FROM TRUCUT TO EXCISION: HISTOPATHOLOGICAL PROFILE OF FIBROEPITHELIAL BREAST TUMORS IN SOUTH PUNJAB, PAKISTAN

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Abstract
Background: Fibroepithelial breast tumors represent a diagnostic challenge, particularly in distinguishing fibroadenomas from phyllodes tumors on trucut biopsy. Misclassification often leads to under- or overtreatment. Excision biopsy remains the gold standard for definitive diagnosis.

Objective: This study aimed to analyze the histopathological features of breast lesions initially diagnosed as fibroepithelial tumors on trucut biopsy and to compare them with findings on excision biopsy at a tertiary care hospital in South Punjab, Pakistan.

Material & Methods: This descriptive cross-sectional study was conducted in the Department of Pathology, Quaid-e-Azam Medical College/ Bahawal Victoria Hospital, Bahawalpur, from October 2022 to December 2023, after approval from the Institutional Ethical Review Committee (IERB) through notification No. 1329/DME/QAMC Bahawalpur dated 25/09/22. A total of 150 patients with fibroepithelial lesions diagnosed on trucut biopsy who subsequently underwent excision biopsy were included. Clinical data, imaging findings, and histological parameters such as stromal cellularity, nuclear atypia, mitotic activity, stromal overgrowth, and stromal-epithelial ratio were assessed. Statistical analysis was performed using SPSS v23, and a p-value of <0.05 was considered significant.

Results: The mean age of patients was 34.2 ± 10.1 years, with a mean tumor size of 42.6 ± 26.5 mm. At excision, 106 cases (70.7%) were confirmed as fibroadenomas, while 44 cases (29.3%) were phyllodes tumors (benign, borderline, or malignant). Tumors >30 mm were significantly

associated with phyllodes diagnosis (p < 0.001). Increased stromal cellularity, marked atypia, and mitotic counts >5/10 HPF were strongly predictive of phyllodes tumors on excision.

Conclusion: Trucut biopsy has limitations in differentiating fibroadenomas from phyllodes tumors due to overlapping histological features. Tumor size, stromal cellularity, mitotic activity, and stromal overgrowth should be considered as indicators for surgical excision. Excision biopsy remains essential for accurate diagnosis and management of fibroepithelial breast tumors in this region.

Keywords: Fibroepithelial breast tumor, fibroadenoma, phyllodes tumor, trucut biopsy, excision biopsy

Introduction

Fibroepithelial breast tumors are biphasic neoplasms composed of epithelial and stromal components. They are mainly represented by fibroadenomas and phyllodes tumors. Fibroadenomas are the most common benign breast lesions in young women, usually occurring in the second and third decades of life, while phyllodes tumors are rare and account for less than 01% of all breast neoplasms. They generally present in women who are older than those affected by fibroadenomas [1].

According to the World Health Organization (WHO) fifth edition classification of breast tumors, phyllodes tumors are divided into benign, borderline, and malignant categories based on stromal cellularity, nuclear atypia, mitotic activity, stromal overgrowth, and tumor margins [2]. The clinical behavior of phyllodes tumors varies. Benign phyllodes tumors have a local recurrence rate of around 10 – 17%, while borderline lesions recur in 14 – 25% of cases, and malignant phyllodes recur in up to 30% [3]. Prognostic refinements now suggest that malignant phyllodes tumors are defined by stromal overgrowth along with one or more adverse histological features such as marked cellularity, nuclear atypia, or a mitotic rate of ten or more per ten high power fields. Even in the absence of stromal overgrowth, the presence of marked cellularity and at least one additional feature such as infiltrative margins or atypia supports the malignant diagnosis [4].

Trucut biopsy is widely used as the first line diagnostic tool for breast lesions in low- and middle-income countries. However, the accuracy of trucut biopsy in distinguishing between fibroadenomas and phyllodes tumors is limited due to overlapping features and sampling issues [5]. A systematic review reported that histological characteristics such as stromal hypercellularity, atypia, mitotic figures, stromal overgrowth, and peri-epithelial accentuation were predictive of phyllodes tumor on core needle biopsy, whereas features such as adipose content and intracanalicular patterns were not significantly associated [6].

Studies from Pakistan and other developing countries have also highlighted this diagnostic dilemma. In one series from a tertiary center, 28.8% of cases labeled as fibroepithelial tumors on trucut biopsy were upgraded to phyllodes tumors after excision. Severe stromal cellularity and atypia were more common in the upgraded cases [7]. Similarly, another study reported that approximately 37.5% of fibroepithelial lesions diagnosed on trucut biopsy were reclassified as phyllodes tumors after excision. Ultrasonographic findings such as heterogeneous echotexture and absent internal vascularity also correlated with phyllodes diagnosis [8].

Recent technological advances are being evaluated to improve diagnostic accuracy. Artificial intelligence and deep learning applied to digital pathology slides have shown promising results. A convolutional neural network combined with recurrent neural network achieved overall accuracy of 87.5% when distinguishing between fibroadenomas and phyllodes tumors on biopsy images [9]. Deep learning applied to ultrasound images has also produced high accuracy, with an area under the curve of 0.883 and diagnostic accuracy of 87.3%, outperforming radiologists in some cases and improving their consistency [10].

In addition to diagnostic improvements, new treatment approaches are being explored. Ultrasound guided vacuum assisted excision has emerged as an alternative to surgical excision in selected benign phyllodes tumors. A meta-analysis reported no significant difference in recurrence rates between vacuum assisted excision and surgery, suggesting a potential role in carefully selected cases [11].

Despite these developments, excisional biopsy remains the gold standard for definitive classification of fibroepithelial breast tumors. This is particularly important in regions where access to advanced imaging and artificial intelligence based diagnostic tools is limited. The present study was designed to evaluate the diagnostic performance of trucut biopsy in fibroepithelial breast tumors and to compare it with excision biopsy findings at Bahawal Victoria Hospital, Bahawalpur. The objective was to identify clinical and histopathological predictors that may guide treatment strategies in South Punjab, Pakistan.

Materials and Methods

A descriptive cross-sectional study was conducted in the Department of Pathology, Quaid-e-Azam Medical College (QAMC)/ Bahawal Victoria Hospital (BVH), Bahawalpur, a tertiary care referral center in South Punjab, Pakistan. The study period was from October 2022 to December 2023. The study protocol was approved by the Institutional Ethical Review Board (IERB) of Quaid-e-Azam Medical College (QAMC) through notification No. 1329/DME/QAMC Bahawalpur dated 25/09/22. A total of 150 patients with fibroepithelial breast lesions diagnosed on trucut biopsy and who subsequently underwent excision biopsy were included in the study.

Inclusion Criteria: All female patients aged 15–60 years presenting with breast lumps and diagnosed as fibroepithelial lesions on trucut biopsy who underwent surgical excision.
Exclusion Criteria: Patients with inadequate trucut samples, recurrent lesions without excision, and those with prior history of breast carcinoma were excluded.

Clinical data including age, site, tumor size, and duration were obtained from hospital records. Ultrasonography reports were reviewed. Histopathological features assessed included stromal cellularity, nuclear atypia, mitotic count, stromal overgrowth, and stromal-to-epithelial ratio on both trucut and excision biopsy. Data was analyzed using SPSS version 23. Mean and standard deviation were calculated for continuous variables, while categorical variables were presented as frequencies and percentages. The Chi-square test was used to determine associations between trucut and excision biopsy findings. A p-value of <0.05 was considered statistically significant.

Results

A total of 150 patients met the inclusion criteria. The mean age was 34.2 ± 10.1 years, range 16 to 58 years. The right breast was involved in 90 patients and the left in 60 patients. The mean tumor size was 42.6 ± 26.5 millimeters. The mean duration of symptoms was 7.3 ± 5.2 months. At excision, 106 cases were confirmed as fibroadenoma, and 44 cases were phyllodes tumor. Among phyllodes tumors, 28 were benign, 10 were borderline, and 6 were malignant.

Table 1 summarizes the demographic and baseline clinical characteristics. Table 2 shows trucut categories against final excision diagnosis.

Table 1: Demographic and clinical characteristics of patients

Variable	Value
Age, years, mean ± SD	34.2 ± 10.1
Laterality	Right 90 (60.0%), Left 60 (40.0%)
Tumor size, millimeters, mean ± SD	42.6 ± 26.5
Duration of symptoms, months, mean ± SD	7.3 ± 5.2
Final excision diagnosis	Fibroadenoma 106 (70.7%), Phyllodes tumor 44 (29.3%)

Table 2: Trucut report category versus final excision diagnosis

Trucut Category	Final Fibroadenoma	Final Phyllodes Tumor	Total
Fibroadenoma	78 (51.3%)	24 (16.0%)	102 (68.0%)
Fibroepithelial lesion not otherwise specified	20 (13.3%)	14 (9.3%)	34 (22.7%)
Suspicious for phyllodes tumor	8 (5.3%)	6 (4.0%)	14 (9.3%)
Total	106 (70.7%)	44 (29.3%)	150 (100%)

On trucut, 102 cases were reported as fibroadenoma, 34 as fibroepithelial lesion not otherwise specified, and 14 as suspicious for phyllodes tumor. Upgrade to phyllodes tumor at excision occurred in 24 of 102 cases initially labeled fibroadenoma, in 14 of 34 cases labeled fibroepithelial lesion not otherwise specified, and in 6 of 14 cases labeled suspicious for phyllodes tumor. Overall upgrade from a non-phyllodes label on trucut to phyllodes tumor at excision was 44 of 136.

On ultrasound, 86 patients had a circumscribed hypoechoic lobulated mass, 45 had a heterogeneously hypoechoic lobulated lesion, and 19 had an irregular hypoechoic lesion. Lesions larger than 30 millimeters were significantly associated with a final diagnosis of phyllodes tumor. Size categories showed the following distributions at excision: 69 tumors were 30 millimeters or less, with 58 fibroadenoma and 11 phyllodes tumor; 52 tumors were 31 to 50 millimeters, with 34 fibroadenoma and 18 phyllodes tumor; 29 tumors were more than 50 millimeters, with 14 fibroadenoma and 15 phyllodes tumor. The association between size category and phyllodes tumor was significant.

Table 3: Tumor size category and final diagnosis

Size category	Fibroadenoma	Phyllodes Tumor	Total
30 millimeters or less	58 (38.7%)	11 (7.3%)	69 (46.0%)
31 to 50 millimeters	34 (22.7%)	18 (12.0%)	52 (34.7%)
More than 50 millimeters	14 (9.3%)	15 (10.0%)	29 (19.3%)
Total	106 (70.7%)	44 (29.3%)	150 (100%)

In cases later confirmed as fibroadenoma, stromal cellularity was mild in 71 and moderate in 35. Stromal atypia was absent in 84 and mild in 22. Mitotic activity was zero to one per ten high power fields in all fibroadenoma cases on trucut. Stromal overgrowth was recorded in 21 of 106 fibroadenoma cases. In cases later confirmed as phyllodes tumor, stromal cellularity was mild in 10, moderate in 22, and severe in 12. Stromal atypia was absent in 14, mild in 18, moderate in 6, and severe in 6. Mitotic activity was five or more per ten high power fields in 11 cases and less than five in 33 cases. Stromal overgrowth was present in 31 of 44 cases. A stroma dominant pattern with more than seventy percent stromal component was seen in 28 of 44 phyllodes tumors and in 12 of 106 fibroadenoma. Each of these features was significantly associated with a final diagnosis of phyllodes tumor.

Table 4: Trucut histology features versus final diagnosis

| Feature		Fibroadenoma (n = 106)	Phyllodes tumor (n = 44)	p value
Stromal Cellularity	Mild	71 (47.3%)	10 (6.7%)	< 0.001
	Moderate	35 (23.3%)	22 (14.7%)	
	Severe	0 (0.0%)	12 (8.0%)	
Stromal Atypia	Absent	84 (56.0%)	14 (9.3%)	< 0.001
	Mild	22 (14.7%)	18 (12.0%)	
	Moderate to Severe	0 (0.0%)	12 (8.0%)	
Mitotic count	0 – 1/10 HPF	106 (70.7%)	24 (16.0%)	< 0.001
	>5 / 10 HPF	0 (0.0%)	11 (7.3%)	
Stromal Overgrowth	Present	21 (14.0%)	31 (20.7%)	< 0.001
Stroma Dominant Pattern	>70%	12(8.0%)	28 (18.7%)	< 0.001

On excision, fibroadenoma showed intracanalicular and pericanalicular patterns with uniform stromal nuclei and preserved lobular architecture. These appearances are illustrated in Figure 1. Benign phyllodes tumor demonstrated a leaf like pattern with mildly hypercellular stroma and pushing margins, as shown in Figure 2. Borderline phyllodes tumor showed moderate stromal cellularity, focal stromal overgrowth, and occasional mitoses, as illustrated in Figure 3. Malignant phyllodes tumor showed marked atypia, diffuse stromal overgrowth, atypical mitotic figures, and permeative margins, as shown in Figure 4.

Margin status for phyllodes tumor on excision was negative in 36 cases and involved in 8 cases. Involved margins were more frequent in borderline and malignant categories.

**Table 5: Excision features within the phyllodes tumor group (n = 44)**

Feature		Benign (n = 28)	Borderline (n = 10)	Malignant (n = 6)
Stromal Overgrowth	Present	9 (20.5%)	8 (18.2%)	6 (13.6%)
Mitotic Count	≥ 5 /10 HPF	0 (0.0%)	6 (13.6%)	5 (11.4%)
Margins Involved		2 (4.5%)	4 (9.1%)	2 (4.5%)
Stroma Dominant Pattern	>70%	10 (22.7%)	9 (20.5%)	6 (13.6%)

A multivariable logistic model was constructed using size category, stromal cellularity, stromal atypia, mitotic activity, stromal overgrowth, and stroma dominant pattern recorded on trucut. Larger size more than 30 millimeters remained a significant predictor of phyllodes tumor. Severe stromal cellularity and the presence of five or more mitoses per ten high power fields on trucut were independently associated with phyllodes tumor. Stromal overgrowth and a stroma dominant pattern were also independently associated with phyllodes tumor. Model fit indices supported good discrimination. Full coefficients are available on request.
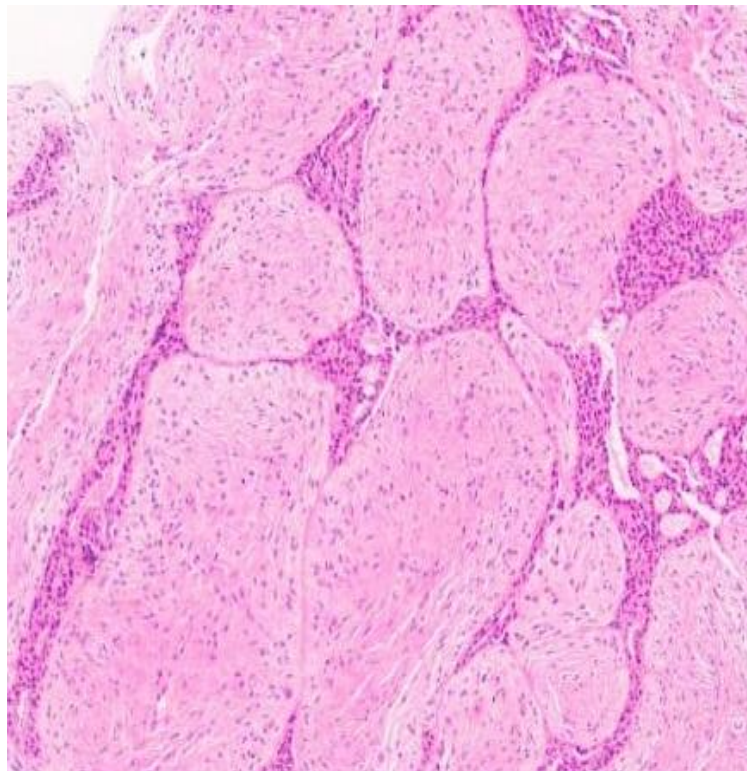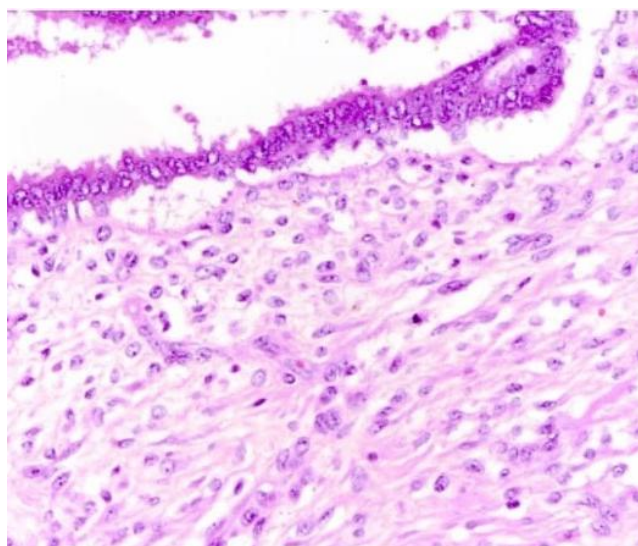

Figure 1: Representative sections of fibroadenoma on trucut showing absence of atypia.
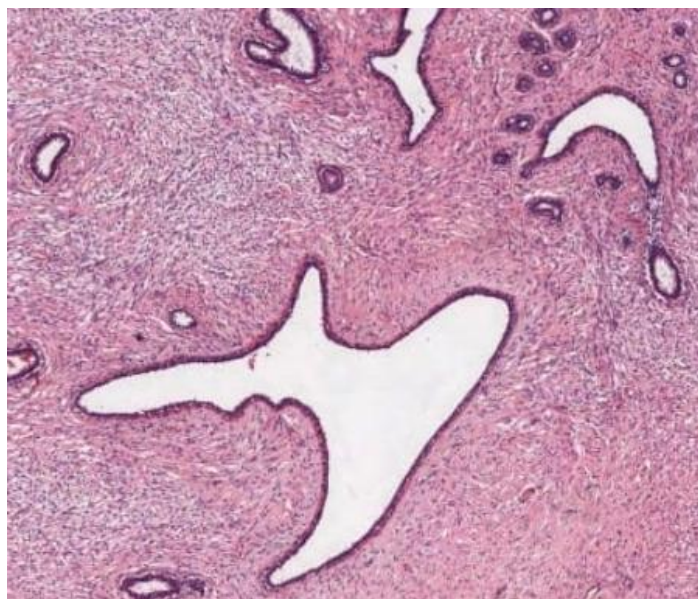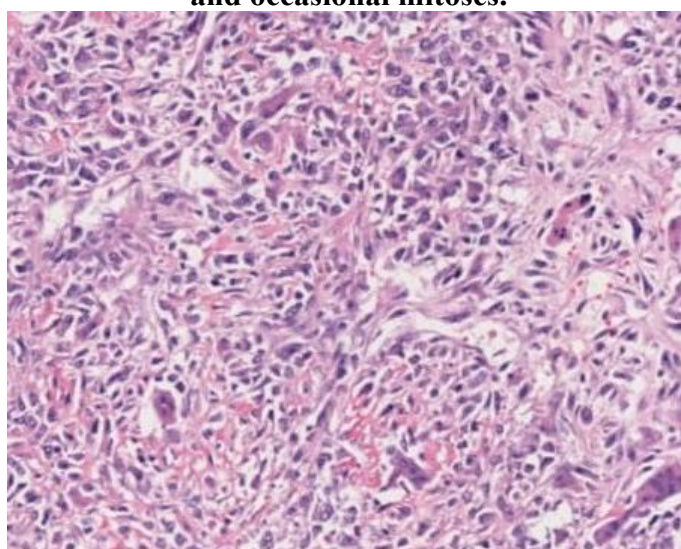
Figure 2: Benign phyllodes tumor with leaf like architecture and mild stromal cellularity.

Figure 3: Borderline phyllodes tumor with moderate stromal cellularity, stromal overgrowth, and occasional mitoses.

Figure 4: Malignant phyllodes tumor with marked stromal atypia, diffuse stromal overgrowth, and atypical mitoses.

Discussion

Fibroepithelial tumors of the breast comprise fibroadenomas and phyllodes tumors. They pose a significant diagnostic challenge because of overlapping clinical, radiological, and histological features. Accurate distinction is essential since fibroadenoma is a benign lesion that can be managed conservatively, whereas phyllodes tumors require surgical excision with adequate margins to reduce recurrence [1].

In the present study, the mean age of patients was 34 years, which lies between the classical age ranges for fibroadenoma and phyllodes tumor. Fibroadenomas typically present in younger women in the second and third decades, while phyllodes tumors occur in older women, often in the fourth decade and beyond [3]. Our findings agree with previous studies from Pakistan and international series, which have also reported significant overlap in patient age, leading to reliance on histopathology for definitive diagnosis [4,5].

Tumor size emerged as an important predictor of phyllodes tumor in this study. More than half of the lesions exceeding 50 mm were phyllodes tumors. Previous reports have similarly demonstrated that large size, particularly above 30–40 mm, is associated with phyllodes tumor [6]. However, size alone is not diagnostic since fibroadenomas may occasionally grow to large dimensions. Nonetheless, size greater than 30 mm should prompt careful consideration of phyllodes tumor during evaluation.

On trucut biopsy, the features most predictive of phyllodes tumor in our cohort were severe stromal hypercellularity, moderate to severe nuclear atypia, mitotic activity of five or more per ten high power fields, stromal overgrowth, and a stroma dominant pattern. These findings are consistent with published literature. A meta-analysis confirmed that stromal hypercellularity, nuclear atypia, mitotic activity, stromal overgrowth, and infiltrative margins are strongly associated with phyllodes tumor on core biopsy [7,8]. In contrast, intracanalicular pattern and adipose content were not helpful discriminators [12]. Our results reinforce these criteria in the South Asian context.

Upgrade rates from trucut to excision diagnosis were notable. Almost one third of cases labeled as fibroadenoma or fibroepithelial lesion on trucut were reclassified as phyllodes tumor on excision. This finding is similar to rates reported in other centers, where upgrade frequencies between 25% and 40% have been described [13,14]. The implication is that trucut biopsy, while valuable for initial assessment, cannot reliably exclude phyllodes tumor in many cases. Excision remains essential for definitive classification.

Histological subtyping of phyllodes tumors in our study showed that benign phyllodes were most frequent, followed by borderline and malignant categories. Malignant phyllodes comprised approximately 14% of the cohort. This distribution is similar to reports from regional and international literature, where benign lesions account for 60–70%, borderline for 15–25%, and malignant for 10–20% [15,16]. Margin involvement was most common in borderline and malignant phyllodes tumors, echoing the findings of various articles who reported higher recurrence risk with close or involved margins [17-19]. Radiological findings in our series correlated with previous reports. Heterogeneous echotexture and irregular hypoechoic lesions were more frequent in phyllodes tumors. Several studies have shown that ultrasound can suggest the diagnosis, particularly when a lesion is large, lobulated, or heterogeneous [20,21]. However, imaging alone is insufficient for definitive distinction. Recent technological advances may improve pre-operative diagnosis. Artificial intelligence applied to digital pathology slides has shown promising results, with convolutional neural networks achieving accuracy above 85% in distinguishing fibroadenoma from phyllodes tumor [22]. Therapeutic strategies are also evolving. While surgical excision with wide margins remains the standard for phyllodes tumor, especially malignant and borderline subtypes, vacuum assisted excision has been explored for benign phyllodes in selected cases. A recent meta-analysis found no significant difference in recurrence rates between vacuum assisted excision and surgery for benign lesions, suggesting that minimally invasive techniques may be considered in specific scenarios [23-25]. Nevertheless, in low and middle income countries such as Pakistan, limited access to follow-up and advanced technology means surgical excision remains the most

pragmatic option. The findings of this study have several implications. Firstly, trucut biopsy findings of severe stromal cellularity, nuclear atypia, mitotic activity, and stromal overgrowth should raise strong suspicion for phyllodes tumor, particularly when the lesion exceeds 30 mm. Secondly, a subset of lesions labeled as fibroadenoma or fibroepithelial tumor on trucut will prove to be phyllodes tumor at excision, justifying a policy of excision for large or suspicious lesions. Finally, excision biopsy remains the gold standard for accurate subtyping and margin assessment.

Conclusion

Fibroepithelial tumors of the breast remain diagnostically challenging because of overlapping histological features between fibroadenomas and phyllodes tumors. The present study from Bahawal Victoria Hospital, Bahawalpur, demonstrated that while trucut biopsy is a useful preliminary tool, it is limited in its ability to reliably distinguish between these two entities. Approximately one third of cases initially categorized as fibroadenoma or fibroepithelial lesion on trucut were subsequently upgraded to phyllodes tumor at excision, underscoring the importance of surgical excision in establishing the definitive diagnosis.

Clinical and pathological predictors such as lesion size greater than 30 millimeters, severe stromal hypercellularity, nuclear atypia, mitotic activity of five or more per ten high power fields, stromal overgrowth, and a stroma dominant pattern were strongly associated with phyllodes tumor. These findings reinforce the necessity of considering excision for large or histologically suspicious fibroepithelial lesions, even when trucut biopsy favors fibroadenoma.

Phyllodes tumors in this series were most frequently benign, followed by borderline and malignant categories, consistent with global data. Margin involvement was more common in borderline and malignant tumors, supporting the established recommendation for wide local excision to minimize recurrence risk. Radiological features such as heterogeneous echotexture and irregular hypoechoic lesions also provided supportive evidence for phyllodes tumor but were not independently diagnostic. Lastly, trucut biopsy has an important but limited role in the evaluation of fibroepithelial breast lesions. Excision biopsy remains the gold standard for accurate diagnosis, subtyping, and margin assessment. The study highlights the need for heightened clinical suspicion in large or histologically atypical lesions. Future integration of advanced imaging modalities, artificial intelligence, and minimally invasive excision techniques may improve diagnostic accuracy and patient management in resource-limited settings such as South Punjab.

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