

Tumor Budding in Invasive Breast Carcinoma: Association With Histopathological Features and Hormone Receptor Status

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Abstract

Background

Tumor budding (TB), characterized by the presence of isolated tumor cells or small clusters of tumor cells at the invasive front or within the tumor parenchyma, is recognized as a potential histopathological indicator of tumor aggressiveness and metastatic potential. The present study evaluated the extent of TB in invasive breast carcinoma and investigated its association with key histopathological characteristics and hormone receptor status.

Methodology

This prospective observational study included 94 histopathologically confirmed cases of invasive breast carcinoma treated with modified radical mastectomy. TB was evaluated on hematoxylin and eosin (H&E)-stained sections and classified as peripheral tumor budding (PTB) and intratumoral tumor budding (iTB), with each categorized as low, intermediate, or high using a study-specific scoring approach adapted from published TB grading methods, rather than a universally validated breast-specific scoring system. Clinicopathological characteristics and immunohistochemical expression of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2/neu were assessed. Associations between TB and clinicopathological variables were evaluated using the chi-square test, with a p-value <0.05 considered statistically significant.

Results

PTB was categorized as low, intermediate, and high in 28 (29.8%), 38 (40.4%), and 28 (29.8%) cases, respectively, whereas iTB was low, intermediate, and high in 34 (36.2%), 46 (48.9%), and 14 (14.9%) cases, respectively. PTB was significantly associated with necrosis, lymph node metastasis, and perineural invasion, whereas iTB was significantly associated with necrosis, lymph node metastasis, and lymphovascular invasion ($p < 0.05$).

Conclusions

TB is significantly associated with selected adverse clinicopathological features in invasive breast carcinoma. Its assessment on routine H&E sections provides a simple and potentially cost-effective histopathological adjunct to conventional pathological evaluation.

Categories: Pathology, Oncology, Healthcare Technology

Keywords: hormone receptor status, intratumoral budding, invasive breast carcinoma, lymphovascular invasion, peripheral tumor budding, tumor budding

Introduction

Breast carcinoma is the most frequently diagnosed malignancy among women worldwide and a leading cause of cancer-related mortality, accounting for nearly a quarter of all cancers in women [1]. In India, breast cancer has become the most common malignancy among women, a trend associated with demographic, reproductive, hormonal, and lifestyle-related factors [2]. These trends underscore the need for cost-effective prognostic markers capable of predicting tumor aggressiveness and guiding therapy [3,4].

Breast carcinoma is a biologically heterogeneous disease [5]. Molecular and immunohistochemical classification into distinct subtypes, including luminal A, luminal B, human epidermal growth factor receptor 2 (HER2)-enriched, and triple-negative subtypes, has transformed clinical management by enabling endocrine and targeted therapy [6]. However, established prognostic parameters such as tumor size,

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Nottingham histological grade, Tumor-Node-Metastasis (TNM) stage, nodal status, and lymphovascular invasion (LVI) provide important prognostic information but may not fully characterize the invasive behavior of individual tumors. Therefore, additional morphological features warrant investigation to determine whether they can complement established clinicopathological parameters in assessing tumor aggressiveness [7].

Tumor budding (TB), defined as isolated single tumor cells or small clusters of up to four cells at the invasive front or within the tumor parenchyma, is considered a morphological correlate of epithelial-mesenchymal transition (EMT) and has emerged as one such marker [8]. First described by Imai in gastric carcinoma [9], TB has since been shown to correlate with lymph node metastasis, vascular invasion, and poor differentiation in colorectal, esophageal, pancreatic, lung, and breast malignancies [10,11]. Two patterns are recognized: peripheral tumor budding (PTB), occurring at the tumor-stroma interface, and intratumoral budding (iTB), located within the tumor parenchyma. Although iTB comprises the same neoplastic cell population as the main tumor, it is identified morphologically as discrete single tumor cells or small clusters of up to four cells separated from larger tumor cell aggregates by intervening tissue. Thus, the distinction between PTB and iTB is based primarily on their anatomical location and morphological arrangement rather than on differences in cellular identity [12-15].

TB is an established International Tumor Budding Consensus Conference (ITBCC)-standardized prognostic parameter in colorectal carcinoma, whereas its prognostic and reporting implications in breast carcinoma remain under investigation [16,17]. In breast carcinoma, high TB has been linked to nodal metastasis and aggressive tumor behavior and reduced disease-free survival, yet it is not part of routine reporting because standardized scoring criteria are still evolving [18]. Its relationship with hormone receptor status also remains inconsistent, with some studies reporting an association between high TB and triple-negative or HER2-enriched tumors and others finding none [19]. At the molecular level, TB has been proposed as a morphological correlate of EMT, during which tumor cells downregulate E-cadherin and upregulate vimentin under the influence of transforming growth factor beta, Wnt/ β -catenin, Snail, Twist, and Zeb1 signalling, thereby acquiring increased migratory and invasive potential [20,21].

TB can be identified on routine hematoxylin and eosin (H&E)-stained sections without additional cost, making it potentially useful in resource-limited settings such as India. Despite accumulating evidence supporting its prognostic relevance, the association of TB with conventional histopathological parameters and hormone receptor status in invasive breast carcinoma remains incompletely characterized. This study was therefore designed to evaluate tumor cell budding in invasive breast carcinoma and to correlate it with clinicopathological parameters, including tumor size, histological grade, LVI, lymph node status, and hormone receptor expression of estrogen receptor (ER), progesterone receptor (PR), and HER2/neu.

Materials And Methods

Study design and participants

This prospective observational study was conducted in the Department of Pathology and Multidisciplinary Research Unit (MRU), Baba Raghav Das Medical College, Gorakhpur, India, from December 17, 2025, to July 30, 2026, over a period of seven months. Patients with histopathologically confirmed invasive breast carcinoma who underwent modified radical mastectomy during the study period were enrolled, irrespective of distant metastatic status, if they fulfilled the remaining eligibility criteria. The required sample size was estimated to be 94, based on a reported prevalence of 14.8%, a 95% confidence level ($Z = 1.96$), and an allowable error of 7%.

Inclusion and exclusion criteria

Patients of all ages and either sex with histopathologically confirmed invasive breast carcinoma, adequate tissue for histopathological and immunohistochemical evaluation, and documented informed written consent were included. Distant metastatic status was not an independent exclusion criterion. Cases with recurrent breast carcinoma, autolyzed or poorly fixed specimens, inadequate tissue for histopathological or immunohistochemical evaluation, absence of informed consent, or a history of neoadjuvant chemotherapy were excluded.

Ethical approval

The study was approved by the Institutional Human Ethical Committee, Baba Raghav Das Medical College (approval number: 267/IHEC/2025).

Histopathological assessment of tumor budding

Grossing, tissue processing, and H&E staining were performed using standard laboratory protocols. Histological grade was assigned using the modified Nottingham histological grading (Elston-Ellis modification of the Bloom-Richardson) system [22,23]. The tumor invasive front was screened using a 4 $\times$ objective to identify areas with prominent TB. Individual tumor buds were subsequently examined and counted using a 40 $\times$ objective. Total optical magnification was determined according to the objective and

eyepiece magnifications of the microscope. TB was assessed using a three-tier scoring system adapted from published TB grading approaches [24,25]. The ITBCC criteria were developed for colorectal carcinoma; the thresholds used in this study should be considered study-specific and not a universally validated breast-specific scoring system. A tumor bud was defined as an isolated single tumor cell or a small cluster of fewer than five tumor cells. PTB was assessed at the tumor-stroma interface, whereas iTB was assessed separately within the tumor parenchyma, away from the invasive front [26]. Individual buds were identified by their discrete morphological arrangement and separation from larger tumor cell aggregates. Separate tumor nodules were not classified as tumor buds. Tumor buds were counted in 10 consecutive microscopic fields using a 40× objective, and the mean number of buds per field was calculated. Based on the mean bud count, cases were categorized as low-grade (0-4 buds/field), intermediate-grade (5-9 buds/field), or high-grade (≥10 buds/field) [27]. This three-tier scoring approach was adapted for the present study from published TB grading approaches and should not be interpreted as a universally validated breast-specific scoring system. Tumor stroma percentage was assessed at 10× magnification in a representative field at the invasive front and categorized as low (<50%) or high (>50%) [28,29].

Tumor budding and clinicopathological associations

ER, PR, HER2/neu, and pancytokeratin expression were assessed on formalin-fixed paraffin-embedded sections using a standard polymer horseradish peroxidase immunohistochemistry technique with appropriate positive and negative controls. ER and PR nuclear staining were scored using the Allred method (proportion score + intensity score; range: 0-8), with a total score of 3-8 considered positive. HER2/neu membranous staining was interpreted according to the recommendations of the American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP), with immunohistochemical expression categorized as 0/1+, 2+, or 3+ [30-32].

Statistical analysis

Statistical analyses were performed using SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages. Associations between TB categories (PTB and iTB) and clinicopathological variables, including tumor size, histological grade, necrosis, lymph node status, LVI, perineural invasion, tumor stroma percentage, age, and hormone receptor status, were assessed using the chi-square (χ^2) test. Fisher's exact test was applied when the assumptions for the chi-square test were not met, and the specific comparisons analyzed using Fisher's exact test are reported accordingly in the results. All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

Results

The study included 94 patients with histopathologically confirmed invasive breast carcinoma. The baseline demographic and histopathological characteristics of the study cohort are summarized in Table 1. Most patients were aged >50 years (56, 59.6%) and were postmenopausal (58, 61.7%). The right breast was involved slightly more frequently than the left breast (49, 52.1% vs. 45, 47.9%). Tumors measuring 2-5 cm were the most common size category, accounting for 49 (52.1%) cases, followed by tumors >5 cm (25, 26.6%) and ≤2 cm (20, 21.3%). Grade II tumors were the most frequent histological grade (42, 44.7%), followed by Grade III (29, 30.9%) and Grade I (23, 24.5%). Invasive breast carcinoma of no special type constituted the predominant histological type (91, 96.8%), while mucinous/medullary carcinomas accounted for 3 (3.2%) cases. Lymphovascular invasion and perineural invasion were present in 41 (43.6%) and 29 (30.9%) cases, respectively, while lymph node metastasis was identified in 49 (52.1%) patients. A ductal carcinoma in situ component was present in 28 (29.8%) tumors, and a high tumor stroma percentage (>50%) was observed in 44 (46.8%) cases.

Parameter	Category	n (%)
Age	≤50 years	38 (40.4)
	>50 years	56 (59.6)
Menopausal status	Premenopausal	36 (38.3)
	Postmenopausal	58 (61.7)
Laterality	Right breast	49 (52.1)
	Left breast	45 (47.9)
Tumor size	≤2 cm (T1)	20 (21.3)
	2–5 cm (T2)	49 (52.1)
	>5 cm (T3)	25 (26.6)
Histological grade	Grade I	23 (24.5)
	Grade II	42 (44.7)
	Grade III	29 (30.9)
Histological type	IBC–NST	91 (96.8)
	Mucinous/Medullary	3 (3.2)
Lymphovascular invasion	Present	41 (43.6)
Perineural invasion	Present	29 (30.9)
Lymph node metastasis	Present	49 (52.1)
DCIS component	Present	28 (29.8)
Tumor stroma percentage	High (>50%)	44 (46.8)

TABLE 1: Baseline demographic and histopathological characteristics of the study cohort (n = 94).

Data are presented as n (%), unless otherwise specified. Percentages are calculated based on the total study population (n = 94).

IBC–NST: invasive breast carcinoma of no special type; DCIS: ductal carcinoma in situ

TB was predominantly of intermediate grade in both compartments. PTB was classified as low, intermediate, and high grade in 28 (29.8%), 38 (40.4%), and 28 (29.8%) cases, respectively, whereas iTB was low, intermediate, and high grade in 34 (36.2%), 46 (48.9%), and 14 (14.9%) cases, respectively (Table 2). TB grade was determined based on the mean number of buds counted across 10 consecutive microscopic fields using a 40× objective. High-grade budding was more frequent in the peripheral compartment than in the intratumoral compartment; however, no statistical comparison between PTB and iTB grades was performed. On H&E examination, low-grade budding appeared as occasional isolated tumor cells or small clusters at the invasive front, whereas high-grade budding was characterized by numerous isolated cells and small tumor cell clusters infiltrating the surrounding stroma (Figures 1A, 1B). Pancytokeratin immunohistochemistry further highlighted these isolated and clustered tumor cells at the invasive front, confirming the presence of tumor buds (Figures 2A, 2B).

Budding type	Tumor budding grade (mean buds per field)	n (%)
PTB	Low (0–4)	28 (29.8)
	Intermediate (5–9)	38 (40.4)
	High (≥10)	28 (29.8)
iTB	Low (0–4)	34 (36.2)
	Intermediate (5–9)	46 (48.9)
	High (≥10)	14 (14.9)

TABLE 2: Distribution and grading of peripheral and intratumoural tumor budding in the study population (n = 94).

Data are presented as n (%). Tumor budding grade was based on the mean number of buds per field across 10 consecutive microscopic fields: low (0–4), intermediate (5–9), and high (≥10).

PTB: peripheral tumor budding; iTB: intratumoural tumor budding

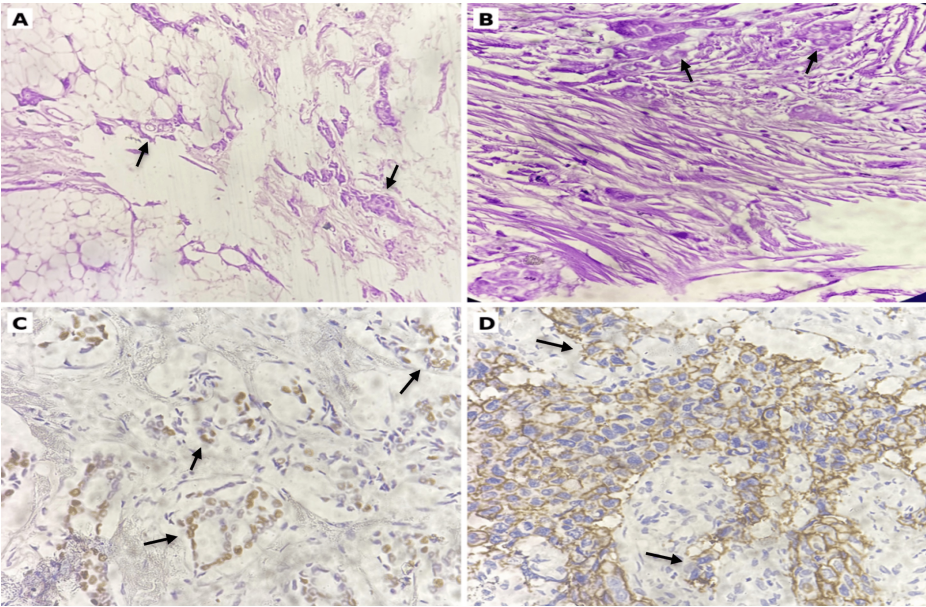


FIGURE 1: Representative histopathological and immunohistochemical features of tumor budding and hormone receptor expression in invasive breast carcinoma.

(A) Low-grade tumor budding at the invasive tumor front (hematoxylin and eosin (H&E), ×10) (arrowheads). (B) High-grade peripheral tumor budding characterized by numerous isolated tumor cells and small tumor cell clusters infiltrating the surrounding stroma (H&E, ×40) (arrowheads). (C) Nuclear immunoreactivity for estrogen receptor (ER) in tumor cells forming tubular structures (immunohistochemistry (IHC), ×40) (arrowheads). (D) Human epidermal growth factor receptor 2 (HER2) overexpression showing intense, complete circumferential membranous staining (3+) in tumor cells (IHC, ×40).

Source: Original images from the present study.

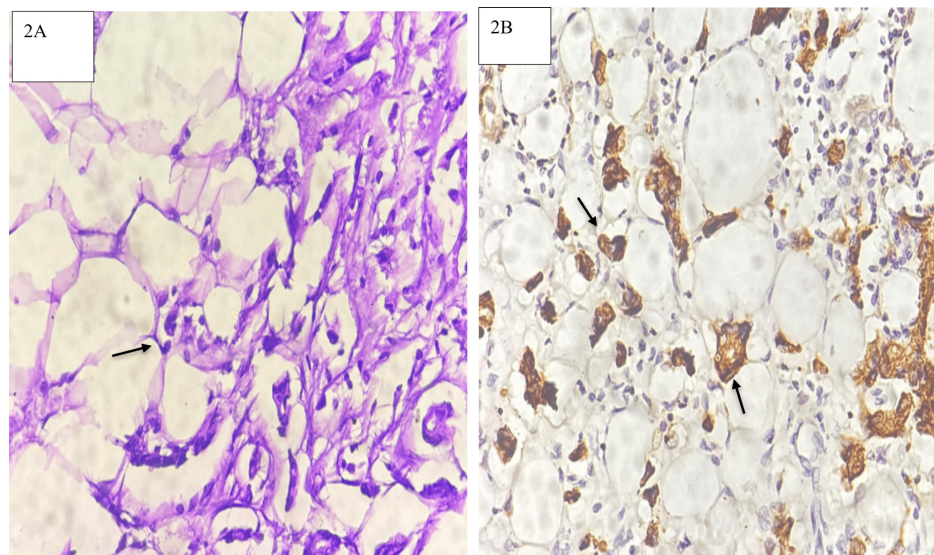


FIGURE 2: Representative histological and immunohistochemical features of tumor budding in invasive breast carcinoma.

(A) Hematoxylin and eosin (H&E)-stained section showing the tumor–stroma interface, with isolated tumor cells and small clusters consistent with tumor budding (arrowheads; 40× objective). (B) Pan-cytokeratin (PanCK) immunohistochemical staining highlighting tumor cells and small tumor-cell clusters in a separate representative field. The H&E and PanCK images are from different fields of view and do not depict the exact same microscopic structures.

Source: Original images from the present study.

Association of tumor budding with adverse histopathological features

PTB showed significant associations with necrosis ($p = 0.021$), lymph node metastasis ($p = 0.010$), and perineural invasion ($p = 0.025$). No statistically significant associations were observed between PTB grade and tumor size >5 cm ($p = 0.106$), LVI ($p = 0.051$), high tumor stroma percentage $>50\%$ ($p = 0.274$), or Grade III histology ($p = 0.095$). Age >50 years was also not significantly associated with PTB grade ($p = 0.952$) (Table 3). Higher PTB grades were significantly associated with necrosis, lymph node metastasis, and perineural invasion.

Parameter	Low PTB	Intermediate PTB	High PTB	Pearson χ^2	P-value
Tumor size >5 cm	4 (16.0%)	10 (40.0%)	11 (44.0%)	4.48	0.106
Necrosis present	7 (18.4%)	14 (36.8%)	17 (44.7%)	7.755	0.021*
Lymph node metastasis	10 (20.4%)	18 (36.7%)	21 (42.9%)	9.237	0.010*
Lymphovascular invasion	8 (19.5%)	16 (39.0%)	17 (41.5%)	5.941	0.051
Perineural invasion	5 (17.2%)	10 (34.5%)	14 (48.3%)	7.395	0.025*
High tumor stroma (>50%)	10 (22.7%)	18 (40.9%)	16 (36.4%)	2.590	0.274
Grade III	6 (20.7%)	10 (34.5%)	13 (44.8%)	4.717	0.095
Age >50 years	17 (30.4%)	23 (41.1%)	16 (28.6%)	0.098	0.952

TABLE 3: Association of PTB with histopathological parameters (n = 94).

Data are presented as n (%), with percentages calculated within each row/category total. Pearson's χ^2 test was used to assess associations between PTB grade and histopathological parameters. P-values <0.05 were considered statistically significant; asterisks (*) indicate statistically significant associations. Significant associations were observed for necrosis, lymph node metastasis, and perineural invasion, whereas tumor size, lymphovascular invasion, high tumor stroma percentage, Grade III histology, and age were not significantly associated with PTB grade.

PTB: peripheral tumor budding

iTB demonstrated significant associations with necrosis ($p < 0.001$), lymph node metastasis ($p = 0.001$), and LVI ($p = 0.026$). In contrast, no statistically significant associations were observed between iTB grade and tumor size >5 cm ($p = 0.142$), perineural invasion ($p = 0.228$), high tumor stroma percentage >50% ($p = 0.712$), or Grade III histology ($p = 0.534$). Age >50 years was also not significantly associated with iTB grade ($p = 0.729$) (Table 4). Overall, higher iTB grades were associated with selected adverse histopathological features, particularly necrosis, lymph node metastasis, and LVI.

Parameter	Low iTB	Intermediate iTB	High iTB	Pearson χ^2	P-value
Tumor size >5 cm	5 (20.0%)	15 (60.0%)	5 (20.0%)	3.910	0.142
Necrosis present	8 (21.1%)	18 (47.4%)	12 (31.6%)	15.986	<0.001
Lymph node metastasis	12 (24.5%)	24 (49.0%)	13 (26.5%)	13.167	0.001
Lymphovascular invasion	10 (24.4%)	21 (51.2%)	10 (24.4%)	7.271	0.026
Perineural invasion	7 (24.1%)	16 (55.2%)	6 (20.7%)	2.958	0.228
High tumor stroma (>50%)	14 (31.8%)	23 (52.3%)	7 (15.9%)	0.679	0.712
Grade III	9 (31.0%)	14 (48.3%)	6 (20.7%)	1.256	0.534
Age >50 years	21 (37.5%)	28 (50.0%)	7 (12.5%)	0.633	0.729

TABLE 4: Association of iTB with histopathological parameters (n = 94).

Data are presented as n (%), with percentages calculated within each row/category total. Pearson's χ^2 test was used to assess associations between iTB grade and histopathological parameters. P-values <0.05 were considered statistically significant. Significant associations were observed for necrosis, lymph node metastasis, and lymphovascular invasion, whereas tumor size, perineural invasion, high tumor stroma percentage, Grade III histology, and age were not significantly associated with iTB grade.

iTB: intratumoral tumor budding

Association of tumor budding with hormone receptor and HER2/neu status

Among the 94 breast carcinoma cases, ER positivity (Allred score: 3-8) was observed in 58 (61.7%), while PR positivity was present in 54 (57.4%). HER2/neu expression was negative (0/1+) in 68 (72.3%), equivocal (2+)

in 8 (8.5%), and positive (3+) in 18 (19.1%) (Table 5). Triple-negative breast cancer, defined by the absence of ER, PR, and HER2/neu expression, was identified in 4 (4.3%) cases. ER immunohistochemistry demonstrated nuclear staining in tumor cells, whereas HER2/neu-positive tumors showed intense, complete circumferential membranous staining corresponding to a 3+ score (Figures 1C, 1D). No statistically significant associations were observed between individual hormone receptor markers and TB grades in the present study. These findings indicate that the association between TB and hormone receptor/HER2 status was not statistically established in this cohort.

Receptor	Category	n (%)
ER	Positive (score 3–8)	58 (61.7)
	Negative (score 0–2)	36 (38.3)
PR	Positive (score 3–8)	54 (57.4)
	Negative (score 0–2)	40 (42.6)
HER2/neu	Negative (0/1+)	68 (72.3)
	Equivocal (2+)	8 (8.5)
	Positive (3+)	18 (19.1)
Triple-negative breast cancer	Present (ER/PR/HER2)	4 (4.3)

TABLE 5: Receptor status and triple-negative breast cancer phenotype among breast carcinoma cases (n = 94).

Data are presented as n (%). ER and PR positivity were defined by an Allred score of 3–8, while HER2/neu expression was categorized as negative (0/1+), equivocal (2+), or positive (3+). Percentages are based on the total study population (n = 94).

ER: estrogen receptor; PR: progesterone receptor; HER2/neu: human epidermal growth factor receptor 2

Discussion

The present prospective cross-sectional study comprised 94 women with invasive breast carcinoma, most in the fifth and sixth decades of life and postmenopausal (61.7%) at diagnosis, a pattern consistent with several contemporary Indian series [20,33]. Invasive carcinoma of no special type predominated (96.8%), and Grade II tumors were the most frequent histological grade (44.7%), findings comparable with recent Indian and international cohorts.

PTB was intermediate in 40.4% and high in 29.8% of cases, while iTB was intermediate in 48.9%. In our cohort, PTB was significantly associated with necrosis, lymph node metastasis, and perineural invasion, whereas iTB was significantly associated with necrosis, lymph node metastasis, and LVI. In this study, PTB and iTB were evaluated separately using predefined study-specific criteria. Because TB assessment methods and scoring thresholds may vary across studies, direct comparisons between cohorts should be interpreted cautiously. Furthermore, the ITBCC criteria were developed for colorectal carcinoma, and the thresholds applied in this study should not be interpreted as a universally validated breast-specific scoring system [34,35]. This pattern mirrors previous observations linking TB with nodal metastasis and an adverse tumor microenvironment in invasive ductal breast carcinoma and has been reproduced in more recent cohorts [36–38]. Increased budding activity has similarly been associated with nodal involvement and aggressive tumor behavior, while significant correlations have been reported between TB, tumor size, histological grade, and nodal metastasis in breast carcinoma cohorts [39,40].

A systematic review and meta-analysis further supported the association between increased TB and adverse clinicopathological features and outcomes [41]. Previous studies have reported associations between TB and adverse clinicopathological features, including lymph node metastasis and LVI. The present findings support an association with selected adverse features in this cohort; however, differences in scoring methods and study populations should be considered when comparing results across studies [3,42]. The proportion of intermediate-grade budding in our cohort was higher than that reported in studies where low-grade budding predominated and lower than in cohorts reporting a majority of high-grade budding [43]. This variation may reflect differences in anatomical definitions of TB, field selection, counting procedures, and scoring thresholds, as well as differences in tumor stage at presentation. These methodological variations highlight the need for clearly defined and reproducible criteria for assessing PTB and iTB in breast carcinoma [44].

ER, PR, and HER2/neu positivity in this cohort (61.7%, 57.4%, and 19.1%, respectively) were broadly comparable with previously published Indian and international series [45]. The association between TB and individual receptor markers was not statistically significant in the present cohort. Therefore, the observed findings do not establish a significant relationship between TB grade and ER, PR, or HER2/neu status. Further studies with larger cohorts are needed to clarify these relationships [46]. Combining tumor bud counts with stromal proteolytic markers may improve prognostic stratification beyond receptor status alone, supporting the concept that TB provides prognostic information complementary to, rather than serving as a surrogate for, receptor-based subtyping [47].

Mechanistically, TB is considered a morphological manifestation of partial EMT, in which cells at the invasive front acquire migratory, apoptosis-resistant phenotypes that facilitate single-cell or collective invasion relatively independent of hormone receptor signaling [48]. Because it can be assessed on routine H&E sections without additional specialized infrastructure, TB may be particularly useful in resource-constrained settings as an adjunct to conventional histopathological evaluation. However, its potential role in treatment stratification and follow-up requires validation in studies incorporating clinical outcomes and survival data [49].

This study has certain limitations. It was conducted at a single tertiary care center, which may limit generalizability; detailed molecular subtyping beyond ER/PR/HER2 was not performed; TB assessment on H&E sections may be subject to interobserver variability; and treatment outcome or survival data were not correlated with budding status. In addition, the present study did not assess interobserver agreement, and therefore the reproducibility of the TB assessment could not be formally evaluated. Future multicentric prospective observational studies incorporating standardized TB assessment, molecular characterization, treatment response, recurrence, and long-term survival are warranted to validate its independent prognostic significance and determine its potential role in routine histopathological reporting and risk stratification of invasive breast carcinoma.

Conclusions

TB, both peripheral and intratumoral, showed significant associations with selected adverse clinicopathological features in invasive breast carcinoma. PTB was significantly associated with necrosis, lymph node metastasis, and perineural invasion, whereas iTB was significantly associated with necrosis, lymph node metastasis, and LVI. The relationship between TB and individual ER, PR, and HER2/neu profiles was not statistically consistent in this cohort. TB can be evaluated on routine H&E sections and may serve as a cost-effective adjunct to conventional histopathological assessment. However, its independent prognostic value requires confirmation through larger multicenter studies incorporating treatment response, recurrence, and survival outcomes. Further studies using standardized and reproducible assessment criteria are warranted to establish its clinical applicability in breast carcinoma.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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