

## REVIEW ARTICLE

# Pearls and pitfalls in breast MRI

I MILLET, MD, E PAGES, MD, D HOA, MD, S MERIGEAUD, MD, F CURROS DOYON, MD, X PRAT, MD  
and P TAOUREL, MD, PhD

Department of Imaging, Lapeyronie Hospital, Montpellier, France

**ABSTRACT.** At our academic institution, we have noticed repeated examples of both false-positive and false-negative MR diagnoses in breast cancer. The most common diagnostic errors in interpreting MRI of the breast are discussed in this review and experience-based advice is provided to avoid similar mistakes. The most common reasons for false-positive diagnoses are misinterpretation of artefacts, confusion between normal enhancing structures and tumours and, above all, insufficient use of the American College of Radiology breast imaging reporting and data system lexicon, whereas false-negative diagnoses are made as a result of missed tiny enhancement, a background-enhancing breast, or enhancement interpreted as benign rather than malignant.

Received 1 September  
2010  
Revised 6 February 2011  
Accepted 17 February 2011

DOI: 10.1259/bjr/47213729

© 2012 The British Institute of  
Radiology

MRI of the breast has evolved into an important adjunctive tool with multiple indications in breast imaging, as recommended by American and European guidelines [1, 2]. Breast MRI is currently the most sensitive detection technique for breast cancer diagnosis. Although breast MRI is classically alleged to have a low specificity and a positive predictive value, comparative studies have shown that breast MRI has about the same specificity as mammography and a significantly higher specificity than breast ultrasound [3–6]. As reported by Kuhl [7], despite its reliability, some difficulties and obstacles have hampered the adoption of MR for clinical practice in many centres, with a lack of expertise in reading breast MR examinations constituting one of the main stumbling blocks in the development of breast MRI in clinical practice. At our busy academic institution, we perform about 1000 breast MRI procedures per year and receive many MR examinations performed by other centres for a second opinion. Our indications are classical according to the published referential and cases may be divided between the following groups: staging before treatment planning, screening of high-risk females, evaluation of response to neoadjuvant chemotherapy, patients with breast augmentation or reconstruction, occult primary breast cancer, breast cancer recurrence and characterisation of equivocal findings [8]. Our MRI (1.5T unit) protocol may be defined as follows: bilateral morphological study using bilateral unenhanced high-spatial resolution  $T_2$  weighted fast spin-echo sequence without fat saturation in the axial plane; bilateral three-dimensional gradient-echo  $T_1$  weighted dynamic sequences in the axial plane; with or without fat saturation according to the radiologist; thickness between 2 and 3 mm according to the breast size; spatial in-plane resolution  $\leq 1 \text{ mm}^2$ ; temporal resolution

60 s. We use intravenous injection of gadolinium chelates at the standard dose of  $0.1 \text{ mmol kg}^{-1}$  with an injection rate of  $2 \text{ ml s}^{-1}$  followed by saline flushing using an automatic injector. For dynamic studies performed both with and without fat saturation, image post-processing includes temporal subtraction; morphological in addition to dynamic analyses with representative curves are performed on native images in incidences of patient motion. Many diagnostic errors have been made, even by breast imaging experts. These mistakes have been responsible for numerous false-positive diagnoses and some missed breast cancers. In reviewing the most common misdiagnoses, we will provide experience-based advice to decrease the rate of false-positive and false-negative diagnosis and further improve MRI breast cancer detection.

### Decreasing the false-positive diagnosis rate

Numerous false-positive diagnoses occur when every enhancement of the breast is considered as a breast cancer finding. In a patient with a breast enhancement, physicians should: confirm that it is a true enhancement and not an artefact; recognise normal enhancing breast structures and analyse the enhancement according to the American College of Radiology breast imaging reporting and data system (BI-RADS) lexicon [9, 10]; and be able to characterise benign lesions.

### Differentiating true enhancement from pseudo-enhancement due to artefacts

Pseudo-enhancement on subtracted images may be due to breast movement between pre- and post-contrast images. Such artefacts appear at the fat–parenchyma

Address correspondence to: Dr Patrice Taourel, Department of Imaging, Lapeyronie Hospital, Montpellier 34000, France. E-mail: p-taourel@chu-montpellier.fr

interface. They are easily recognised in most cases, especially when the displacement occurs in the plane of the slice, since two adjacent artefacts are displayed on the same slice: a bright one (pseudo-enhancement) resulting from fat minus parenchyma subtraction and a dark one due to parenchyma minus fat subtraction. Differentiation becomes difficult when the displacement is not in the same plane as that of MRI sequence acquisition; *i.e.* superior–inferior displacement if the acquisition is axial (Figure 1), or right–left displacement if the acquisition is sagittal. Native pre- and post-contrast images should be compared in order to distinguish motion artefact from true enhancement. As most breast displacements are due to pectoralis muscle contraction, the modification in the shape of the pectoralis muscle can be identified by comparing native pre- and post-contrast acquisitions.

### Recognising normal enhancing structures

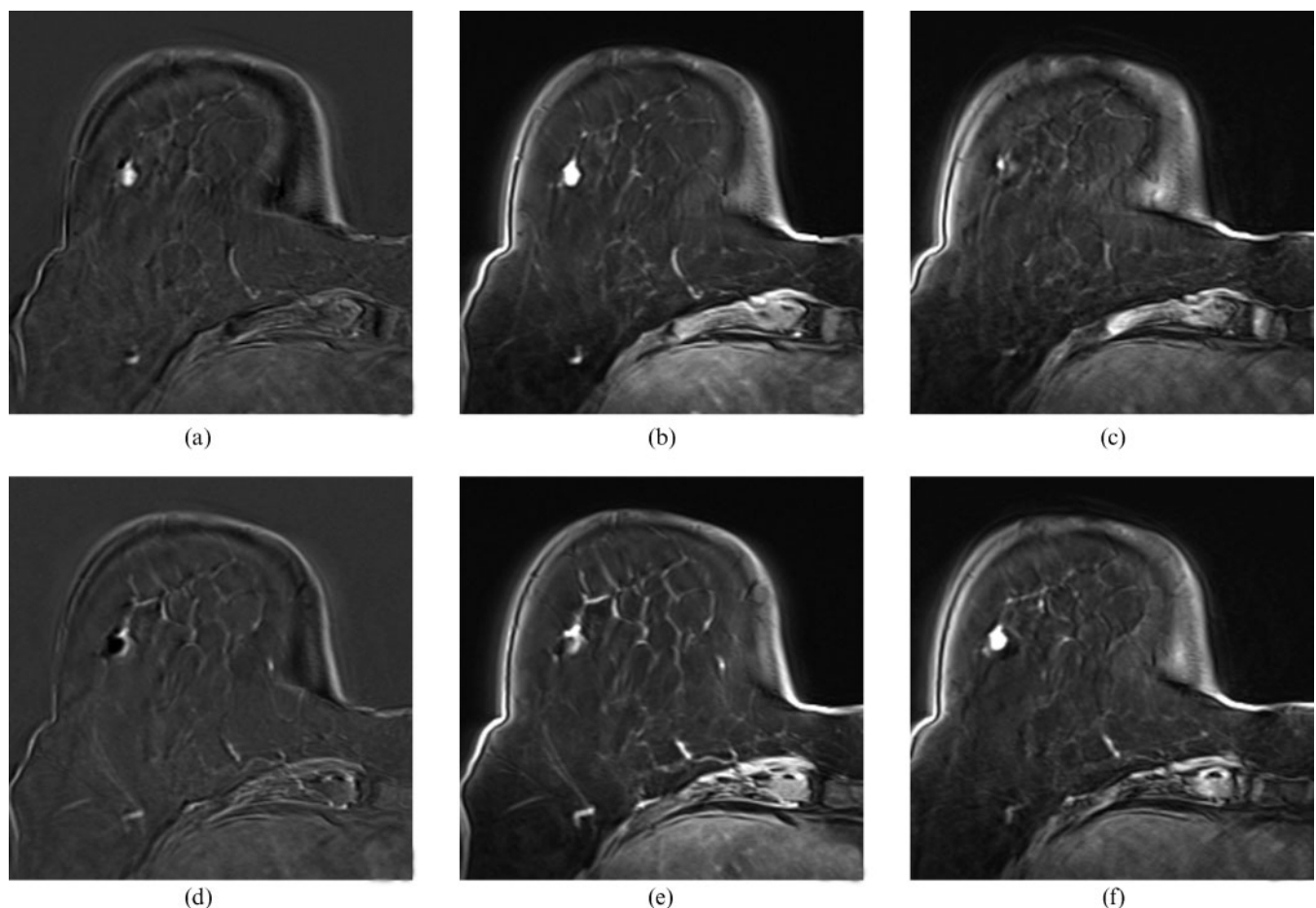
Some normal breast structures, such as vessels, nipples and intramammary lymph nodes, may normally enhance

and should not be diagnosed as tumours. Otherwise normal breast parenchyma may also enhance.

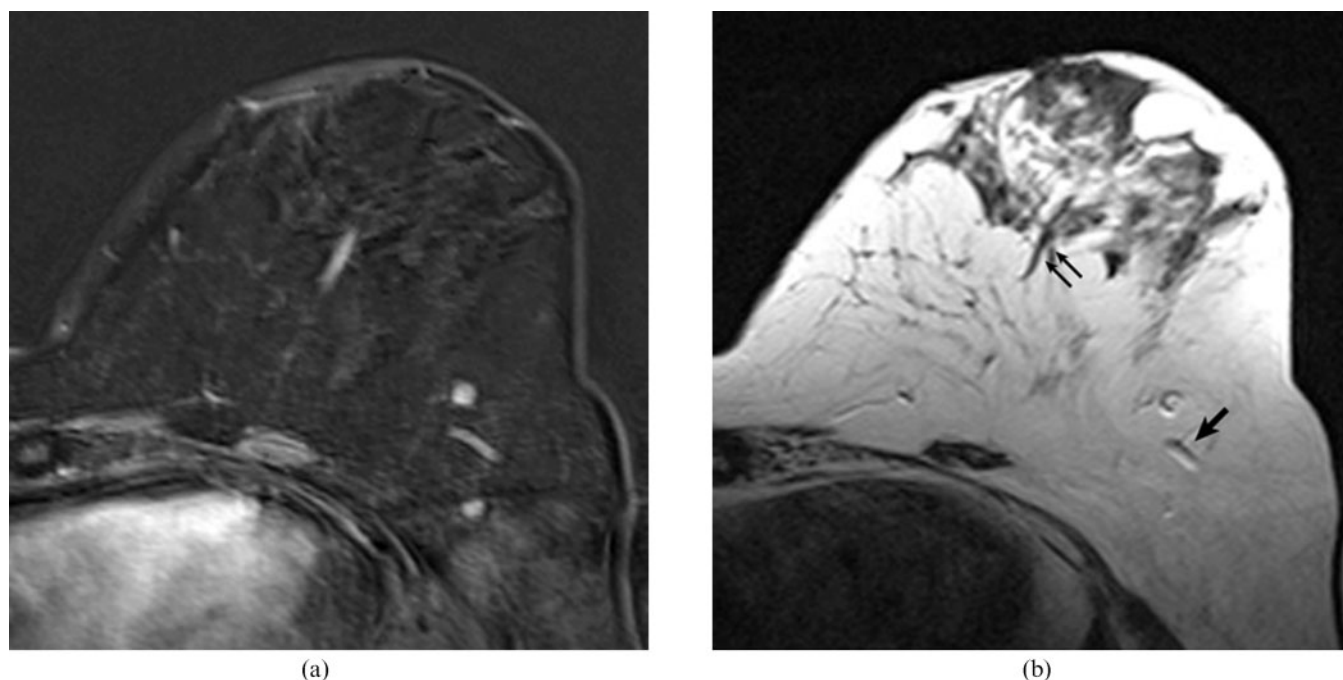
Vessels are easily recognised by their course, which should be assessed in cine-view mode, by their topography (they are often localised at the parenchyma and fat junctions or within fat layers) and by their high signal intensity on  $T_2$  weighted sequences, although this may be lost in high-velocity vessels (Figure 2).

Nipples enhance normally to varying intensities in breast MRI [11, 12]. This enhancement is due to the rich blood supply in the nipple–areolar complex. A normal nipple may be misinterpreted as a mass when it is inverted or flattened against the anterior surface of the coil due to the large size of the breast [11]. To determine that an enhancing lesion is actually a nipple, viewing the anatomic image without contrast injection, comparing with the other side and performing three-dimensional reformatting can be helpful.

Intramammary lymph nodes are present in up to 47% of breasts [13]. Although they are usually located in the upper outer quadrant, they may appear anywhere in the breast. They are identified by MRI, as well as by other imaging modalities, on the basis of morphological



**Figure 1.** Pseudo-enhancement due to a subtraction artefact. (a) At level "a", a pseudo-enhancement is seen on the subtraction image due to subtraction between a mass in hypersignal on the (b) axial fat-saturated  $T_1$  weighted image after contrast and the fat in hyposignal on the (c) axial fat-saturated  $T_1$  weighted image before contrast. (d) At level "b", 6 mm lower, the feature is inverted with a hyposignal on the subtraction image due to subtraction between fat in hyposignal on the (e) axial fat-saturated  $T_1$  weighted image after contrast and the mass in hypersignal on the (f) axial fat-saturated  $T_1$  weighted image before contrast. Pseudo-enhancement of the mass is due to its movement in a coronal plane between sequences before and after intravenous contrast.



**Figure 2.** Normal enhancing breast structures. (a) On the subtracted axial image of the left breast, four enhancing structures are seen: two are linear and two are nodular. (b) On the  $T_2$  weighted image, the two nodules have a location within fat and a hypersignal highly suggestive of lymph nodes, and the two linear structures are suggestive of vessels with one in hypersignal (arrow) and the other in hyposignal (double arrows) because of a difference in velocities.

criteria. Normal lymph nodes have a well-defined margin, contain a fatty hilum, are adjacent to a vessel and have a round, oval or (more typically) reniform shape. They also show high signal intensity on  $T_2$  weighted images (Figure 2). Conversely, enhancement characteristics are not helpful because normal lymph nodes may avidly enhance [11].

Normal fibroglandular tissue, especially in pre-menopausal patients, generally exhibits a low level of enhancement soon after contrast administration with gradual, progressive and faint enhancement over time (background enhancement [14]). Enhancement is bilateral and symmetric. Sometimes, multiple bilateral foci predominantly located at the outer part of the breast are enhanced. These transiently enhancing foci are usually observed during the second half of the menstrual cycle and around menstruation; therefore, breast imaging should be performed during the second week of the menstrual cycle in order to minimise the risk of false-positive diagnosis [14]. Such parenchymal enhancement can also be found in menopausal females under hormone replacement therapy. Progesterone can cause abnormal enhancement in 50% of cases [15]. Where possible, hormone replacement therapy should be discontinued 4–6 weeks before performing breast MRI. Anti-oestrogen medication may suppress these enhancements, as shown in some trials including those involving non-menopausal females with risk factors or premenstrual mastalgia [16, 17]. At the time of writing, because of the adverse effects involved, we do not recommend administration of anti-oestrogen treatment only to reduce physiological breast enhancement. However, anti-oestrogen treatment for breast cancer may significantly impede physiological breast enhancement and new breast enhancement classified as evolutive may appear when anti-oestrogen treatment is stopped [16].

#### *Analysing enhancement according to the BI-RADS classification in order to characterise benign lesions*

When interpreting an enhancement, the first step is to determine the type of enhancement according to the following categories in the BI-RADS lexicon [9, 10]. A lesion is classified as a mass, an area of non-mass-like enhancement or a focus. The distinction between these categories is critical because it paves the way for further diagnostic pathways [18] that each requires a different set of diagnostic criteria for characterising benign lesions.

#### *Mass*

A mass is a three-dimensional, space-occupying lesion measuring  $\geq 5$  mm. It is usually visible on pre-contrast  $T_1$  or  $T_2$  weighted images. It constitutes the most common MRI lesion. In a study of 995 lesions designed to determine the prevalence and predictive values of MR features, masses accounted for 62.7% of the cases [19]. Typical causes of mass are breast cancers, fibroadenomas, papillomas, fat necrosis, atypical forms of benign proliferative breast disease, sclerosing adenosis, inflammatory lesions and intramammary lymph nodes. In patients with an enhanced mass, seeking benign lesion criteria will decrease the false-positive diagnosis rate. Benign lesion criteria are as follows:

(1) Smooth margins, characterised by well-defined and sharply demarcated borders. This is the feature with the highest benign lesion predictive value [20, 21]: 97–100% of masses with smooth margins are reported as benign [20, 21]. Margins also represent the best agreement-rated feature [22]. It is important to note that margin analysis depends on the spatial resolution, so an irregular border may appear to be relatively smooth when insufficient resolution is used. Furthermore, a mass with smooth



margins may appear to be poorly delineated on subtracted images owing to misregistration as a result of slight motion between pre- and post-contrast sequences (radiographic artefact); conversely, the irregular border of a mass may not be clearly visible on the subtraction (Figure 3). Margin analysis should therefore be performed on anatomical sequences on the first post-contrast native image in order to avoid misregistration in addition to tumoral washout and progressive enhancement of the surrounding breast tissue, which could impair lesion analysis.

(2) Round or oval mass shape. This has also been found to be predictive of benignity, but did not contribute to prediction when tested with a multivariate model [23] because round or oval shapes are encountered in masses with smooth margins.

(3) Homogeneous enhancement within the mass. This is highly suggestive of benignity in tumours  $\geq 1$  cm; however, in the smallest tumours, the reliability of this finding is lower [23] because the spatial resolution may limit evaluation and because small breast cancers usually have a homogeneous content.

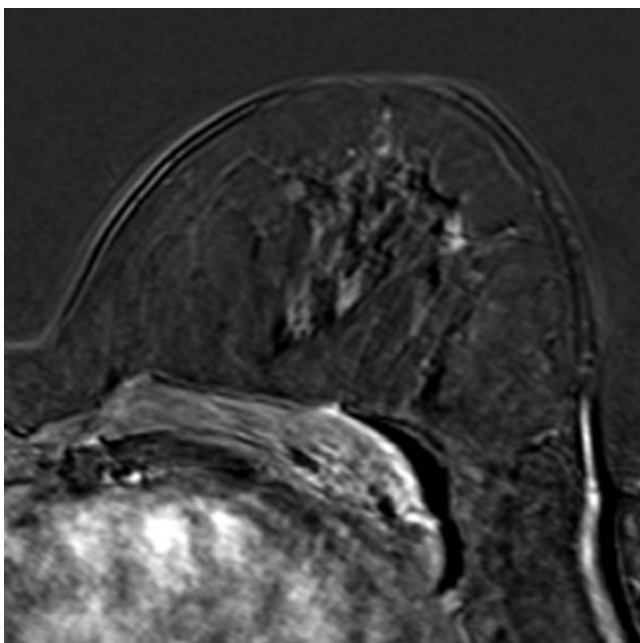
(4) Fat content within the mass. This should be investigated in unenhanced  $T_1$  or  $T_2$  weighted sequences without fat suppression, which gives a hyperintense fat signal. Fat content occupying a part of a mass is specific to benign lesions, namely hamartoma, fibroadenoma, intramammary lymph nodes or fat necrosis. In the case of fat necrosis, even if the lesion appears irregular in both shape and margin, with a rim enhancement, the key to diagnosis is a fat-specific (Figure 4) internal signal on unenhanced sequences without fat suppression [24].

(5) Strong hypersignal on non-fat-suppressed  $T_2$  weighted sequences. This is classically considered to be a clear sign of fibroadenoma [25]; however, this finding has recently been questioned, with  $T_2$  hypersignals

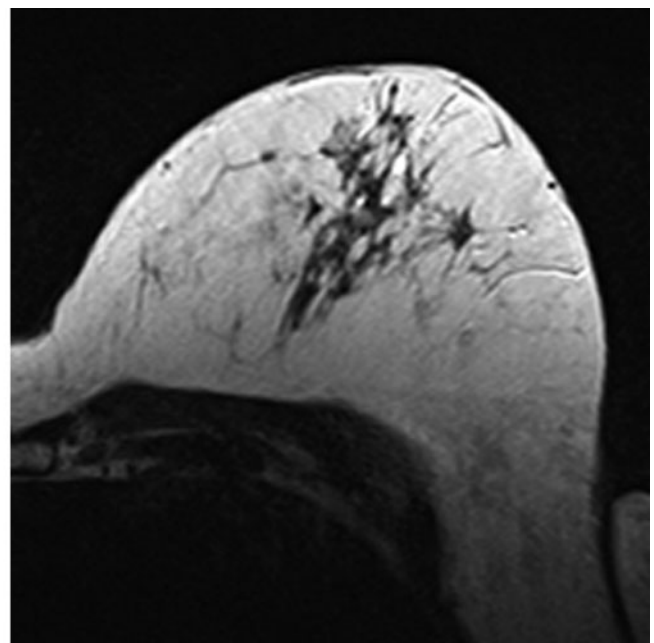
described in several breast cancers including (predominantly) mucinous carcinomas, invasive ductal carcinomas, metaplastic carcinomas and intracystic papillary carcinomas [26, 27]. In our experience (Figure 5), as in the cases reported in these studies, the mass on  $T_2$  weighted sequences generally does not have a homogeneous hyperintense sequence, whereas, in fibroadenomas, the hyperintense signal is homogeneous, except where there are thin septa [28]. Consequently, we consider masses with homogeneously high signals on  $T_2$  weighted sequences and homogeneous enhancement to be highly suggestive of benign lesions.

(6) Rim enhancement. Although this is regarded as suggestive of malignancy [29], a regular enhanced rim, which may be thick, may be seen around cysts (Figure 6), seromas and circumscribed fat necrosis. Differentiating these entities from a malignancy is based on mass content assessment, with a strong and hyperintense fluid-specific signal shown in cysts (Figure 6) and seromas and a fat-specific signal shown in circumscribed fat necrosis.

(7) Enhancement kinetics. These are particularly helpful in confirming benignity if the lesion has a benign morphological appearance. However, it should be kept in mind that rapid and strong enhancement may be encountered in fibroadenomas and in intramammary lymph nodes [30]. In these cases, the discrepancy between a morphological benign appearance and a kinetic malignant appearance may be resolved via detailed evaluation of mammography and ultrasound findings. In the remaining unresolved cases, the centrifugal contrast uptake pattern may help in diagnosing a fibroadenoma, whereas a centripetal spread of contrast is more common in carcinomas [19, 31]. A thinner slice thickness may also indicate fat-containing centres, which are typical in lymph nodes [30, 32].

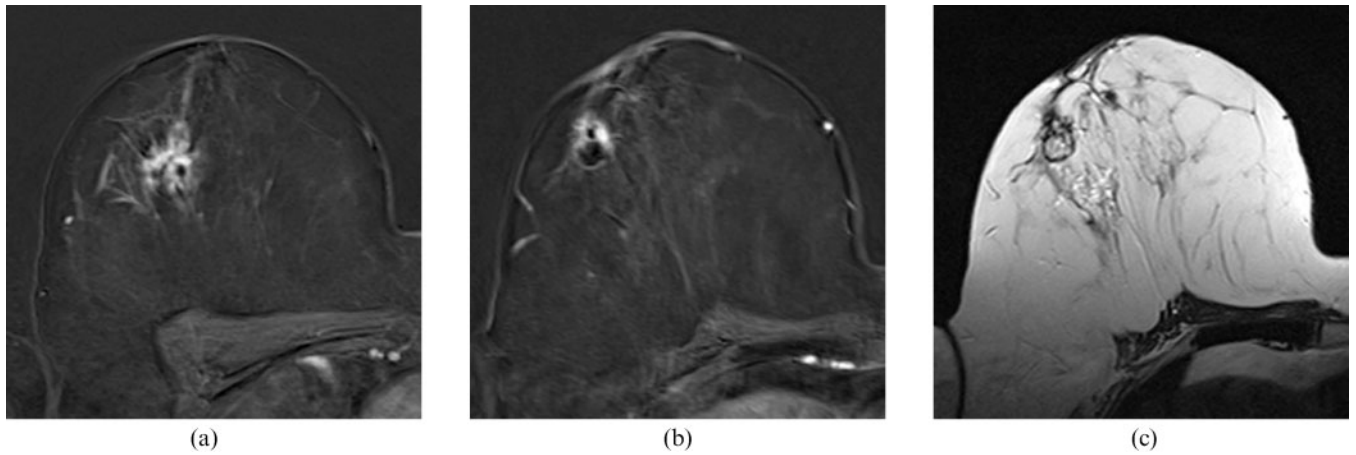


(a)



(b)

**Figure 3.** Invasive breast cancer with morphological findings better seen on native images. (a) On the subtracted axial slice, the outline of the enhancement is hardly analysable. (b) On the  $T_2$  weighted image, the stellar outline of the mass is obvious.



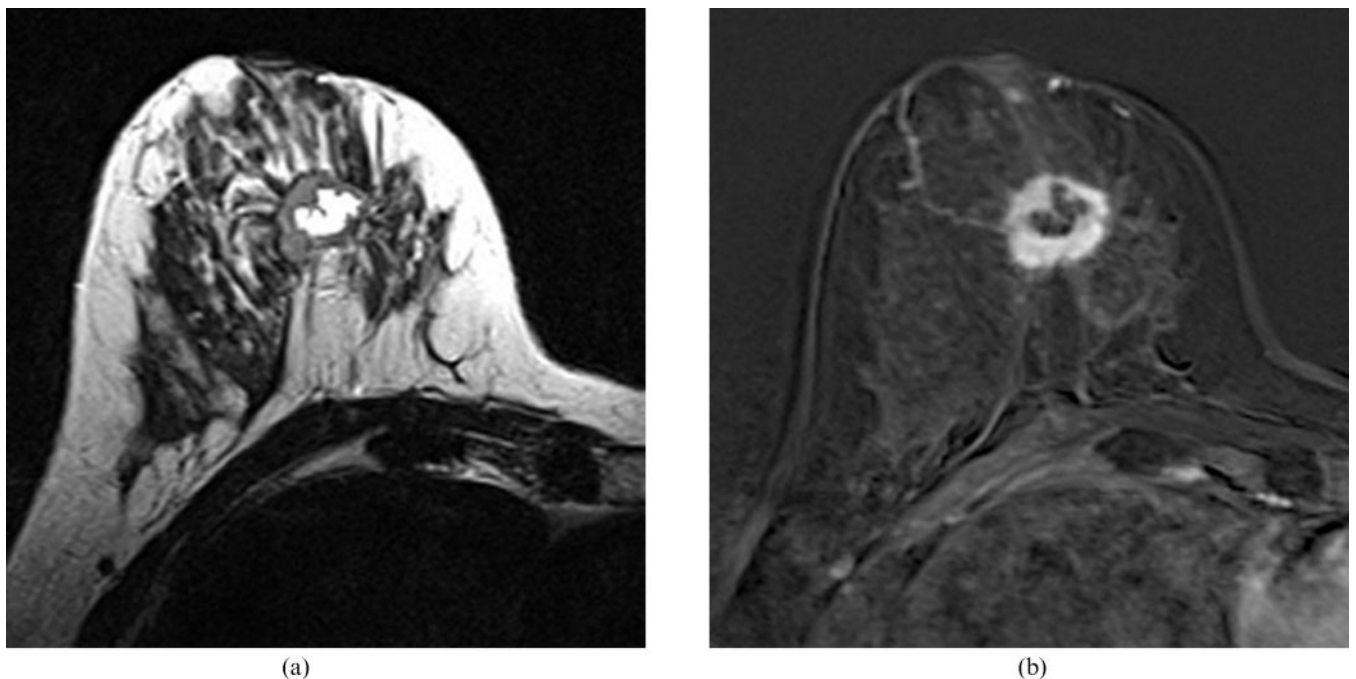
**Figure 4.** Rim of enhancement around a fat necrosis. (a) Axial subtracted image from the dynamic  $T_1$  weighted series: non-mass enhancement corresponding to an invasive breast cancer. 1 year after conservative treatment, (b) subtracted and (c)  $T_2$  weighted axial images. A rim enhancement is seen around the fat necrosis. Note also that the retraction of skin is clearly seen on the  $T_2$  weighted sequence.

Correlations with mammography and ultrasound findings are useful in confirming lesion benignity; masses  $\geq 1$  cm are generally found on conventional examinations and decisions on the need for biopsy should be made according to the findings of examinations showing the most suspicious features. Moreover, patients' ages and risk factors are important when interpreting breast MRIs. For instance, rapid and strong fibroadenoma enhancement is a common finding in pre-menopausal patients and must not lead to a false-positive cancer diagnosis. Conversely, smooth margins and benign morphology of a mass should be considered with caution in patients with Breast Cancer 1 (*BRCA1*) mutations, given the high frequency of breast cancer

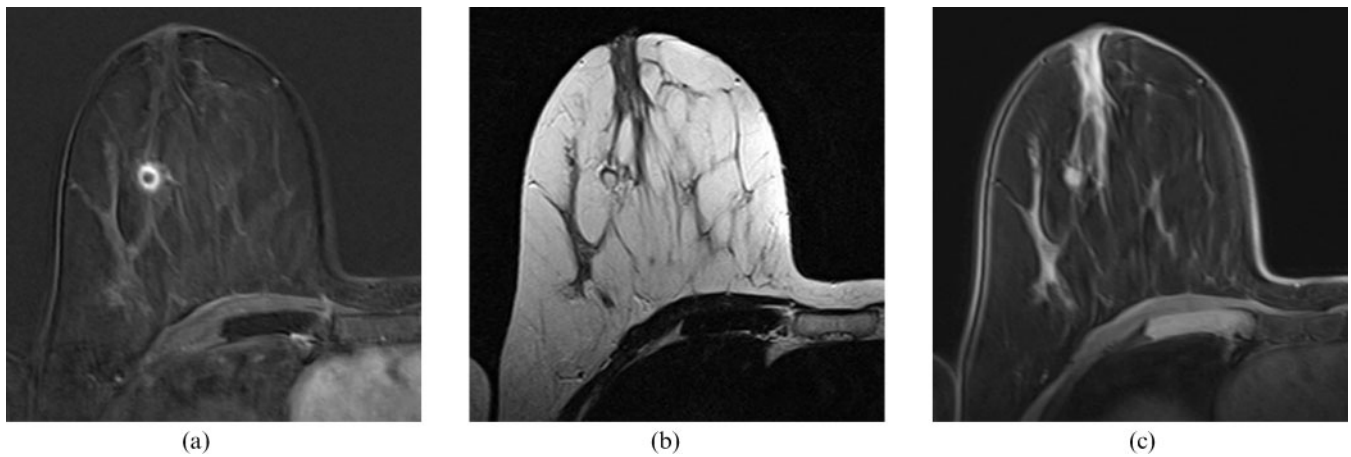
with benign appearance in *BRCA1*-mutated patients [33, 34].

#### Non-mass-like enhancement

Non-mass-like enhancement refers to enhancement of an area that is neither a mass nor a focus. The enhancement pattern is distinct from that of normal surrounding tissue. There is no space-occupying effect and the lesion is not seen on unenhanced sequences. Typical causes of non-mass-like enhancement include mastopathic changes, fibrocystic changes due to hormonal stimulation, inflammatory changes for benign lesions or ductal carcinoma *in situ* (DCIS), invasive lobular carcinoma and some cases of oestrogen receptor-negative



**Figure 5.** Hypersignal on a  $T_2$  weighted sequence in invasive ductal carcinoma. (a) Axial  $T_2$  weighted image showing a circumscribed tumour with a central region of high signal intensity. (b) Axial subtraction image showing thick and irregular enhancement surrounding a hypointense area corresponding to necrosis within the tumour.



**Figure 6.** Thick enhanced rim around a cyst. (a) Axial subtraction image showing a thick and regular enhanced rim around a hyposignal area. (b) On the axial  $T_2$  weighted image and (c) on the axial fat-saturated  $T_1$  weighted image, the non-enhanced area has a high signal intensity suggesting a cyst, which was confirmed by ultrasound.

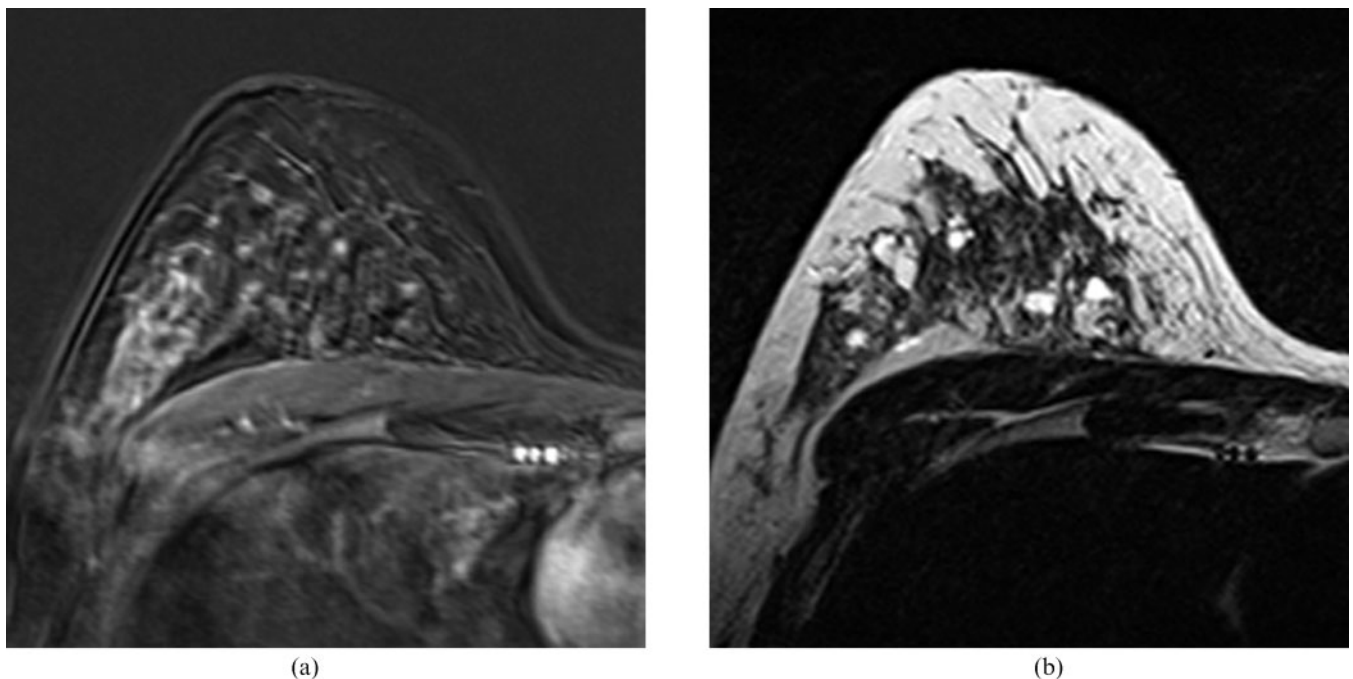
invasive ductal carcinoma. Non-mass-like enhancement is the major cause of false-positive breast findings [35]. In patients with a non-mass-like enhancement, seeking benign lesion criteria may decrease the false-positive diagnosis rate. These criteria are as follows:

(1) Bilateral symmetric non-mass-like enhancement, which is highly suggestive of benign changes [18].

(2) Presence of several cysts (microcysts or macrocysts) visible on  $T_2$  weighted images and distributed over the enhanced area (Figure 7). This feature is highly indicative of fibrocystic mastopathy [36]. We believe that it is not sufficiently used, because many studies in which MRI features of fibrocystic changes were analysed did not report  $T_2$  weighted sequences in their protocol [37, 38].

(3) Diffuse enhancement. This is a good indication of benign changes where there is a lack of clinical, ultrasonic or mammographic signs. Indeed, diffuse breast neoplasia within the entire breast parenchyma generally displays clinical, mammographic or ultrasonic signs. Diffuse enhancement may be localised to a breast in a non-menopausal patient with a history of cancer in the contralateral breast in which physiological enhancement has been impeded by radiotherapy.

(4) Distribution and internal enhancement patterns are also important descriptors in the BI-RADS lexicon. However, their accuracy in distinguishing benign from malignant lesions in localised enhancement is debatable [23]. We consider that a lesion is likely to be benign where



**Figure 7.** Regional non-mass-like enhancement in fibrocystic change of the breast. (a) Axial subtraction shows a non-mass enhancement on the outer part of the right breast. (b) Axial  $T_2$  weighted image showing numerous cysts within the enhanced area. Note also cysts in the inner part of the breast close to the pectoralis muscle.



there is localised enhancement that is both regional in terms of distribution (rather than ductal or segmental) and stippled (composed of multiple enhancing dotted foci) in terms of internal pattern, and when it occurs in a non-menopausal patient without strong risk factors and any supporting abnormality noted on mammography or ultrasound images.

**Focus**

A focus is a tiny enhancement dot measuring <5 mm in size. It is not a space-occupying lesion. A focus is usually due to benign lesions such as papillomas, fibroadenomas, intramammary lymph nodes or focal fibrocystic changes. It seldom represents a focal small invasive cancer or DCIS. In a retrospective study of 666 MRI-guided localisations, Liberman et al [39] concluded that biopsy is rarely necessary for lesions <5 mm because of the associated low (3%) likelihood of cancer; only 1 of the 47 foci classified as BI-RADS 3 in the prospective multi-institutional American College of Radiology Imaging Network study was malignant [40]. A focus is usually too small to be well characterised morphologically, and a smooth outline must not be considered as an additional argument for benignity. Furthermore, enhancement quantitative analysis with curves is not possible for foci, and the enhancement intensity and the presence of washout must be visually analysed. Finally, correlations with ultrasound or mammography findings generally do not provide any support for foci. The strategy must therefore be chosen based on the patient's risk factors and other MRI data. We consider foci as BI-RADS 2 when they are numerous and/or bilateral and an isolated focus as BI-RADS 3 when there is neither washout nor *BRCA* mutation. In a study evaluating probable benign breast MRI lesions, no malignancy was shown in the follow-up of foci with persistent enhancement [41]. We consider isolated foci with either washout or *BRCA* mutation as BI-RADS 4, for which we recommend biopsy under MRI guidance.

In clinical practice, after identifying and classifying an enhancement, the strategy is to look for correlations on a mammogram or a targeted second-look ultrasound. Where correlations are present, the biopsy decision should be based on the examination resulting in the most serious findings. Enhancement patterns in patients with no supporting signal on mammography or ultrasound, for whom diagnoses are either negative without

the need for close MRI follow-up or likely to be benign requiring MRI but no biopsy, are summarised in Table 1.

**Decreased false-negative rate**

Of all the breast imaging techniques that are currently available, MR offers the highest sensitivity for both invasive and intraductal cancers. In the literature data [5, 31, 42, 43], the sensitivity of MRI was higher than that of mammography, regardless of the mammography density or breast cancer type. Although breast cancers, particularly invasive forms, are seldom overlooked, false-negative diagnoses may occur.

Undiagnosed breast cancer on MRI may be due to a possible lack of enhancement or a missed or misinterpreted enhancement.

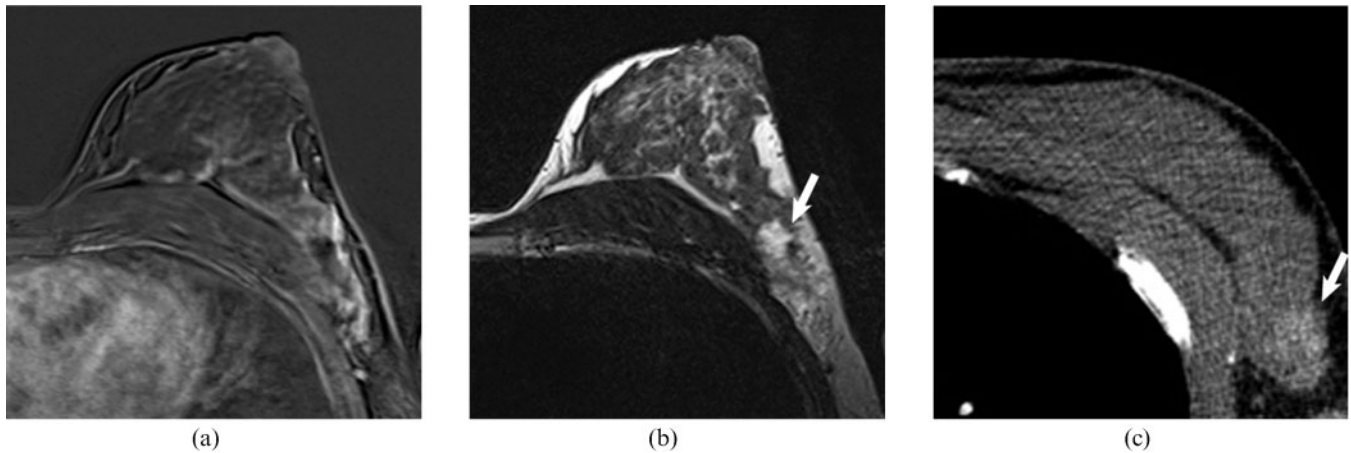
**Breast cancer with no enhancement**

Enhancement of a lesion on MRI depends on its neovascularisation. This neovascularisation with an increased microvessel permeability is the prerequisite for contrast agent pooling in and around malignant lesions. The degree of angiogenesis is variable and related to the degree of vascular endothelial growth factor expression [44], and it is lower in DCIS than in invasive carcinomas. This explains why the lack of enhancement is more common in DCIS than in invasive carcinomas. In a retrospective multicentric study assessing cases of false-negative diagnoses in breast MRI in females with risk factors, two-thirds of the non-enhanced breast cancers were DCIS [45]. Tumour angiogenesis is generally assumed to not begin before the tumour has reached a diameter of about 3 mm, thus explaining the false-negative diagnoses made in cases of very small invasive carcinomas [46]. The possible lack of enhancement in invasive breast cancer >5 mm in diameter is rare and more difficult to explain. In particular, this has been observed in cases of inflammatory carcinoma [30]. It has been hypothesised that these tumours obtain nutrients through diffusion and not from genuine tumour vessels, which would explain their lack of contrast enhancement [47, 48]. In the management of lesions that are suspicious on mammography or ultrasound (BI-RADS 4 or 5) that breast MRI is not useful because lesions cannot be

**Table 1.** Enhancement patterns suggestive of benignity

	Negative MRI (BI-RADS 2)	MRI follow-up (BI-RADS 3)
Mass	Cyst Content: non-enhancing high $T_2$ hypersignal; thin enhancing rim Lymph node, fat necrosis Content: $T_1$ , $T_2$ hypersignal within the fat-specific mass	Smooth border + homogeneous enhancement ( $\pm$ non-enhancing septa) + $T_2$ hypersignal and/or kinetic progressive enhancement + non- <i>BRCA1</i> patient
Non-mass-like	Bilateral and symmetric Numerous $T_2$ hypersignal cysts within the enhanced area	Diffuse unilateral enhancement Regional patchy enhancement with stipple pattern
Focus	Multiple and/or bilateral Single + no washout + no <i>BRCA</i> patient	Single + either washout or <i>BRCA</i> patient

BI-RADS, The American College of Radiology breast imaging reporting and data system; BI-RADS 2, when foci are numerous and/or bilateral; BI-RADS 3, an isolated focus when there is neither washout nor *BRCA* mutation; *BRCA*, breast cancer gene.



**Figure 8.** Clinically palpable breast cancer in the left axillary area with no enhancement on MRI. (a) Axial subtraction image does not show any enhanced mass in the axillary area. (b) Axial  $T_2$  weighted image clearly shows a high signal intensity mass with irregular margins, corresponding to the palpable breast cancer (arrow). (c) On CT examination performed for breast cancer staging, the mass is paradoxically enhanced and clearly seen in the outer part of the breast (arrow).

classified as benign based on the results of a normal MRI. Furthermore, a careful reading of anatomical MRI sequences is necessary in order to detect morphologically suspicious masses, even in cases where the mass is not enhanced (Figure 8).

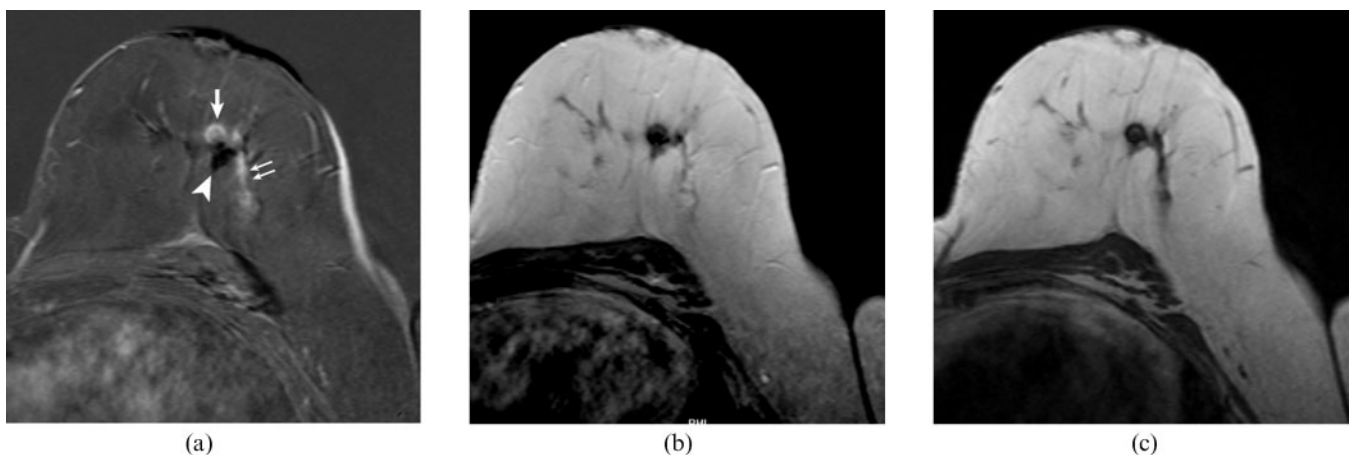
Checking for adequate contrast bolus administration must be carried out before interpreting a complete lack of enhancement on an MR examination. Lack of contrast enhancement in the heart, absence of normal breast vessels or nipple enhancement including internal mammary arteries may reflect a missed contrast material bolus [8].

#### Missed enhancement

The two main reasons for failing to detect lesional enhancement are small tumour size and background enhancement in the surrounding normal fibroglandular

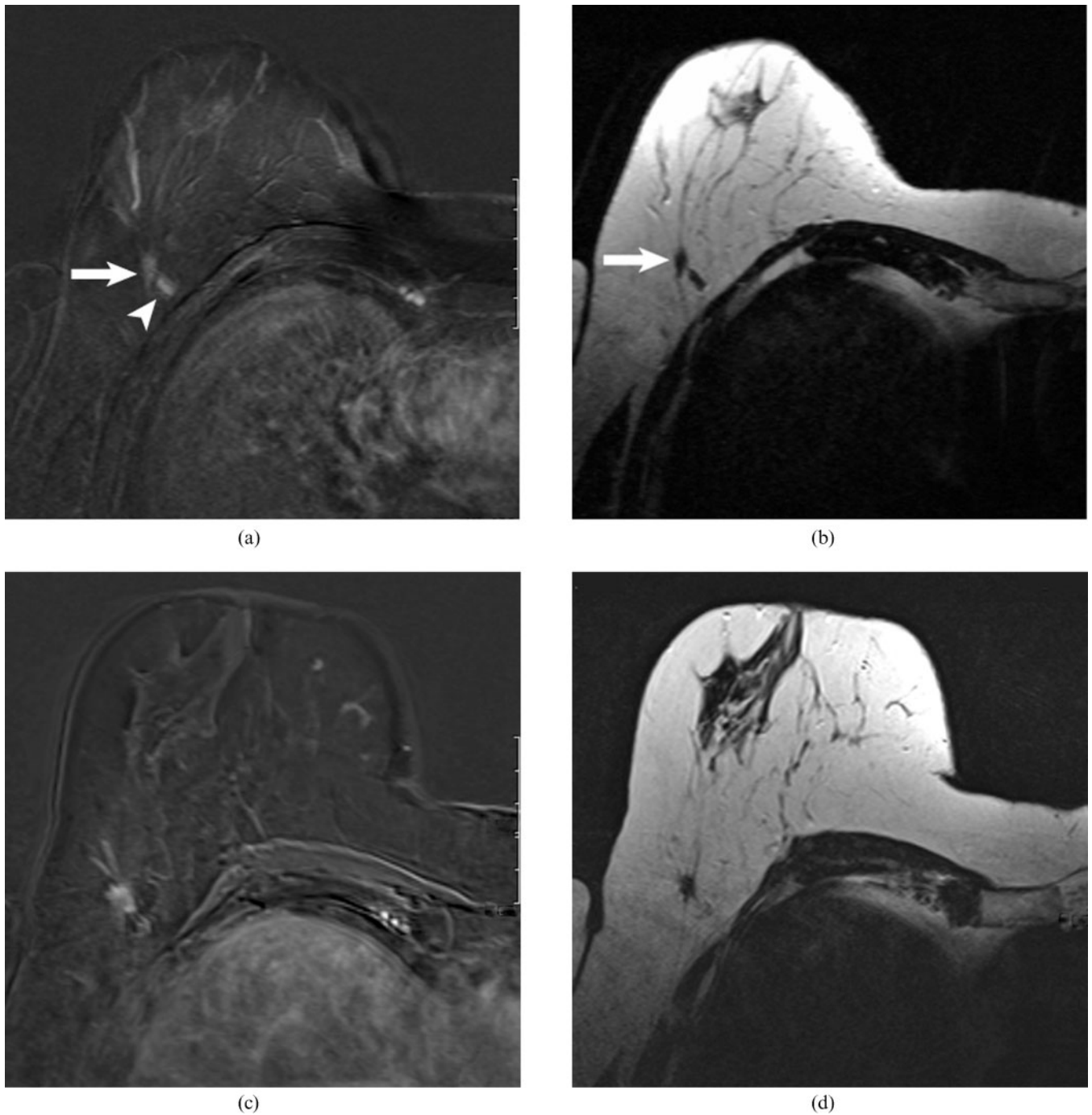
tissue that may mask the enhancing cancer [48]. In a series that assessed the prevalence and characteristics of malignant breast lesions not identified by 1.0 T MRI [46], cancer was missed on 83% of false-negative studies because of strong background enhancement in the fibroglandular tissue around the cancer. Therefore, as recommended by Kuhl [7], the background enhancement must be graded into four categories (as is the case for the breast density on mammograms) and communicated in the MR report, in order to obtain information about the expected MR sensitivity. Furthermore, in cases of strong background enhancement, it is crucial to pay special attention to the first post-contrast acquisition in order to better detect a tumour enhancing earlier than the surrounding parenchyma.

Misregistration due to motion between pulse sequence images leads to subtraction artefacts and pseudo-enhancement, so true enhancement may be overlooked on the subtracted images (Figure 9). In these cases, it is



**Figure 9.** True linear enhancement due to a ductal carcinoma *in situ* (DCIS) close to a pseudo-enhancement due to an artefact. (a) Axial subtraction showing two enhancements: a rim enhancement (arrow) and a linear enhancement (double arrows). Note a dark nodule behind the rim enhancement suggestive of an artefact (arrowhead). The comparison between axial native  $T_1$  weighted images (b) before and (c) after contrast showing that only the linear enhancement is true, the nodule in hyposignal is not truly enhanced and the pseudo-enhancement is due to a subtraction artefact. Biopsy of the linear enhancement under MRI guidance showed a DCIS.





**Figure 10.** Missed breast cancer in a female with risk factors. (a) Axial subtraction showing an enhanced mass (arrow) close to a vessel (arrowhead). (b) The hypointense mass is clearly seen (arrow) on the axial  $T_2$  weighted image. However, this mass was missed. 1 year later, the mass had grown and was well individualised on both (c) axial subtraction and (d) axial  $T_2$  weighted images.

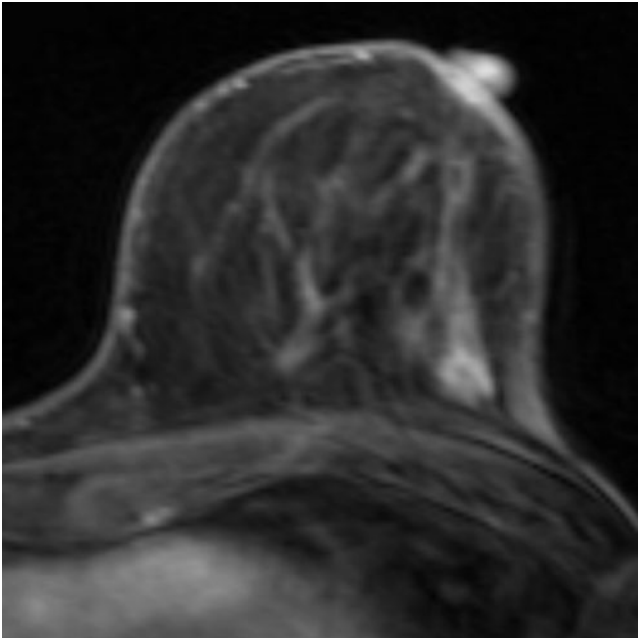
very important to interpret MR examinations on post-contrast native images and to compare pre- and post-contrast native images.

Even with a lack of background enhancement and with correctly subtracted images, tumoral enhancement may be missed because of its location. In our experience, enhancements located close to a normally enhanced structure such as a vessel (Figure 10), or (more rarely) close to the nipple, may be confused with normally enhancing structures, and enhancement located in the axillary area may be poorly analysed because of cardiac artefacts in the phase encoding direction. Finally, when a breast MRI appears normal,

adequate coverage of the breast may be checked [49]. Inadequate coverage resulting from an undersized field of view may result in superior, inferior or lateral portions of the breast not being included in the sequence.

#### *Misinterpreted enhancement*

Misinterpreted enhancement corresponds to a detected malignant enhancement classified as benign. This misinterpretation may be due to morphological or kinetic criteria, or to lesion stability.



**Figure 11.** Breast cancer with non-enhancing septa. Axial subtraction showing an enhanced mass with non-enhancing septa. Note that the mass margins are irregular. The mass was biopsied under ultrasound guidance with a diagnosis of invasive breast cancer.

Although morphological findings are important in lesion characterisation, breast cancers may have a benign appearance. In particular, 30% of familial breast cancers revealed by a mass show benign morphological features with a round or oval shape, smooth margins and homogeneous internal enhancement [34]. It should be considered that all enhancing masses in females with genetic risks are suitable for biopsy when there is a lack of typical cyst or fat necrosis findings.

A fat-containing mass probably corresponds to a benign tumour. However, it should be noted that, in a non-mass-like enhancement, the enhancement growth pattern leaves fat islands between enhancing areas. Invasive lobular carcinomas do not typically present as space-occupying lesions owing to their "Indian file" invasion pattern [50].

Non-enhancing internal septations were initially described to have a high specificity in fibroadenoma diagnosis; however, this feature has recently been described in phyllode tumours and cancers [19] and thus has little value when considered alone (Figure 11).

Persistent enhancement is classically suggestive of benign lesions. However, persistent enhancement in 45% of lesions that proved to be cancerous was reported in a multi-institutional trial [19]. Regardless of the enhancement kinetics, any suspicious morphological feature should prompt biopsy. This is particularly true for high-risk patients, as shown by the Magnetic Resonance Imaging for Breast Screening (MARIBS) trial [45], in which 7 of 12 misinterpreted breast cancers had a benign kinetic pattern.

Lastly, as is the case in mammography or ultrasound, MRI lesion stability is not an absolute finding of benignity; in our experience, some breast cancers have a highly irregular growth pattern with periods of

tumour-size stability. Even in high-risk patients known to have more evolutive tumours, the lesion may remain stable: in the dismissed breast cancers of the MARIBS study [45], 2 of the 12 misinterpreted breast cancers had a stable-size tumour in 2 consecutive screenings.

## Conclusion

Although the use of contrast-enhanced MRI of the breast has increased both the sensitivity and the specificity of breast cancer detection, common causes of false-positive and rarer causes of false-negative diagnoses still occur. Knowing these causes and some rules for interpreting breast MRI could help reduce the number of misinterpretations. However, it would be impossible to achieve 100% sensitivity without decreasing the specificity to a level that would make breast MRI clinically unreliable.

## References

1. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman CD, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin* 2007;57:75–89. Erratum in: *CA Cancer J Clin* 2007;57:185.
2. Mann RM, Kuhl CK, Kinkel K, Boetes C. Breast MRI: guidelines from the European Society of Breast Imaging. *Eur Radiol* 2008;18:1307–18.
3. Liberman L, Morris EA, Dershaw DD, Abramson AF, Tan LK. MR imaging of the ipsilateral breast in women with percutaneously proven breast cancer. *AJR Am J Roentgenol* 2003;180:901–10.
4. Kuhl CK, Schmutzler RK, Leutner CC, Kempe A, Wardelmann E, Hocke A, et al. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. *Radiology* 2000;215:267–79.
5. Warner E, Plewes DB, Shumak RS, Catzavelos GC, Di Prospero LS, Yaffe MJ, et al. Comparison of breast magnetic resonance imaging, mammography, and ultrasound for surveillance of women at high risk for hereditary breast cancer. *J Clin Oncol* 2001;19:3524–31.
6. Stoutjesdijk MJ, Boetes C, Jager GJ, Beex L, Bult P, Hendriks JH, et al. Magnetic resonance imaging and mammography in women with a hereditary risk of breast cancer. *J Natl Cancer Inst* 2001;93:1095–102.
7. Kuhl C. The current status of breast MR imaging. Part I. Choice of technique, image interpretation, diagnostic accuracy, and transfer to clinical practice. *Radiology* 2007;244:356–78.
8. Sardanelli F, Boetes C, Borisch B, Decker T, Federico M, Gilbert FJ, et al. Magnetic resonance imaging of the breast: recommendations from the EUSOMA working group. *Eur J Cancer* 2010;45:1296–316.
9. Schnell MD, Ikeda DM. Lesion Diagnosis Working Group report. *J Magn Reson Imaging* 1999;10:982–90.
10. Morris EA. Breast MR imaging lexicon updated. *Magn Reson Imaging Clin N Am* 2006;14:293–303.
11. Ojeda-Fournier H, Choe KA, Mahoney MC. Recognizing and interpreting artifacts and pitfalls in MR imaging of the breast. *Radiographics* 2007;27:S147–64.
12. Friedman EP, Hall-Craggs MA, Mumtaz H, Schneidau A. Breast MR and the appearance of the normal and abnormal nipple. *Clin Radiol* 1997;52:854–61.
13. Spillane AJ, Donnellan M, Matthews AR. Clinical significance of intramammary lymph nodes. *Breast* 1999;8:143–6.

14. Macura KJ, Ouwerkerk R, Jacobs MA, Bluemke DA. Patterns of enhancement on breast MR images: interpretation and imaging pitfalls. *Radiographics* 2006;26:1719–34.
15. Delille JP, Slanetz PJ, Yeh ED, Kopans DB, Halpern EF, Garrido L. Hormone replacement therapy in postmenopausal women: breast tissue perfusion determined with MR imaging—initial observations. *Radiology* 2005;235:36–41.
16. Eng-Wong J, Orzano-Birgani J, Chow CK, Venzon D, Yao J, Galbo CE, et al. Effect of raloxifene on mammographic density and breast magnetic resonance imaging in premenopausal women at increased risk for breast cancer. *Cancer Epidemiol Biomarkers Prev* 2008;17:1696–701.
17. Oksa S, Parkkola R, Luukkaala T, Maenpaa J. Breast magnetic resonance imaging findings in women treated with toremifene for premenstrual mastalgia. *Acta Radiol* 2009;50:984–9.
18. Agrawal G, Su MY, Nalcioğlu O, Feig SA, Chen JH. Significance of breast lesion descriptors in the ACR BI-RADS MRI lexicon. *Cancer* 2009;115:1363–80.
19. Schnall MD, Blume J, Bluemke DA, DeAngelis GA, DeBruhl N, Harms S, et al. Diagnostic architectural and dynamic features at breast MR imaging: multicenter study. *Radiology* 2006;238:42–53.
20. Szabo BK, Aspelin P, Wiberg MK, Bone B. Dynamic MR imaging of the breast. Analysis of kinetic and morphologic diagnostic criteria. *Acta Radiol* 2003;44:379–86.
21. Nunes LW, Schnall MD, Siegelman ES, Langlotz CP, Orel SG, Sullivan D, et al. Diagnostic performance characteristics of architectural features revealed by high spatial-resolution MR imaging of the breast. *AJR Am J Roentgenol* 1997;169:409–15.
22. Beresford MJ, Padhani AR, Taylor NJ, Ah-See ML, Stirling JJ, Makris A, et al. Inter- and intraobserver variability in the evaluation of dynamic breast cancer MRI. *J Magn Reson Imaging* 2006;24:1316–25.
23. Gutierrez RL, DeMartini WB, Eby PR, Kurland BF, Peacock S, Lehman CD. BI-RADS lesion characteristics predict likelihood of malignancy in breast MRI for masses but not for nonmasslike enhancement. *AJR Am J Roentgenol* 2009;193:994–1000.
24. Daly CP, Jaeger B, Sill DS. Variable appearances of fat necrosis on breast MRI. *AJR Am J Roentgenol* 2008;191:1374–80.
25. Kuhl CK, Klaschik S, Mielcarek P, Gieseke J, Wardelmann E, Schild HH. Do  $T_2$ -weighted pulse sequences help with the differential diagnosis of enhancing lesions in dynamic breast MRI? *J Magn Reson Imaging* 1999;9:187–96.
26. Yuen S, Uematsu T, Kasami M, Tanaka K, Kimura K, Sanuki J, et al. Breast carcinomas with strong high-signal intensity on  $T_2$ -weighted MR images: pathological characteristics and differential diagnosis. *J Magn Reson Imaging* 2007;25:502–10.
27. Santamaria G, Velasco M, Bargallo X, Caparros X, Farrus B, Luis Fernandez P. Radiologic and pathologic findings in breast tumors with high signal intensity on  $T_2$ -weighted MR images. *Radiographics* 2010;30:533–48.
28. Wurdinger S, Herzog AB, Fischer DR, Marx C, Raabe G, Schneider A, et al. Differentiation of phyllodes breast tumors from fibroadenomas on MRI. *AJR Am J Roentgenol* 2005;185:1317–21.
29. Kobayashi M, Kawashima H, Matsui O, Zen Y, Suzuki M, Inokuchi M, et al. Two different types of ring-like enhancement on dynamic MR imaging in breast cancer: correlation with the histopathologic findings. *J Magn Reson Imaging* 2008;28:1435–43.
30. Kurz KD, Roy S, Modder U, Skaane P, Saleh A. Typical atypical findings on dynamic MRI of the breast. *Eur J Radiol* 2010;76:195–210.
31. Kuhl CK, Schild HH, Morakkabati N. Dynamic bilateral contrast-enhanced MR imaging of the breast: trade-off between spatial and temporal resolution. *Radiology* 2005;236:789–800.
32. Gallardo X, Sentis M, Castaner E, Andreu X, Darnell A, Canalias J. Enhancement of intramammary lymph nodes with lymphoid hyperplasia: a potential pitfall in breast MRI. *Eur Radiol* 1998;8:1662–5.
33. Gilbert FJ, Warren RM, Kwan-Lim G, Thompson DJ, Eeles RA, Evans DG, et al. Cancers in BRCA1 and BRCA2 carriers and in women at high risk for breast cancer: MR imaging and mammographic features. *Radiology* 2009;252:358–68.
34. Schrading S, Kuhl CK. Mammographic, US, and MR imaging phenotypes of familial breast cancer. *Radiology* 2008;246:58–70.
35. Baltzer PA, Benndorf M, Dietzel M, Gajda M, Runnebaum IB, Kaiser WA. False-positive findings at contrast-enhanced breast MRI: a BI-RADS descriptor study. *AJR Am J Roentgenol* 2010;194:1658–63.
36. Thomassin-Naggara I, Salem C, Darai E, Bazot M, Uzan S, Marsault C, et al. Non-masslike enhancement on breast MRI: interpretation pearls. *J Radiol* 2009;90:269–75.
37. Chen JH, Liu H, Baek HM, Nalcioğlu O, Su MY. Magnetic resonance imaging features of fibrocystic change of the breast. *Magn Reson Imaging* 2008;26:1207–14.
38. Chen JH, Nalcioğlu O, Su MY. Fibrocystic change of the breast presenting as a focal lesion mimicking breast cancer in MR imaging. *J Magn Reson Imaging* 2008;28:1499–505.
39. Liberman L, Mason G, Morris EA, Dershaw DD. Does size matter? Positive predictive value of MRI-detected breast lesions as a function of lesion size. *AJR Am J Roentgenol* 2006;186:426–30.
40. Weinstein SP, Hanna LG, Gatsonis C, Schnall MD, Rosen MA, Lehman CD. Frequency of malignancy seen in probably benign lesions at contrast-enhanced breast MR imaging: findings from ACRIN 6667. *Radiology* 2010;255:731–7.
41. Eby PR, DeMartini WB, Gutierrez RL, Saini MH, Peacock S, Lehman CD. Characteristics of probably benign breast MRI lesions. *AJR Am J Roentgenol* 2009;193:861–7.
42. Kriege M, Brekelmans CT, Boetes C, Besnard PE, Zonderland HM, Obdeijn IM, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N Engl J Med* 2004;351:427–37.
43. Leach MO, Boggis CR, Dixon AK, Easton DF, Eeles RA, Evans DG, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet* 2005;365:1769–78.
44. Folkman J. What is the evidence that tumors are angiogenesis dependent? *J Natl Cancer Inst* 1990;82:4–6.
45. Obdeijn IM, Loo CE, Rijnsburger AJ, Wasser MN, Bergers E, Kok T, et al. Assessment of false-negative cases of breast MR imaging in women with a familial or genetic predisposition. *Breast Cancer Res Treat* 2010;119:399–407.
46. Teifke A, Hlawatsch A, Beier T, Werner Vomweg T, Schadmand S, Schmidt M, et al. Undetected malignancies of the breast: dynamic contrast-enhanced MR imaging at 1.0 T. *Radiology* 2002;224:881–8.
47. Kuhl CK. Concepts for differential diagnosis in breast MR imaging. *Magn Reson Imaging Clin N Am* 2006;14:305–28.
48. Shimauchi A, Jansen SA, Abe H, Jaskowiak N, Schmidt RA, Newstead GM. Breast cancers not detected at MRI: review of false-negative lesions. *AJR Am J Roentgenol* 2010;194:1674–9.
49. Harvey JA, Hendrick RE, Coll JM, Nicholson BT, Burkholder BT, Cohen MA. Breast MR imaging artifacts: how to recognize and fix them. *Radiographics* 2007;27 Suppl 1:S131–45.
50. Boetes C, Veltman J, van Die L, Bult P, Wobbes T, Barentsz JO. The role of MRI in invasive lobular carcinoma. *Breast Cancer Res Treat* 2004;86:31–7.