

# Utility of Trucut Biopsy in Diagnosing Phyllodes Tumor

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ABSTRACT

Breast phyllodes are rare fibroepithelial neoplasms. Various classifications adopted to grade them into benign, borderline and malignant but the presently used one is the WHO classification of 2012. Trucut biopsy is a sensitive prediagnostic tool to grade phyllodes. But features can sometimes be overlapping making it difficult to grade it. In this study, an effort has been made to compare the morphology of trucut and histopathology specimens. Sensitivity of the trucut bopsy in diagnosing benign and malignant phyllodes is calculated and is being compared with other studies. Hence due to varied morphological features sole diagnosis should not be based on trucut biopsy.

**KEYWORDS:** Breast, phyllodes, trucut

## INTRODUCTION

Phyllodes tumor is a rare fibroepithelial neoplasm with malignant phyllodes having high risk of recurrence and metastasis. It accounts for 0.3%–0.5% of female breast tumors.<sup>[1]</sup> In 1838, Johannes Muller coined the term cystosarcoma phyllodes while, later in 1981, the term phyllodes tumor was adopted by the WHO.<sup>[2]</sup> At present, it has been classified as benign, borderline, and malignant according to several characteristics such as margins, stromal overgrowth, atypia, and mitosis. These tumors originate from periductal stroma and comprise stromal and epithelial elements.<sup>[3]</sup> The epithelial component is benign while the hyperproliferative stromal component is malignant. Diagnosis of phyllodes tumor on fine-needle aspiration cytology is difficult. Thus, preoperative imaging and biopsy remain the preliminary diagnostic tool for phyllodes tumor. Diagnosis remains challenging, especially in distinction of phyllodes from other fibroepithelial lesions, such as giant fibroadenoma both on imaging and in trucut. This uncertainty in diagnosis makes it difficult to further streamline the treatment. We present here a series of 20 patients comparing their histopathological diagnosis on resected specimens with their respective trucut biopsies.

## MATERIALS AND METHODS

Around 3200 histopathology specimens of the breast (trucut and resected specimens) were received

during 5 years of our study (January 2012–December 2017). A total of 20 patients with a diagnosis of phyllodes tumor on surgical specimen with their corresponding trucuts were received during the period of study.

## Observations

1. Patients ranged in age from 14 to 66 years with a mean age of 37.9 years. They all presented with a painless lump with three patients having associated ulceration and discharge from the breast and two having associated pain. One patient presented with a history of recurrent lump [Table 1]
2. Thirteen cases (65%) presented with a left-sided lump and seven cases with a right-sided lump
3. The duration of the lump ranged from 6 months to 6 years [Table 2]. Mammography and contrast-enhanced computed tomography were performed only in two cases [Figure 1a]
4. The tumor size varied from 5 cm × 4 cm to 30 cm × 25 cm. Thirteen cases (65%) were >10 cm, fulfilling the criteria of giant phyllodes
5. Nine (45%) patients underwent lumpectomy, whereas four (20%) had modified radical mastectomy (MRM), and the remaining seven (35%) had simple mastectomy [Figure 1b-d]

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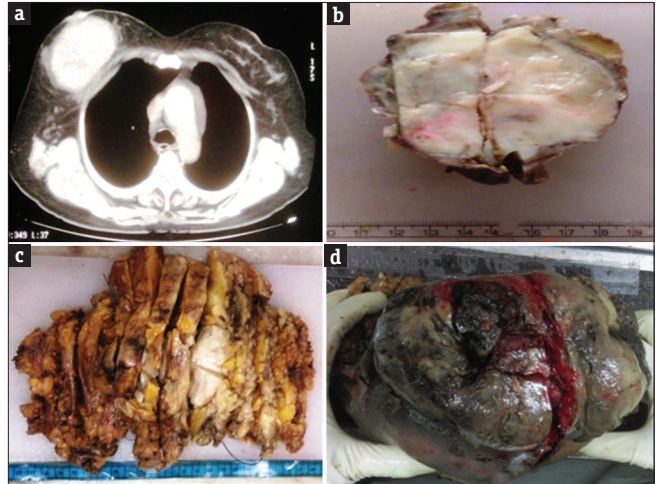
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6. On trucut biopsies of the patients, the following four stromal features were assessed: stromal cellularity, stromal atypia, mitosis, and relative proportion of the stroma to the epithelium. On the basis of these features, 14 cases (70%) were diagnosed to be benign phyllodes while 6 (30%) had malignant features [Table 3]
7. Histomorphologic features of final surgical specimen (lumpectomy/mastectomy) were studied on the basis of the WHO 2012 grading system for phyllodes tumor. Seven (35%) cases were found to be benign [Figure 2a and b], four (20%) were found to be borderline [Figure 2c and d], while nine (45%) were found to be malignant [Figure 3a, b and Table 4]
8. Two cases had associated heterologous elements showing chondrosarcomatous [Figure 3c] and leiomyosarcomatous [Figure 3d] differentiation, while one showed only chondrosarcomatous elements
9. Lymph nodes isolated showed reactive changes only with the absence of any tumor

10. Three cases with diagnosis of benign phyllodes on trucut were finally diagnosed as malignant phyllodes on final histopathology report
11. Four cases diagnosed as benign on trucut were diagnosed as borderline phyllodes eventually [Table 5]
12. Sensitivity of trucut in diagnosing benign phyllodes was 100%, and specificity was 46.15%. Positive predictive value was 50% and negative predictive value was 100%



**Figure 1:** (a) Postcontrast-enhanced computed tomography chest image in the mediastinal window showing a well-defined enhancing mass lesion in the right breast. (b) Cut section showing benign phyllodes. (c) Cut section of borderline phyllodes showing gray-white well-defined lesion. (d) Cut section of malignant phyllodes showing an infiltrative lesion with areas of hemorrhage

**Table 1: The following WHO 2012 grading system was used for classifying phyllodes**

Histologic features	Benign	Borderline	Malignant
Stromal cellularity	Mild	Moderate	Marked
Stromal atypia	Mild	Moderate	Marked
Mitosis	<5/10 HPF	5-9/10 HPF	>10/10 HPF
Stromal overgrowth	Absent	Absent/focal	Present
Tumor margins	Well defined	Well defined	Infiltrative

HPF: High-power field

**Table 2: Clinical features, duration, and type of surgical intervention in patients with phyllodes tumor**

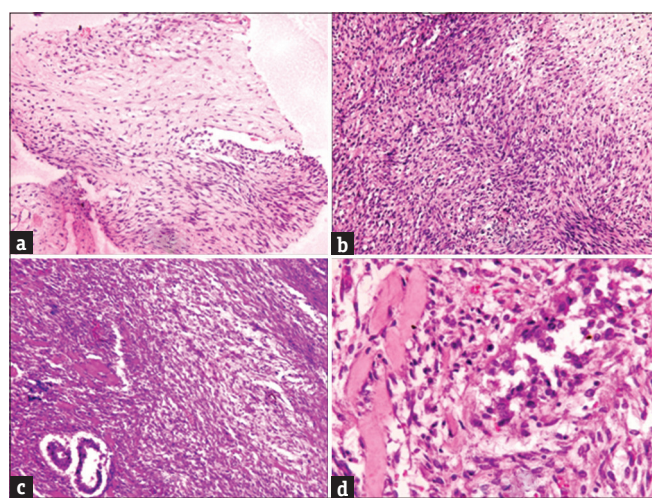
Age (years)	Complaints	Duration	Laterality	Quadrant	Surgery
43	Lump	6 years	Left	Upper outer	Lumpectomy
30	Lump	3 years	Right	All	MRM
66	Lump	2 years	Left	All	MRM
32	Lump	6 months	Left	Upper outer	Lumpectomy
24	Lump	1 year	Left	All	Mastectomy
66	Lump, ulceration	4 years	Left	All	Mastectomy
33	Lump	6 months	Right	Upper and lower outer	MRM
14	Lump	1 year	Left	All	Lumpectomy
45	Lump	1 year	Right	All	Lumpectomy
46	Lump	1 year	Left	Upper and lower outer	Lumpectomy
24	Lump, ulceration	4 years	Right	Upper outer	Lumpectomy
30	Lump, ulceration	1 year	Left	All	MRM
55	Lump, pain	1 year	Left	Upper outer and inner	Mastectomy
30	Lump	1 year	Right	All	Lumpectomy
21	Recurrent lump	2 years	Left	All	MRM
50	Lump	1 year	Right	All	Mastectomy
42	Lump, pain	8 months	Left	Upper and lower inner	Mastectomy
50	Lump	2 years	Right	Upper and lower inner	Mastectomy
32	Lump	1 year	Left	All	Lumpectomy
25	Lump	1 year	Left	Upper outer	Lumpectomy

MRM: Modified radical mastectomy

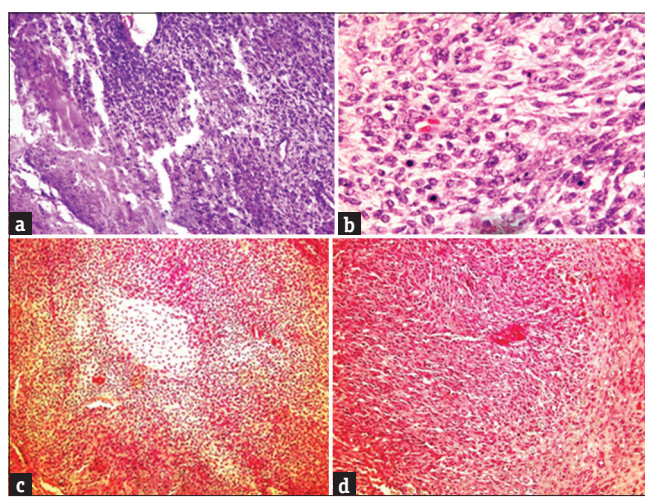
**Table 3: Histomorphologic features on trucuts**

Stromal atypia	Stromal mitosis	Stromal cellularity	Stromal overgrowth	Diagnosis
Mild	Occasional	Mild	Absent	Benign
Marked	Frequent	Marked	Focal	Malignant
Marked	Frequent	Marked	Focal	Malignant
Mild	1-2/10 HPF	Mild	Absent	Benign
Mild	Occasional	Mild	Absent	Benign
Mild	Occasional	Mild	Absent	Benign
Mild	Occasional	Mild	Absent	Benign
Mild	1-2/10 HPF	Mild	Absent	Benign
Mild	3-4/10 HPF	Mild	Absent	Benign
Mild	Occasional	Mild	Absent	Benign
Marked	Frequent	Marked	Present	Malignant
Marked	Frequent	Marked	Present	Malignant
Mild	Occasional	Mild	Absent	Benign
Mild	1/10 HPF	Mild	Absent	Benign
Moderate	4/HPF	Marked	Present	Malignant
Mild	Occasional	Mild	Absent	Benign
Mild	Occasional	Mild	Absent	Benign
Marked	Frequent	Marked	Focal	Malignant
Mild	1/10 HPF	Mild	Absent	Benign
Mild	Occasional	Mild	Absent	Benign

HPF: High-power field



**Figure 2:** (a) Photomicrograph of trucut of benign phyllodes showing mild increase in stromal cellularity (H and E,  $\times 100$ ). (b) Photomicrograph of the corresponding mastectomy specimen consistent with trucut findings (H and E,  $\times 100$ ). (c) Photomicrograph of trucut of borderline phyllodes showing moderate increase in stromal cellularity. An entrapped duct is noted (H and E,  $\times 100$ ). (d) Photomicrograph of the corresponding mastectomy specimen consistent with trucut findings (H and E,  $\times 100$ )



**Figure 3:** (a) Photomicrograph of trucut of malignant phyllodes showing increase in stromal cellularity along with mitotic figures (H and E,  $\times 100$ ). (b) Photomicrograph of the corresponding mastectomy specimen consistent with trucut findings (H and E,  $\times 100$ ). (c) Photomicrograph showing chondrosarcomatous element in malignant phyllodes (H and E,  $\times 400$ ). (d) Photomicrograph showing leiomyosarcomatous element in malignant phyllodes (H and E,  $\times 400$ )

13. Sensitivity of trucut in diagnosing malignant phyllodes was 66.6% and specificity was 100%. Positive predictive value was 100% while negative predictive value was 78.5%.

## DISCUSSION

Phyllodes tumors are rare fibroepithelial lesions. They occur in women aged 35–55 years of age<sup>[4]</sup> and usually present as a painless lump with slow progression. It has

an equal propensity to occur in either of the breast with a rare bilateral presentation<sup>[5]</sup> and is more commonly found in the upper outer quadrant. In our study, the mean age was found to be 37.9 years while the youngest patient was 14 years. The most common presentation was painless lump in the breast; however, three patients had associated skin involvement and discharge from the lump. The left breast (65%) was more affected than the right with no patient having bilateral involvement in

**Table 4: Histomorphologic features on histopathologically resected specimens**

Tumor size	Stromal cellularity	Atypia	Mitosis	Stromal overgrowth	Margins	Necrosis	Diagnosis
11×9×7	Marked	Marked	Frequent	Present	Infiltrative	Absent	Malignant
15×12×10	Marked	Marked	Frequent	Present	Infiltrative	Absent	Malignant
29×15×7	Marked	Marked	Frequent	Present	Infiltrative	Present	Malignant
7×6×4	Marked	Marked	2-3/HPF	Present	Infiltrative	Absent	Malignant
20×16×10	Mild-mod	Mod	5/10 HPF	Absent	Well defined	Absent	Borderline
18×15×15	Marked	Marked	Frequent	Present	Infiltrative	Present	Malignant
6×4×3	Mild	Mild	3-4/10 HPF	Absent	Well defined	Absent	Benign
8×7×4	Mild	Mild	3-4/10 HPF	Absent	Well defined	Absent	Benign
10×7×6	Mild -mod	Mod	5-6/10 HPF	Focal	Well defined	Absent	Borderline
9×9×3	Mild	Mild	1-2/10 HPF	Absent	Well defined	Absent	Benign
6×4×3	Marked	Marked	Frequent	Present	Infiltrative	Present	Malignant
30×25×10	Marked	Marked	10/10 HPF	Present	Infiltrative	Present	Malignant
8×6×4	Mild	Mild	1/10 HPF	Absent	Well defined	Absent	Benign
20×14×6	Moderate	Mod	7/10 HPF	Present	Well defined	Absent	Borderline
22×15×6	Marked	Marked	12/10 HPF	Present	Infiltrative	Absent	Malignant
20×14×7.5	Mild	Mod	7/10 HPF	Focal	Well defined	Absent	Borderline
15×14×10	Mild	Mild	1-2/10 HPF	Absent	Well defined	Absent	Benign
12×11×6	Marked	Marked	10/10 HPF	Present	Infiltrative	Present	Malignant
20×20×8.5	Mild	Mild	Occasional	Absent	Well defined	Absent	Benign
5×4×3	Mild	Mild	1-2/10 HPF	Absent	Well defined	Absent	Benign

HPF: High-power field

**Table 5: Comparison of diagnosis in trucut and histopathologically resected specimens**

Trucut biopsy	Histopathology specimen
Benign	Malignant with heterologous elements
Malignant	Malignant
Malignant	Malignant
Benign	Malignant
Benign	Borderline
Benign	Malignant
Benign	Benign
Benign	Benign
Benign	Borderline
Benign	Borderline
Benign	Benign
Malignant	Malignant
Malignant	Malignant
Benign	Benign
Benign	Borderline
Malignant	Malignant
Benign	Borderline
Benign	Benign
Malignant	Malignant with heterologous elements
Benign	Benign
Benign	Benign

our series. In the present series, all the quadrants were involved in 55% cases with the upper outer quadrant being involved in 35%.

The most favored theory on pathogenesis of phyllodes is epithelial-stromal interactions. Frequent MDM12 somatic mutations are identified in fibroadenoma and

phyllodes, suggesting a common origin for these two.<sup>[6,7]</sup> Size of phyllodes tumor varies from 1 cm to 40 cm.<sup>[8]</sup> About 20% tumors grow larger than 10 cm, when they are named as giant phyllodes. In the present study, the tumor size varied from 5 cm × 4 cm to 30 cm × 25 cm with 65% of cases presenting as giant phyllodes. Duration of presenting complaints in our study ranged from 6 months to 6 years.

Palpable axillary lymphadenopathy has been reported in up to 20% with 5% presenting with positive nodes.<sup>[9]</sup> Patients with lymph node metastasis have a poor prognosis. The mode of metastasis is commonly hematogenous and rarely lymph nodes are involved. Common sites of metastasis include lung, soft tissue, and bone. In the present series, lymph nodes isolated from patients showed reactive changes, and no lymphatic metastasis was identified.

On gross, phyllodes appear as solid, lobulated, and gray-white in color with hemorrhagic, necrotic, and cystic areas within. Phyllodes tumors are biphasic with both mesenchymal and epithelial components. A characteristic leaf-like architecture is present with epithelial components forming benign ducts while the hypercellular stroma forming the malignant counterpart. These fibroblasts can also differentiate into heterologous elements such as fat, cartilage, smooth muscle, and striated muscle. The presence of these components indicates poor prognosis.<sup>[10]</sup> In our study, two cases showed heterologous differentiation

with chondrosarcomatous [Figure 3c] and leiomyosarcomatous [Figure 3d] elements.

Mammography, ultrasonography, and magnetic resonance imaging (MRI) are routine imaging diagnostic modalities. However, none of them are characteristic of phyllodes and features overlap with fibroadenoma.<sup>[10,11]</sup> Accurate cytological diagnosis of phyllodes by fine-needle aspiration cytology (FNAC) is also difficult, especially in differentiating benign phyllodes from fibroadenoma. The presence of hypercellular stromal fragments and stromal elements being more numerous than epithelial ones is suggestive of phyllodes tumor on cytology.<sup>[5]</sup> Radiological investigations including mammogram, ultrasound, and FNAC have poor diagnostic performance.<sup>[12]</sup>

Surgical treatment is the mainstay of treatment for phyllodes. Wide local excision with at least 1 cm tumor-free margins should be kept. Since excision with required margins is impossible in giant phyllodes, mastectomy should be done for larger tumors and also in cases of recurrent tumors, especially of malignant histology.<sup>[13]</sup> Mastectomy may also be required for tumors between 5 and 10 cm in diameter depending on the size and location of phyllodes. Trucut biopsy is considered the most valuable pre-diagnostic test for phyllodes tumor. It has greater accuracy than other methods in diagnosing phyllodes but has limited clinical significance. Accurate diagnostic rates of core needle biopsy are variable, but most studies show below 50%.<sup>[13]</sup> Komenaka *et al.* found sensitivity to be 99% with negative predictive value and positive predictive value of 93% and 83%, respectively, while the accuracy rates of 76%.<sup>[14]</sup> Ward *et al.* reported accurate diagnostic rate of core needle biopsy to be 63%.<sup>[15]</sup> In our study, sensitivity of trucut in diagnosing benign phyllodes was 100% and specificity was 46.15% while sensitivity of trucut in diagnosing malignant phyllodes was 66.6% and specificity was 100%. Jacob *et al.* found that four stromal features (cellularity, nuclear atypia, mitoses, and amount of stroma) in core needle biopsy specimen differed significantly between cases that were fibroadenoma or phyllodes at excision.<sup>[16,17]</sup>

Lymph node dissection is not recommended as nodal metastasis is rare. Bhargav *et al.* stated that regardless of the histological grade, wide local excision should be the first choice of treatment and all patients with recurrence should undergo mastectomy.<sup>[18]</sup> Ben Hassouna *et al.* proposed mastectomy as the preferred surgical approach for malignant phyllodes.<sup>[19]</sup> Chest wall invasion appears to be an uncommon event with phyllodes tumors.<sup>[20]</sup> In our series, wide local excision was done in nine patients, mastectomy was performed in seven while MRM was performed in four cases. The role of

adjuvant radiotherapy and chemotherapy in phyllodes is uncertain.

In the present study, the WHO 2012 classification was used in evaluating the surgical specimens.<sup>[21]</sup> Parameters used were stromal cellularity, atypia, mitosis per 10 HPF, stromal overgrowth, and tumor margins. These histologic parameters were evaluated as follows in surgical specimens.<sup>[22]</sup> Stromal cellularity was evaluated in most cellular areas and graded as mild, moderate, and severe. Stromal atypia was also graded as mild, moderate, and severe depending on size, pleomorphism, and presence of nucleoli. Mitotic activity was evaluated in more cellular areas and quantified per 10 HPF. Stromal overgrowth was defined by stromal proliferation without accompanying epithelial elements in at least one low-power field. Tumor margins were graded as well defined, focally infiltrative, and infiltrative. The term infiltrative was used when projection of tumor stroma was seen into the peritumoral stroma or adipose tissue. In summary, trucut is a good pre-diagnostic method but its accuracy rates become limited. Features of benign phyllodes can easily overlap with those of cellular fibroadenoma. Furthermore, features of benign and borderline phyllodes are quite overlapping; in these cases, mitosis appears to be the most important parameter. Sarcoma breast and metaplastic carcinoma can also be close differential diagnosis of malignant phyllodes if epithelial components are absent. Hence, due to varied morphological features of phyllodes, its sole diagnosis should not be based on trucut. Excision biopsy provides the final confirmation of the diagnosis.

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#### Conflicts of interest

There are no conflicts of interest.

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