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Contrast-enhanced spectral mammography: Impact of the qualitative morphology descriptors on the diagnosis of breast lesions

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ABSTRACT

Objective: To analyze the morphology and enhancement characteristics of breast lesions on contrast-enhanced spectral mammography (CESM) and to assess their impact on the differentiation between benign and malignant lesions.
Materials and method: This ethics committee approved study included 168 consecutive patients with 211 breast lesions over 18 months. Lesions classified as non-enhancing and enhancing and then the latter group was subdivided into mass and non-mass. Mass lesions descriptors included: shape, margins, pattern and degree of internal enhancement. Non-mass lesions descriptors included: distribution, pattern and degree of internal enhancement. The impact of each descriptor on diagnosis individually assessed using Chi test and the validity compared in both benign and malignant lesions. The overall performance of CESM were also calculated.
Results: The study included 102 benign (48.3%) and 109 malignant (51.7%) lesions. Enhancement was encountered in 145/211 (68.7%) lesions. They further classified into enhancing mass (99/145, 68.3%) and non-mass lesions (46/145, 31.7%). Contrast uptake was significantly more frequent in malignant breast lesions (p value ≤0.001). Irregular mass lesions with intense and heterogeneous enhancement patterns correlated with a malignant pathology (p value ≤0.001). CESM showed an overall sensitivity of 88.99% and specificity of 83.33%. The positive and negative likelihood ratios were 5.34 and 0.13 respectively.
Conclusion: The assessment of the morphology and enhancement characteristics of breast lesions on CESM enhances the performance of digital mammography in the differentiation between benign and malignant breast lesions.

1. Introduction

Up-to-date, mammography appears to be the most consistent method for the early detection of breast cancer; yet, it has both limited sensitivity and specificity in the detection and diagnosis of breast lesions, especially in dense breasts. Moreover the full extent of the disease may not be clearly depicted. In reference to this, mammography misses about 20% of invasive breast cancers [1,2].

The use of an intravenous injected iodinated contrast agent could help increase the sensitivity of digital mammography by adding information on tumor angiogenesis. The contrast agent can be used to highlight areas of unusual blood flow. Two approaches have been made for clinical implementation of contrast-enhanced mammography, namely; single-energy (SE) and dual-energy (DE) imaging. In each technique, pairs of mammograms are acquired, which are then subtracted in order to cancel the appearance of healthy breast tissue and thus permit the sensitive detection and specific characterization of lesions [3].

In the single energy or temporal subtraction technique high-energy images are acquired before and after contrast medium injection while in the dual energy technique the acquisition of a pair of low and high-energy images occurs only after contrast medium injection. The dual energy technique does not provide information

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about the kinetics of tumor enhancement but allows the acquisition of multiple views of the same breast or bilateral examination and is less sensitive to patient motion than the temporal technique. This feature allows for better morphology assessment [4].

At present, there are no standardized interpretation criteria for the evaluation of breast lesions on CESM. The different patterns of contrast uptake and the morphology descriptors of enhancing lesions which allow characterization of benign and malignant breast lesions on CESM are still a subject of research.

In this study, the enhancement characteristics and morphology descriptors of breast lesions on contrast-enhanced spectral mammography (CESM) are analyzed to assess their impact on the differentiation between benign and malignant breast lesions.

2. Materials and methods

2.1. Patients

This study is a retrospective analysis that included 168 consecutive patients with 211 breast lesions in the period from January 2012 to June 2013. The study was approved by the Scientific Research Review Board of the Radiology Department, and waiver of informed consent was applied for the used data of the included cases.

Indication of contrast injection was to (i) further evaluate heterogeneous dense breast parenchyma (27/211; 12.8%) or (ii) clarify already identified mammography abnormalities (184/211; 87.2%) namely mass lesions, areas of parenchyma distortion, focal asymmetries or suspicious microcalcifications.

Patients with renal impairment, pregnant patients and those giving history of allergy to contrast media were excluded from the study.

Reference standard was histopathology after core or surgical biopsy, as well as follow-up (for 1year) of lesions classified as benign.

2.2. Digital mammography system

Dual energy contrast-enhanced spectral mammography (CESM) was performed using Senographe Essential; (Seno DS; GE, Buc, France) that is adapted to obtain low and high-energy images for each mammography view. The low-energy image is comparable to the standard mammography image and the high-energy image shows the contrast-enhanced areas.

2.3. Technique of examination

The examination consists of an intravenous injection of an iodinated contrast agent (iohexol, 300 mg I/ml) at a dose of 1.5 ml/kg through a catheter introduced in the ante-cubital vein before application of compression to avoid interference with the normal vascular dynamics of the breast. This is followed by a 2-min wait before a mammography exam is performed in exactly the same positions as the standard examination. Low- and high-energy images are consecutively acquired in each view during a single compression to minimize motion artifact. Low-energy images were acquired at peak kilovoltage values ranging from 26 to 31 kVp, which is below the k-edge of iodine. High-energy images were acquired at 45–49 kVp, which is above the k-edge of iodine. Iodine-enhanced images are calculated by weighted logarithmic subtraction of the two images through appropriate image processing and thus the visibility of the parenchyma is reduced and contrast-enhanced images are generated.

2.4. Image analysis

Mammograms were analyzed according to the Breast Imaging Reporting and Data System (BI-RADS) lexicon designed by the American College of Radiology [5].

Analysis was performed by independent double reading using two different radiologists for each of the standard mammograms and CESM images. Readers were blinded about each other analysis, the pathology reports and follow up outcome.

Regarding CESM images; the presence or absence of contrast enhancement was assessed on the subtraction images. The assessment of the low-energy images was also essential to identify non-enhancing suspicious clusters of microcalcifications, areas of parenchymal distortion, focal asymmetries and to evaluate the morphologic features of non-enhancing mass lesions.

Lesions were classified as enhancing and non-enhancing. Enhancing lesions were further classified as mass versus non-mass.

A mass lesion was described when a three dimensional space-occupying lesion ≥5 mm was seen in both mammography views. Mass lesions morphology descriptors included: mass shape (oval, rounded or irregular), margins (well-defined, ill-defined or spiculated), internal enhancement pattern (homogeneous, heterogeneous or ring) and degree of enhancement.

Non-mass enhancement was described when the enhancement was an area with no space-occupying or 3D volume effect. Non-mass lesions morphology descriptors included: distribution of enhancement, internal enhancement pattern and degree of enhancement.

2.5. Statistical analysis

Data were statistically described in terms of frequencies and percentages. The impact of the individual morphology descriptors on the diagnosis of breast lesions was assessed using Chi square (χ^2) test. The validity of each descriptor was compared in both benign and malignant lesions. p values less than 0.05 were considered statistically significant. The positive and negative predictive values and the likelihood ratios (LR) were calculated using the sensitivity and specificity to assess each morphology descriptor individually. A LR greater than 1 indicates a strong association with a diagnosis of malignancy. A LR less than 1 indicates a strong association with the absence of malignancy. Likelihood ratios that lie close to 1 indicate little practical significance. After validating the impact of these signs in differentiating benign from malignant breast lesions, the overall performance of CESM was evaluated.

3. Results

3.1. Classification of lesions

The study included 211 breast lesions: 102/211 (48.3%) benign and 109/211 (51.7%) malignant. The reference standard was histopathology of core or surgical biopsy specimens in 128/211 (60.7%) lesions and a scheduled follow-up study for 1 year in 83/211 (28.9%) lesions that showed typical benign morphology descriptors.

Malignant lesions included: 81/211 (38.4%) invasive duct carcinomas (IDC), 4/211 (1.95%) invasive lobular carcinomas (ILC), 14/211 (6.6%) mixed invasive duct and lobular carcinoma, 2/211 (0.95%) mucinous carcinomas, 2/211 (0.95%) primary non-Hodgkin's lymphoma, 3/211 (1.4%) DCIS, and 3/211 (1.4%) metastatic lesions to the breast.

Benign lesions included: 21/211 (10%) fibro-adenomas, 45/211 (21.3%) adenosis and fibro-cystic changes, 23/211(10. 9%) benign post operative breast changes; 6/211 (2.8%) abscess cavities and infected cysts, 4/211(1.9%) intra-mammary lymph nodes in atypical