# Evaluation of Benign Breast Diseases With or Without Atypical Epithelial Hyperplasia Accompanying Radial Scars

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**ABSTRACT**

**Objective:** A radial scar (RS) is a benign breast lesion (BBL) that has an obscure etiology. RS is easily confused with breast carcinoma and therefore correct identification radiologically and pathologically is important. The aim of this study was to determine the incidence of atypical lesions by evaluating RS detected with BBL and to investigate whether atypia and RS are related to their characteristics.

**Materials and Methods:** A total of 1.370 patients with a diagnosis of BBL postoperatively in a single department were analyzed retrospectively. Forty-six confirmed RS/complex sclerosing lesion (CSL) cases were selected. The demographic and clinical characteristics of the patients and the relationship between RS and other BBL were evaluated. In addition, the relationship between RS/CSL and the presence of atypia was interpreted.

**Results:** The mean age was 45.17±8.72 years. Spiculated lesion (34.8%) on mammography and microcalcification (37%) on histopathological examination were the most common features. The most common BBL accompanying RS/CSL was adenosis. Atypical epithelial hyperplasia (AEH) was presented in 15 (32.6%) of those diagnosed with RS. Although all patients were benign, the frequency of AEH accompanying RS was found to be significantly higher. The mean size of RS was 10.8±8.4 mm (2-30 mm). The size of RS/CSL was not significantly associated with atypia.

**Conclusion:** RS/CSLs usually present as suspicious lesions that must be distinguished radiologically from malignancy. However RS, which can be present with malign breast lesions, can be also seen with all BBL. Therefore, core biopsy and/or excisional biopsy continue to be important for definitive histopathological diagnosis.

**Keywords:** Radial scar; complex sclerosing lesion; benign breast lesions; spiculated lesion

**Key Points**

- Radial scar (RS) often has a spicule appearance mimicking breast carcinoma on mammography, so the definitive diagnosis of the lesion with mammography is difficult.
- The high incidence of atypical epithelial hyperplasia accompanying RS in the study suggests that RS is strongly associated with atypia.
- The follow up of RS without atypia requires a multidisciplinary approach.

## Introduction

Radial scar (RS) and complex sclerosing lesion (CSL) may be confusing, benign breast lesions (BBL). RS is a proliferative BBL that includes central sclerosis. Distortion and pseudo-infiltrative appearance have been confused with carcinoma (1). When the size is smaller than 1 cm, the lesion is termed RS, whereas, if it is bigger than 1 cm, it is designated a CSL (1, 2). Small lesions usually present as incidental microscopic findings but the mammographic findings of large lesions are typical (2, 3). The incidence of RS and CSL is reported to be 0.03–0.09% in all core needle biopsies (CNB) (4, 5). RS pathogenesis is not exactly clear. Inflammatory process, chronic ischemia, previous trauma and surgical operations may all play a role in the pathogenesis of RS

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(6). RS is characterized by a central area of fibroelastosis with radiating ducts and lobules. These ducts and lobules have the appearance of spicules on mammography, which often mimics breast carcinoma (1, 7). Therefore, it is difficult for a definitive mammographic diagnosis of this lesion (6, 7). The results of studies examining the relationship between breast cancer and RS are controversial. Currently, it is unclear whether RS/CSL only act as an independent risk factor in increasing breast cancer or are in themselves premalignant (6, 8). Although RS/CSL is mostly associated with malignancy by clinicans, it can frequently be seen with various BBLs. Proliferative BBLs, with or without atypia, may accompany RS (5, 6, 8).

The aim of this study was to determine the benefits of imaging modalities and core needle biopsy and to investigate the frequency of benign lesions in the breast associated with RS. Furthermore, the association of RS with or without atypical BBL was assessed.

## Materials and Methods

Between 1995-2015, 1.370 operated cases were diagnosed with BBL and retrospectively analyzed at Istanbul University, Faculty of Medicine Surgery, Department C Clinical Services. Forty-nine cases with histopathology confirming cases of RS or CSL were selected.

As the aim was to consider etiologically non-traumatic and idiopathic RS in patients without history of breast operation, 3 of 49 (6.1%) cases that had excisional biopsies performed on the same breast previously were excluded. Demographic and clinical characteristics of the remaining 46 patients including age, menopausal status, age at menarche, lactation period, number of births, family history of cancer, oral contraceptive use, hormonal therapy, complaint, palpability of lesions, and side of lesions were evaluated.

Ultrasonography, mammography, and magnetic resonance imaging (MRI) results were also evaluated by size and Breast Imaging Reporting and Data System (BI-RADS) score. If the lesion was 1.0 cm or less, the lesion was designated RS and if greater than 1.0 cm it was defined as CSL.

We gathered and reviewed follow-up reports in order to examine the risk of developing carcinoma or other lesions. Lesions accompanying RS were further investigated to assess the relationship between RS and other benign lesions

### Statistical Analysis

The Statistical Package for the Social Sciences (SPSS), version 25.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. While evaluating the study data, chi-square tests (Pearson chi-square, Yates chi-square, Fisher's Exact test) were used for qualitative comparisons between groups and to produce descriptive statistics. The results were evaluated within the 95% confidence interval and significance was assummed when $p<0.05$.

## Results

The mean ± standard deviation (range) age of the patients was 45.17±8.72 (22–61) years. Seven patients (15.2%) had a family history of breast cancer. Fourteen (30.4%) patients had palpable mass at presentation. The lesion was in the right breast in 47.8% and in the left breast in 52.2%. Demographic and clinical characteristics of the patients are given in Table 1. Twenty-five cases (54.3%) cases were identified by the mammography screening program (MSP).

Table 1. Demographic and clinical characteristics of patients

| | n | % |
|---|---|---|
| **Age** | 45.17±8.72 (22–61) | |
| **Age groups** | | |
| 20-30 | 3 | 6.5 |
| 31-40 | 8 | 17.4 |
| 41-50 | 21 | 45.7 |
| 50+ | 14 | 30.4 |
| Premenopausal | 31 | 67.4 |
| Postmenopausal | 15 | 32.6 |
| Used oral contraceptives | 10 | 21.7 |
| Family history of breast cancer | 7 | 15.2 |
| Age at menarche (year) | 13.5±1.4 | |
| Lactation period (month) | 22.72±19.31 | |
| | **n** | **%** |
| **Presenting symptoms** | | |
| Screening | 25 | 54.3 |
| Mass | 13 | 28.3 |
| Pain | 5 | 10.9 |
| Mass+pain | 3 | 6.5 |
| **Imaging techniques** | | |
| Ultrasound | 46 | 100 |
| Mammogram | 37 | 80.4 |
| Magnetic Resonance Imaging | 16 | 34.7 |
| **MMG findings (total 37 patients)** | | |
| Microcalcifications | 19 | 51.3 |
| Spiculated lesion | 16 | 43.2 |
| Opacity | 11 | 29.7 |
| Asymmetric density | 3 | 8.1 |
| Distortion | 2 | 5.4 |
| **CNB findings (total 24 patients)** | | |
| Pure RS/CSL | 8 | 33.3 |
| Intraductal papilloma | 3 | 12.5 |
| Stromal fibrosis | 3 | 12.5 |
| Fibroadenoma | 2 | 8.8 |
| ADH | 2 | 8.8 |
| Adenosis | 1 | 4.1 |
| Phyllodes tumour | 1 | 4.1 |
| RS&Adenozis&DCIS | 1 | 4.1 |
| RS&Intraductal papilloma | 1 | 4.1 |
| Fibroadenolipoma | 1 | 4.1 |
| Sclerosing adenosis | 1 | 4.1 |
| **Surgery techniques** | | |
| Wire localization biopsy | 31 | 67.4 |
| Excisional biopsy | 14 | 30.4 |
| Radioguided occult lesion localization & surgical biopsy | 1 | 2.2 |

RS: radial scar; CSL: complex sclerozing lesion; ADH: Atypical ductal hyperplasia; DCIS: ductal carcinoma *in situ*; RS: radial scar

Microcalcification was detected in 19/37 (51.3%) of the mammograms, and spiculated lesion was observed in 16/37 (43.2%). Distributions of mammography findings appear in Table 1. Six patients (23.1%) were designated as BIRADS III, 14 as BIRADS IV (53.8%) and six as BIRADS V (23.1%). Mammographic appearance is shown in Figure 1. RS/CSL was detected in only 10 (41.7%) of 24 CNB performed. In the other 14 CNB results, the presence of RS was not identified but other benign lesions were detected. Histopathological results of 24 core biopsy specimens are shown in Table 1.

Radiologically suspicious lesions were excised without CNB in 22 patients. Of the 22 patients, 16 who had not undergone CNB, were excised with wire-guidance. The lesions were excised due to a spicule contour mass in 8 (50%) patients, microcalcifications in 5 (31.25%), lobulated contour in 2 (12.5%), and suspicious contrast enhancement in MRI in 1 (6.25%) case. When pathology results of 5 patients who underwent biopsy due to microcalcification were evaluated, the mean RS dimension was 3.8±2.5 mm. The most common surgical method was wire localization excision with a frequency of 67.4%.

RS was detected in 34 cases (73.9%) while CSL was found in 11 cases (23.9%). Only 1 (2.2%) had both RS and CSL. RS/CSL were multiple in 8 cases (17.4%) whereas 38 lesions (82.6%) were single. Five (10.9%) cases had pure RS/CSL. The most common RS/CSL accompanying lesion was adenosis (39.1%) (Figure 2 shows CSL, sclerosing, papilloma and adenosis). Microcalcification was identified in 17 of 46 (36.9%) cases by histopathological examination. The distribution of BBL accompanying RS is shown in Table 2.

The mean size of RS/CSL was 10.8±8.4 mm 2–30 mm). RS size was less than 5 mm in 22 (47.83%) patients and greater than 5 mm in 24 (52.17%) patients. RS/CSL size was less than 1 cm in 31 (67.4%) patients and greater than 1 cm in 15 (32.6%) patients. Atypical epithelial hyperplasia (AEH) was seen with a frequency of 32.6% (15/46). Twelve patients had atypical ductal hyperplasia (ADH), two patient had atypical lobular hyperplasia (ALH), and one patient had both ADH and ALH. The incidence of atypia in patients with RS according to age is given in Table 3. There was no statistical relationship between the age of patients and the presence of AEH.
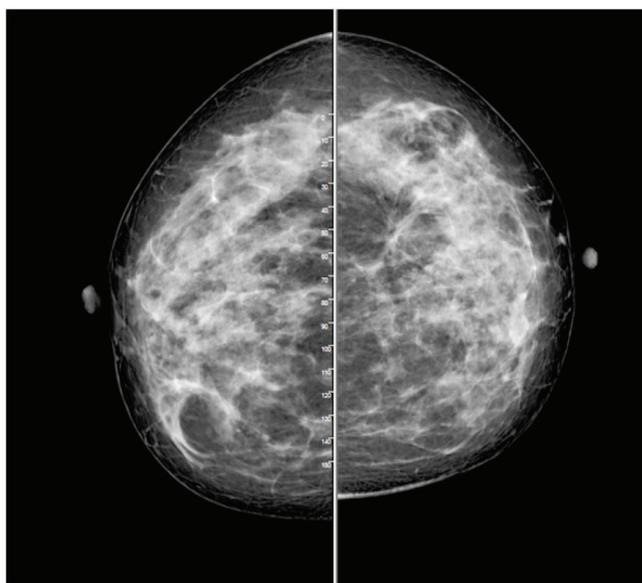


**Figure 1.** RS mammographic appearence

*RS: radial scar*

While 33.3% percent of 24 cases (with RS dimension 0.5 cm or larger) had AEH, 66.7% percent didn't have AEH. In contrast, in 22 cases with RS smaller than 0.5 cm, 32.8% percent had AEH and 68.2% didn't have AEH. Taking a cut-off at 1 cm, while 26.7% percent of 15 cases (with CSL 1 cm and larger) had AEH, 73.3% didn't have AEH. Whereas 35.5% percent of 31 cases with RS smaller than 1 cm had AEH, 64.5% didn't have AEH. No statistically significant correlation was found between RS/CSL size and atypia (Table 4). Among 15 RS with AEH, three cases were multiple, while 12 cases were solitary. AEH was present in 3 of 8 (37.5%) multiple lesions, and it was found in 12 of 38 solitary lesions (31.6%). The number of lesions did not reveal any statistically significant relation with atypia.

Benign phyllodes tumor, hamartoma, and lobular carcinoma in situ (LCIS) was an accompanying lesion in three different patients. In a 35-year-old patient diagnosed with hamartoma, a rare breast tumor, RS was detected in this hamartoma. In the wire localization biopsy of a 53-year-old postmenopausal patient, RS was accompanied by LCIS. The mean follow-up period of the patients was 48 months, and RS recurrence and malignancy did not develop in any of the patients during the follow-up period.
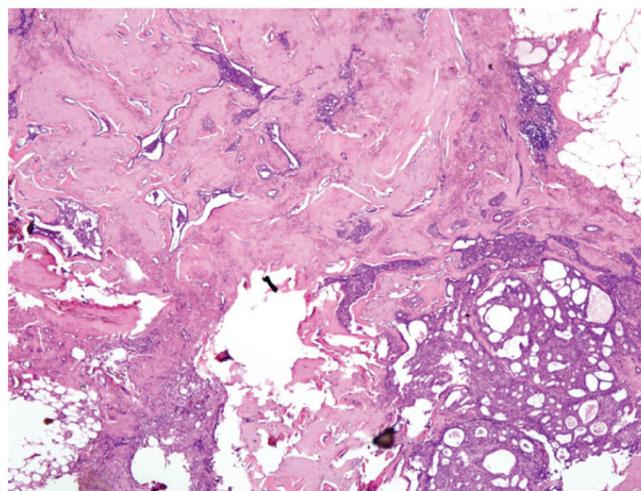


**Figure 2.** CSL with sclerosan papilloma, adenosis and radial scar (H&E, x100)

Table 2. Associated benign breast lesions with radial scar

| Concominant benign breast lesions | n | % |
|---|---|---|
| Adenosis | 18 | 39.1 |
| Intraductal papilloma | 16 | 34.8 |
| Ductal ectasia | 16 | 34.8 |
| Apocrine metaplasia | 15 | 32.6 |
| Fibroadenoma | 12 | 26.1 |
| Sclerosing adenosis | 12 | 26.1 |
| ADH | 12 | 26.1 |
| Florid ductal hyperplasia | 10 | 21.7 |
| Ductal hyperplasia | 2 | 4.4 |
| ALH | 2 | 4.4 |
| ADH &ALH | 1 | 2.2 |

ADH: atypical ductal hyperplasia; ALH: atypical lobular hyperplasia

Table 3. Relationship between age and atypia in patients with RS

| | AEH | | | |
|---|---|---|---|---|
| Age | Absent n (%) | Present n (%) | Total n (%) | p |
| 20-30 | 2 (6.5) | 1 (6.7) | 3 (6.5) | 0.593 |
| 31-40 | 4 (12.9) | 4 (26.7) | 8 (17.4) | |
| 41-50 | 16 (51.6) | 5 (33.3) | 21 (45.7) | |
| 50+ | 9 (29.0) | 5 (33.3) | 14 (30.4) | |
| Total n (%) | 31 (100.0) | 15 (100.0) | 46 (100.0) | |

AEH: atypical epithelial hyperplasia; RS: radial scar

Table 4. Size of RS/CSL-AEH relations

| Size (cm) | AEH | | |
|---|---|---|---|
| | Absent n (%) | Present n (%) | Total n (%) |
| **Cut off 0.5 cm** | | | |
| <0.5 | 15 (48.4) | 7 (46.7) | 22 (47.8) |
| >0.5 | 16 (51.6) | 8 (53.3) | 24 (52.2) |
| Total, n (%) | 31 (100.0) | 15 (100.0) | 46 (100.0) |
| **Cut off 1 cm** | | | |
| <1 | 20 (64.5) | 11 (73.3) | 31 (67.4) |
| 1 + | 11 (35.5) | 4 (26.7) | 15 (32.6) |
| Total, n (%) | 31 (100.0) | 15 (100.0) | 46 (100.0) |

AEH: atypical epithelial hyperplasia; RS: radial scar

## Discussion and Conclusion

Fenoglio and Lattes first described RS as "sclerosing papillary proliferation". In 1975 Hamperl et al. named it "Strahlige Narbenquot", translated as "radial scar" (9, 10). RS are usually incidental microscopic findings in excised breast tissue (11). In the present study, RS was not detected in 14 (58%) of 24 patients who underwent CNB, and these were found as incidental RS accompanying other BBL as a result of histopathological examination of excisional biopsies. Mammography was performed in 37 patients. RS was suspected on mammography images in only seven (18.9%) of these. King et al. (6) reported that only 19 of 45 cases were diagnosed by mammography, which is similar to our results.

RS is generally encountered in premenopausal women. This lesion is uncommon before 40 years old and after 60 years old (6, 12). The mean age in our series was 45.17±8.72 and around two thirds of the patients were premenopausal. Patients with RS routinely have non-palpable lesion. Egyed et al. (13) determined the rate of palpable RS lesions as 6.5%. Our cases were selected from excisional biopsy, which results in pure RS or accompanying BBL with RS. Our high rates of palpable lesions can be explained by the presence of other BBL such as fibroadenomas and papillomas with RS. The RS's precise incidence is unknown, but with the increasing use of MSP, RS is seen more often (2, 14).

In the present study, 54.3% of the patients were detected as a result of biopsies performed from suspicious lesions on mammography screening. In mammography, RS is defined as a central radiolucency, presence of multiple long and thin spicules, varying appearance in different projections, and radiolucent linear structures parallel to the spicules (15). The central areas contain fat and this fat appears as a "black star". A '"black star" aspect is typical of RS but it is not specific to RS (16). The varying appearances seen in different projections in mammography can be attributed to small invasive carcinoma seen simultaneously. This appears to be one reason for the confusion between small-sized breast carcinoma and RS (17). In a study, 52.8% of RS was presented as architectural distortion where 27.8% has spiculated opacity. In the same study, the frequency of microcalcification was reported as 19.4% (11). In another study 50% was detected as an architectural distortion, where calcifications were 29%, and masses made up 21% (3). The most common mammography finding we detected was microcalcifications in 51.3%. In 43.2% of our cases, spiculated lesions were detected, while opacity was the other common finding (29.7%). Opric et al. (12) reported that RS was seen more frequently in the glandular breast rather than lipomatous breast tissue. On histopathological examination, RS is morphologically similar to breast carcinoma, especially because of the creamy-yellow elastotic center which is common for both and fibroelastotic area with entrapped ducts. The ducts consist of dual epithelial and myoepithelial rows (12). This feature is one of the most significant similarities between RS and tubular carcinoma, which may often cause confusion during diagnosis (18). Cawson et al. (17) showed that the sensitivity rate of stereotactic biopsy was 85% while the sensitivity rate of ultrasound-guided core needle biopsy was 63% in a definitive diagnosis of RS/CSL (19).

RS/CSL can be single, multiple, or appear in clusters (5). In one study, a single lesion was detected with a frequency of 87%, while it was reported that 13.0% had two or more lesions (8). In our study, RS was solitary in 38 cases (82.6 %), while in eight cases (17.4%) there were multiple lesions. Five (10.8%) cases had pure RS/CSL. The average size as of RS has been reported as 1.01 cm and 1.42 cm (13, 20). In the present study, the average size of RS/CSL was 1.08 cm (0.2–3). Previous studies have suggested that malignancy occurs more frequently in larger and multiple RS (19, 20). Bacci et al. (1) reported that upgrade malignancy lesions were notably larger in size than non-upgraded lesions, but they could not define a statistically significant threshold. However, other studies have reported no relation between the size of the lesion and the risk of developing breast cancer (14). In the present study, there was no significant association between RS number and atypia. While AEH was seen in 37.5% of cases with multiple lesions, it was detected in 31.6% of cases with solitary lesions. We did not find a significant relationship between RS number and atypia. Also, there was no relation between RS size and atypia. When the cut-off value was taken as 1 cm for RS size, no statistically significant difference was found in terms of AEH detection rates. Similarly, when the RS dimension was evaluated as values below and above 5 mm, we did not find a statistically significant difference between the RS dimension and AEH. When age groups and presence of AEH were evaluated, although there were fewer cases with atypia in the 20–30 year-old age range, there was no statistically significant relationship between age groups and the presence of AEH. Similarly, in a study, when BBL cases with RS and high-risk lesions with RS were compared, the mean age was reported as 49 and 50 years, respectively (7).

RS/CSL may be found concurrently with a range of proliferative epithelial lesions, such as sclerosing adenosis and papillomas. Besides,

it may be associated with non-proliferative benign lesions, like simple cysts and fibroadenomas (21). In the present study, adenosis was the most common lesion accompanying RS/CSL (39.1%) while Opric et al. (12) found 23.1% adenosis in their study.

Jacobs et al. (19) suggested that RS was an independent risk factor for breast cancer. In contrast, Berg et al. (8) reported that RS was not an independent risk factor for cancer but that RS was associated with concomitant atypical hyperplasia. It is claimed that RS represents a natural pattern of carcinogenesis that starts from a proliferative lesion and then progresses to an atypical and then carcinomatous lesion (20). ADH is considered a marker for ductal carcinoma *in situ*, and invasive ductal carcinoma. In recent years, they have been found to be molecularly similar to each other. In studies, ADH is detected in 5–20% of all breast biopsies (22). Berg et al. (8) encountered atypia in proliferative lesions with RS more than proliferative lesions without RS. In one study, ADH or LCIS was observed in 15 of 164 patients with RS (14). Osborn et al. (23) reported that 18% of RSs were accompanied by atypia. In the present study, AEH was present in 15 cases (32.6%), while 12 patients had ADH, two had ALH, and one patient had both ADH and ALH. Although all our patients had benign lesions, the frequency of ADH accompanying RS was found to be significantly higher (32.6%). Recent studies have shown low up-grade to malignancy in RS without atypia. Therefore, it has recently been highlighted that radiological follow-up after CNB may be preferred to an excision in RS without atypia and malignancy (24-26). Some investigators have reported that excised RS/CSL was associated with atypical hyperplasia, *in situ* and invasive carcinoma on follow-up (14). Five of 149 patients who were followed for 68 months developed cancer according to the study of Bunting et al. (14). In comparison, in the pressent study, the mean of follow-up was 48 months, and none of the patients developed breast cancer by last follow-up.

In conclusion, 32.6% of the patients with RS had AEH. No correlation was found between the presence of atypia and RS size, number of RS, and patient age. Although all our patients had benign lesions, the incidence of AEH accompanying RS was higher than generally reported in the literature. This suggests that RS has a strong relationship with atypia. There is a consensus that surgical excision is required in the presence of atypia accompanying RS in CNB. However, cases without atypia are still clinically challenging. We believe that if RS patients without atypia are to followed up, it would be safer to follow up with core-needle biopsy, especially in specialized breast centers and with an emphasis on radiology-pathology cooperation.

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