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Correlation Between Enhancement Intensity in Contrast Enhancement Spectral Mammography and Types of Kinetic Curves in Magnetic Resonance Imaging

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Due to the decreased sensitivity of mammography in glandular breasts, new diagnostic modalities, like contrast-enhanced spectral mammography (CESM) and digital breast tomosynthesis (DBT) have been developed. The aim of this study was to compare qualitative enhancement levels on CESM with type of kinetic enhancement curves on MRI examination.

Material/Methods: Patients qualified for the CESM examination presented some diagnostic doubts – suspected multifocality, multicentricity, or having dense glandular breast tissue. The enhancement level on CESM was described as weak, medium, or strong. Enhancement on achieved MR images was assessed on the basis of enhancement kinetic curves. The level of enhancement on CESM was associated with enhancement curves type on MRI. All lesions detected on CESM and MRI were histopathologically verified.

Results: The study involved 107 lesions diagnosed in 94 patients: 71 lesions (66%) appeared to be infiltrating on histopathological examination, 9 lesions (8%) were non-infiltrating cancers, and 27 lesions (25%) were benign. Data analysis revealed that lesions with wash-out curve on MRI most often presented strong enhancement on CESM, while in lesions with progressive enhancement curve, strong enhancement on CESM was the rarest. The relationship between enhancement level on CESM and curve type on contrast-enhanced MRI depends on the nature of the lesion. The type of MRI curve was found to be associated with enhancement level on CESM.

Conclusions: We compared subjective assessments of contrast enhancement on CESM with enhancement kinetic curves on MRI. The results showed that the level of enhancement on CESM and type of kinetic curves on MRI depends on the lesion type.

MeSH Keywords: Breast Neoplasms • Magnetic Resonance Imaging • Mammography

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Background

Breast cancer is the most common malignant disease among women. Mammography is a basic method used in breast cancer diagnostics. However, the sensitivity and specificity of mammography depend on breast anatomy.

The sensitivity of mammography is significantly lower in dense glandular breasts in comparison with fatty breasts, and specificity has similar problems. According to data in the literature, the sensitivity of mammography in glandular breasts ranges from 52.4% to 60%, while specificity ranges from 90.5% to 98.7% [1–3]. Due to the decreased sensitivity of mammography in glandular breasts, new diagnostic modalities for breast cancer detection have been developed. Some of these new methods, including contrast-enhanced spectral mammography (CESM) and digital breast tomosynthesis (DBT), are based on mammographic principles. CESM is a relatively new diagnostic method, cleared by the Food and Drug Administration in 2011, and quickly developing since then. The examination is performed 2 min after intravenous injection of an iodinated contrast medium, when images from low- and high-energy exposures are obtained. We follow the protocol of image acquisition: "not suspected" breast in CC projection, "suspected" breast in CC, "not suspected breast in MLO, and "suspected" breast in MLO [4]. The protocol varies among hospitals, but the overall goal of performing the examination in under 7 min from the time of contrast injection is achieved [5,6]. The exposure techniques are automatically adjusted by the mammography system according to breast anatomy and amount of glandular tissue within the breast. The radiologist can review the low-energy images (comparable with mammography images) and subtraction images with attenuated glandular tissue and visible contrast enhancement foci. Consequently, CESM enables assessment not only of symptoms visible in conventional mammography, like microcalcifications, architectural distortions, or masses, but also enhancement foci, which may be related to lesions detected on mammography or exist as additional ones. Enhancement on CESM can be evaluated qualitatively and quantitatively, but it is not possible to assess contrast enhancement kinetics.

The utility of MRI in breast cancer diagnostics has been documented in many publications. It is considered to be a very good diagnostic method, particularly useful in evaluation of young women with dense, glandular breast anatomy. On contrast-enhanced MRI examinations, it is possible to evaluate the morphology and dynamics of enhancement of focal lesions. Dynamic parameters are assessed by using contrast enhancement curves, which are helpful in determining the nature of breast lesions. The aim of this study was to compare qualitative enhancement levels on contrast-enhanced spectral mammography with kinetic enhancement curves on magnetic resonance imaging examination. Increasing our knowledge of those patterns may help radiologist to categorize difficult-to-assess lesions in a more effective way and thus reduce the number of unnecessary biopsies performed.

Material and Methods

CESM examinations (routinely used in our department) were performed with the GE Senographe Essential full-field digital mammography system. Patients qualified for the examination presented some diagnostic doubts, meaning that multifocality or multicentricity was suspected on mammography or ultrasound examination, or the patient had a dense glandular breast anatomy or glandular-fatty heterogeneous breast anatomy. The examination was performed using the following protocol [7]: 2 min after administration of Iopromide (1.5 ml/kg of body weight), mammography acquisitions started on the breast without suspected pathology, followed by the breast with pathology suspected in preliminary mammography or ultrasonography examination. Enhancement level on CESM was described as weak, medium, or strong (Figure 1).

Since the assessment of the enhancement level is subjective, 2 independent radiologists (with 5 and 7 years of experience with CESM) were involved in the task. For contrast-enhanced MRI sequences, patients were administered Gadovist at 0.1 ml/kg of body weight by automatic contrast injector. Enhancement on MRI was assessed on the basis of enhancement curves, which were automatically drawn by the apparatus and analyzed by radiologists. Following the method described in the literature [8,9], MRI enhancement curves were described as continuously increasing – progressive enhancement pattern (typical for benign lesions), plateau (can be present for benign and malignant lesions), and wash-out type (for malignant lesions) (Figure 2). The level of enhancement on CESM was associated with enhancement curves type on MRI.

Statistical methods

The chi-square test of independence was used to assess the relationship between the studied variables. The type of lesions, type of MRI curve, and type of CESM enhancement were analyzed. A significance level α=0.05 was accepted for all tests.

Histopathological examination

All lesions detected on CESM and MRI were histopathologically verified. After performing imaging examinations, lesions underwent core biopsy or vacuum-assisted core biopsy. The verification method depended on lesion size and its availability on imaging examination. Most biopsies were performed under ultrasonography guidance. In case of enhancing

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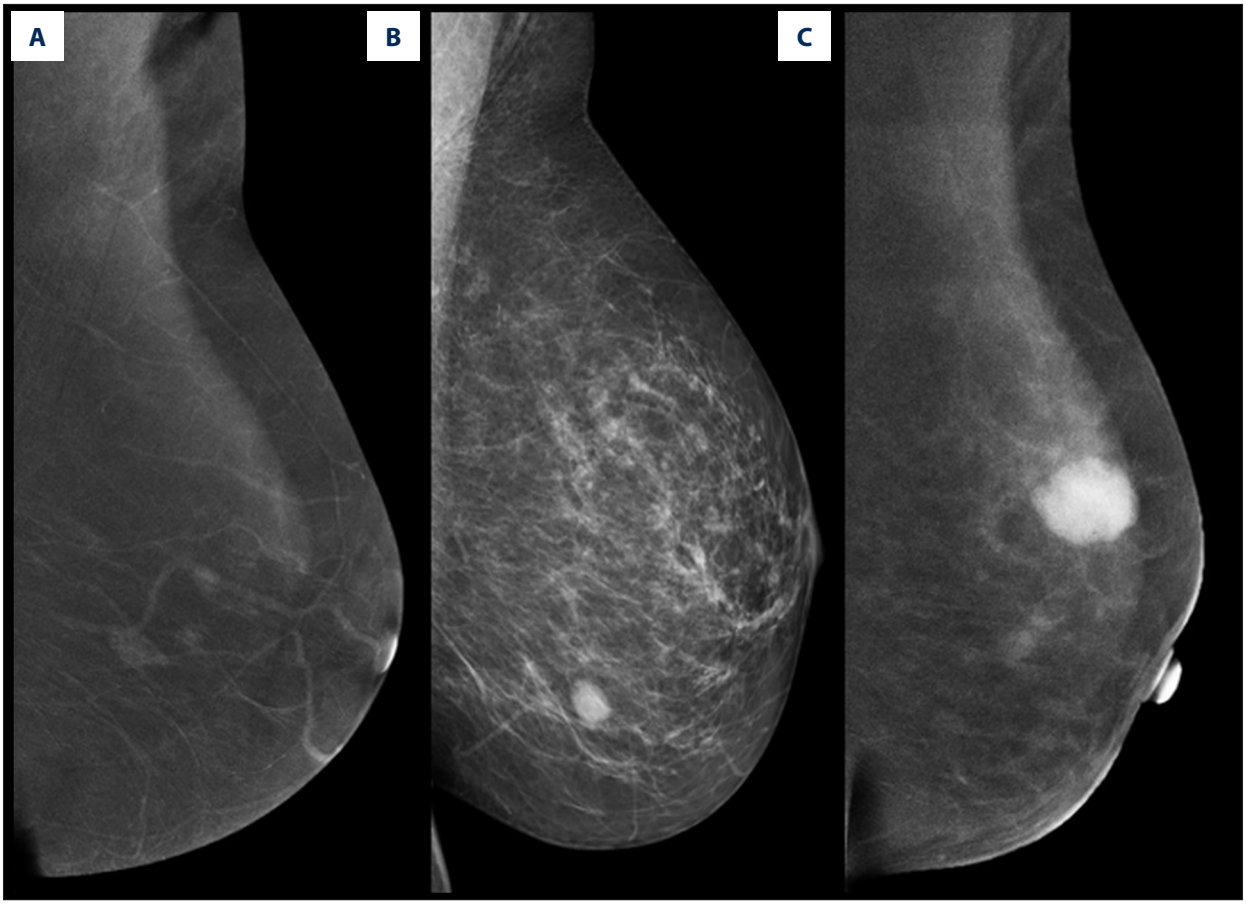

Figure 1. Example images of: (**A**) weak; (**B**) medium; (**C**) strong CESM enhancement.

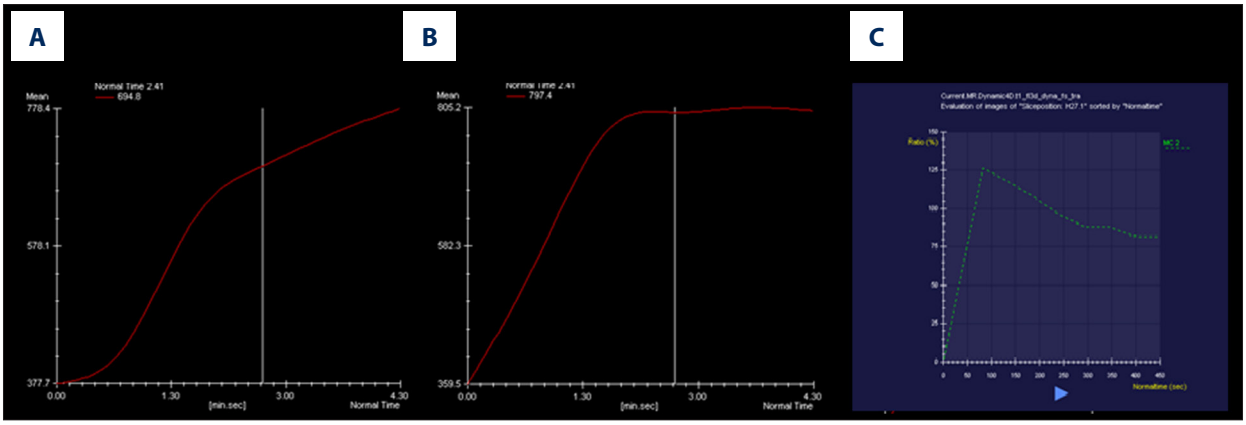

Figure 2. Examples of kinetic CE-MRI curves. (**A**) Type I (persistent); (**B**) type II (plateau); (**C**) type III (wash-out).

microcalcifications on CESM or MRI, the biopsy was guided on mammography. All lesions that appeared to be cancers were subjected to surgery. Specimens obtained with core biopsy or vacuum-assisted core biopsy were fixed in formalin and then embedded in paraffin blocks. After being cut into 4–5-µm slices, the standard hematoxylin and eosin staining procedure was performed. If cancer cells were present, additional immunohistochemical staining was performed to determine the subtype of cancer better (such as ER, PR, and HER expression and Ki-67 index).

Results

The study sample included 107 lesions diagnosed in 94 patients: 71 lesions (66%) appeared to be infiltrating on histopathological

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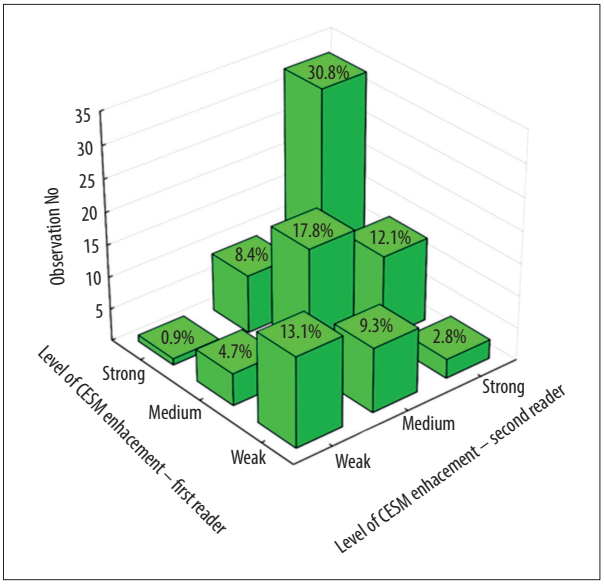

Figure 3. Levels of CESM enhancement – values obtained by readers 1 and 2.

examination, 9 lesions (8%) were non-infiltrating cancers, and 27 lesions (25%) were benign.

Level of enhancement on CESM

The level of enhancement depended on the nature of the lesion (p=0.007 for the first reader, p=0.015 for the second reader, and p=0.0002 for cumulated readings). In case of benign lesions, the level of enhancement on CESM was most frequently weak or medium, and rarely strong. However, for malignant lesions, the level of enhancement was most often strong on CESM, and less frequently medium or low (Figure 3).

The agreement between the 2 readers on levels of enhancement was 76.7%. Differences in assessment of enhancement on CESM between the 2 readers are presented in the diagram below (Table 1).

MRI enhancement curves assessment.

Data analysis revealed that the type of curve on MRI is correlated with lesion type. In case of malignant lesions, the wash-out type curve was the most frequent (72.5%), followed by plateau (18.8%). The progressive enhancement pattern was most common in benign lesions (70.4%), while wash-out type was rarely observed. Within the examined group of patients, the progressive enhancement pattern was characteristic for benign lesions (70.4%) (p<0.001).

Comparisons between lesion type and enhancement curve on MRI are presented in Table 2.

Data analysis revealed that lesions with wash-out curve on MRI most often presented strong enhancement on CESM (53.3% for the first reader, 61% for the second reader, and 57.5% for cumulated readings), while in case of lesions with progressive enhancement curve, strong enhancement on CESM was

Table 1. Differences in assessment of enhancement on CESM between the 2 readers.

Type of lesion	CESM – level of enhancement			
	Weak	Medium	Strong	Total
Benign	R1=9 (33.3%) R2=8 (29.6%) Cumulated readings=31.5%	R1=14 (51.9%) R2=13 (48.2%) Cumulated readings=50.0%	R1=4 (14.8%) R2=6 (22.2%) Cumulated readings=18.5%	27
Cancer	R1=18 (22.5%) R2=12 (15.0%) Cumulated readings=18.7%	R1=23 (28.8%) R2=25 (31.3%) Cumulated readings=30.0%	R1=39 (48.7%) R2=43 (53.7%) Cumulated readings=51.3%	80
Total	R1=27 R2=20	R1=37 R2=38	R1=43 R2=49	107

Table 2. Comparison between lesion type and enhancement curve on MRI.

Type of lesion	Type of curve			
	Type I – persistent	Type II – plateau	Type III – wash-out	Total
Benign	19 (70.4%)	6 (22.2%)	2 (7.4%)	27
Cancer	7 (8.8%)	15 (18.8%)	58 (72.5%)	80
Total	26	21	60	107

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Table 3. Correlation between level of CESM enhancement and type of curve in breast CE-MRI.

Type of enhancement	Type of curve			
	Type I – persistent	Type II – plateau	Type III – wash-out	Total
Strong	R1=3 (11.5%) R2=6 (23.1%) CR=17.3%	R1=8 (38.1%) R2=6 (28.6%) CR=33.3%	R1=32 (53.3%) R2=37 (61.6%) CR=57.5%	R1=43 R2=49
Medium	R1=12 (46.2%) R2=13 (50.0%) CR=48.1%	R1=6 (28.6%) R2=9 (42.9%) CR=35.7%	R1=19 (31.7%) R2=16 (26.7%) CR=29.2%	R1=37 R2=38
Weak	R1=11 (42.3%) R2=7 (26.9%) CR=34.6%	R1=7 (33.3%) R2=6 (28.6%) CR=31.0%	R1=9 (15.0%) R2=7 (11.7%) CR=13.3%	R1=27 R2=20
Total	26	21	60	107

the rarest (11.5%, 23.1%, and 17.3%, respectively, as above). The relationship between enhancement level on CESM and curve type on contrast-enhanced MRI depends on the nature of the lesion. If a cancer was present, strong- or medium-level enhancement was dominant and the curve type on MRI was either plateau or wash-out. If the lesion was benign, weak enhancement was more common than strong on CESM, and non-characteristic curve type was most common on MRI contrast image. The type of MRI curve was found to be related with enhancement level on CESM (p=0.004 for first reader, p=0.006 for the second reader, and p<0.0001 for cumulated readings) (Table 3).

Discussion

MRI is a diagnostic method with proven efficiency in breast cancer diagnostics. During this examination after contrast medium administration, 5–7 acquisitions are performed in a short time, which allows visualization of contrast enhancement foci, as well as enhancement dynamics assessment. As such, morphologic and dynamic features of enhancing lesions can be evaluated on MRI; this helps their evaluation and classification as benign, malignant, or requiring follow-up. On CESM morphologic features, lesion enhancement and possibly the level of enhancement (qualitatively and quantitatively) can be evaluated. With CESM, only 1 acquisition is obtained in CC projection and 1 in MLO projection; as such, drawing kinetic contrast up-take/wash-out curves after contrast medium administration, as possible with MRI dynamic sequences, is not possible (although some experienced users looking at the enhancement level in CC and MLO may get an idea of the speed of up-take/wash-out).

Our study compared a subjective assessment of contrast enhancement on CESM with enhancement kinetic curves on MRI. The results showed that level of enhancement on CESM depends on lesion type (p=0.007 for the first reader and p=0.015 for the second reader). In case of benign lesions, the level of enhancement on CESM was most frequently weak or medium, and rarely strong. On the contrary, for malignant lesions, the level of enhancement was most often strong on CESM, and more rarely medium and low.

Type of kinetic curves on MRI image depends on lesion type. In case of breast cancer, the wash-out type curve was the most frequent (72.5%) and followed by plateau (18.8%). Progressive enhancement pattern was most commonly seen in case of benign lesions (70.4%) (p<0.001).

Having compared enhancement curves on MRI with CESM for lesions with wash-out curve type, we most often see strong enhancement on CESM (53.3%), while for lesions with progressive curve, strong CESM enhancement was the rarest (11.5%). Analysis revealed that curve type on MRI is associated with enhancement level on CESM (p=0.04).

In previous publications, CESM and MRI were compared only in reference to their sensitivity and specificity. In terms of effectiveness in dense glandular breasts imaging, MRI sensitivity ranges from 81% to 97.8% and specificity is around 61% [2,10,11]. CESM sensitivity varies from up to 90.5% specificity to around 76.1% [1].

Our study has certain limitations than should be considered, First, it lacked quantitative assessment on spectral mammography. Qualitative assessment is subjective and may not reflect the actual level of enhancement on CESM, which can be reliably determined in quantitative assessment. The differences in the evaluation were discussed by the interobservers and they both agreed that the main factor of these results was based on subjective view of certain lesion and the overall clinical

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experience of each individual, since no histopathological factor of the tumor was involved when making the evaluation.

The second limiting factor is the lack of BPE assessment from the breast MRI studies. However, the correlation between the BPE and the enhancement intensity, as well as the assessment of BPE in CESM, are the topic of currently on-going studies. Tools like radiomics or Artificial Intelligence would help in unifying the results and should be taken under consideration. Other limitations include the small number of lesions analyzed on both imaging methods, and the lack of a control group.

Conclusions

Our study showed that a relationship exists between characteristic features of MRI and CESM (kinetic contrast curves and enhancement level, respectively), and each is related to the nature of the lesion. Our results bring these 2 imaging methods even closer to being regarded as the optimal reference modalities for use in breast cancer diagnosis.

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