

## Original Research Article

# STUDY OF HISTOMORPHOLOGICAL PATTERNS OF DCIS ASSOCIATED WITH INVASIVE DUCTAL CARCINOMA

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### ABSTRACT

**Background:** Ductal carcinoma in situ (DCIS) frequently coexists with infiltrating duct carcinoma (IDC) of the breast and represents the non-invasive precursor component within the spectrum of breast carcinogenesis. Evaluating the histomorphological patterns of DCIS occurring alongside IDC provides important insights into tumor biology, aggressiveness, and potential prognostic implications. The aim is to study the histomorphological patterns of DCIS associated with IDC.

**Materials and Methods:** Cross-sectional, descriptive study done in the department of Pathology, SVS Medical college, Mahbubnagar for duration of one-year ie from September 2024- september 2025.

**Results:** DCIS was identified in the majority of IDC cases, with solid being the most common architectural pattern, followed by comedo and cribriform patterns. Mixed patterns were frequent, accounting for a substantial proportion of cases where more than one subtype of DCIS coexisted. High-grade DCIS showed a strong association with comedo necrosis and was more commonly present in tumors of higher histological grade. Cases with comedo or mixed architectural patterns demonstrated increased frequency of necrosis and a higher likelihood of lymphovascular invasion in the invasive component. No significant difference was observed in age distribution or tumor size in relation to DCIS subtype.

**Conclusion:** DCIS accompanying IDC displays diverse architectural patterns, with solid and comedo types being most prevalent. High-grade nuclear features and comedo necrosis are more frequently associated with aggressive invasive carcinoma characteristics. Understanding the histomorphological spectrum of DCIS in association with IDC is essential, as it may provide prognostic information and help refine therapeutic decision-making.

**Keywords:** Ductal carcinoma in situ (DCIS), Infiltrating duct carcinoma (IDC).

## INTRODUCTION

Breast cancer is the most common malignancy among women worldwide and remains a leading cause of cancer-related morbidity and mortality. Histologically, invasive duct carcinoma (IDC) of no special type constitutes the predominant subtype, accounting for nearly 70–80% of all invasive breast cancers. A significant proportion of IDC cases demonstrate an associated in situ component, most commonly ductal carcinoma in situ (DCIS), which

represents a non-invasive neoplastic proliferation confined to the terminal ductal-lobular units. DCIS is widely recognized as the direct precursor lesion to IDC and forms an integral part of the multistep progression model of breast carcinogenesis.<sup>[1]</sup>

DCIS is characterized by a wide spectrum of architectural patterns, nuclear grades, and necrotic features, reflecting considerable biological heterogeneity. The architectural subtypes—solid, comedo, cribriform, micropapillary, and papillary—often coexist in various combinations, giving rise to

mixed-pattern lesions. Nuclear grading further refines this diversity, with high-grade DCIS frequently demonstrating marked pleomorphism, prominent nucleoli, increased mitotic activity, and an association with comedo-type necrosis. These histomorphological variations are not merely descriptive; they have important clinical implications, as they correlate with recurrence risk, progression potential, and prognostic behavior.<sup>[2]</sup>

The coexistence of DCIS with invasive carcinoma is of particular interest. Several studies have emphasized that the characteristics of the in-situ component can influence the biology of the invasive tumor. High-grade DCIS, extensive comedo necrosis, and mixed architectural patterns have been linked with aggressive features in the invasive component, including higher histological grade, lymphovascular invasion, and nodal metastasis. Understanding these associations is essential, as they may help refine risk stratification, influence treatment planning—especially decisions regarding margin assessment, radiotherapy, and systemic therapy—and contribute to more accurate prognostication.<sup>[3]</sup>

Despite substantial research, variations in the distribution of architectural patterns, frequency of mixed patterns, and prevalence of nuclear grades have been reported across populations. Ethnic, genetic, and environmental differences, diagnostic thresholds, and institutional reporting practices may contribute to these disparities. Furthermore, the correlation between DCIS morphology and the histopathological characteristics of the invasive component is still evolving, with some studies showing strong associations while others report inconsistent findings.<sup>[4-7]</sup>

In this context, detailed assessment of the histomorphological features of DCIS occurring alongside IDC is essential, particularly in diverse clinical settings. Evaluating the spectrum of DCIS architecture, nuclear grade, and necrotic patterns—and correlating these with the invasive tumor features—can enhance our understanding of tumor progression and provide insights relevant to both pathologists and clinicians.

**Aim of the study:** To study of histomorphological patterns of DCIS associated with invasive ductal carcinoma (no special type)”

#### **Objectives**

- To study the histomorphological patterns of DCIS associated with IDC
- To analyze their frequency, architectural subtypes, nuclear grading, necrosis
- To Correlate with the histological features of the invasive component

## **MATERIALS AND METHODS**

Institutional Ethics Committee approval was obtained prior to study initiation.

**Study Design:** Cross-sectional, descriptive study

**Place of study:** Department of Pathology, SVS Mediacollege, Mahbubnagar

**Study duration:** one year ie from -ie from September 2024- september 2025

**Sample size:** 70

#### **Inclusion Criteria**

- Histologically confirmed IDC (Not Otherwise Specified and special subtypes where IDC component is present)
- Presence of an in situ ductal component (DCIS) in the same specimen
- Adequate tissue preservation and representative sections available for evaluation

#### **Exclusion Criteria**

- Specimens with invasive carcinoma lacking DCIS
- Pure DCIS without invasive carcinoma
- Recurrent tumors or previously treated (post-chemotherapy/post-radiotherapy) breast cancers
- Inadequate, autolyzed, or poorly preserved tissue samples

#### **Methodology**

##### **Specimen Processing and Histopathological Evaluation**

All specimens were fixed in 10% neutral buffered formalin for adequate duration, followed by routine tissue processing. Representative tissue sections (average 10–15 blocks per mastectomy specimen and 3–6 blocks per lumpectomy specimen) were embedded in paraffin, sectioned at 4–5 μm thickness, and stained with Hematoxylin and Eosin (H&E).

Microscopic evaluation was performed by two independent pathologists to minimize interobserver variation.

##### **Assessment of DCIS Component**

DCIS was classified using established morphological criteria based on:

##### **Architectural Pattern**

- Solid
- Comedo
- Cribriform
- Micropapillary
- Papillary
- Mixed pattern (presence of >1 architectural subtype)

##### **Nuclear Grading**

**Graded as low, intermediate, or high, based on:**

- Nuclear size and pleomorphism
  - Chromatin characteristics
  - Presence of nucleoli
  - Mitotic activity
- (According to WHO and modified Lagios criteria.)

##### **Necrosis**

**Presence of comedo-type necrosis was specifically noted and classified as:**

- Present
- Absent

The extent of DCIS (focal vs. extensive) was recorded where applicable.

### Assessment of the Invasive Component

The IDC portion was evaluated for the following parameters:

- Histological Grade (Nottingham modification of Scarff-Bloom-Richardson system)
- Lymphovascular Invasion (LVI) – present/absent
- Stromal Reaction – desmoplastic, inflammatory, or mixed
- Perineural Invasion – present/absent
- Tumor Size – measured in centimeters
- Axillary Lymph Node Status – number of nodes examined and number positive

Correlation was made between DCIS architectural pattern, nuclear grade, necrosis, and invasive tumor features, especially tumor grade, LVI, and lymph node metastasis.

**Data Collection and Statistical Analysis:** All findings were entered into a structured datasheet. Statistical analysis was performed using SPSS (version XX) or equivalent statistical software. Descriptive statistics (frequency, percentages, mean, standard deviation) were used for baseline parameters. Chi-square test or Fisher's exact test was used to determine associations between DCIS patterns and invasive carcinoma

characteristics. A p-value < 0.05 was considered statistically significant.

## RESULTS

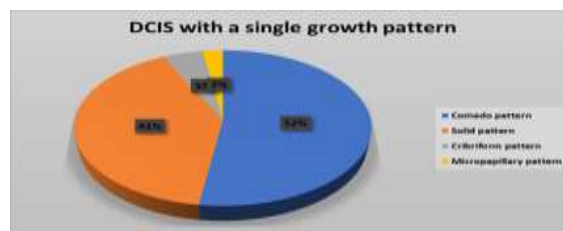
**Age wise distribution of occurrence of DCIS with IDC:** In the present study comprising 70 cases of invasive duct carcinoma with coexistent DCIS, the highest incidence was observed in the 50–60-year age group, accounting for 35 cases (50%). This was followed by the 40–50-year age group with 18 cases (25.7%). The 60–70-year age group constituted 11 cases (15.7%), while patients above 70 years formed the smallest subset with 6 cases (8.6%). Overall, the majority of cases occurred between the fourth and sixth decades of life, indicating a peak incidence in middle-aged to early postmenopausal women.

**Patterns of DCIS:** In the present study, single-pattern DCIS was observed in 42 cases (60%), while mixed architectural patterns were identified in 28 cases (40%). Thus, single-pattern DCIS constituted the majority, although a substantial proportion of cases exhibited mixed morphology, reflecting the inherent histological heterogeneity of the in situ component associated with invasive duct carcinoma.

**Table 1: DCIS with a single growth pattern.**

Single DCIS Pattern	Number of Cases	Percentage (%)
Comedo pattern	22	52.4%
Solid pattern	17	40.5%
Cribriform pattern	2	4.8%
Micropapillary pattern	1	2.4%
Total	42	100%

Among the 42 cases exhibiting a single architectural pattern of DCIS, the comedo pattern was the most common, accounting for 22 cases (52.4%). This was followed by the solid pattern in 17 cases (40.5%). Cribriform and micropapillary patterns were less frequently encountered, comprising 2 cases (4.8%) and 1 case (2.4%), respectively. Thus, high-grade patterns such as comedo and solid predominated among the single-pattern DCIS lesions.

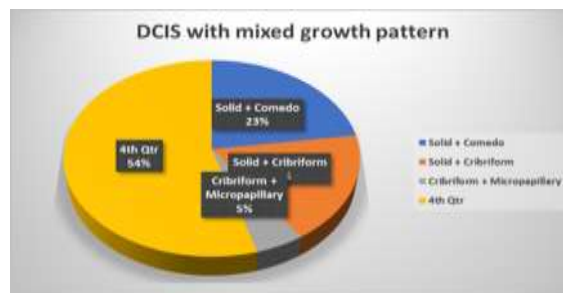


**Figure 1: Pie diagram showing DCIS with a single growth pattern.**

**Table 2: DCIS with mixed growth pattern**

Mixed DCIS Pattern	Number of Cases	Percentage (%)
Solid + Comedo	14	50.0%
Solid + Cribriform	11	39.3%
Cribriform + Micropapillary	3	10.7%
Total	28	100%

Among the 28 cases showing mixed architectural patterns of DCIS, the Solid + Comedo combination was the most common, observed in 14 cases (50%). This was followed by the Solid + Cribriform pattern in 11 cases (39.3%). The Cribriform + Micropapillary combination was less frequent, accounting for 3 cases (10.7%). Overall, mixed patterns were dominated by combinations involving solid and comedo components, reflecting the predominance of high-grade morphological variants in DCIS associated with invasive carcinoma.



**Figure 2: Pie diagram showing DCIS with a mixed growth pattern.**

Among high-grade DCIS cases (N = 42), the majority were associated with Bloom–Richardson Grade III invasive carcinoma (19 cases, 45.2%), followed by Grade II (16 cases, 38.1%) and Grade I (7 cases, 16.7%). Intermediate-grade DCIS (N = 22) most frequently corresponded to Grade II IDC (11 cases, 50%), followed by Grade I (6 cases, 27.3%) and Grade III (5 cases, 22.7%). In contrast, low-grade DCIS (N = 6) showed a strong association with low-

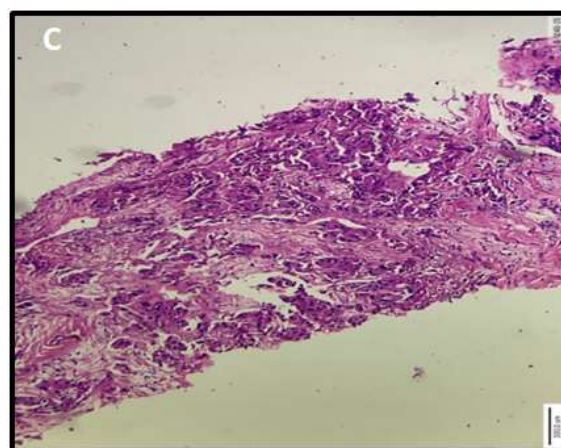
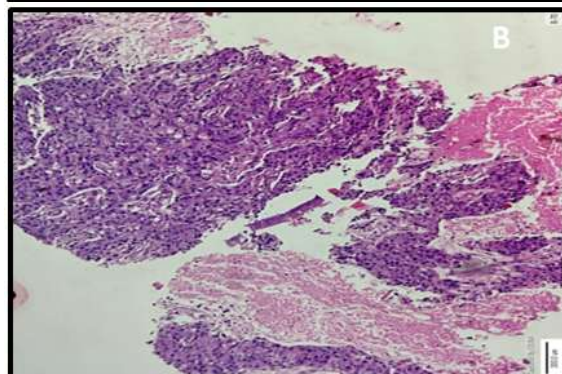
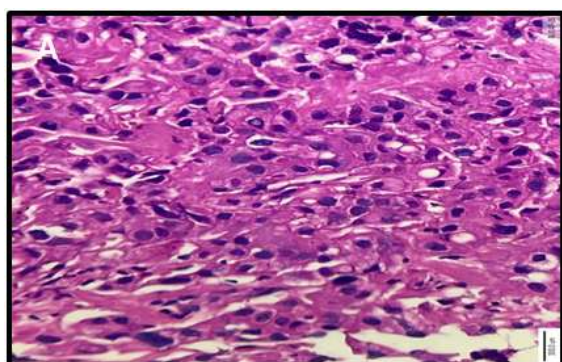
grade invasive carcinomas, with 5 cases (83.3%) corresponding to Grade I IDC and only 1 case (16.7%) associated with Grade II IDC; none were associated with Grade III. These findings indicate a clear correlation between the nuclear grade of DCIS and the histological grade of the invasive component, with high-grade DCIS more frequently accompanying higher-grade IDC.

**Table 3: Association of DCIS grading with Bloom Richardson grading of IDC.**

Bloom–Richardson Grade	High-Grade DCIS (N = 42)	Intermediate-Grade DCIS (N = 22)	Low-Grade DCIS (N = 6)
Grade I	7(16.7%)	6(27.3%)	5(83.3%)
Grade II	16( 38.1%)	11(50.0%)	1(16.7%)
Grade III	19(45.2%)	5( 22.7%)	-
Total	42( 100%)	22(100%)	6(100%)

### Statistical Association Between DCIS Grade and IDC Grade

A Chi-square test of independence was performed to evaluate the association between DCIS nuclear grade and the Bloom–Richardson histological grade of invasive duct carcinoma (IDC). The observed distribution showed that high-grade DCIS frequently corresponded to Grade III IDC, whereas low-grade DCIS was predominantly associated with Grade I IDC. Intermediate-grade DCIS demonstrated a moderate overlap with Grade II IDC. with p value < 0.01. The Chi-square value (14.92) exceeded the critical value for 4 degrees of freedom at the 0.01 level ( $\chi^2 = 13.28$ ), indicating a statistically significant association. This means the relationship between DCIS grade and IDC grade is unlikely to have occurred by chance, confirming a strong, positive correlation between the nuclear grade of DCIS and the histological grade of the invasive component.



**Figure 3: Histopathological images**

**A.40x H and E shows Desmoplastic stroma**

**B.10x H and E shows Foci of hemorrhage and necrosis are seen.**

**C.10X H and E shows Invasive tumor cells arranged in cords, nests, trabeculae, sheets, or tubules infiltrating fibrous stroma**

## DISCUSSION

The present study evaluated the architectural patterns and nuclear grades of the in situ (DCIS) component associated with invasive breast carcinoma and compared the findings with previously published literature.

### Comparative studies related to age distribution

In the present study the majority of cases occurred between the fourth and sixth decades of life, indicating a peak incidence in middle-aged to early postmenopausal women. In the study by Apoorva et al,<sup>[7]</sup> study the mean age of patients with IDC and coexisting DCIS was 46.4 ± 11.7 years, indicating a predominance in premenopausal and perimenopausal women. Similarly, Gao et al,<sup>[8]</sup> study also noted that the peak incidence of DCIS with invasive carcinoma occurred in the 40–55-year age group, with only 18% of cases seen beyond 60 years of age. Basu et al,<sup>[9]</sup> study reported a comparable mean age (47.3 years), confirming that DCIS–IDC coexistence is uncommon at the extremes of reproductive age (2).

In contrast, Vikram et al,<sup>[10]</sup> observed fewer cases in women above 60 years (27%), reinforcing that mixed invasive and in situ disease is primarily a mid-life pathology.

Comparative studies related to architectural patterns

In the present study, single-pattern DCIS was observed in 42 cases (60%), while mixed architectural patterns were identified in 28 cases (40%). Thus, single-pattern DCIS constituted the majority, although a substantial proportion of cases exhibited mixed morphology, reflecting the inherent histological heterogeneity of the in situ component associated with invasive duct carcinoma. Apoorva et al,<sup>[7]</sup> reported pure (single) DCIS patterns in 60% of cases and mixed patterns in 40%. Comparable distributions were described by Vikram et al,<sup>[15]</sup> (55% single; 45% mixed), and earlier works by Sanders et al,<sup>[11]</sup> (58% single; 42% mixed) and Renshaw & Gould,<sup>[12]</sup> (52% single; 48% mixed) also fall within this range (3–5). These findings collectively indicate that mixed architectural patterns are present in nearly half of DCIS lesions, suggesting significant morphological heterogeneity.

#### **Comparative studies related to the single (pure) architectural subtypes**

In the present study, Among the 42 cases exhibiting a single architectural pattern of DCIS, the comedo pattern was the most common, accounting for 22 cases (52.4%). This was followed by the solid pattern in 17 cases (40.5%). Cribriform and micropapillary patterns were less frequently encountered, comprising 2 cases (4.8%) and 1 case (2.4%), respectively. Thus, high-grade patterns such as comedo and solid predominated among the single-pattern DCIS lesions. Apoorva et al,<sup>[7]</sup> found that the solid pattern (27.5%) was most common, followed by comedo (17.5%), cribriform (12.5%), and micropapillary (2.5%). Similar distributions are described by Page et al,<sup>[13]</sup> who reported solid (30%), cribriform (25%), and comedo (20%) patterns as the predominant types (6). The EORTC 10853 trial by Bijker et al,<sup>[14]</sup> also demonstrated a high proportion of solid and cribriform DCIS. These consistent findings suggest that the solid and comedo patterns account for the majority of pure DCIS lesions.

#### **Comparative studies related to the mixed architectural subtypes**

In the present study Mixed architectural combinations in the present study, such as solid + comedo, solid + cribriform, and cribriform + micropapillary, match closely with the observations by Vikram et al,<sup>[10]</sup> who reported solid + comedo (52%) and solid + cribriform (42%) as the most frequent mixed patterns. Studies by Matsen et al,<sup>[15]</sup> Bharathi et al,<sup>[16]</sup> and Liberman et al,<sup>[17]</sup> similarly emphasize that solid + comedo represents the most biologically aggressive and most common mixed pattern of DCIS (8–10). These combinations are particularly significant because they frequently correlate with higher nuclear grades and larger in situ disease extent.

With respect to nuclear grading, in our study among high-grade DCIS cases (N = 42), the majority were associated with Bloom–Richardson Grade III invasive carcinoma (19 cases, 45.2%), followed by Grade II (16 cases, 38.1%) and Grade I (7 cases, 16.7%). Intermediate-grade DCIS (N = 22) most frequently corresponded to Grade II IDC (11 cases, 50%), followed by Grade I (6 cases, 27.3%) and Grade III (5 cases, 22.7%). where as Apoorva et al,<sup>[7]</sup> reported high-grade DCIS in 45%, intermediate grade in 43%, and low grade in 12%. These figures align with modern studies such as Wong et al,<sup>[18]</sup> who also reported a predominance of high-grade DCIS, especially in lesions associated with invasive carcinoma.

Overall, the comparison of the present study with multiple published series demonstrates a high degree of concordance. The predominance of the solid and comedo patterns, the frequent occurrence of mixed architectural combinations, and the high proportion of high-grade nuclei reflect the biological aggressiveness of DCIS that coexists with invasive carcinoma. Literature also supports that mixed-pattern and high-grade DCIS show a stronger association with high-grade invasive ductal carcinoma, multifocality, and higher recurrence potential. These correlations underline the importance of detailed morphological assessment of the in situ component for prognostication and management planning.

## **CONCLUSION**

In this study of 70 cases of invasive duct carcinoma with an associated in situ component, ductal carcinoma in situ (DCIS) demonstrated considerable architectural and nuclear heterogeneity. The majority of lesions exhibited single architectural patterns, predominantly comedo and solid types, while a substantial proportion showed mixed patterns, most commonly the solid + comedo combination. High-grade nuclear features were the most frequent, underscoring the biologically aggressive nature of DCIS when coexisting with invasive carcinoma.

A statistically significant association was identified between DCIS nuclear grade and the Bloom–Richardson grade of the invasive component ( $\chi^2 = 14.92$ ,  $p < 0.01$ ). High-grade DCIS showed a strong correlation with high-grade IDC, whereas low-grade DCIS was predominantly associated with low-grade invasive tumors. This concordance highlights the continuum of progression from in situ to invasive disease and reinforces the relevance of DCIS morphology in predicting invasive tumor behavior.

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