



Radial Scar: a management dilemma

Charlotte Marguerite Lucille Trombadori¹ · Anna D'Angelo² · Francesca Ferrara¹ · Angela Santoro³ · Paolo Belli² · Riccardo Manfredi^{1,2}

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Abstract

Radial scar (RS) or complex sclerosing lesions (CSL) if > 10 mm is a benign lesion with an increasing incidence of diagnosis (ranging from 0.6 to 3.7%) and represents a challenge both for radiologists and for pathologists. The digital mammography and digital breast tomosynthesis appearances of RS are well documented, according to the literature. On ultrasound, variable aspects can be detected. Magnetic resonance imaging contribution to differential diagnosis with carcinoma is growing. As for the management, a vacuum-assisted biopsy (VAB) with large core is recommended after a percutaneous diagnosis of RS due to potential sampling error. According to the recent International Consensus Conference, a RS/CSL lesion, which is visible on imaging, should undergo therapeutic excision with VAB. Thereafter, surveillance is justified. The aim of this review is to provide a practical guide for the recognition of RS on imaging, illustrating radiological findings according to the most recent literature, and to delineate the management strategies that follow.

Keywords Radial scar · B3-lesions · Vacuum-assisted biopsy · Radial scar management

Abbreviations

ABUS	Automated Breast Ultrasound
BLES	Breast Lesion Excision System
CNB	Core Needle Biopsy
CSL	Complex Sclerosing Lesions
DBT	Digital Breast Tomosynthesis
DM	Digital Mammography
HHUS	Hand-Held Ultrasound
G	Gauge
MRI	Magnetic Resonance Imaging
NHS	National Health Service

RS	Radial Scar
US	Ultrasound
VAB	Vacuum-Assisted Biopsy
VAE	Vacuum-Assisted Excision

Background

Radial scar (RS) is a benign breast lesion classified with the B-coding system as a lesion with uncertain malignant potential (B3-lesion) [1].

It is histologically characterized by a central area mimicking a scar, containing one to several ducts showing

Charlotte Marguerite Lucille Trombadori and Anna D'Angelo contributed equally to this work.

✉ Charlotte Marguerite Lucille Trombadori
charlotte.trombadori@gmail.com

✉ Anna D'Angelo
anna.dangelo@policlinicogemelli.it

Francesca Ferrara
francesca.ferrara26@gmail.com

Angela Santoro
angela.santoro@policlinicogemelli.it

Paolo Belli
paolo.belli@policlinicogemelli.it

Riccardo Manfredi
riccardo.manfredi@policlinicogemelli.it

¹ Università Cattolica del Sacro Cuore, Dipartimento Universitario di Scienze Radiologiche ed Ematologiche, Largo Francesco Vito 1, 00168 Rome, Italy

² UOC Radiologia Generale ed Interventistica Generale, Area Diagnostica per Immagini, Dipartimento Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

³ UOC di Gineco-patologia e Patologia Mammaria, Dipartimento per la Salute della Donna e del Bambino e della Salute Pubblica, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

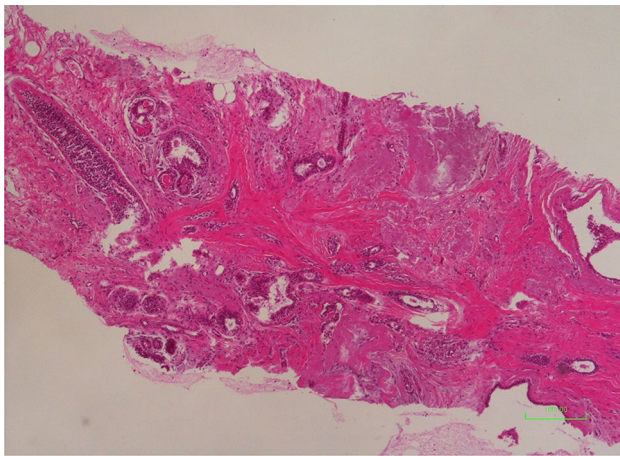


Fig. 1 Surgical specimen shows typical aspect of RS: lesion with stellate architecture, prominent fibroelastosis with basophilic elastic material, obliterated ducts, compressed tubular structures with two cell layers (including myoepithelium, CK14+) and hyalinized stroma. (Hematoxylin–eosin stain [H&E]; magnification×4)

obliterative mastopathy and surrounded by elastic fibers. In addition, other ducts converge into the scar-like area in a stellate fashion [2, 3] (Fig. 1). When larger than 10 mm, a lesion presenting these features is called complex sclerosing lesion (CSL).

Etiology of RS remains obscure, although several theories have been proposed.

Some authors [4] suggested it may begin as a reaction to an unknown injury, that heals with focal areas of fibrosis and elastosis contracting centrally and forming the characteristic stellate appearance.

Battersby and Anderson [5] suggested a role for chronic inflammation and demonstrated that RS is a lesion characterized by the presence of central myofibroblast activity, parenchymal degeneration and sclerosis, characterized by an early stage with a prevalence of myofibroblasts and a late stage with more prominent elastosis and fewer myofibroblasts.

Other authors postulated that RS [6] arises as a manifestation of fibrocystic changes, considering that the frequency of RS is higher among women with fibrocystic disease.

RS is seen more frequently in women 30–60 years old [7] and it is generally clinically occult and often not palpable regardless of size and superficiality within the breast [8].

It is usually diagnosed at image-guided biopsy and has an incidence ranging from 0.6 to 3.7% that is growing in the last years due to the introduction of population-based screening programs and the increasing use of digital breast tomosynthesis (DBT) [9].

Considering the mammographic frequency, Tabar and Dean found a prevalence of 0.9 radial scars every 1000, in screening examinations [10].

In autopsy series, the incidence of RS has ranged from 14 to 28% depending on the frequency of the section sampling method, since it is not rare for a breast to contain multiple RS that are often millimetric.

RS represents a trick for breast radiologists, because of its morphologic similarity with malignancy resulting in a difficult differential diagnosis, and for the pathologists, because of its association with other proliferative lesions and the possibility of founding foci of intraductal or invasive carcinoma within or adjacent to the lesion. Hence, the importance of the diagnosis and management remains controversial.

The aim of this review is to provide a practical guide for the recognition of RS on imaging, illustrating radiological findings according to the most recent literature and delineate the management strategies that follows.

Imaging findings

Imaging is crucial for diagnosis of RS, in some cases, found occasionally during routine radiological screening. In the last years, the role of DBT as a screening and diagnostic tool has been demonstrated to help the radiologist detecting mammographic architectural distortions, resulting in an increasing incidence of both carcinoma and RS [11–13].

The use of magnetic resonance imaging (MRI) in diagnosis or in evaluation of RS is still controversial; it may

Table 1 RS/CSL imaging findings

DM/DBT	US	MRI
“Black Star”: central radiolucency radiating long, thin spicules	Irregularly shaped hypoechoic mass/distorted parenchymal area: ill-defined borders	Stellate architectural distortion: no mass effect mild or no enhancement
“White Star”: stellate opacity	Round or oval mass: circumscribed margins	Irregular and spiculated “tumor-like” mass
Group of microcalcifications	Focal area of shadowing with no discernible mass	Oval or round mass: smooth margins
	Not visible	Mass or architectural distortion without enhancement

be used as a problem-solving tool for inconclusive clinical or mammographic findings, or to rule out malignancy in patients diagnosed with RS after core needle biopsy (CNB) resulting in a valuable help for management assessment [14].

The main imaging findings are resumed in Table 1.

Digital mammography (DM) and digital breast tomosynthesis (DBT)

The most typical appearance on digital mammography (DM) and on DBT of RS is the architectural distortion, the “black star” (Fig. 2 and 3), described by Tabar and Dean [10] including five criteria:

- Central radiolucency;
- Radiating long, thin spicules;
- Varying appearance in different projection;

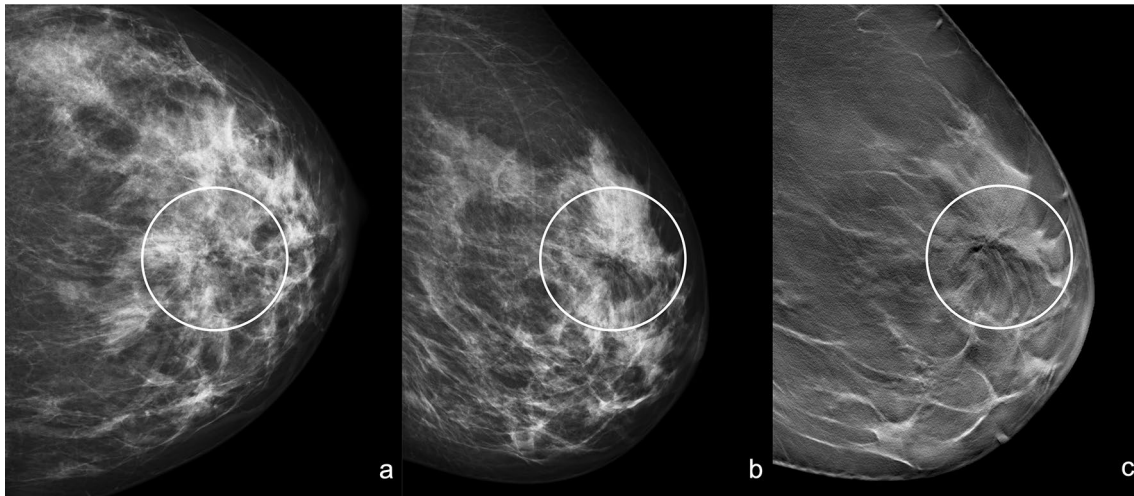


Fig. 2 “Black Star”: Left craniocaudal (a) and mediolateral oblique (b) mammograms show an area of architectural distortion with radiolucent core in the union of upper quadrants (white circle). Left medi-

olateral oblique tomosynthesis (c) confirms the area of architectural distortion and shows better the radiolucent core with the radiating long thin spicules (white circle)

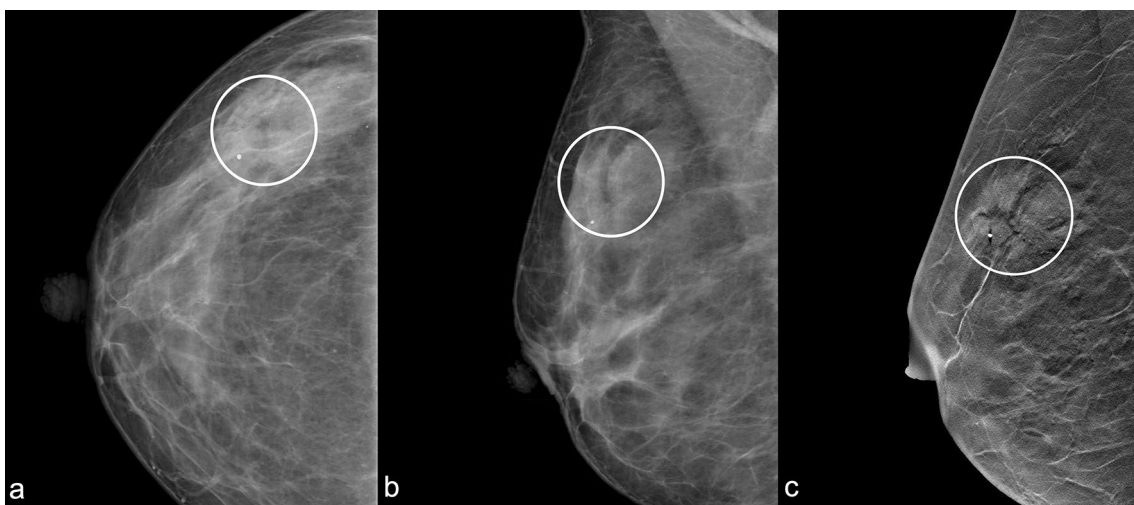
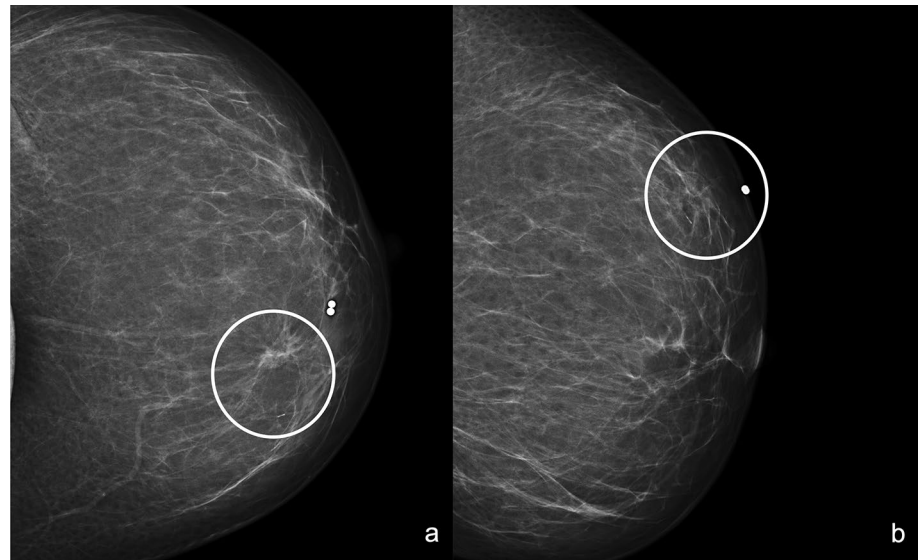


Fig. 3 “Black Star”: Right craniocaudal (a) and mediolateral oblique (b) mammograms show an area of architectural distortion with radiolucent core in the upper-outer quadrant (white circle). Right mediolat-

eral oblique tomosynthesis (c) shows better the architectural distortion and the radiolucent core (white circle)

Fig. 4 “White Star”: Left craniocaudal (a) and mediolateral oblique (b) mammograms reveal a stellate opacity with ill-defined borders and spiked linear extensions (white circle) in the upper- inner quadrant. Radiopaque metallic landmark was positioned before surgery



- Radiolucent linear structures parallel to the spicules;
- Absence of palpable lesion/skin changes.

The presence of radiolucent core does not exclude malignancy; in fact, it is challenging to differentiate the central radiolucent core from superimposed background fat [15].

RS can also appear as a stellate opacity (the “white star”) (Fig. 4) that is a mass having irregular borders and spiked linear extensions, which lead out toward adjacent tissue; the morphology is similar to carcinoma and differential diagnosis is even more difficult.

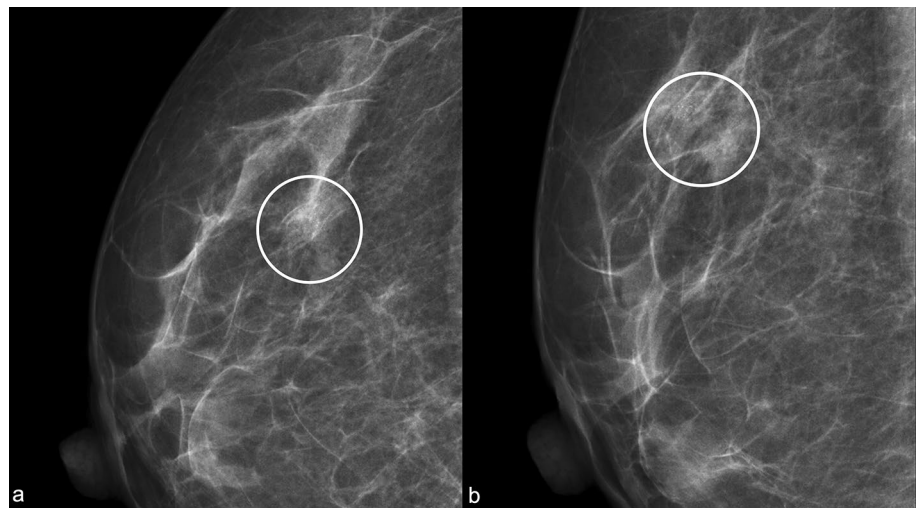
Cohen et al. [7] described how several studies tried to retrospectively identify cases of spiculated masses with features suggesting that the lesion excised was a RS [15–17]. At surgery, 17–59% of lesions were misclassified, particularly because of the misleading presence of radiolucent centers.

This finding emphasizes the struggle of differentiating RS and carcinoma at DM.

Some studies suggested that length of spicules of a spiculated lesion contributes to differential diagnosis of RS versus carcinoma: the longer the spicules are compared to the lesion diameter, the more likely the stellate lesion is benign [18, 19]; more specifically, considering (D) the diameter of the stellate lesion including spicules and (d) the lesion diameter, Hagay [20] stated that a D/d ratio higher than two suggests benignancy.

Rarely, RS appears on DM like a group of microcalcifications (Fig. 5). Calcifications are often related to the benign proliferative fibrocystic changes and sclerosing adenosis that coexist within and around those lesions. Anyway, morphologic characteristics of these calcifications are often non-specific resulting inadequate to differentiate benign from malignant disease [7]. Miller CL et al.

Fig. 5 Right craniocaudal (a) and mediolateral oblique (b) mammograms show an area of microcalcifications with in the upper-outer quadrant (white circle)



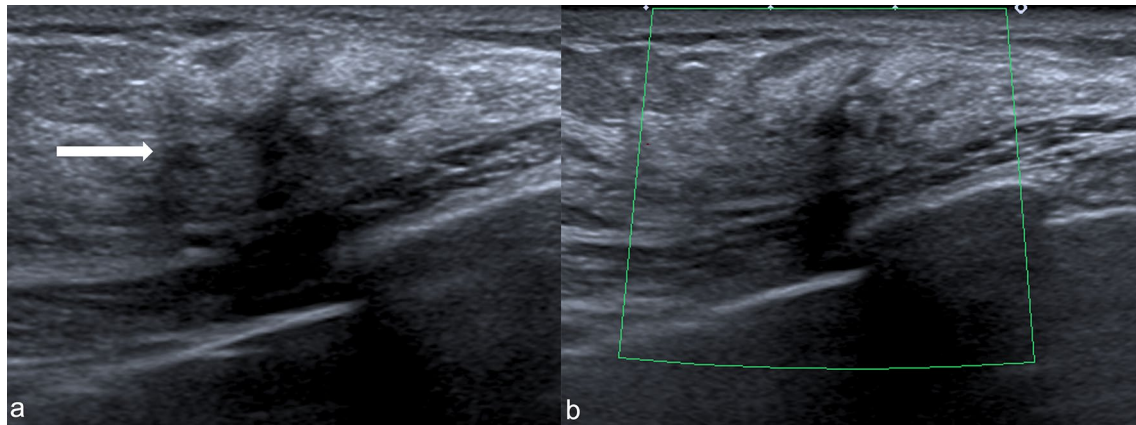


Fig. 6 US demonstrates an irregularly shaped hypoechoic distorted parenchymal area, showing ill-defined borders, with posterior acoustic shadowing (white arrow)

[21] reported that the radiological appearances of a mass or architectural distortion on DM or ultrasound (US) are more likely to be upgraded to carcinoma compared with RS's presenting as calcifications.

Numerous studies have demonstrated that DBT increases detection of RS [22, 23], mostly in recognizing and defining tomographic characteristics of benign architectural distortion like symmetric spiculation with spoke-wheel morphology and central-lucency on mammographic imaging [12, 13]. Nevertheless, there are still no DBT-specific features to allow a certain differentiation of RS from cancer.

Ultrasound (US)

On US, RS can have variable aspects. It is not always sonographically visible, and it is demonstrated that finding an architectural distortion without correlative findings on US was less likely to represent malignancy than architectural distortion with correlative sonographic findings [12, 24]; nevertheless, an architectural distortion on DM with no US findings needs further investigation with stereo-biopsy.

When visible, RS can appear as [7]:

- Irregularly shaped hypoechoic mass or distorted parenchymal area, showing ill-defined borders, with or without posterior acoustic shadowing, virtually identical to a carcinoma of the breast (Fig. 6);
- Round or oval mass with circumscribed margins and without posterior acoustic enhancement or shadowing (Fig. 7);
- Focal area of shadowing with no discernible mass (Fig. 8).

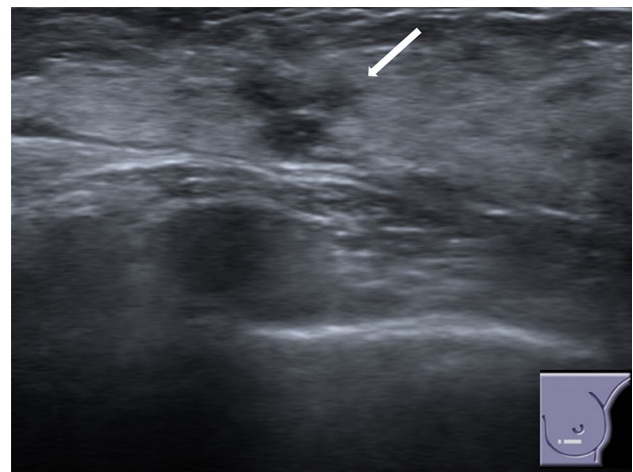


Fig. 7 US shows a mass with circumscribed margins without posterior acoustic shadowing (white arrow)

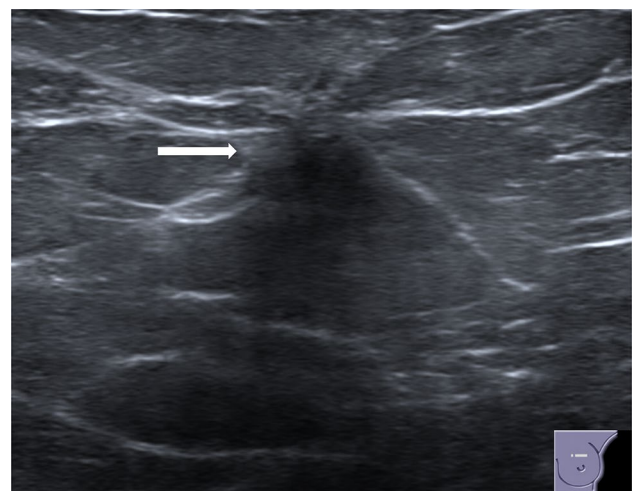


Fig. 8 US shows a focal area of shadowing with no discernible mass (white arrow)

Cawson et al. [25] have defined US findings that suggest the likelihood of RS instead of cancer:

- Absence of echogenic halo;
- Presence of tiny sonographic cysts;
- Absence of shadowing and breast architecture disruption.

The introduction of breast elastography was investigated in the literature [26–28], suggesting that frequently RS has an inherent stiffness comparable to that of invasive breast cancer, leading to false-positive elastography results. For this reason, breast elastography does not appear reliable for differentiating RS from malignant lesions.

In a recent study, Vourtsis and Kachulis [29] evaluated the use of automated breast ultrasound (ABUS) compared to conventional hand-held US (HHUS) in the visualization and characterization of breast lesions. The authors showed that ABUS confers an added value on the coronal plane, helping in recognition of architectural distortion. Particularly, ABUS allows the detection of RS that was not recognized at DM or HHUS.

Anyway, RS can't be reliably differentiated from malignancy on the basis of DM/DBT features alone, correlation with US is fundamental and biopsy is always recommended.

Magnetic resonance imaging (MRI)

The use of MRI in breast imaging has progressively increased over last decades and its capacity to predict the presence of malignancy in B3-lesions has been investigated in various studies [30, 31].

When RS is visible at MRI, three patterns of presentations have been identified, according to the literature [14]:

- Irregular or spiculated “tumor-like” mass. These lesions show the same morphology and enhancement kinetics of invasive breast cancer (Fig. 9);
- Stellate “architectural distortion,” without mass effect, with mild or no enhancement;
- Benign-looking oval or round mass with smooth margins and mild and gradual enhancement.

In some cases, RS could appear as an architectural distortion/mass without contrast enhancement (Fig. 10).

Several studies have investigated the role of MRI examinations in predicting the unfavorable evolution of lesions [32, 33], and a negative predictive value of 97.6–100% has been found for differentiating between benign and malignant RS lesions. These results suggest that in case of absent or modest enhancement, the possibility of malignancy can be excluded.

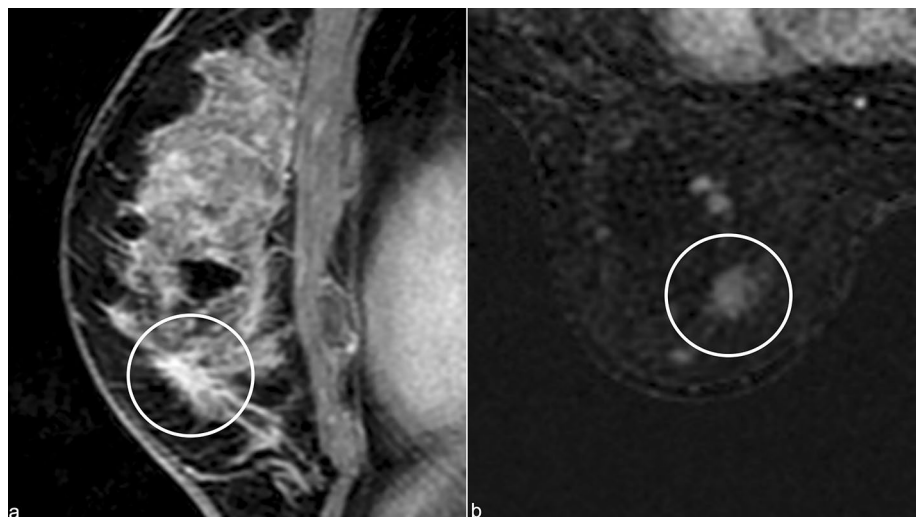
More recently, Santucci et al. [34], according to these statements, showed that upgrade was often associated with evident contrast-enhanced lesions. In contrast, Amitai et al. [11] found that MRI has low accuracy in differentiating invasive cancer from RS, with positive predictive value of 30%. In conclusion, in most of the cases, a clear-cut distinction of a RS versus invasive cancer is not possible. However, the role of MRI remains important to exclude the presence of other lesions either in the affected or in the contralateral breast; in fact, MRI detects many additional enhancing lesions unseen with DM and US [35].

RS and malignancy

The rate of upgrade to carcinoma in RS's excision specimens varies widely in the literature.

First autopsy studies provided an overall rate of malignancy of 8.6% (32/374 cases) in RS [6]. Afterward, upgrade

Fig. 9 Sagittal MRI contrast material-enhanced T1-weighted image (a) and axial MRI subtracted early contrast-enhanced image (b) show an enhancing mass with irregular borders (white circle)



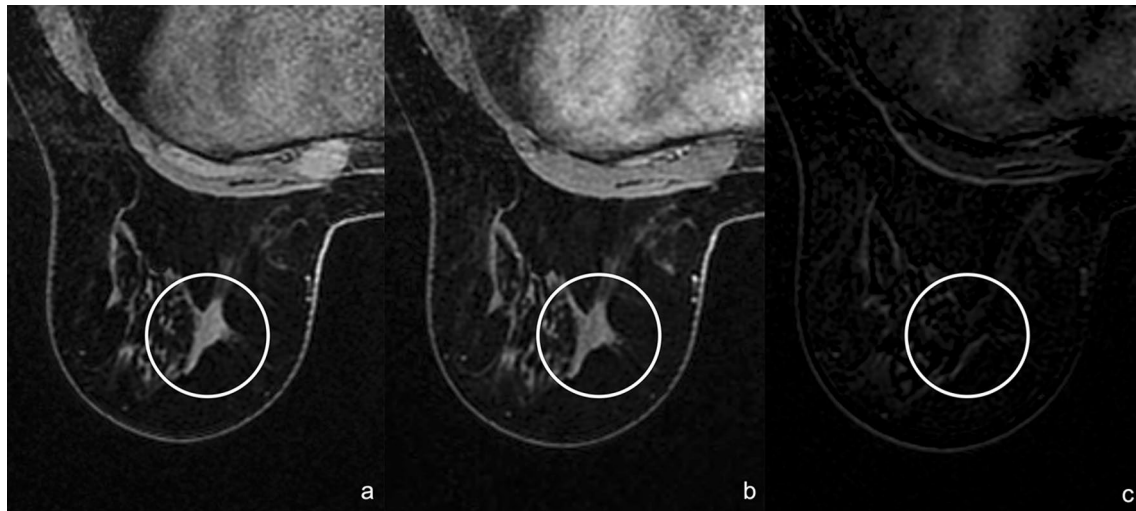


Fig. 10 Axial MRI precontrast T1-weighted image (a), early contrast-enhanced T1-weighted image (b) and early T1-weighted subtraction show an architectural distortion without enhancement (white circle)

rates diagnosed on CNB have ranged from 0 to 40% [36]. These studies were limited by the lack of radiological–pathological correlations, consistent criteria for excision, and clinical follow-up for patients who forego excision. Moreover, some papers highlighted the often eccentric and peripheral location of cancers present within RS locations that can conceivably evade a sampling needle [37].

There is a general agreement that RS alone is a benign lesion, but several studies in the literature acknowledge that the upgrade rate of RS depends on the presence or absence of associated atypia.

RS with no associated epithelial atypia has a very low rate of upgrade (< 10%) [38]. In fact, studies with carefully performed radiological–pathological correlations indicated that the upgrade rate for “RS without atypia” is 2% [39]. Moreover, several recent publications reported no cases upstaged to malignancy in the “RS without atypia” group [9]. Conversely, radial scars with atypia on biopsy show higher upgrade rates, with a range from 28% [40] to 36% [41] among the literature. A study of Ferreira et al. [42] found that the presence of atypia in the initial CNB was associated with an approximately 10 times higher risk for upstage at surgical excision.

In the last decade, the implementation of biopsy protocols using vacuum-assisted biopsy (VAB) with large needles (7–13 Gauge (G)) has permitted more extensive target lesion sampling at biopsy [43]. This has been associated with a progressive decline in the rate of underestimation of malignancy associated with the presence of RS alone on CNB [43]; in particular, a study of Linda et al. demonstrated that the biopsy underestimation rate of malignancy decreased from 9% for 14 G biopsies to 5% for 11 G biopsies [44].

The exact nature of the relationship between RS and neoplasia remains poorly understood.

Data from the Nurses’ Health Study suggested a stronger association between RS and hormone receptor-negative carcinomas [45] colliding with early clinical studies that reported RS to be most frequently found in conjunction with tubular carcinoma [46].

RS in some cases could be, indeed, misinterpreted as low-grade invasive ductal or tubular carcinoma. Eusebi et al. [47] addressed the distinctions between RS, infiltrating epitheliosis and tubular carcinoma. In most cases, hematoxylin and eosin and immunohistochemical staining for a surrounding layer of myoepithelial cells can differentiate RS from invasive cancer [48].

Further, gene mutations have been recently identified in the PIK3CA pathway in RS that are particularly prevalent in luminal-type, hormone receptor-positive breast cancers, offering additional insight into the pathogenesis of RS [49]. No consistent correlation has been demonstrated between malignancy at excision of RS and parity, menopausal status and clinical presentation. The only variable with a statistically significant relation to upgrading was the average age (> 50 years), associated with a slightly higher risk [50].

The most likely hypothesis is that the coexistence with high-risk lesions or the presence of breast tissue field, in addition to allowing development of RS may predispose tissue in the affected field to the development of carcinoma that is not etiologically related to RS [7, 51].

Management

The management of RS is still debated. The majority of different academic institutions did not provide the same management recommendations for RS, this suggests that there is still a deep heterogeneity in the management of RS between breast imagers. RS represents approximately 0.09% of all CNB [52].

According to the recent International Consensus Conference, therapeutic excision with VAB or vacuum-assisted excision (VAE) is recommended after percutaneous diagnosis of RS [2], because of the potential sampling error due to the eccentric and peripheral location of invasive carcinoma present within RS, that can escape to a sampling needle [37, 53, 54]. In fact, adequate sampling of the periphery, as well as the center of the RS, improves the detection rate of associated atypia/malignancy [55]. In the past years, when a CNB returned a RS lesion, surgical excision was always suggested considering the potential sampling error. Nowadays, the aim of VAE is to take about 4 g of tissue, and the purpose is to equate a surgical biopsy, without the associated complications. The amount of tissue is estimated by multiplying the number of cores with estimated weight of each core dependent on the needle size [54, 56]; generally, a 7 or 8 G needle is used.

Thereafter, surveillance is justified [2].

Regarding surveillance, the National Health Service (NHS) Breast Screening multidisciplinary working group [38] recently suggested flowcharts for the management of RS, differentiating two pathways depending on the presence or the absence of atypia. In their opinion, VAE is always recommended in cases of RS with atypia, and if no additional atypia is found, surveillance with annual mammography is suggested. In cases where further atypia is found, the management should include open surgical excision [57]. In an interesting study of Özçağlayan et al. [58], breast lesion excision system (BLES) has been evaluated as a secure procedure that can provide high diagnostic success and serve as a therapeutic method in high-risk lesions, such as RS, with high complete excision rates.

The management is more controversial in cases without atypia. According to the NHS Breast Screening multidisciplinary working group [38], even in cases without atypia, VAE is always recommended, and the decision is based on the result obtained on histology; more specifically, if no atypia is retrieved after VAE, a three-yearly mammography is proposed. Some recent studies demonstrated that conservative management with imaging follow-up could be considered if the appropriate biopsy techniques are used and the pathology returns as isolated RS without atypia [38].

On a recent meta-analysis, Farshid et al. [59] focused on atypia and the extent of sampling as two potential factors

to take into account for the substantial variation in reported upgrade rates. They observed that RS without atypia was the group of lesions with the lowest upgrade rate (1%) (95% CI 0–4%). Upgrade rates were significantly lower also for the group assessed by the 8–11G VAB than those by smaller biopsies. The authors concluded that imaging surveillance could be a reasonable option for RS without atypia assessed by 8–11G VAB. Likewise, Bacci et al. [60] found that VAB with a large core is reliable to exclude malignancy and allows avoiding surgical excision when there is no discordance between radiological and histological findings, and no associated atypia on biopsy. Eghtedari et al. [61] observed that in a group of 54 patients with a CNB histological result of RS without atypia, no case developed malignancy during the 2 years of follow-up (95% confidence interval 0–7%).

The recommendations could change according to lesion size. In a Slovenian study, Gašljević et al. [55] suggested that RS without atypia and smaller than 20 mm can be followed radiologically. Conversely, lesions larger than 20 mm, sampled with a smaller core and/or showing atypia, should be excised.

In addition, Linda et al. [14], as mentioned above, have demonstrated that MRI has a negative predictive value of 97.6% in evaluating malignant transformation in non-enhancing RS. Therefore, they concluded that an imaging follow-up could be suitable for non-enhancing RS, with a follow-up protocol of short interval MRI (every 6 months for 2 years) as a surveillance tool for patients with small RS without atypia on CNB.

Regarding suspicious lesions only MRI-visible, resulting to be a RS/CSL after MRI-guided biopsy, many studies in literature have evaluated the rates of upgrade to malignancy, showing a discordance. Some studies [62–64] revealed no upgrade to malignancy, others [65, 66] reported an overall upgrade to malignancy ranging from 15 to 23.1%. High upgrade rates could be explained by the lack of accuracy of the MRI biopsy technique. In fact, the number and dimension of samples may be responsible for the difference in upgrade rates. Ferreira et al. [42] indicated lower upgrade rates of RS with greater number of fragments obtained at biopsy and in RS subjected to VAB than in those subjected to core biopsy. In a recent study, Okamoto et al. [67] stated that when MRI biopsy is vacuum assisted, the risk of upgrade and malignancy is significantly lower with less indication for excisional biopsy.

It was tried to develop a predictive scoring system based on clinical–radiological–pathological data to choose the most appropriate management in US-detected B3 lesions [68]. The authors categorized RS as a “low-risk B3 lesion” and proposed a personalized strategy in every individual patient, considering the patient demographics, imaging features, and pathological results, with the objective of

selecting the right management, reducing the frequency of benign surgical excision.

Grippo et al. [69] recently evaluated its feasibility based on clinical, pathological, and radiological data. It is assumed that a RS lesion with associated atypia should undergo therapeutic excision with VAB.

A multidisciplinary approach may be appropriate in patients with a diagnosis of RS without atypia, to decide on personalized management, which may include imaging surveillance or surgical excision based on patient risk factors, comorbid conditions, and their history of concurrent breast cancer.

In future studies, different imaging examinations features should be tested “in combination” to assess malignancy probability. Furthermore, emerging techniques, like radiomics (the extraction of tissue characteristics of tumor phenotype from images generating features not appreciated by the naked eye) and artificial intelligence, are showing promising results in evaluation of breast cancer [70] and in the future may provide additional information on the assessment of malignancy also in B3-lesions, integrating molecular and genetic findings.

Conclusion

This review reported almost all the presentation patterns of RS through different imaging techniques already well-described among the literature and the updates on management.

It is important for the breast radiologist to be familiar with these features, in order to make an accurate differential diagnosis.

At present, no imaging examination can yet provide sufficient elements to certainly exclude malignancy. Despite this, all of them (DM/DBT, US, and MRI) provide a contribution in making the correct decision and, therefore, should all be performed. Moreover, biopsy is always recommended, and afterward, a systematic multidisciplinary evaluation is crucial. Besides, when the “wait-and-see” pathway is undertaken, it requires accurate and complete imaging examination protocols.

Additional studies including closer radiology–pathology correlations and development of artificial intelligence could help to reduce unnecessary excision biopsy and surgical procedures.

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Declarations

Conflict of interest The authors declare that they have no competing interests.

Ethical approval and consent to participate All patients have signed consent forms agreeing that their images and data could be used for educational and research purposes.

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