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Breast microcalcifications: The lesions in anatomical pathology

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KEYWORDS
Urogenital;
Breast;
Mammography

Abstract Microcalcifications are actually indirect signs of pathological processes, and only a few of these processes may be correctly correlated to the morphologic pattern of calcifications. This is true of the microcalcifications typically classified as benign by the 4th edition of the BI-RADS Atlas, except for round and punctuate microcalcifications. This is also the case of polymorphous fine and linear fine microcalcifications most often, but not exclusively, associated with DCIS with necrosis. For other types of microcalcifications, other parameters are analyzed in a more global approach: the associated clinical or mammographical signs; the context, especially genetic; the spatial distribution; the number; the evolution over time. The radiologist should compare the images with the anatomy of the terminal ductal-lobular unit, from where most cancers arise, and estimates the risk by taking into account the clinical context and the antecedents.

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Breast microcalcifications are present in about 30% of all malignant breast lesions, in over half of the malignant infraclinical breast lesions, and lead to depict 85 to 95% of all cases of ductal carcinoma in situ in screening campaigns.

Definition and technical requirements

The term microcalcification refers to calcifications of whom diameter is inferior to 1 mm, knowing that current spatial resolution mammographs make small objects to be detected without magnification for a size ranged between 100 and 200 \( \mu \)m.

Detection is, in principle, based on the images obtained with a magnification of 1, on installations complying with the prevailing quality control standards.

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2211-5684/S – see front matter © 2014 Éditions françaises de radiologie. Published by Elsevier Masson SAS. All rights reserved.
Characterization requires images with a magnification of at least 1.5, using the smallest focal spot of 0.1 mm, according to the French legislation. The specifications for the French breast cancer screening program indicates that the installation should be able to provide images with geometric magnification, except for installations providing a spatial resolution of 50 µm, for which magnification by electronic methods are authorised [1].

Physiopathology

The most common breast calcifications are dystrophic and occur in different, sometimes associated, pathological processes: inflammation, infection, benign tumour, malignant tumour.

They may occur in the stroma of a fibrous lesion with a connective component (fibroadenoma), or in the stroma reaction of a malignant tumour.

In the ductal-lobular structures, they appear with two distinct mechanisms:

- an accumulation of secretions of mucin in the lumen of the duct or lobular acini or in the cavities formed by the lesion, such as low or intermediate grade DCIS, that calcify secondarily taking a round or amorphous shape of different size, of more or less large size depending on whether or not the lumen is dilated [2]. These microcalcifications are not specific to neoplastic lesions and may be found in all pathological processes involving the terminal ductal-lobular unit, including simple or sclerosing adenosis, simple or atypical ductal or lobular epithelial hyperplasia;

- a calcification process of endoluminal necrotic material consisting of cell debris and secretions produced by various pathological entities including comedocarcinoma, that will fit closely around the lumen of the ductal-lobular structures providing linear, sometimes granular microcalcifications, depending on the amount of material accumulated in the lumen [2].

These often easily recognised microcalcifications are frequently associated with high-grade ductal carcinoma in situ but are also, although more rarely, found in extensive low and intermediate lesions or even in benign lesions such as epithelial metaplasia [3].

Most breast calcifications are made of calcium phosphate, a small are made of calcium oxalate in case of ductal lithiasis (weddelites).

Another type results from metaplasia by cells that metabolize calcium in the collagen in response to a post-traumatic, post-therapeutic cytosteatonecrosis or following a haematoma like that occur in the bone tissue.

Morphological analysis and assessment of the risk: general principles

Correlation between the radiological images and the anatomy of the terminal ductal-lobular unit

By analyzing microcalcifications, the radiologist systematically looks for signs compatible with a carcinoma in situ. In the ductal and lobular forms, it arises in the terminal ductal-lobular unit (TDLU). It is therefore necessary to be fully familiar with the histological characteristics of TDLU in order to be able to establish a link between the morphology of the microcalcifications, their distribution, and their ductal-lobular origin.

The breast has average 15 to 20 lobes or segments that give rise to a main duct ending in a lactiferous sinus in the nipple.

Each duct divides from the nipple to the periphery in sub-segment ducts and then into 20 to 40 terminal ducts.

Each terminal duct collects 10 to 100 glandular acini that define a lobule (Fig. 1).

The entire length of the walls of the ducts, to the canciuli and the acini, are formed by a continuous surface epithelium in periphery surrounded by a discontinuous layer of

myo-epithelial cells. This layer is coated with a layer of slack connective tissue poor in collagen and rich in cells called basal membrane, the crossing of which determines the micro-invasive and then invasive nature of a tumor [3].

The microcalcifications associated with the development of a carcinoma in situ arise in the lumen of the acini and terminal ducts, by calcium production on the secretion material or on the zones of necrosis. They only indirectly attest to the cell proliferation of the carcinoma, that will then progress in a retrograde direction, within the lobule or an anterograde direction in the ducts toward the nipple. The microcalcifications may seem to be discontinuous and indicate multi-focality. Multifocal DCIS lesions are actually rare and most often may correspond to a single lesion extending to several ducts by contiguity [4].

**Size of the microcalcifications**

Roughly, large microcalcifications of about one millimetre are more often benign than those whose size is under 0.5 mm.

However, there are exceptions since coarse heteroge- neous or dystrophic calcifications over one millimetre in size may associate with malignant lesions.

**Number of microcalcifications**

A group of 10 or more microcalcifications in a volume inferior to 1 cm³ is more suspect than a group of 5 of identical morphology.

In Barreau’s study, the high number of microcalcifications in a cluster was correlated with the high grade of DCIS and the presence of necrosis [5].

**Site of origin**

The site of the formation or accumulation of calcifications may determine their morphology:
- round or punctuate, of normal size or dilated, in the lobular acini, most often associated with benign lesions or low grade carcinoma in situ;
- linear in the lumen of a small duct by calcification of a zone of necrosis associated with a high grade ductal carcinoma in situ or by rod-like calcifications of secretions accumulated in a larger duct as a consequence of a galactophoritis;
- coarse in the connective tissue of an adenofibroma or in the stroma reaction of invasive carcinoma.

**Distribution according to the aetiology**

The pathological process that produces the microcalcifications may determine their distribution:
- round clustered distribution or regional distribution in the lumen of multiple lobular acini in case of adenosis, lesions involving a risk or certain DCIS;
- segmental arrangement in the caniculi and ducts of a lobe in case of extensive DCIS;
- diffuse distribution in case of fibrocystic dystrophy in cysts or dilated acini.

**Evolution over time: is stability a guarantee of benignness?**

Stability over time is classically considered to be less sus- pect, suggesting benign histology. This concept applies when a mammography image is classified ACR 3. A control after 4 or 6 months, then 6 months later, then 1 year later is the usual follow-up schedule for an anomaly thought to be probably benign with a risk of malignancy that does not exceed 2% during the assessment of practices.

In the analysis of microcalcifications, decision of follow- up should only apply to certain microcalcifications featuring non-suspect semiological criteria:
- a few, round or punctuate clustered microcalcifications;
- a few, amorphous microcalcifications in a small round or oval cluster, onset calcification process of a fibroade- noma;
- coarse, heterogeneous microcalcifications, grouped on a small volume, suggesting a calcified fibroadenoma.

For other microcalcifications not combining these criteria, the stability over time should not be considered to be probably benign.

Lev-Toaff, in a series of 105 cases of malignant microcalcifications, analysed the evolution of the anomalies by comparison with the previous mammograph performed 8 to 63 months before (mean: 25.4 months). The microcalcifications were unchanged in 24.8% of the cases [6].

**Associated mammography signs**

Opacity associated with the microcalcifications increases the probability of malignancy, mostly invasive carcinoma.

**Clinical context and antecedents**

Microcalcifications that may be considered as probably benign in the general population are more suspect in case of an anomaly in the clinical examination, a personal history of breast cancer or a genetic predisposition.

Clustered classification that would have been classified as ACR 3 in the general population often leads to biopsy in a woman with a genetic risk.

Microcalcifications appearing not typical of cystostateoncrosis in a treated breast should undergo histological verification.

**The different types of microcalcifications: what are the risks?**

By definition, calcifications over one millimetre, such as pop-corn-like calcifications and large rod-like calcifications are excluded.

**The BI-RADS system of the American College of Radiology**

It was developed in order to standardise the description and recommendations for the care of anomalies detected by mammography, and as a result, facilitate communication between radiologists and referring physicians.
It is useful to evaluate the assessment of the radiological practices and helps to standardise practices.

It is also a unique way to be able to compare publications by using a common language that was sadly missing in the past (for example, the same type of microcalcifications could be labelled lobular, round or granular in different publications published before the BI-RADS system, or even in recent publications that do not use it).

The section dealing with microcalcifications is inspired by previous classifications, such as Le Gall’s classification.

It defines the descriptive elements concerning the morphology of the different types of breast calcifications, and describes three categories: typically benign, intermediate risk of malignancy, higher probability of malignancy. It adds descriptive elements concerning the spatial distribution of the calcifications:

- the scattered or diffuse nature;
- the regional distribution, corresponding to calcifications scattered over a large volume (>2 cc of breast tissue) without a ductal distribution;
- clustered calcifications, containing at least 5 microcalcifications in a small volume of tissue (<1 cc);
- the linear distribution suggesting ductal extension;
- the segmental distribution, of triangular shape with the tip directed towards the nipple, suggesting a neoplastic process extending into a lobe or a segment of the breast.

In practice, these modifiers, as a function of the spatial distribution, will modulate the degree of suspicion of round/punctuate and amorphous microcalcifications: less suspicion in case of scattered or diffuse distribution, slightly less in case of regional distribution, higher suspicion in case of grouping in a focal point or cluster, of segmental or linear distribution.

The current version is the 4th edition published in 2003 [7]. It has modified some elements of the morphological description by splitting the former "polymorphous" category into two categories: "coarsely heterogeneous" and "fine polymorphous". In the typically benign category, it includes round and punctuate microcalcifications, and this point is a subject of controversy in the literature.

Typically benign microcalcifications that don’t require histological verification

Cutaneous or dermal calcifications

They do not generate diagnostic problems in mammography, appearing round, lucent-centred and ring-shaped and with a light centre. They predominate in the sub-mammary, axillary, areolar and parasternal regions, more rich in subcutaneous glands. When their cutaneous origin has not been clearly demonstrated, it may be useful to obtain some complementary views tangential to the skin.

Vascular calcifications

They are more frequent with age and predominate along the external mammary vessels. They may form a marker of atherosclerosis and coronary risk. They are easily recognised when they present as a long tram-track patterns along vessels, in particular in diabetic patients. They raise more interpretation problems when discontinuous at the beginning of the calcification process, due to their linear distribution, and in this case, they may require to histological verification.

Lucent-centered calcifications of cytosteateonecrosis

They are round or oval and range from 1 mm to 1 cm, with a light centre and thick wall. They correspond to calcified cytosteateonecrosis, of post-traumatic or post-therapeutic origin, in particular after radiotherapy.

Eggshell or parietal calcifications

They are thin, less than 1 mm, in the periphery of a cyst or a zone of cytosteateonecrosis.

Milk of calcium calcifications

They correspond to the sedimentation of calcified secretion inside cysts. Sedimentation is only confirmed by performing a lateral-medial view, revealing the characteristic crescentic teacups shape.

On the cranial-caudal view, the central part appears amorphous, due to the accumulation of the calcified fluid at the bottom of the cyst.

Certain authors have recommended to perform complementary "hanging breast" views in order to prove the mobile sedimentary nature in this position.

Their benign appearance should preclude the verification of the absence of other more suspect microcalcifications nearby.

Calcified surgical sutures

They are obvious when the calcifying process is complete, but may raise problems of interpretation in cases of partial calcification.

Dystrophic calcifications

They appear in zones exposed to a trauma or radiation. Their shape is coarse, over 0.5 mm. Other calcifications suggesting cytosteateonecrosis (lucent-centered calcifications, eggshell calcifications) are frequently associated.

Radio-histological correlations

Microcalcifications that may be classed as benign or suspect: round or punctuate microcalcifications

They are included in the category of typically benign calcifications in the 4th edition of the BI-RADS system by the American College of Radiology (Fig. 2). Nevertheless, the authors indicate that an isolated group (cluster) of punctuate calcifications may require close follow-up, or even a biopsy, if present on the same side as a breast cancer [7].
This choice has given rise to a controversy in the literature and certain authors propose classifying these microcalcifications as suspect.

They classically consist of microcalcifications arising in the lumen of lobular acini, called round when they exceed 0.5 mm and punctuate below 0.5 mm.

In a great many recent publications, they do not seem to be individualised as such in the ‘‘typically benign’’ category, with a rate of cancer reported as null in this category [8–10]. However, in certain studies, certain punctuate microcalcifications may be classified as amorphous microcalcifications, or even fine polymorphous microcalcifications, as the studies on the inter- and intra-observer reproducibility have revealed great disparities [11].

Le Gall’s work reported the presence of malignancy associated with regular punctuate microcalcifications in 19% of the cases [12].

De Lafontan reported a malignancy of 10% of cancer for punctuate microcalcifications [13].

In a meta-analysis on 40 publications and 10,665 cases of microcalcifications, Rominger reported a global rate of malignancy for round and punctuate microcalcifications of 9% (6–13%), of 14% (11–19%) in the sub-group that benefited from systematic histological verification and 0.5% (0.08–2.57%) in a sub-group that benefited from 2 years of follow-up [14].

Holland reported that the round or punctuate microcalcifications are those usually found in well-differentiated DCIS [15]. Evans reported that round and punctuate microcalcifications are more frequently associated with positive margins during excision surgery of DCIS than polymorphous and fine linear microcalcifications, and suggests that these microcalcifications are more often associated with DCIS comprising non-calcified extensions not seen in mammography [16].

Evans indicated that these round microcalcifications are more frequent in cribriform DCIS without necrosis [17].

Barreau reported, in 58 cases of DCIS detected by round microcalcifications, 65.6% grade I DCIS, 17.2% grade 2 DCIS and 17.2% grade 3 DCIS [5].

Evans found punctuate microcalcifications in 22% of the low grade DCIS, 20% of the intermediate grade DCIS and 9% of the high grade DCIS [18].

Figure 2. Round and punctuate microcalcifications: a: lateral medial view: infracentimetric focus at the union of the outer quadrants of the right breast (arrow); b: lateral medial and (c) cranio-caudal view with magnification: clustered punctuate microcalcifications (arrow) with several round calcifications (small arrow) with angular contours comprising more than 10 elements classified as ACR 4B; d: vacuum assisted breast macrobiopsies: Presence of representative microcalcifications (arrows); e: histology (low magnification): simple, non-atypical, focally hyperplastic, cylindrical metaplasia. Microcalcifications (blue arrows) in the lumen of the acini of a lobule (red arrows); f: histology (high magnification): simple cylindrical, non-atypical, focally hyperplastic metaplasia. Microcalcifications in the lumen of the acini of a lobule (red arrows). Epithelial lesions of cylindrical non-atypical metaplasia (blue arrow). Presence of several aspects of grade 2 lobular neoplasm (LIN 2) (yellow arrows).
These microcalcifications may be found in all pathological processes involving the terminal ductal-lobular unit, including simple or sclerosing adenosis, ductal or lobular, simple or atypical, epithelial hyperplasia.

In 2002, the ANAES proposed considering as probably benign (ACR 3), a few round or punctuate microcalcifications (the threshold of 10 microcalcifications was often reported) in small round isolated clusters and proposed a histological verification for more numerous round or punctuate microcalcifications (ACR 4) and/or those grouped in clusters with neither round nor oval margins [18].

In his meta-analysis, Rominger indicated that the different items of descriptions of the spatial distribution of round or punctuate microcalcifications are associated with an overall rate of malignancy that remains superior to 2%, and recommends classifying them as ACR4 whatever the mode of distribution or number. For the different descriptions, he reports: in small clusters, 7.66% of malignancy (2.49–21.23%); diffuse, 5.67% (0.36–50.05%); regional 22.63% (3.27–71.65%); segmental 21.41% (8.73–43.72%); linear 21.74% (4.33–63.03%) [14].

Figure 3. Amorphous microcalcifications: a: lateral medial view; Microcalcifications extending over 3 cm in the upper outer quadrant of the right breast, poorly visible (arrows); b: lateral medial and (c) cranio-caudal view magnification: association of abundant amorphous microcalcifications, with regional distribution (arrows) classified as ACR 4A, and several rare coarse heterogeneous microcalcifications (small arrow); d: vacuum assisted breast macropiöses: poorly visible representative microcalcifications (arrows); e: histology (low magnification): fibrous fatty breast tissue comprising several aspects of sclerosing adenosis. Microcalcifications distributed in several lobules (arrows); f: histology (high magnification): fibrous fatty breast tissue comprising several aspects of sclerosing adenosis. Microcalcifications filling the lumen of the lobular acini where the epithelium is no longer visible (red arrows). Zone of intralobular fibrosis (blue arrow).

Suspect microcalcifications or intermediate level of concern

Amorphous or indistinct microcalcifications

Also called tiny or hazy microcalcifications, about 200 to 300 μm, they are less conspicuous than the other microcalcifications and require technically optimised mammograms (Fig. 3).

They are found in the benign pathological processes (fibrocystic dystrophy), lesions at risk or non-comedo carcinoma in situ.

Descriptor items of the spatial distribution play a major role in the assessment of the risk associated with these microcalcifications: scattered or diffuse, they are considered to be probably benign; in clustered, regional, segmental or linear, they are considered as suspect.

In 2002, the ANAES proposed classifying as probably benign ACR 3, a few amorphous microcalcifications in small, round or oval, amorphous clusters, not abundant microcalcifications, suggesting the beginning of calcification process of a fibroadenoma, and proposed classifying as suspect ACR 4, abundant and grouped microcalcifications [19].
Barreau reported, in 146 cases of DCIS detected by amorphous microcalcifications, 71.6% grade 1 DCIS, 13.2% grade 2 DCIS and 15.2% grade 3 DCIS [5].

Berg reported a rate of malignancy of 20% for amorphous microcalcifications. De Lafontan reported a malignancy of 19% [20].

In his series, in the sub-group of amorphous microcalcifications, Burnside reported 7% invasive carcinoma, 7% DCIS, 13% lesions at risk [8].

Bent et al. reported a rate of malignancy of 20%, 10% invasive carcinoma and 10% DCIS [9].

Shin et al. reported 7% invasive carcinoma, 24% DCIS, 8% lesions at risk [10].

In his meta-analysis, Rominger reported a rate of malignancy of 27% for amorphous microcalcifications and a global rate always exceeding 2%, whatever the descriptor items of spatial distribution, including scattered microcalcifications where the rate was 6.98% (0.94—37.16%) [14].

Coarse heterogeneous microcalcifications
Recently individualised, they refer to microcalcifications exceeding 0.5 mm those are easily visible, irregular, tending to coalesce (Fig. 4). The size remains inferior to that of dystrophic calcifications and superior to that of fine polymorphous calcifications.

They correspond to the usual appearance of fibroadenomatous lesions or fibrotic lesions, but may also be found in malignant lesions. Modifiers of the spatial distribution should be taken into account in estimating the risk of malignancy: probable calcified fibroadenoma in case of compact clustered microcalcifications grouped over a small volume, suspect lesion in the case of segmental distribution.

Burnside reported, in his series, in the sub-group of 14 cases of coarse heterogeneous microcalcifications, only one case of DCIS, no cases of invasive carcinoma, or lesions at risk [8].

In 10 cases, Bent et al. reported 2 cases of DCIS and no cases of invasive carcinoma [9].

In 110 cases, Shin et al. reported 6% invasive carcinoma, 25% DCIS, 12% lesions involving a risk [10].

In his meta-analysis, Rominger reported 13% (7—20%) of malignancy for coarse heterogeneous microcalcifications, 12.02% (5.22—25.29%) when they are in small focal spots, 25% (8.34—89.11%) when they are regional, 16.67% (0.95—80.64%) when they are linear [14].

Figure 4. Coarse heterogeneous microcalcifications: a: CC view without magnification: focus of outer retromammary clustered microcalcifications of 5 mm (arrow); b: front and (c) profile view with magnification: presence of about ten coarse heterogeneous microcalcifications with a linear distribution, classified as ACR 4B (arrow); d: vacuum assisted breast macrobiopsies: representative microcalcifications with low contrast (arrow); e: histology (low magnification): nodular lesion of 0.4 cm with a margin of fibrous fatty tissue poor in glandular structures, corresponding to a fibroadenoma with fibrous stroma, with big scattered calcifications. Nodule with distinct margins (tips of arrows). Large microcalcifications (blue arrows) and small microcalcifications (small arrow); f: histology (high magnification): nodular lesion of 0.4 cm with a margin of fibrous fatty tissue poor in glandular structures, corresponding to a fibroadenoma with fibrous stroma, with big scattered calcifications. Calcifications developed within the stroma (arrows) without epithelial structure.
Microcalcifications with a higher probability of malignancy

They are easily visible and usually feature a spatial distribution suggesting ductal neoplasm. They are often associated with calcified necrosis moulded in the ducts in case of high-grade comedo carcinoma or intermediate grade DCIS with necrosis.

Fine polymorphous microcalcifications

Recently individualised, they correspond to calcifications whose size is under 0.5 mm, and are more visible than amorphous microcalcifications (Fig. 5).

They suggest malignancy as first choice and require histological verification.

Barreau reported, for 103 cases of DCIS detected by fine polymorphous microcalcifications, 44.6% grade 1 DCIS, 16.9% grade 2 DCIS and 38.5% grade 3 DCIS [5].

In a series of 77 cases of fine polymorphous microcalcifications, Hofvind reported the presence of high grade DCIS in 69% [21].

Burnside reported in his series, in the sub-group of fine polymorphous microcalcifications, 15% invasive carcinoma, 15% DCIS, 3% lesions at risk [8].

Bent et al. reported 28% malignancy, 12% invasive carcinoma and 16% DCIS [9].

In 58 cases, Shin et al. reported 26% invasive carcinoma, 60% DCIS, 3% lesions at risk [10].

In his meta-analysis, Rominger reported a rate of malignancy of 50% (43–58%) [14].

Fine linear or fine linear branched calcifications

They are linear or irregular curvilinear, sometimes discontinuous, under 0.5 mm (Fig. 6). They are easily visible and usually identified as suspect, classified ACR 4, or even ACR 5 when the distribution is segmental.

Barreau reported, in 21 cases of DCIS detected by fine linear branched microcalcifications, 30% grade 1 DCIS, 11.4% grade 2 DCIS and 58.6% grade 3 DCIS [5].

Evans found fine linear microcalcifications in 58% of the high grade DCIS, 38% of the intermediate grade DCIS and 26% of the low grade DCIS [18]. He indicated that these microcalcifications are not only found in high grade DCIS and that the incidence of linear microcalcifications increases with the extent of the microcalcifications, whatever the grade of the DCIS. He reported that the incidence of linear microcalcifications in a small cluster, under 10 mm, of high grade DCIS

![Figure 5](image_url) Fine polymorphous microcalcifications: a: strict profile view: outer retromammmary microcalcifications extending over 3 cm (arrow); b: profile and (c) front view with magnification: fine polymorphous microcalcifications with linear distribution classified as ACR 4C (arrows); d: vacuum assisted breast macrobiopsies: representative microcalcifications (arrows); e: histology (low magnification): high grade nuclear ductal carcinoma in situ with necrosis and microcalcifications, of the comedocarcinoma type. Necrosis without calcifications in the lumen of a duct (red arrow). Necrosis with fine calcifications (yellow arrow). Calcifications without visible necrosis (blue arrow); f: histology (high magnification): High grade nuclear ductal carcinoma in situ with necrosis and microcalcifications, of the comedocarcinoma type. Calcifications developed on areas of necrosis in the lumen of the ducts (blue arrows). Calcifications without visible associated necrosis (red arrow).
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is identical to that found in an intermediate grade DCIS of 21 to 30 mm and in a low grade DCIS of over 30 mm.

Hofvind reported, in series of 62 cases of fine linear microcalcifications, the presence of high grade DCIS in 84% [21].

Burnside reported in his series, in the sub-group of fine linear calcifications, 32% invasive carcinoma, 21% DCIS, 5% lesions at risk [8].

Bent et al. reported 70% malignancy, 22% invasive carcinoma and 48% DCIS [9].

In 35 cases, Shin et al. reported 23% invasive carcinoma, 69% DCIS, 6% lesions involving a risk [10].

In his meta-analysis, Rominger reported a rate of malignancy of 78% (68–86%) [14].

**Conclusion**

Microcalcifications are actually indirect signs of pathological processes, some of which may only be correctly identified according to their morphology. This is true for the microcalcifications classified as typically benign in the 4th edition of the BI-RADS system, except for round and punctuate microcalcifications. This is also true of fine polymorphous and fine linear microcalcifications that are more often, but not exclusively, associated with ductal carcinoma in situ with necrosis.

For other types of microcalcifications, other parameters are analyzed in a more global approach:

- the signs associated and, first, the findings of the clinical examination, and the associated mammographic opacities;
- the context and in particular the genetic risk of breast cancer;
- the type of spatial distribution;
- the number;
- the stability over time, which does not eliminate malignancy when the microcalcifications are suspect.

This multiparameter approach is even more complex due to the poor inter-observer as well as intra-observer reproducibility, in classifying the different microcalcifications by morphological type.

Moreover, it is especially difficult to classify microcalcifications by morphological type when several types are found in the same area, which is a frequent case (Fig. 7). The rule is to choose the risk associated with the most suspect microcalcifications. In practice, the determination of the uniform or polymorphous...
nature of fine microcalcifications is subject to a great subjectivity. A multidisciplinary radio-surgical analysis during a formal exchange may be the way to standardise practices when confronted with difficult cases.

**TAKE-HOME MESSAGES**

- Microcalcifications are under 1 mm. Magnification of 1.5 using the smallest focal spot of 0.1 mm are required for their characterisation.
- They are indirect sign of different pathological process: inflammation, infection, benign lesions, malignant lesions.
- Microcalcifications associated with malignant lesions develop at the terminal ductallobular unit.
- Microcalcifications classified as typically benign in the 4th edition of the BI-RADS system do not require histological verification, except for certain round or punctuate microcalcifications.
- Round or punctuate microcalcifications as well as amorphous or indistinct microcalcifications are developed on secretions in the lobular acini.

They may be associated with benign lesions or ductal carcinoma in situ, usually without necrosis.
- Coarse heterogeneous microcalcifications may be associated with fibroadenomas or fibrosis lesions, but may be associated with malignancy.
- Fine polymorphous and fine linear microcalcifications are developed in the terminal ducts of the terminal ductallobular unit and are often associated with ductal carcinoma in situ with necrosis. They progress in the ducts towards the nipple.
- Fine or polymorphous and fine linear microcalcifications are suspect and classified ACR 4 or 5.
- Round or punctuate microcalcifications, amorphous or indistinct microcalcifications and coarse heterogeneous microcalcifications are classified ACR 2, 3, 4 or 5 according to their spatial distribution, number, evolution over time, associated clinical signs, antecedents and the genetic predisposition to breast cancer.
Case report

A 44-year-old woman with antecedents of ductal carcinoma in situ of the upper inner quadrant of the right breast, treated by conservative surgery followed by radiotherapy (Fig. 8).

Detection of two small focal clusters of microcalcifications on the right breast (arrow and arrow head) on a mammogram performed 1 year after the end of the treatment (Fig. 8a–c).

Questions

1. Indicate the morphological type and spatial distribution of the upper and medial microcalcifications (arrow head) according to the BI-RADS system by the American College of Radiology.
2. Indicate the morphological type and spatial distribution of the upper and central microcalcifications (arrow) according to the BI-RADS system by the American College of Radiology.
3. What ACR classification do you propose for both anomalies? What do you recommend?

Answers

1. The microcalcifications are fine polymorphous, in small focal clusters of less than 1 cm.
2. The microcalcifications are fine linear with a linear distribution.
3. The clustered microcalcifications of fine polymorphous upper and medial quadrant may be classified as ACR 4C. They are often associated with high-grade ductal carcinomas in situ with necrosis. In a meta-analysis on 10,665 cases of breast microcalcifications, Rominger reported a rate of malignancy of 50% (43–58%) for fine polymorphous microcalcifications. In this case, they may be classified as ACR 5 considering their appearance in a breast previously treated for ductal carcinoma in situ, thereby increasing the risk of cancer. The aligned fine linear microcalcifications may be classified as ACR 5. They are most often associated with high-grade ductal carcinomas with necrosis. Rominger reported a rate of malignancy of 78% (68–86%) for this type of microcalcifications. Their appearance in a breast previously treated for ductal carcinoma in situ increases the risk of cancer [22].

Figure 8. Fine polymorphous microcalcifications of the upper inner quadrant: a: front view without magnification; b: front view with magnification; c: profile view with magnification; d: macrobiopsies targeting the focal point of fine polymorphous microcalcifications in the upper inner quadrant. Representative samples (arrows); e: histology (low magnification): high grade ductal carcinoma in situ with necrosis and microcalcifications. Calcifications in the lumen of a duct without necrosis (white arrow). Non-calciﬁed necrosis in the lumen of a duct (black arrow); f: histology (high magnification): High grade ductal carcinoma in situ with necrosis and microcalcifications. Anarchic cell proliferation with atypia of the epithelium of a duct (asterisk). Necrosis during calcification in the lumen of a duct (white arrow) near a zone of calcified necrosis (black arrow). Endoluminal calcifications without associated necrosis (tip of arrow).
Surgery is indicated. First, macrobiopsies are indicated (Fig. 8d–f) in order to confirm the diagnosis of a local recurrence, and increase a proposal for non-conservative surgery, a first line option for a recurrence in an irradiated breast.

Disclosure of interest


Co-financing of the lodging and travel expenses for the 2011 SOFOMS Congress in Montpellier by Bard France.

A. Leroux: co-financing of the lodging and travel expenses for the Carrefour Pathologie in Paris in 2011 and 2012 by Roche.

C. Barlier and P. Génin declare that they have no conflicts of interest concerning this article.

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