Non-masslike enhancement in breast MRI: the pearls of interpretation?

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Abstract

The MR Breast Imaging Reporting and Data System (BI-RADS) lexicon of the American College of Radiology (ACR) includes a new lesion category defined as non-masslike enhancement. The purpose of this paper is to review the definition of this new entity, illustrate the main imaging features described in the BI-RADS lexicon and to propose a diagnostic approach based on data from the literature in order to achieve diagnosis and optimal patient management.

Key words: Breast. MRI. Non-masslike enhancement. MRI. Diagnosis.

How can I detect a non-masslike enhancement?

A non-masslike enhancement is the enhancement of an area that is not a mass (no spatial volume). According to the definition in the lexicon “it includes more or less extensive areas whose internal features have only become possible with the development of MR guided biopsies because it cannot be obtained with conventional imaging techniques. The most frequent non-masslike enhancement is usually diffuse and bilateral, of ductal origin, and may also still be called diffuse parenchymal enhancement. It usually occurs in young pre-menopausal woman. It makes detection and interpretation of contrast uptake difficult. The prevalence in the general population of non-masslike enhancements is significantly lower than that of mass enhancement with 13% versus 76% (2) respectively, although 57% of non-palpable invasive carcinomas may present as non-masslike enhancements (3). While the presence of a mass usually reveals an invasive malignant lesion or a benign tumor, non-masslike enhancements may be either malignant lesions, which are usually an intraductal process, or more frequently a diffuse benign disease (fibrocystic mastopathy), an inflammatory disease, or even physiological enhancement. Thus, thorough knowledge of these imaging features is essential to make a diagnosis, especially since the interpretation of non-masslike enhancements is poorer with conventional imaging techniques. La Trenta, et al. identified an anomaly on retrospective ultrasound for 25% of masses compared to only 11% of non-masses (4). As a result, the management and treatment of non-masslike enhancements are more complex, and in particular obtaining histological proof is more difficult. A retrospective breast ultrasound must be performed to limit the number of MR guided biopsies, which are still not generally available. Therefore the aim of this review is to provide the definition of non-masslike enhancements, describe the main forms found in the lexicon, and discuss management in the presence of these lesions.
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How can I diagnose a non-masslike enhancement?

The description of non-masslike enhancements should be based on a comparison with the contralateral breast. This includes studying the distribution, internal features of enhancement as well as the pharmacokinetics of contrast uptake. Any associated features should also be noted (associated T1- and T2- image anomalies) as well as the presence of other areas of contrast uptake such as ipsilateral or contralateral masses.

Distribution

Symmetric features

Symmetric contrast uptake strongly suggests a benign lesion. Thus, axial or sagittal images must systematically be obtained in both breasts (fig. 2).

Diffuse or localised

Interpretation is based on the saying “the more extensive enhancement is, the less suspicious it is”.

Diffuse non-masslike enhancement involves the entire breast. It may be symmetric or asymmetric (fig. 3).

By definition localised non-masslike enhancements only involve one area of the breast. These are defined according to their distribution:

- A focal non-masslike enhancement will involve less than 25% of a breast quadrant and may be singular or multiple (fig. 4);
- Regional non-masslike enhancement involves more than 25% of a breast quadrant and can also be singular or multiple (fig. 5);
- Ductal non-masslike enhancement presents a linear or branched path of enhancement that follows the galactophoric system (fig. 6);
- Non-ductal linear enhancement follows a line that does not point towards the nipple (fig. 7);
- Segmental enhancement presents a triangular region of enhancement which points towards the nipple (fig. 8).

Internal features of enhancement

Non-masslike enhancements may be clumped (fig. 9), heterogenous (fig. 10), homogeneous (fig. 11) or stippled (fig. 12) according to the BI-RADS classification. Another feature of internal enhancement has also recently been described in the literature: ring-like non-masslike enhancement (5) (fig. 13).

Pharmacokinetics of contrast uptake

The pharmacokinetics of contrast uptake in non-masslike enhancements are identical to those in masses. A type 1 contrast uptake curve corresponds to increasing, progressive uptake (benign picture). A type 2 curve corresponds to moderate uptake with a plateau and no secondary washout (undetermined picture). A type 3 curve corresponds to rapid (before the 3rd minute) intense (≥100%), uptake with secondary washout (malignant picture).

Associated features

When evaluating non-masslike enhancements, features associated with benign lesions (microysts on T2-weighted images in stippled NME strongly suggesting a diagnosis of fibrocystic mastopathy) or malignant lesions (detection of a mass or associated architectural distortions visible on unenhanced T1-weighted images) must be investigated. The presence of a retracted nipple, skin retraction, edema, or associated adenopathies make a non-masslike enhancement more suspicious. On the other hand, detection of internal fat on T1-weighted images before and after contrast enhanced subtraction would systematically exclude by identifying this enhancement on post-contrast enhanced images, then confirming that there is no visible mass on the pre-contrast sequences to confirm the diagnosis of a non-masslike enhancement. Also, all images must be obtained on the same anatomical plane for optimal comparison of images before and after contrast enhancement. 3D (MIP) with volume reconstruction may also be help to determine the form of the non-masslike enhancement or may be used for reconstruction of coronal images to visualize the galactophoric system. Another approach includes obtaining sagittal views during the dynamic sequence of the breast being studied (5). Tomazaki, et al. emphasized the importance of using this method in case of segmental non-masslike enhancements because the distribution of this entity is easier to identify on coronal images (6). To obtain these reconstructions and the best possible images of contrast uptake, pixel size must be isometric (the same size in all three spatial planes).
images would lower the positive predictive value for malignancy in this same non-masslike enhancement.

What approach should I take to a non-masslike enhancement?

The distribution of a non-masslike enhancement is the most important imaging feature whatever the mathematical model used. ($A_2=0.78-0.84$) (2).

Diffuse symmetric enhancement

The presence of diffuse, symmetric enhancement and the patient’s medical history is usually enough to make a diagnosis. The two main etiologies are:

- **Diffuse parenchymal breast enhancement** found in pre-menopausal patients especially when MRI is performed at the end of the cycle. Thus, breast MRI should be performed between the 7th and the 17th day of the cycle. This same parenchymal enhancement can be found in menopausal women who are taking hormone replacement therapy. Progesterones can cause abnormal enhancement in 50% of cases (7). Once again, hormonal treatments should be discontinued between 4 and 6 weeks before performing breast MRI. It is important to respect these recommendations because diffuse parenchymal enhancement makes it difficult to detect and analyse contrast uptake. Thus, it is important to mention the grade of diffuse parenchymal enhancement at the beginning of the report which is separate from breast density, and rate it from 1 to 4. When it is significant, making interpretation difficult, it may be preferable to perform another MRI later.

Fig. 4: **Single focal non-masslike enhancement.** Axial T1-weighted image after gadolinium injection (2nd minute) and subtraction.

Fig. 5: **Regional non-masslike enhancement only partially masked by diffuse parenchymal enhancement.** Axial T1-weighted image after gadolinium injection (2nd minute) and subtraction.

Fig. 6: **Branched, retroareolar ductal non-masslike enhancement.** Sagittal T1-weighted image after gadolinium injection (2nd minute) and subtraction.

Fig. 7: **Linear, non ductal non-masslike enhancement in the periphery of the gland corresponding to a vessel.** Axial T1-weighted image after gadolinium injection (2nd minute) and subtraction.

Fig. 8: **Segmental non-masslike enhancement.** Sagittal T1-weighted image after gadolinium injection (2nd minute) and subtraction.
Fibrocystic mastopathy is the second etiology of diffuse, symmetric enhancement. This usually includes stippled type enhancements associated with microcysts that are visible on T2-images and which are evenly distributed throughout the breast. (fig. 14).

Enhancement without a localized mass and/or an asymmetric mass

We will list the different non-masslike enhancements in descending order according to their positive predictive value (PPV) for malignancy (table I).

Segmental NME is the most suspicious of the non-masslike enhancements. Its PPV for malignancy is high in most studies in the literature and even reaches 100% in the study by Tozaki, et al. (6). The latter explains these results by the method of image acquisition in that study, and states that coronal views of the galactophoric architecture should limit the number of false positive results. This NME is usually a sign of malignant disease (fig. 15).

The prevalence and positive predictive value of ductal enhancement varies. These differences in prevalence may depend on the population studied. In a selected population (high risk patients, or patients with cancer) (8), the frequency of ductal enhancement was 21% compared to 5% in an unselected population (9). Moreover, the positive predictive value for malignancy varied from 26% to 84% depending on the authors (8, 10). The study by Liberman provided a response by showing the importance of context (8). These authors showed that the presence of an ipsilateral carcinoma increased the PPV for malignancy from 22% to 50%. On the other hand, family history, menopausal status and a personal history of breast cancer did not change the PPV of NME in that same study (8). Internal features must also be taken into account. A clumped ductal NME is more suggestive of malignancy than a homogenous ductal NME (35% versus 14% malignancy) (8), which confirms the study.
by Tozaki (5). Ductal NME is mainly the sign of a ductal pathology which may be carcinomatous (in situ ductal carcinoma) or inflammatory (ectasiant galactophoritis) (fig. 16).

In the literature the PPV of regional and focal NME also vary significantly. Regional or focal NME had a PPV of approximately 21% in the study by Schnall (2). Morakabati did not find any malignant lesions in regional (n = 10) or focal (n = 4) NME (9). Thus, other elements must be considered, in particular the internal features of NME. When enhancement is homogeneous or stippled, the PPV for malignancy is low, with values below 5% if it is homogeneous and 25% if it is stippled, suggesting in this case an area of fibrocystic dystrophy (fig. 17).

When enhancement is heterogeneous, reticular, clumped or ring-like the risk of malignancy is greater. Reticular enhancement is most frequently found in inflammatory carcinomas (fig. 18). Ring-like enhancement was recently described in the study by Tozaki with a PPV for malignancy of 96%. This hypothesis has already been proposed by Heywang Kobrunner who reported a poor prognostic value in the presence of increased contrast uptake on the periphery of an enhanced image (11).

Finally, linear non-ductal NME has a very low PPV for malignancy because this usually corresponds to vascular enhancement.

### Contrast uptake curves

The importance of contrast uptake curves in the characterisation of non-masslike enhancements varies in the literature. In the study by Bartella et al. NME corresponding to malignant entities usually presented with plateau shaped curves, and less frequently included secondary washout (3). In the study by Nunes et al., a low-intensity regional NME had a PPV for malignancy of 8% while a moderate or high-intensity regional NME had a PPV of 58% (10). However, no significant difference in contrast uptake curves could be found to differentiate benign from malignant diseases, which was also confirmed in the study by Goto (12).

The feasibility of obtaining uptake curves for non-masslike enhancements is a technical problem that must be taken into account. When the NME is heterogeneous or stippled, it may be difficult or even impossible to place a region of interest without being at least partially in the adjacent gland. Thus the uptake kinetics may be falsely reassuring and should not be the major element under consideration when evaluating an NME.

Finally evaluation of non-masslike enhancements should include data from the patient’s medical history (hormonal sta-
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The presence of microcalcifications on a mammogram in the area of a segmental or ductal NME increases the negative predictive value, and stereotactic tissue biopsy can be performed in this case. Although retrospective ultrasound performed after MRI is less pertinent for analysing masses, it should be systematic in the presence of a non-masslike enhancement (3). Ultrasound guided tissue samples can then be obtained if an anomaly is detected in the same anatomical area. Figure 19 provides a decision tree for the management of NME discovered during breast MRI (11).

Fig. 17: Fibrocystic dystrophy of the upper outer quadrant of the right breast.

\[a\]
Axial T1-weighted image after gadolinium injection (2nd minute) and subtraction. Regional, stippled non-masslike enhancement.

\[b\]
Axial T2-weighted image with fat saturation. Presence of associated microcysts throughout the visible breast tissue.

Fig. 18: Inflammatory cancer in the outer quadrants of the left breast. Axial T-weighted image after injection of gadolinium (2nd minute) and subtraction. Reticular non-masslike enhancement associated with a hypertrophic gland and edema with cutaneous and subcutaneous thickening.

Fig. 19: Decision tree for non-masslike enhancements (11).
References