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Arch Basic Clin Res 2026;8(2):143-149
**DOI:** 10.4274/ABCR.2026.25402

Research Article

# The Relationship Between Mammographic Features of BI-RADS 4 and 5 Calcifications and Pathological Diagnoses

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**Cite this article as:** Seyfettin A, Büyükceran EU, Eskalen Z, et al. The relationship between mammographic features of BI-RADS 4 and 5 calcifications and pathological diagnoses. *Arch Basic Clin Res*.2026;8(2):143-149.

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## ABSTRACT

**Objective:** To evaluate the relationship between mammographic features of BI-RADS category 4 and 5 breast calcifications and their corresponding pathological diagnoses, and to determine whether specific morphological or distribution patterns are predictive of malignancy.

**Methods:** This retrospective study included 54 patients who underwent biopsy for suspicious breast calcifications between August 2021 and March 2024. Among these patients, 30 underwent stereotactic vacuum-assisted biopsy, and 24 underwent wire-guided localization followed by excisional biopsy. The mammographic morphology and distribution patterns of the calcifications were assessed using the BI-RADS lexicon, and the corresponding histopathological diagnoses were recorded. The association between mammographic features and pathological outcomes was subsequently analyzed.

**Results:** Fine pleomorphic calcifications were the most common morphology (40.7%). A grouped distribution was the predominant pattern (61.1%). Benign lesions were mostly categorized as BI-RADS 4A, B3 lesions as BI-RADS 4B, and DCIS cases as BI-RADS 4C ($P$ = 0.03). The Grouped distribution was more frequent among benign and B3 lesions, whereas DCIS exhibited more frequent linear and segmental patterns ($P$ = 0.01). Malignancy rates were highest for fine linear/branching and fine pleomorphic morphologies.

**Conclusion:** A significant association exists between the mammographic characteristics of BI-RADS 4 and 5 calcifications and their pathological outcomes. In our study, fine pleomorphic morphology and linear or segmental distribution patterns consistently indicated a increased likelihood of malignancy, particularly ductal carcinoma *in situ*, whereas benign and B3 lesions were more commonly associated with grouped distribution patterns. These results highlight that detailed evaluation of calcification morphology and distribution on mammography can improve diagnostic confidence, aid in distinguishing higher-risk lesions, and contribute to more informed biopsy decision-making.

**Keywords:** BI-RADS, breast calcifications, mammography, breast malignancy, pathology correlation

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**Received:** January 12, 2026
**Revision Requested:** February 20, 2026 **Accepted:** May 25, 2026 **Publication Date:** July, 14, 2026

**This study presented as an oral presentation at the TÜKRAD 2024 Congress.**

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## INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy among women worldwide, and early detection constitutes one of the principal determinants in reducing disease-related mortality.[1] Mammography, as the primary imaging modality for breast cancer screening, plays a pivotal role in the detection of microcalcifications, which may represent one of the earliest radiological manifestations of ductal carcinoma *in situ* (DCIS) and invasive carcinoma.[2] Breast calcifications are among the most frequently encountered findings in mammographic practice and represent one of the most challenging features for radiologists in terms of diagnostic interpretation.[3] The mammographic evaluation of breast calcifications constitutes a well-recognized diagnostic challenge in breast imaging, largely attributable to the substantial overlap in morphological and distributional characteristics between benign entities and malignant lesions.[4]

To address the diagnostic challenges associated with the overlapping mammographic appearances of breast calcifications, the Breast Imaging Reporting and Data System (BI-RADS) was developed to standardize lesion description and stratify malignancy risk based on morphological and distributional criteria.[5]

Despite advances in mammographic interpretation and standardized classification, suspicious breast calcifications often require image-guided tissue sampling, as stereotactic core needle biopsy remains the reference standard for distinguishing benign from malignant findings on mammography.[6]

The aim of this study is to systematically evaluate the association between the morphological and distributional mammographic characteristics of non-mass-associated BI-RADS category 4 and 5 breast calcifications and their corresponding histopathological diagnoses, and to assess the diagnostic value of specific mammographic patterns for predicting malignancy, with particular emphasis on early-stage breast cancer. Through a detailed analysis of the correlation between mammographic findings and pathological outcomes in cases with isolated calcifications, this study aims to facilitate earlier detection of malignancy while minimizing unnecessary invasive procedures.

### MAIN POINTS

- A significant association was identified between the mammographic morphology and distribution patterns of BI-RADS 4-5 calcifications and their corresponding pathological diagnoses.
- Fine pleomorphic and fine linear/branching calcifications were associated with the highest malignancy rates and were strong predictors of malignancy, particularly of ductal carcinoma *in situ*.
- Linear and segmental distribution patterns were observed more frequently in malignant lesions, whereas benign and B3 lesions predominantly demonstrated grouped distributions.
- Detailed assessment of calcification morphology and distribution improves the accuracy of malignancy risk estimation and strengthens biopsy decision-making.

## MATERIAL AND METHODS

In this retrospective study, 54 patients who underwent interventional procedures for non-mass-associated suspicious breast calcifications detected on mammography at the Ankara Güven Hospital Breast Unit between August 2021 and March 2024 were evaluated. Of these patients, 30 underwent stereotactic vacuum-assisted biopsy, while 24 underwent wire-guided excisional biopsy. The mammographic features and corresponding histopathological diagnoses of all cases were reviewed retrospectively. Ethical approval for this study was obtained from the Erzincan Binali Yıldırım University Non-Interventional Clinical Research Ethics Committee (approval date: 18.09.2025, decision no: 2025-16/08).

All mammographic examinations were retrospectively evaluated by two breast radiologists with 20 and 3 years' experience, respectively. The senior radiologist reviewed all cases, and consensus-based final assessments were established. Both radiologists were blinded to histopathological outcomes. Interobserver agreement analysis was not performed; final assessments were based on consensus between the two radiologists. Breast calcifications were evaluated in accordance with the criteria defined in the American College of Radiology (ACR) BI-RADS® Atlas, Fifth Edition. Standard mammographic views were reviewed, and magnification views were used when available to allow detailed evaluation of calcification morphology. Calcifications were classified based on their morphological characteristics as amorphous, coarse heterogeneous, fine pleomorphic, fine linear, fine linear branching, and punctate. In addition, the distribution patterns of calcifications were assessed and categorized as diffuse, regional, grouped, linear, or segmental.[7]

Suspicious breast calcifications were assigned BI-RADS assessment categories based on a combined evaluation of calcification morphology and distribution patterns, in accordance with the ACR BI-RADS® Atlas, Fifth Edition. Subcategorization of BI-RADS category 4 lesions (4A, 4B, and 4C) was performed using established criteria integrating morphologic descriptors and distribution characteristics, as previously described in the literature. Amorphous calcifications with a regional or grouped distribution were categorized as BI-RADS 4A, whereas those with a linear or segmental distribution were classified as BI-RADS 4B. Coarse heterogeneous calcifications were categorized as BI-RADS 4B regardless of their distribution pattern. Fine pleomorphic calcifications with grouped distribution were classified as BI-RADS 4B, while those exhibiting linear or segmental distribution were assigned BI-RADS 4C. Calcifications with fine linear or fine-linear branching morphology were categorized as BI-RADS 4C when grouped, and as BI-RADS 5 when associated with a linear or segmental distribution, particularly when newly developed. Additionally, punctate calcifications demonstrating interval increase and clustering on follow-up mammography were categorized as BI-RADS 4A.[8]

Stereotactic vacuum-assisted biopsies were performed in the mammography unit with the patient seated upright, using a full-field digital mammography system (MAMMOMAT Revelation, Siemens Healthineers, Erlangen, Germany). Prior to the procedure, the skin overlying the target area was cleansed with an antiseptic solution, and the procedure was carried out under sterile conditions. Local anesthesia was administered using 1% lidocaine to ensure adequate analgesia.

After target localization under mammographic guidance and breast compression, tissue sampling was performed using a 10-gauge vacuum-assisted biopsy system (EnCor, USA). During the procedure, an initial 360° probe rotation was performed and multiple tissue samples were obtained. Specimen radiography was subsequently performed, and the retrieved samples were evaluated to confirm that they adequately represented the target calcifications. If the lesion was not considered sufficiently represented, an additional 360° rotation of the probe was performed.

Histopathological evaluation of biopsy or surgical excision specimens was performed by an experienced breast pathologist with 10 years' experience, and diagnoses were categorized according to the 2019 World Health Organization Classification of Tumours of the Breast. Pathological outcomes were classified as benign lesions, B3 lesions, DCIS, and invasive breast carcinoma. B3 lesions include atypical ductal hyperplasia, flat epithelial atypia, classic lobular intraepithelial neoplasia, radial scar, complex sclerosing lesion, papillary lesions, and benign or borderline phyllodes tumors.[9]

### Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (SPSS), version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation or median (minimum-maximum), as appropriate, while categorical variables were expressed as frequencies and percentages. Associations between mammographic characteristics of breast calcifications, including morphological features and distribution patterns, and histopathological outcomes were evaluated using the chi-square test. Comparisons were primarily conducted between benign and malignant pathological groups to assess the diagnostic significance of specific mammographic patterns. A two-tailed *P* value of less than 0.05 was considered statistically significant.

## RESULTS

The mammographic characteristics of calcifications in the 54 included cases are summarized in Table 1. With respect to morphology, the most frequently observed calcification type was fine pleomorphic, which was identified in 22 cases (40.7%). This was followed by amorphous calcifications in 12 cases (22.2%) and punctate calcifications in 10 cases (18.5%). Coarse heterogeneous calcifications were observed in 8 cases (14.8%), whereas fine linear calcifications were identified in 2 cases (3.7%). The majority of calcifications demonstrated a grouped distribution (33 cases, 61.1%). Regional distribution was observed in 11 cases (20.4%), while linear and segmental distributions were each identified in 5 cases (9.3%). According to BI-RADS assessment categories, 45% of cases were classified as BI-RADS 4A, 33% as BI-RADS 4B, 20% as BI-RADS 4C, and 2% as BI-RADS 5.

Among the 54 cases included in the study, histopathological examination revealed DCIS in 20 cases (37%), benign lesions in 18 cases (33%), and B3 lesions in 15 cases (28%). Invasive carcinoma was identified in 1 case (2%). In patients who underwent subsequent surgical excision following stereotactic vacuum-assisted biopsy, no histopathological diagnostic upgrade was observed. Because only one patient was diagnosed with invasive carcinoma, this subgroup was not included in the statistical analysis owing to the insufficient sample size.

Benign and B3 lesions more frequently showed grouped distributions, whereas DCIS lesions were more commonly associated with linear and segmental distributions; this difference was statistically significant ($P$ = 0.01). When distribution patterns were ranked by malignancy rate, the highest rate occurred in the segmental distribution, followed by the linear, grouped, and regional distributions.

Although differences in calcification morphology among pathological diagnosis groups did not reach statistical significance, malignancy rates decreased in the following order: fine linear or fine linear branching, fine pleomorphic, coarse heterogeneous, amorphous, and punctate calcifications. Detailed results regarding morphology and distribution patterns are presented in Table 2.

Independent of these findings, benign lesions were most frequently classified as BI-RADS 4A; B3 lesions were predominantly categorized as BI-RADS 4B; and DCIS cases were most commonly assigned to BI-RADS 4C. This distribution demonstrated a statistically significant association between BI-RADS assessment categories and histopathological diagnoses ($P$ = 0.03).

### Representative Cases

#### Case 1

A screening mammography examination demonstrated grouped amorphous calcifications in the retroareolar region of the left breast. Based on the morphological appearance and

**Table 1.** Mammographic Morphological and Distributional Characteristics of Breast Calcifications

| | N | % |
|---|---|---|
| **Morphology** | | |
| Amorphous | 12 | 22.2 |
| Fine linear | 2 | 3.7 |
| Fine pleomorphic | 22 | 40.7 |
| Coarse heterogeneous | 8 | 14.8 |
| Punctate | 10 | 18.5 |
| **Distribution** | | |
| Regional | 11 | 20.4 |
| Grouped | 33 | 61.1 |
| Linear | 5 | 9.3 |
| Segmental | 5 | 9.3 |

distribution pattern, the findings were categorized as BI-RADS 4A. The Craniocaudal mammographic view demonstrated the calcifications (Figure 1a), and subsequent magnification views were obtained to further characterize their morphology (Figure 1b). Stereotactic vacuum-assisted biopsy was subsequently performed, and radiographic images acquired during the biopsy procedure demonstrated accurate targeting of the calcifications (Figure 1c). Specimen radiography confirmed adequate sampling of the calcifications (Figure 1d). Histopathological examination revealed columnar cell change without atypia accompanied by apocrine metaplasia, consistent with a benign diagnosis.

### Case 2

Mammography revealed grouped fine pleomorphic calcifications in the retroareolar region of the left breast, which were assessed as BI-RADS 4B. The craniocaudal mammographic view demonstrated the clustered calcifications (Figure 2a). Stereotactic vacuum-assisted biopsy was subsequently performed, and the scout image obtained during the biopsy procedure confirmed accurate localization of the target area (Figure 2b). Specimen radiography verified successful retrieval of the calcifications (Figure 2c). Histopathological examination revealed atypical lobular hyperplasia, consistent with a B3 lesion.

### Case 3

Mammographic evaluation, performed in the setting of bloody nipple discharge, revealed newly developed, segmental, fine linear, and pleomorphic calcifications in the lower inner quadrant of the right breast, raising high suspicion for malignancy. The findings were categorized as BI-RADS 5. The c raniocaudal mammographic view demonstrated a segmental distribution of calcifications (Figure 3a), and magnification views further delineated the calcifications' fine linear and pleomorphic morphology (Figure 3b). Stereotactic vacuum-assisted biopsy was subsequently performed, and images obtained during the procedure confirmed accurate targeting of the calcifications (Figure 3c). Specimen radiography demonstrated successful retrieval of the calcifications (Figure 3d). Histopathological examination confirmed the diagnosis of DCIS, which was consistent with the highly suspicious imaging features.

**Table 2.** Association of Calcification Morphology, Distribution Patterns, and BI-RADS Assessment Categories with Histopathological Diagnosis in Non-Mass-Associated Suspicious Breast Calcifications

| Category | Subgroup | Benign n (%) | B3 n (%) | DCIS n (%) | *P* value |
|---|---|---|---|---|---|
| Morphology | Amorphous | 4 (22.2) | 5 (33.3) | 3 (15.0) | 0.29 |
| | Fine linear | 0 (0.0) | 0 (0.0) | 2 (10.0) | |
| | Fine pleomorphic | 3 (16.7) | 7 (46.7) | 11 (55.0) | |
| | Coarse heterogeneous | 3 (16.7) | 3 (20.0) | 2 (10.0) | |
| | Punctate | 8 (44.4) | 0 (0.0) | 2 (10.0) | |
| Distribution | Regional | 4 (22.2) | 3 (20.0) | 3 (15.0) | **0.01** |
| | Grouped | 14 (77.8) | 10 (66.7) | 9 (45.0) | |
| | Linear | 0 (0.0) | 2 (13.3) | 3 (15.0) | |
| | Segmental | 0 (0.0) | 0 (0.0) | 5 (25.0) | |
| BI-RADS | 4A | 18 (100.0) | 2 (13.3) | 4 (20.0) | **0.03** |
| | 4B | 0 (0.0) | 10 (66.7) | 7 (35.0) | |
| | 4C | 0 (0.0) | 3 (20.0) | 8 (40.0) | |
| | 5 | 0 (0.0) | 0 (0.0) | 1 (5.0) | |

DCIS, ductal carcinoma in situ; BI-RADS, Breast Imaging Reporting and Data System. The invasive carcinoma subgroup (n=1) was excluded from the statistical analysis because only one case was identified.

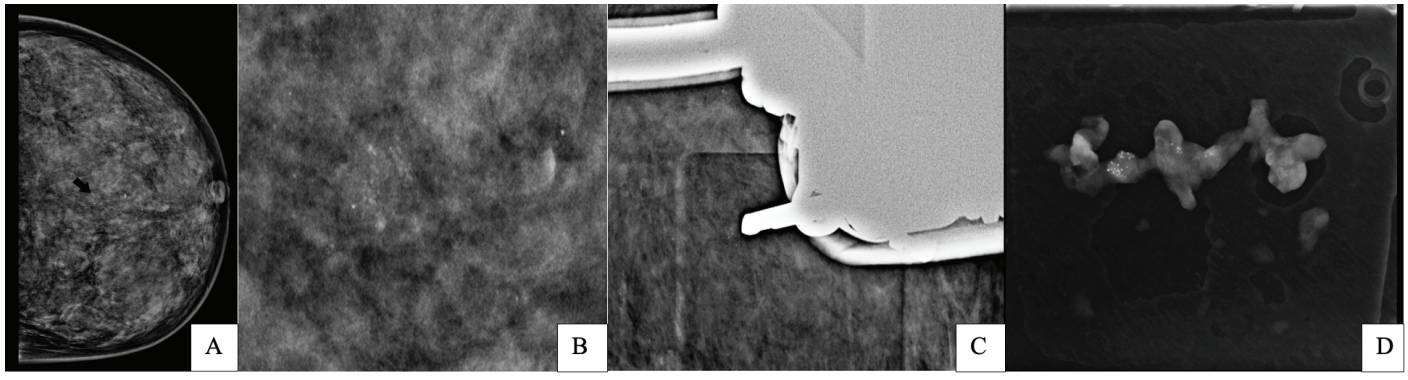



**Figure 1.** BI-RADS 4A calcifications. (a) Craniocaudal mammographic view shows grouped amorphous calcifications in the retroareolar region of the left breast (arrow). (b) Magnification view further characterizes the amorphous morphology. (c) Stereotactic vacuum-assisted biopsy image confirms accurate targeting. (d) Specimen radiograph demonstrates retrieval of calcifications.

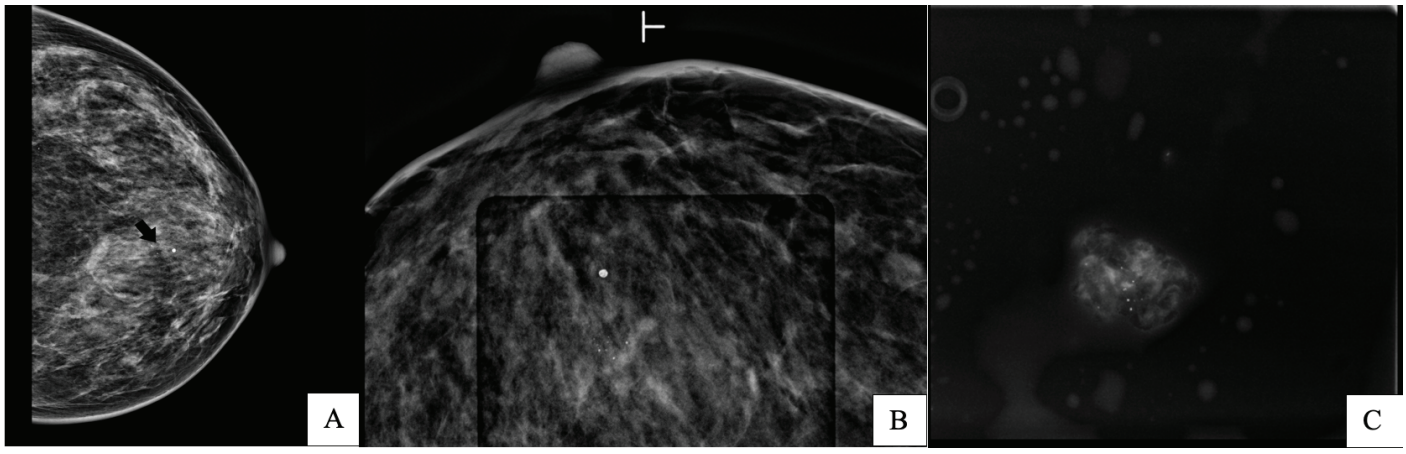



**Figure 2.** BI-RADS 4B calcifications. (a) Craniocaudal mammographic view demonstrates grouped fine pleomorphic calcifications in the retroareolar region of the left breast (arrow). (b) Scout image obtained during stereotactic vacuum-assisted biopsy confirms accurate localization. (c) Specimen radiograph demonstrates retrieval of calcifications.

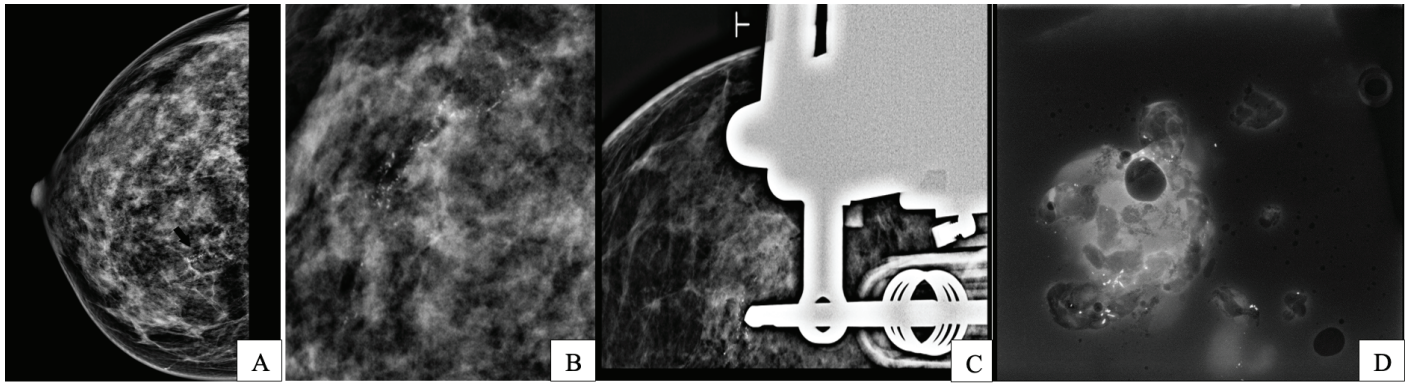



**Figure 3.** BI-RADS 5 calcifications. (a) Craniocaudal mammographic view demonstrates newly developed segmental fine linear and pleomorphic calcifications in the lower inner quadrant of the right breast (arrow). (b) Magnification view highlights the fine linear and pleomorphic morphology. (c) Stereotactic vacuum-assisted biopsy image confirms accurate targeting. (d) Specimen radiograph demonstrates retrieval of calcifications.

## DISCUSSION

In this study, the relationship between mammographic features of non-mass-associated suspicious breast calcifications and histopathological diagnoses was evaluated. The findings demonstrated that calcification distribution patterns and BI-RADS assessment categories were significantly associated with pathological outcomes, whereas morphological characteristics alone were not sufficiently discriminative. In particular, grouped distribution patterns were more frequently observed in benign and B3 lesions, while linear and segmental distribution patterns were more strongly associated with DCIS. These results underscore the importance of calcification distribution patterns and BI-RADS classification in evaluating suspicious breast calcifications and guiding clinical decision-making.

Distribution patterns of calcification were significantly associated with histopathological diagnoses. The higher frequency of grouped distribution in benign and B3 lesions suggests that this pattern predominantly reflects localized and limited proliferative processes. In contrast, the stronger association of linear and segmental distribution patterns with DCIS may be explained by these patterns, which represent pathological processes that extend along the ductal system. Consistent with previous reports, linear and segmental distributions of calcifications, indicative of ductal spread, are associated with a higher risk of malignancy, particularly DCIS.[8,10-12] In this context, the assessment of distribution patterns emerges as an independent and robust indicator for the differential diagnosis of non–mass-associated suspicious breast calcifications.

Analysis of calcification morphology revealed no statistically significant association with histopathological diagnoses, although there was a trend toward higher malignancy rates in certain suspicious morphological subtypes. This finding may be attributed to the well-documented overlap in the mammographic morphologies of calcifications between benign and malignant lesions. Although fine linear, fine linear branching, and fine pleomorphic calcifications have traditionally been associated with an increased risk of malignancy, these morphologic patterns may also be encountered in benign or borderline lesions, thereby limiting their specificity in differential diagnosis.[13] Accordingly, calcification morphology, while informative, appears insufficient as a standalone predictor

of malignancy and should be interpreted in conjunction with distribution patterns and the overall imaging context, particularly in cases of suspicious, non-mass-associated breast calcifications.

Evaluation of BI-RADS assessment categories revealed a significant correlation between the categories and histopathological outcomes in this cohort. The predominance of benign lesions within the BI-RADS 4A category is consistent with prior reports describing this subgroup as comprising findings with a relatively low probability of malignancy.[14,15] In contrast, B3 lesions were more frequently classified as BI-RADS 4B, reflecting their intermediate and uncertain malignant potential. DCIS was most commonly associated with BI-RADS 4C, highlighting the ability of BI-RADS subcategorization to capture progressively increasing malignancy risk. Previous studies have demonstrated that subdivision of BI-RADS category 4 into 4A, 4B, and 4C facilitates more homogeneous risk stratification and supports clinical decision-making by balancing the avoidance of unnecessary invasive procedures with the early detection of breast cancer.[16-20] Nevertheless, given the broad range of malignancy probabilities encompassed by BI-RADS category 4, imaging findings alone remain insufficient for a definitive diagnosis, particularly for calcification-based lesions. Accordingly, histopathological confirmation remains essential for the management of non–mass-associated suspicious breast calcifications classified as BI-RADS 4 and 5.

### Study Limitations

This study has several limitations that should be acknowledged. First, the retrospective design may be associated with inherent selection bias and limited control over imaging acquisition parameters and follow-up protocols. Second, the relatively small sample size may have reduced the statistical power of the analyses and limited the generalizability of the findings. Because only one patient in the cohort was diagnosed with invasive carcinoma, the invasive carcinoma subgroup could not be included in the statistical analyses, precluding a comprehensive evaluation of invasive malignancies. Furthermore, the limited number of cases in specific subgroups restricted detailed statistical analyses of combined morphology-distribution patterns and their associations with histopathological diagnoses, particularly for less frequent combinations such as segmental amorphous or regional fine pleomorphic calcifications.

## CONCLUSION

Subcategorization of suspicious breast calcifications based on distribution patterns and BI-RADS assessment categories contributes to more accurate estimation of malignancy risk and more appropriate clinical management. Our findings emphasize that integrating distribution patterns with standardized BI-RADS subcategories improves risk stratification beyond morphologic assessment alone, thereby helping to balance avoidance of unnecessary invasive procedures with timely detection of early breast cancer. Nevertheless, given the inherent limitations of retrospective analyses and the complexity of calcification-based lesions, further prospective studies with larger patient cohorts are warranted. Future research incorporating additional imaging parameters, such as contrast-enhanced mammography and artificial intelligence-based decision support systems, may further refine diagnostic accuracy and optimize management strategies for non-mass-associated suspicious breast calcifications.

### Ethics

**Ethics Committee Approval:** Ethical approval for this study was obtained from the Erzincan Binali Yıldırım University Non-Interventional Clinical Research Ethics Committee (approval date: 18.09.2025, decision no: 2025-16/08).

**Informed Consent:** Due to the nature of the retrospective study, written informed consent form was waived.

### Footnotes

### Author Contributions

Concept Design – A.S., E.U.B., Z.E., A.B., K.B.M., E.K., S.G.; Data Collection or Processing – A.S., A.B.; Analysis or Interpretation – A.S., S.G.; Literature Review – Z.E., K.B.M.; Writing, Reviewing and Editing – A.S., E.U.B., Z.E., A.B., K.B.M., E.K., S.G.

**Declaration of Interest:** The authors declared no conflicts of interest.

**Funding:** The authors declare that this study has received no financial support.

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