THE PLANET

Original Article

Tumor Microenvironment Features and Pathologic Characteristics of Invasive Breast Carcinoma

Mohd Mejbahul Bahar[1], Mosammat Mira Pervin[2], Rifat Zia Hossain[3*]

ARTICLE INFO

Received: 9 Mar 2026
Accepted: 12 Mar 2026
Published Online: 18 Mar 2026

DOI: 10.5281/zenodo.19497764

Volume: 9, Number: 2, Page: 62-65

e-ISSN: 2789-5912
ISSN: 2617-0817

*Corresponding author

ABSTRACT

Background: The tumor microenvironment plays a central role in breast cancer progression and therapeutic response. Interactions between immune cells and stromal components influence tumor behavior and may provide prognostic information. However, data correlating routine histopathologic microenvironment features with pathologic characteristics remain limited in resource-constrained settings. This study aimed to evaluate tumor microenvironment features and analyze their association with selected pathologic characteristics in invasive breast carcinoma. **Methods & Materials:** This cross-sectional observational study was conducted at the Department of Surgery, Bangladesh Medical University, Dhaka, from January to December 2025. A total of 125 patients with histologically confirmed invasive breast carcinoma were included. Core biopsy specimens were assessed for lymphocytic response and desmoplasia. Surgical specimens were evaluated for intratumoral necrosis, microcalcification, lymphovascular invasion, perineural invasion, ductal carcinoma in situ component and tumor border configuration. Data were analyzed using SPSS version 25.0. **Results:** The mean age was 46.8 ± 13.3 years, with 41.6% aged ≥50 years. Mild lymphocytic response was observed in 87.2% of tumors, while 60.8% demonstrated moderate desmoplasia. Intratumoral necrosis was present in 34.4% of cases and microcalcification in 8.0%. Lymphovascular invasion and perineural invasion were identified in 5.6% and 4.8% of tumors, respectively. A significant association was found between desmoplasia and lymphocytic response (p=0.002), whereas no significant association was observed between desmoplasia and intratumoral necrosis. **Conclusion:** Tumor microenvironment features, particularly desmoplasia and lymphocytic response, demonstrate significant interrelationship in invasive breast carcinoma. Systematic evaluation of these parameters may enhance understanding of tumor biology and support clinical decision-making.

Keywords: Breast carcinoma, Tumor microenvironment, Tumor, Histopathology.

1. *Assistant Professor, Department of Colorectal Surgery, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh (ORCID: 0009-0000-1638-2507)*
2. *Associate Professor, Department of Surgical Oncology, Bangladesh Medical University (BMU), Dhaka, Bangladesh (ORCID: 0009-0002-9869-6570)*
3. *Assistant Professor, Department of Oncology, Bangladesh Medical University (BMU), Dhaka, Bangladesh (ORCID: 0009-0008-0165-2576)*

INTRODUCTION

Breast cancer remains the most frequently diagnosed malignancy among women worldwide and represents a major contributor to cancer-related morbidity and mortality. Although advances in screening, molecular classification and targeted therapy have improved outcomes, disease progression and therapeutic response vary substantially among patients. Increasing evidence indicates that these variations are not determined solely by intrinsic tumor biology but are also influenced by the tumor microenvironment. The tumor microenvironment comprises a complex network of stromal cells, immune cells, extracellular matrix components and signaling molecules that interact dynamically with malignant epithelial cells and influence tumor behavior, progression and response to therapy [1,2].

The immune component of the tumor microenvironment has attracted significant attention in recent years because of its critical role in tumor development and host antitumor responses. Tumor-infiltrating lymphocytes (TILs), macrophages, neutrophils and other immune cells contribute to a complex immunologic landscape that may either suppress or promote tumor growth. Previous studies have demonstrated that higher levels of tumor-infiltrating lymphocytes are associated with improved prognosis and enhanced response to systemic therapies in several subtypes of breast cancer [3,4]. Conversely, certain immune cell populations may promote tumor progression through immune evasion, chronic inflammation and remodeling of the tumor stroma [5,6]. These interactions highlight the dual role of immune components within the tumor microenvironment.

Beyond immune cells, the structural and stromal elements of the tumor microenvironment also play a critical role in breast cancer progression. Cancer-associated fibroblasts, extracellular matrix deposition and desmoplastic reactions are important determinants of tumor architecture and local invasion. These stromal components influence tumor cell proliferation, angiogenesis and metastatic potential through complex biochemical signaling pathways [7]. Desmoplasia, characterized by the proliferation of fibroblasts and dense collagen deposition around malignant cells, has been associated with aggressive tumor behavior and altered tumor-stromal interactions.

Recent advances in tumor biology emphasize the importance of understanding the spatial and functional heterogeneity of the tumor microenvironment. Variations in immune cell infiltration, stromal composition and lymphoid structures can provide valuable prognostic and predictive information. For instance, tertiary lymphoid structures and B-cell–mediated immune responses have been shown to correlate with enhanced antitumor immunity in certain breast cancer subtypes [8]. Similarly, tumor-associated macrophages have been implicated in modulating tumor progression through regulation of immune responses, angiogenesis and tissue remodeling [9].

Despite growing interest in the tumor microenvironment, data regarding its pathological characteristics in invasive breast carcinoma remain limited in many clinical settings, particularly in developing countries. Most existing studies have

focused on molecular biomarkers or therapeutic implications, while comparatively fewer investigations have systematically evaluated histopathological features of the tumor microenvironment in routine diagnostic specimens. Understanding these features may provide important insights into tumor biology and could contribute to improved prognostic assessment and personalized treatment strategies.

Therefore, the present study aimed to evaluate key tumor microenvironment features and their association with pathological characteristics in patients with invasive breast carcinoma. By analyzing tumor-infiltrating lymphocytes, stromal responses and related histopathological parameters in core biopsy and surgical specimens, this study seeks to provide a clearer understanding of the interaction between tumor cells and their surrounding microenvironment in breast cancer.

OBJECTIVES

This study aimed to evaluate tumor microenvironment features and analyze their association with selected pathologic characteristics in invasive breast carcinoma.

METHODS & MATERIALS

This cross-sectional observational study was conducted at the Department of Surgery, Bangladesh Medical University (BMU), Dhaka, Bangladesh. The study period extended from January to December 2025. The study population comprised patients diagnosed with invasive breast carcinoma who underwent core needle biopsy and subsequent histopathologic evaluation. A total of 125 consecutive cases were included in the analysis.

Sample Selection

Inclusion criteria:

- Female patients with histologically confirmed invasive breast carcinoma.
- Availability of adequate core biopsy specimens for tumor microenvironment assessment.
- Complete histopathologic reports including stromal and invasive features.

Exclusion criteria:

- Patients with recurrent breast carcinoma.
- Cases treated with neoadjuvant chemotherapy or radiotherapy before biopsy.
- Inadequate or poorly preserved biopsy specimens.
- Incomplete clinical or histopathologic data.

Data Collection Procedure

Data were collected prospectively from patients presenting with clinically and radiologically suspected breast carcinoma. After detailed clinical evaluation, core needle biopsies were performed under aseptic precautions using standard techniques. Tissue specimens were fixed in 10% neutral buffered formalin and processed for routine histopathological examination. Paraffin-embedded sections were stained with hematoxylin and eosin for microscopic evaluation. Tumor microenvironment features, including lymphocytic response and degree of desmoplasia, were assessed on core biopsy slides. Lymphocytic response was categorized as mild or moderate based on the density and distribution of tumor-infiltrating lymphocytes. Desmoplasia was graded as mild or moderate according to stromal fibrosis and fibroblastic proliferation. Subsequent surgical specimens were reviewed to document pathologic characteristics such as intratumoral necrosis, microcalcification, lymphovascular invasion, perineural invasion, presence of ductal carcinoma in situ component and tumor border configuration. All slides were examined independently by experienced pathologists to ensure consistency. Discrepancies were resolved through joint review and consensus discussion. Clinical and demographic data were recorded using a structured data collection form. Patient confidentiality was properly maintained. Informed consent was obtained from all participants before inclusion in the study.

Statistical Analysis

Data were analyzed using SPSS version 25.0. Descriptive statistics were expressed as frequency, percentage, mean and standard deviation. Associations between categorical variables were assessed using the chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULT

Table I presents the age distribution of the study population. The age distribution shows that 41.6% of patients were aged ≥50 years. Patients aged <40 years constituted 32.8% of the cohort. The 40–49-year age group represented 25.6% of cases. The mean age was 46.8 ± 13.3 years.

Table I
Age Distribution of study population (*n*=125).

Characteristic		Frequency (n)	Percentage (%)
Age (Years)	<40	41	32.8
	40–49	32	25.6
	≥50	52	41.6
	Mean ± SD	46.8 ± 13.3	

Table II shows that a mild lymphocytic response was observed in 87.2% of cases. Moderate lymphocytic infiltration was present in 12.8% of tumors. Moderate desmoplasia was identified in 60.8% of cases. Mild desmoplasia was noted in 39.2% of tumors.

Table II
Tumor Microenvironment Features on Core Biopsy (*n*=125).

Feature	Predominant Category	Frequency (n)	Percentage (%)
Lymphocytic response	Mild	109	87.2
	Moderate	16	12.8
Desmoplasia	Mild	49	39.2
	Moderate	76	60.8

Table III shows that intratumoral necrosis was present in 34.4% of cases. Microcalcification was detected in 8.0% of tumors. Lymphovascular invasion was observed in 5.6% of cases. Perineural invasion was identified in 4.8% of tumors. A ductal carcinoma in situ component was present in 4.8% of cases. An infiltrative tumor border was reported in 13.6% of tumors.

Table III
Histopathologic Characteristics of Invasive Breast Carcinoma (*n*=125).

Feature	Predominant Category	Frequency (n)	Percentage (%)
Intratumoral necrosis	Present	43	34.4
	Not seen	82	65.6
Microcalcification	Present	10	8.0
	Not seen	115	92.0
Lymphovascular invasion	Present	7	5.6
	Not seen	118	94.4
Perineural invasion	Present	6	4.8
	Not seen	119	95.2
DCIS component	Present	6	4.8
	Not seen	119	95.2
Tumor border	Infiltrating	17	13.6

Table IV shows a significant association between desmoplasia and lymphocytic response (p=0.002). Among cases with moderate desmoplasia, 94.7% had mild lymphocytic response. In contrast, 75.5% of tumors with mild desmoplasia showed mild lymphocytic response. No statistically significant association was found between desmoplasia and intratumoral necrosis (p=0.251). Intratumoral necrosis was present in 40.8% of mild desmoplasia cases and 30.3% of moderate desmoplasia cases.

Table IV
Association between Degree of Desmoplasia and Selected Pathologic Features (*n*=125).

Feature		Desmoplasia		p-value
		Mild (n=49)	Moderate (n=76)	
Lymphocytic Response	Mild	37 (75.5%)	72 (94.7%)	0.002
	Moderate	12 (24.5%)	4 (5.3%)	
Intratumoral Necrosis	Not Seen	29 (59.2%)	53 (69.7%)	0.251
	Present	20 (40.8%)	23 (30.3%)	

DISCUSSION

The present study evaluated tumor microenvironment features and their association with selected pathologic characteristics in invasive breast carcinoma. A predominance of mild lymphocytic response and moderate desmoplasia was observed on core biopsy, with a significant association between desmoplasia and lymphocytic infiltration. These findings highlight the structural and immune landscape of breast tumors within a routine histopathologic framework.

The high frequency of mild lymphocytic response in this cohort aligns with prior observations that immune infiltration in breast cancer is heterogeneous and subtype-dependent. Burugu et al. emphasized that immune infiltrates vary considerably across tumors and may reflect underlying tumor biology [10,11]. Salgado et al. standardized the evaluation of tumor-infiltrating lymphocytes and underscored their relevance as reproducible markers in routine sections [3]. Although the majority of tumors in the present study demonstrated only mild infiltration, this pattern may represent a relatively immunologically quiescent microenvironment. Denkert et al. showed that higher lymphocytic infiltration is associated with improved outcomes, particularly in aggressive subtypes [4]. The predominance of mild infiltration in our series may therefore suggest limited baseline immune activation in a substantial proportion of cases.

Desmoplasia was moderate in more than half of the tumors, reflecting a prominent stromal response. Giorello et al. described cancer-associated fibroblasts as central mediators of extracellular matrix remodeling and stromal expansion [7]. Costa et al. further demonstrated fibroblast heterogeneity and its contribution to immunosuppressive niches within breast tumors [11]. The predominance of moderate desmoplasia in our study supports the concept that stromal remodeling is a common feature of invasive breast carcinoma. Roeke et al. reported that stromal proportion has prognostic implications, reinforcing the biological significance of desmoplastic response [12].

A statistically significant association was identified between desmoplasia and lymphocytic response. Tumors with moderate desmoplasia more frequently exhibited mild lymphocytic infiltration. This inverse pattern may reflect stromal barriers limiting immune cell penetration. Monteran and Erez discussed how cancer-associated fibroblasts can promote immunosuppression through extracellular matrix deposition and cytokine modulation [13]. Lakins et al. demonstrated that stromal elements may induce deletion of cytotoxic T cells, thereby protecting tumor cells [14]. The observed association in this study may therefore indicate a functional interplay between fibrotic stroma and reduced immune infiltration.

Intratumoral necrosis was present in approximately one-third of cases, yet no significant association with desmoplasia was observed. Necrosis is generally considered a marker of aggressive tumor biology and hypoxic stress. Annaratone et al. highlighted the multifaceted nature of the tumor microenvironment, where hypoxia and stromal composition may not always correlate directly [15]. The lack of statistical association in our findings suggests that desmoplastic intensity alone may not predict necrotic change.

Microcalcifications were identified in a minority of tumors. Zheng et al. demonstrated associations between mammographic calcifications and specific clinicopathologic features in a large cohort [16]. Scimeca et al. proposed that microcalcifications may actively contribute to tumor progression through macrophage-mediated epithelial–mesenchymal transition [17]. The relatively low prevalence of microcalcifications in this study may reflect differences in detection methods or tumor characteristics.

Lymphovascular and perineural invasion were infrequent in this cohort. Mantovani et al. emphasized that tumor-associated macrophages facilitate invasion and metastatic dissemination [18]. Qiu et al. described macrophage-driven mechanisms promoting angiogenesis and vascular invasion [9]. Although our study did not explore macrophage subtypes directly, the low rates of lymphovascular invasion may indicate variable microenvironmental support for metastatic spread in this population.

The presence of a ductal carcinoma in situ component was limited. Beguinot et al.

reported biologically distinct immune subgroups in ductal carcinoma in situ, suggesting that immune contexture evolves during progression to invasive disease [19]. The low proportion of in situ components in our series may represent tumors presenting at a predominantly invasive stage.

Recent advances in immunotherapy underscore the clinical relevance of tumor microenvironment characterization. Bertucci and Gonçalves discussed the emerging role of PD-1 and PD-L1 blockade in breast cancer management [20]. Schmid et al. demonstrated improved outcomes with immune checkpoint inhibitors in triple-negative breast cancer [21]. The effectiveness of such therapies is closely linked to pre-existing immune activation within the tumor. Waldman et al. highlighted that successful immunotherapy often requires an immunologically active microenvironment [22]. Therefore, routine assessment of lymphocytic response and stromal patterns may provide indirect insight into therapeutic susceptibility.

Collectively, the findings of this study reinforce the structural and immunologic heterogeneity of invasive breast carcinoma. The significant association between desmoplasia and lymphocytic response underscores the interconnected nature of stromal and immune compartments. Systematic evaluation of these features on core biopsy may contribute to a more integrated understanding of tumor biology in routine clinical practice.

CONCLUSION

Tumor microenvironment assessment revealed a predominant mild lymphocytic response and moderate desmoplasia in invasive breast carcinoma. A significant association between desmoplasia and lymphocytic infiltration highlights stromal–immune interplay. Routine histopathologic evaluation of these features may provide clinically relevant insights into tumor biology and potential therapeutic responsiveness.

ACKNOWLEDGMENT

I would like to express my sincere gratitude for the invaluable support and cooperation provided by the staff, participants and my co-authors/colleagues who contributed to this study.

CONFLICTS OF INTEREST

There are no conflicts of interest.

REFERENCES

1. Soysal SD, Tzankov A, Muenst SE. Role of the tumor microenvironment in breast cancer. Pathobiology. 2015 Aug 31;82(3-4):142-52.
2. Stakheyeva M, Riabov V, Mitrofanova I, Litviakov N, Choynzonov E, Cherdyntseva N, Kzhyshkowska J. Role of the immune component of tumor microenvironment in the efficiency of cancer treatment: perspectives for the personalized therapy. Current pharmaceutical design. 2017 Sep 1;23(32):4807-26.
3. Salgado R, Denkert C, Demaria S, Sirtaine N, Klauschen F, Pruneri G, Wienert S, Van den Eynden G, Baehner FL, Pénault-Llorca F, Perez EA. The evaluation of tumor-infiltrating lymphocytes (TILs) in breast cancer: recommendations by an International TILs Working Group 2014. Annals of oncology. 2015 Feb 1;26(2):259-71.
4. Denkert C, Von Minckwitz G, Darb-Esfahani S, Lederer B, Heppner BI, Weber KE, Budczies J, Huober J, Klauschen F, Furlanetto J, Schmitt WD. Tumour-infiltrating lymphocytes and prognosis in different subtypes of breast cancer: a pooled analysis of 3771 patients treated with neoadjuvant therapy. The lancet oncology. 2018 Jan 1;19(1):40-50.
5. Wu L, Saxena S, Awaji M, Singh RK. Tumor-associated neutrophils in cancer: going pro. Cancers. 2019 Apr 19;11(4):564.
6. Pereira ER, Jones D, Jung K, Padera TP. The lymph node microenvironment and its role in the progression of metastatic cancer. InSeminars in cell & developmental biology 2015 Feb 1 (Vol. 38, pp. 98-105). Academic Press.
7. Giorello MB, Borzone FR, Labovsky V, Piccioni FV, Chasseing NA. Cancer-associated fibroblasts in the breast tumor microenvironment. Journal of mammary gland biology and neoplasia. 2021 Jun;26(2):135-55.
8. Garaud S, Buisseret L, Solinas C, Gu-Trantien C, de Wind A, Van den Eynden G, Naveaux C, Lodewyckx JN, Boisson A, Duvillier H, Craciun L. Tumor-infiltrating B cells signal functional humoral immune responses in breast cancer. JCI insight. 2019 Sep 19;4(18): e129641.
9. Qiu SQ, Waaijer SJ, Zwager MC, de Vries EG, van der Vegt B, Schröder CP. Tumor-associated macrophages in breast cancer: Innocent bystander or important player? Cancer treatment reviews. 2018 Nov 1; 70:178-89.
10. Burugu S, Asleh-Aburaya K, Nielsen TO. Immune infiltrates in the breast cancer microenvironment: detection, characterization and clinical implication. Breast cancer. 2017 Jan;24(1):3-15.
11. Costa A, Kieffer Y, Scholer-Dahirel A, Pelon F, Bourachot B, Cardon M, Sirven P, Magagna I, Fuhrmann L, Bernard C, Bonneau C. Fibroblast heterogeneity and immunosuppressive environment in human breast cancer. Cancer cell. 2018 Mar 12;33(3):463-79.
12. Roeke T, Sobral-Leite M, Dekker TJ, Wesseling J, Smit VT, Tollenaar RA, Schmidt MK, Mesker WE. The prognostic value of the tumour-stroma ratio in primary operable invasive cancer of the breast: a validation study. Breast cancer research and treatment. 2017 Nov;166(2):435-45.
13. Monteran L, Erez N. The dark side of fibroblasts: cancer-associated fibroblasts as mediators of immunosuppression in the tumor microenvironment. Frontiers in immunology. 2019 Aug 2; 10:1835.
14. Lakins MA, Ghorani E, Munir H, Martins CP, Shields JD. Cancer-associated fibroblasts induce antigen-specific deletion of CD8+ T Cells to protect tumour cells. Nature communications. 2018 Mar 5;9(1):948.
15. Annaratone L, Cascardi E, Vissio E, Sarotto I, Chmielik E, Sapino A, Berrino E, Marchiò C. The multifaceted nature of tumor microenvironment in breast carcinomas. Pathobiology. 2020 May 19;87(2):125-42.
16. Zheng K, Tan JX, Li F, Wei YX, Yin XD, Su XL, Li HY, Liu QL, Ma BL, Ou JH, Li H. Relationship between mammographic calcifications and the clinicopathologic characteristics of breast cancer in Western China: a retrospective multi-center study of 7317 female patients. Breast Cancer Research and Treatment. 2017 Nov;166(2):569-82.
17. Scimeca M, Bonfiglio R, Menichini E, Albonici L, Urbano N, De Caro MT, Mauriello A, Schillaci O, Gambacurta A, Bonanno E. Microcalcifications drive breast cancer occurrence and development by macrophage-mediated epithelial to mesenchymal transition. International journal of molecular sciences. 2019 Nov 11;20(22):5633.
18. Mantovani A, Marchesi F, Malesci A, Laghi L, Allavena P. Tumour-associated macrophages as treatment targets in oncology. Nature reviews Clinical oncology. 2017 Jul;14(7):399-416.
19. Beguinot M, Dauplat MM, Kwiatkowski F, Lebouedec G, Tixier L, Pomel C, Penault-Llorca F, Radosevic-Robin N. Analysis of tumour-infiltrating lymphocytes reveals two new biologically different subgroups of breast ductal carcinoma in situ. BMC cancer. 2018 Feb 3;18(1):129.
20. Bertucci F, Gonçalves A. Immunotherapy in breast cancer: the emerging role of PD-1 and PD-L1. Current oncology reports. 2017 Oct;19(10):64.
21. Schmid P, Adams S, Rugo HS, Schneeweiss A, Barrios CH, Iwata H, Diéras V, Hegg R, Im SA, Shaw Wright G, Henschel V. Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. New England journal of medicine. 2018 Nov 29;379(22):2108-21.
22. Waldman AD, Fritz JM. Lenardo MJJNRI. A guide to cancer immunotherapy: from T cell basic science to clinical practice. 2020;20(11):651-8.