mammography in their detection and delineation of their extent. Our aim in this study was to compare the diagnostic performance of contrast-enhanced digital mammography and dynamic contrast-enhanced magnetic resonance imaging (MRI) in diagnosis of breast lesions. This study included one hundred female patients with breast lesions. They underwent full-field digital mammography with a complementary ultrasound examination, contrast-enhanced digital mammography, and dynamic contrast-enhanced MRI. The findings encountered by the three imaging modalities were evaluated independently, and the results were compared with final histopathology. In the current study, dynamic contrast-enhanced MRI study was the most sensitive modality in the detection of the index lesion and achieved a sensitivity of 93.8% and 92% accuracy as compared to contrast-enhanced digital mammography, which achieved a sensitivity of 92.8% and 91% accuracy. Although dynamic contrast-enhanced MRI is the most sensitive imaging modality for detecting the index lesion; contrast-enhanced digital mammography achieved comparable overall accuracy. Future studies are warranted to confirm such findings.

Keywords: Cancer, MRI study, Breast Lesions, Mammography

Full length article **Corresponding Author*, e-mail: : dr.3laa.zidan@gmail.com

1. Introduction

The diagnostic assessment of patients with breast symptoms is based on the multidisciplinary triple diagnostic method. This includes clinical assessment, imaging assessment, and (where appropriate) needle biopsy [1]. It is important to find an accurate and cost-effective way to detect and diagnose early breast cancers in women across various ages, races, risk levels, economic levels, and geographic settings. Contrast-enhanced breast MRI is currently the most sensitive technique to detect and stage breast cancer [2]. Despite its high sensitivity, breast MRI has been reported to have variable specificity, ranging from 81% to 99% in international multicenter studies of high-risk women. Other limitations of breast MRI include high equipment and examination costs, limited scanner availability, the inability to detect breast cancers based on calcifications, and variable sensitivity to in situ cancers [3]. Contrast-enhanced spectral mammography (CESM) is a novel imaging technique combining digital mammography with an intravenous injection of iodinated contrast agent able to depict angiogenesis in breast cancer [4]. The current study aimed to compare contrast-enhanced spectral mammography (CESM) and breast magnetic resonance imaging (MRI) in high-risk breast lesions.

2. Material and Methods

2.1 Study setting and design.

A prospective cross-sectional study was conducted at Radiology Department of South Egypt cancer Institute, Assiut University-Egypt in the period between 2020 and 2023.

2.2 Ethical consideration

The study was conducted according to the principles of the Declaration of Helsinki and was approved by the Hospital's Ethics Committee. The purpose of the study was explained to all participants, and written informed consent was obtained. The study was approved by Assiut Faculty of Medicine, Institutional Review Board.

2.3 Selection criteria

2.3.1 Inclusion criteria

Any woman aged 21 years old or more with suspicious breast lesions (BIRADS $\geq$ 3) diagnosed by sonomammography was eligible for the study.

2.3.2 Exclusion criteria

Any woman with one of the criteria was excluded from the study include pregnant or lactating women, women who had already undergone surgery for breast cancer before enrolment in the study, women with breast implants or other metallic implants, women undergoing neoadjuvant chemotherapy. All patients were subjected to the following.

1. History taking and physical evaluation
2. Conventional mammography
3. Contrast-Enhanced Spectral Mammography

All CESM examinations will be performed with Amulet Innovality, Fujifilm's. Both low- and high-energy images were acquired without an antiscatter grid. For breasts with a thickness greater than 70 mm, an antiscatter grid was used. An antiscatter grid is usually placed between the detector and the breast to reduce the amount of Compton-scattered x-rays. Exposures were obtained with an automatic image acquisition technique for both energies and standard PRIME acquisition parameters for the low-energy images. The low-energy image acquisition and processing parameters were therefore equivalent to standard mammograms. The total number of mammography views in this study was 640. AGD (mGy) was obtained from the acquisitions monitor for each examination and compared as a function of breast thickness.

2.4 Contrast enhanced MRI

All contrast-enhanced MRI examinations were performed with a 1.5T MRI system (Philips, Netherlands).
Readings were performed on a dedicated workstation (syngo.Breast Care; Siemens Healthcare) with high-resolution monitors (8MP Monitor, 12 BIT, Monitor-Pixel: 0,17 mm × 0,17 mm; Brightness/Luminance: >2100 cd/m2). Before data collection, all readers analyzed a series of twenty test cases with CESM to become familiar with the typical image appearance of the device used.

2.5. Biopsy and histopathology

In all the included patients, image-guided biopsy of the most suspicious lesion was performed.

2.6 Statistical analysis

Data was collected and analyzed by using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). The Shapiro test was used to determine compliance of the data to normal distribution. We compared the specificity, sensitivity, negative predictive value (NPV), positive predictive value (PPV), and the accuracy of CI-MRI and CESM using a ROC curve. The level of confidence was kept at 95% and hence, p value less than 0.05 was considered statistically significant.

3. Result and Discussion

Breast cancer is the most frequently diagnosed type of cancer worldwide. While the incidence of breast cancer has been increasing, breast cancer mortality has not shown a corresponding increase. This can be attributed to advancements achieved in imaging and treatment methods. Conventional mammography is currently the most widely proven breast imaging method for reducing breast cancer-related deaths through screening and early detection [5]. The sensitivity of mammography is reduced 30-48% in women with dense breasts due to the masking effect of overlapping breast tissue.

The reduced sensitivity of mammography in the setting of dense breast tissue can be overcome by the intravenous injection of contrast material [6]. Due to the increased neoangiogenesis and immature vascular structure in malignant lesions, there is greater uptake of contrast material in malignant lesions compared to benign lesions. This leads to an increased contrast difference between malignant lesions and normal parenchyma, thereby enhancing the sensitivity of imaging [6]. Breast magnetic resonance imaging (MRI) is the most utilized breast imaging modality worldwide in daily practice that incorporates intravenous contrast material. In today's practice, MRI is known to have the highest sensitivity and is the gold-standard imaging modality for breast cancer detection [7]. However, the long examination time, high cost, limited accessibility, and contraindications associated with MRI have prompted researchers to explore alternative contrast-enhanced imaging methods [8]. The use of contrast material with mammography has been regarded as a potential solution to address these challenges effectively. In CEM, with the dual-energy technique, both low and high energy images are acquired simultaneously after the administration of contrast agent. The low energy images in this method are analogous to digital mammography [9].

The recombined images, generated from both low and high energy images, reduce the visibility of glandular tissue, and enhance the visibility of contrast-enhancing lesions. The recombined images can be considered analogous to the subtraction images obtained in MRI [10]. CEM can be accurately described as a hybrid imaging technique that integrates the properties and advantages of both digital mammography (DM) and MRI. CEM combines the high spatial resolution and ability to visualize suspicious microcalcifications provided by DM that utilizes X-rays with the high contrast resolution achieved through the administration of contrast material, like MRI. By integrating these two modalities, CEM offers improved lesion characterization [10-11]. The goal of this study is to compare the diagnostic accuracy including assessment of sensitivity and specificity of two contrast-enhanced breast imaging methods, CEM and MRI, in the diagnosis and characterization of breast lesions. A total of 65 (65%) women had malignant lesions. The most frequency malignant lesions were IDC (40%) and DCIS (23%). Two patients had ILC. Dynamic contrast-enhanced MRI study was the most sensitive modality in the detection of the index lesion and achieved a sensitivity of 93.8% and 92% accuracy as compared to contrast-enhanced digital mammography, which achieved a sensitivity of 92.8% and 91% accuracy. CEM and MRI exhibit varied strengths and weaknesses due to differences in imaging methodology. MRI can provide more information about lesions by evaluating T1 signal, T2 signal, diffusion, and dynamic contrast characteristics. MRI can image the chest wall and the entire axilla [11].

Table 1: Baseline data of the studied patients

	No= 100
Age (years)	45.09 ± 8.90
Range	25-60
Body mass index (kg/m^2)	26.09 ± 2.17
Menopausal status	
Pre-menopause	43 (43%)
Post-menopause	57 (57%)
Residence	
Rural	70 (70%)
Urban	30 (30%)
Family history of breast cancer	10 (10%)

Data expressed as mean (SD), range, frequency (percentage)

Table 2: Histopathological results among the studied patients

	No= 100
Malignant lesions	**65 (65%)**
IDC	40 (40%)
DCIS	23 (23%)
ILC	2 (2%)
Benign lesions	**35 (35%)**
Fibrocystic changes	20 (20%)
Papilloma	8 (8%)
Inflammatory changes	4 (4%)
Fibroadenoma	3 (3%)

Data expressed as frequency (percentage). IDC: invasive ductal carcinoma; DCIS: ductal carcinoma in-situ; ILC: invasive ductal carcinoma

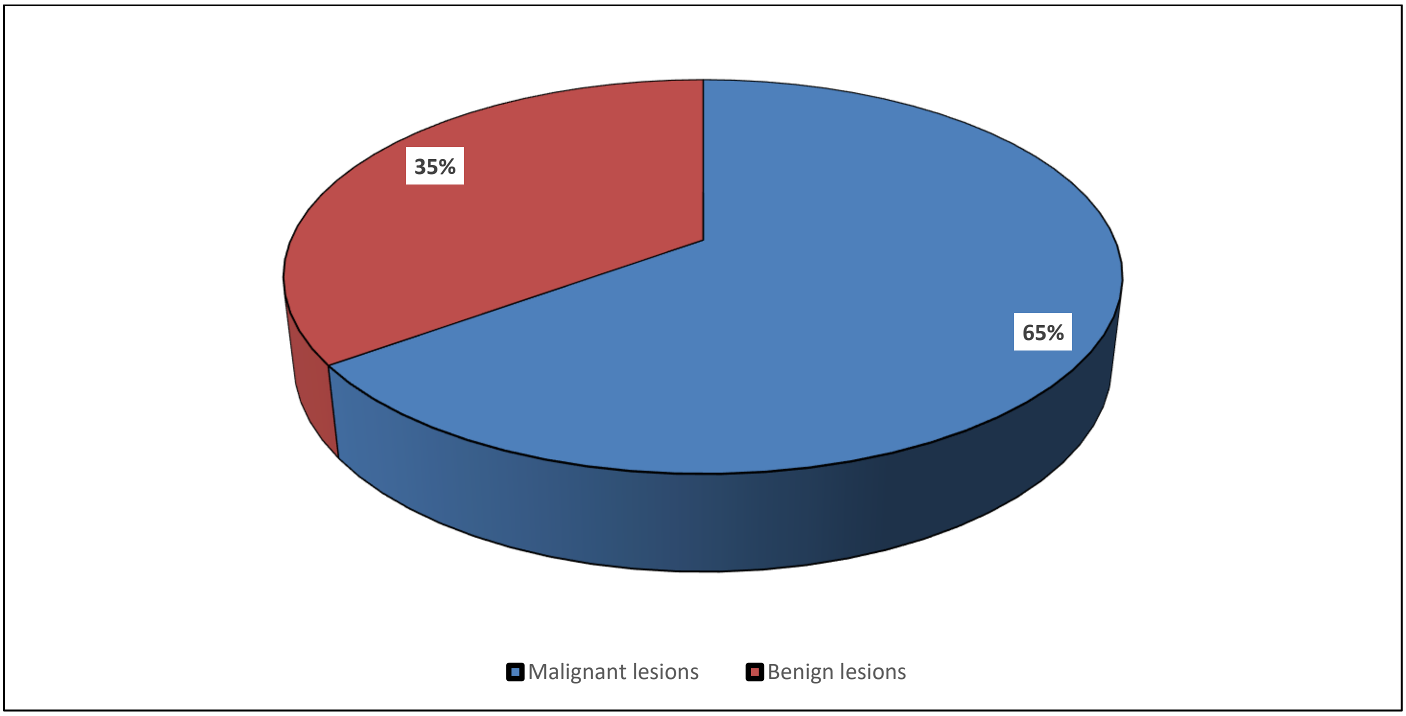

Figure 1: Histopathological nature of the lesions among the studied patients

Table 3: Cross-tabulation between final diagnosis and CESM

Diagnosis based on CESM	Final diagnosis		Total
	Malignant	Benign	
Malignant	60	4	64
Benign	5	31	36
Total	65	35	100

CESM: contrast enhanced spectral mammography.

Table 4: Cross-tabulation between final diagnosis and CE-MRI

Diagnosis based on CE-MRI	Final diagnosis		Total
	Malignant	Benign	
Malignant	61	4	65
Benign	4	31	35
Total	65	35	100

CE-MRI: contrast enhanced magnetic resonance imaging.

Table 5: Accuracy of CESM vs. CE-MRI in detection nature of breast lesion

	CESM	CE-MRI
Sensitivity	92.3%	93.8%
Specificity	88.6%	88.6%
Positive predictive value	93.8%	93.8%
Negative predictive value	86.1%	88.6%
Accuracy	91%	92%
Area under curve	0.90	0.91
P value	< 0.001	< 0.001

CESM: contrast enhanced spectral mammography; CE-MRI: contrast enhanced magnetic resonance imaging.

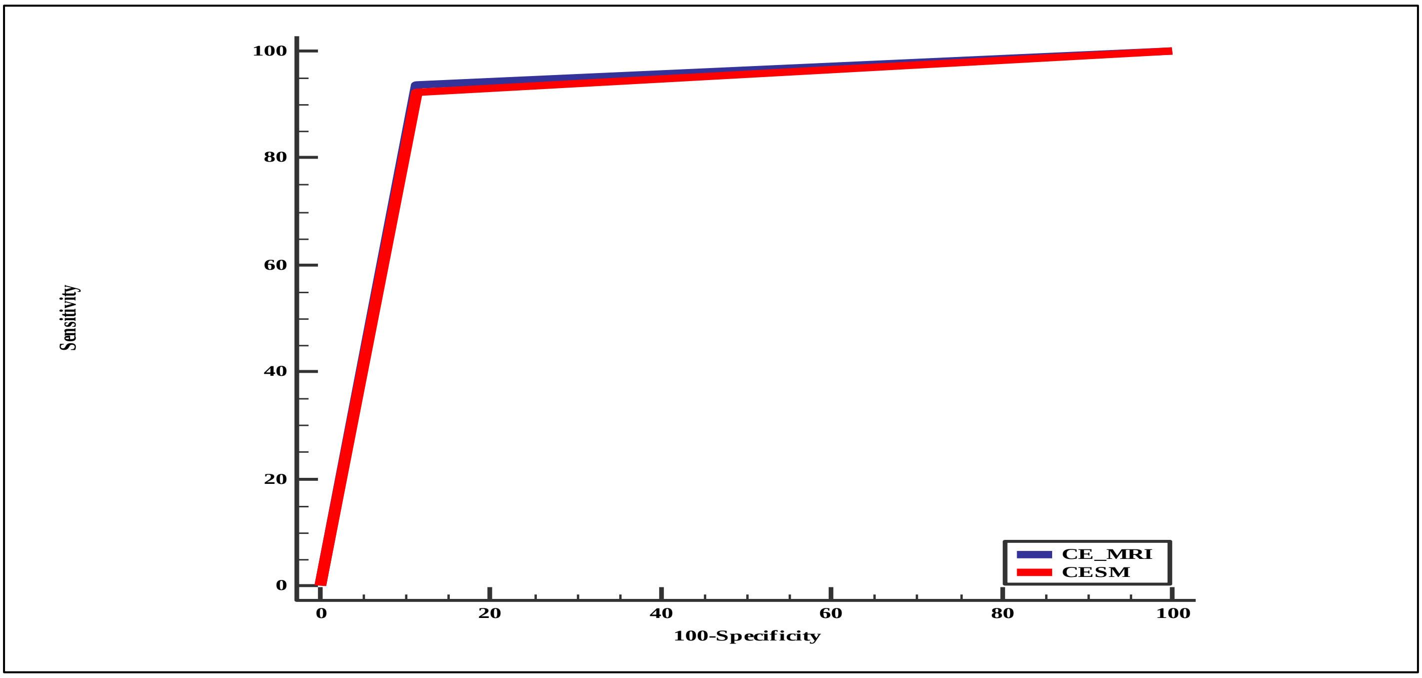

Figure 2: Accuracy and cross-tabulation between final diagnosis with CESM and CE-MRI in the current study

Histopathological results among studied patients (table 2, figure 1): A total of 65 (65%) women had malignant lesions. The most frequency malignant lesions were IDC (40%) and DCIS (23%). Two patients had ILC. Accuracy and cross-tabulation between final diagnosis with CESM and CE-MRI in the current study (tables 3-5, figure 2). Dynamic contrast-enhanced MRI study was the most sensitive modality in the detection of the index lesion and achieved a sensitivity of 93.8% and 92% accuracy as compared to contrast-enhanced digital mammography, which achieved a sensitivity of 92.8% and 91% accuracy. Also, 35 (35%) patients had benign lesions. Fibrocystic changes were frequently present in 20 (20%) women. Papilloma, inflammatory changes and fibroadenoma were reported in 8 (8%), 4 (4%) and 3 (3%) patients, respectively. CEM has high spatial resolution which allows for a clearer evaluation of the shape and margins of lesions, contributing to increased specificity by accurately identifying significant shape and margin features of benign lesions. CEM can detect calcifications. In cases of some DCIS, which may not exhibit contrast enhancement on MRI, CEM can still detect it with the assistance of calcifications [12]. While the detection of typical benign calcifications can lead to correctly diagnosing benign lesions, the detection of suspicious calcifications can also result in false-positive lesions and lower the specificity of CEM [12].

In the evaluation of meta-analyses, Suter et al examined eight studies in their 2020 publication and reported the sensitivity of CEM as 85% and specificity as 77% [4]. Aristokli et al examined twenty-six studies in their 2022 publication and reported the sensitivity of CEM as 90.5% and specificity as 52.6%. For MRI, they reported the sensitivity as 94.6% and specificity as 74.2% [13]. In the study of Acar et al, the lower sensitivity of CEM compared to MRI was attributed to two lesions located outside the imaging field, but this difference was not statistically significant (98.40% vs. 100%) [14]. In most studies, including ours, CEM demonstrated higher specificity without a statistically significant difference. However, two studies reported notable low specificity. In a study comparing CEM and MRI, Lee Felker et al reported a specificity of 17% for CEM and 4% for MRI. They also reported forty-five false positives for MRI and 5 false positives for CEM. The low specificity in this study was attributed to the limited number of benign lesions (n=22) included in the analysis [15]. Lee et al compared CEM and MRI in invasive breast cancers. For all lesions (primary and secondary), the sensitivity of CEM was reported as 92%, specificity as 74.43%, PPV as 95.83%, and NPV as 55.56%. The sensitivity of MRI was reported as 94.73%, with specificity and NPV reported as 0%. The low specificity and NPV were attributed to the inclusion of only six benign lesions in the study [16]. Based on the reviewed studies, including our own, it can be concluded that the diagnostic performance of CEM is like MRI. Some studies reported higher diagnostic values for CEM and others for MRI, but in most cases, the difference between the two modalities is not statistically significant. Baseline data of the studied patients (table 1): Mean age (SD) of the studied women was 45.09 (8.90) with range between 25 and 60 years old. A total of 43 (43%) women were pre-menopause and 57 (57%) patients were post-menopause. Majority of women came from rural areas. Only ten (10%) patients had a positive family history of breast cancer.

4. Conclusions

In the diagnosis of breast lesions, CEM and MRI were evaluated, and it was found that MRI had higher sensitivity, while CEM had similar specificity. However, there was no significant statistical difference between the two methods. Considering this, CEM can be considered as an alternative to MRI in the characterization and classification of breast lesions. Future studies are warranted to confirm such results.

References

[1] T.B. Bevers, B.L. Niell, J.L. Baker, D.L. Bennett, E. Bonaccio, M.S. Camp, S. Chikarmane, E.F. Conant, M. Eghtedari, M.R. Flanagan. (2023). NCCN Guidelines® insights: breast cancer screening and diagnosis, version 1.2023: featured updates to the NCCN guidelines. Journal of the National Comprehensive Cancer Network. 21(9): 900-909.

[2] A.M. Scaranelo. (2022). What's hot in breast MRI. Canadian Association of Radiologists Journal. 73(1): 125-140.

[3] H. Bougias, N. Stogiannos. (2022). Breast MRI: Where are we currently standing? Journal of Medical Imaging and Radiation Sciences. 53(2): 203-211.

[4] M.B. Suter, F. Pesapane, G.M. Agazzi, T. Gagliardi, O. Nigro, A. Bozzini, F. Priolo, S. Penco, E. Cassano, C. Chini. (2020). Diagnostic accuracy of contrast-enhanced spectral mammography for breast lesions: A systematic review and meta-analysis. The Breast. 53: 8-17.

[5] D.S. Polat, W.P. Evans, B.E. Dogan. (2020). Contrast-enhanced digital mammography: technique, clinical applications, and pitfalls. American journal of roentgenology. 215(5): 1267-1278.

[6] T.M. Kolb, J. Lichy, J.H. Newhouse. (2002). Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology. 225(1): 165-175.

[7] R.M. Mann, N. Cho, L. Moy. (2019). Breast MRI: state of the art. Radiology. 292(3): 520-536.

[8] A. Cozzi, V. Magni, M. Zanardo, S. Schiaffino, F. Sardanelli. (2022). Contrast-enhanced mammography: a systematic review and meta-analysis of diagnostic performance. Radiology. 302(3): 568-581.

[9] L.M. Neeter, M.Q. Robbe, T.J. van Nijnatten, M.S. Jochelson, H. Raat, J.E. Wildberger, M.L. Smidt, P.J. Nelemans, M.B. Lobbes. (2023). Comparing the diagnostic performance of contrast-enhanced mammography and breast MRI: a systematic review and meta-analysis. Journal of Cancer. 14(1): 174.

[10] P. Clauser, B. Krug, H. Bickel, M. Dietzel, K. Pinker, V.-F. Neuhaus, M.A. Marino, M. Moschetta, N. Troiano, T.H. Helbich. (2021). Diffusion-weighted imaging allows for downgrading MR BI-RADS 4 lesions in contrast-enhanced MRI of the breast to avoid unnecessary biopsy. Clinical cancer research. 27(7): 1941-1948.

[11] H. Dijkstra, M.D. Dorrius, M. Wielema, R.M. Pijnappel, M. Oudkerk, P.E. Sijens. (2016). Quantitative DWI implemented after DCE-MRI yields increased specificity for BI-RADS 3 and 4 breast lesions. Journal of Magnetic Resonance Imaging. 44(6): 1642-1649.

[12] H. Rahbar, Z. Zhang, T.L. Chenevert, J. Romanoff, A.E. Kitsch, L.G. Hanna, S.M. Harvey, L. Moy, W.B. DeMartini, B. Dogan. (2019). Utility of diffusion-weighted imaging to decrease unnecessary biopsies prompted by breast MRI: a trial of the ECOG-ACRIN cancer research group (A6702). Clinical cancer research. 25(6): 1756-1765.

[13] N. Aristokli, I. Polycarpou, S. Themistocleous, D. Sophocleous, I. Mamais. (2022). Comparison of the diagnostic performance of Magnetic Resonance Imaging (MRI), ultrasound and mammography for detection of breast cancer based on tumor type, breast density and patient's history: A review. Radiography. 28(3): 848-856.

[14] Ç.R. Açar, S. Orguc. (2024). Comparison of Performance in Diagnosis and Characterization of Breast Lesions: Contrast-Enhanced Mammography vs. Breast Magnetic Resonance Imaging. Clinical Breast Cancer. doi: 10.1016/j.clbc.2024.04.007.

[15] S.A. Lee-Felker, L. Tekchandani, M. Thomas, E. Gupta, D. Andrews-Tang, A. Roth, J. Sayre, G. Rahbar. (2017). Newly diagnosed breast cancer: comparison of contrast-enhanced spectral mammography and breast MR imaging in the evaluation of extent of disease. Radiology. 285(2): 389-400.

[16] S.C. Lee, L. Hovanessian-Larsen, D. Stahl, S. Cen, X. Lei, B. Desai, M. Yamashita. (2021). Accuracy of contrast-enhanced spectral mammography compared with MRI for invasive breast cancers: prospective study in population of predominantly underrepresented minorities. Clinical Imaging. 80: 364-370.