Risk Factors for Recurrence and Disease Management of Phyllodes Tumors

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Treatment

- Surgical Management
  - Adjuvant Radiation Therapy
  - Combine Therapy
  - Adjuvant Endocrine Therapy
  - Systemic Therapy
• Core principle of local therapy
  : local excision to negative margins

  : at least a 1 cm margin


  : more than 2 cm margin

• Ultrasound-guided, vacuum assisted breast biopsy for management of benign phyllodes tumors
  - only 1 out of 31 tumors had recurred after a mean of 6 years

• Technical considerations in lumpectomy
- Tunneling through the fibro glandular tissue from a periareolar incision is contraindicated with phyllodes tumor excisions because of the potential for tumor seeding.

- Even a curvilinear incision directly over the mass without removal of skin may be too small to obtain adequate surgical margins.

- Full thickness excisions from skin to chest wall muscle can be very helpful in achieving the 1 cm desired surgical margins.
• Axillary staging
  - Routine axillary dissection is unnecessary.
  - If suspicious lymph nodes
    : directed axillary ultrasound with fine needle aspiration
    or, preferably, core needle sampling
    → If this work-up is negative
      : sentinel lymph node biopsy can be considered
  - In the absence of such suspicion, neither sentinel node biopsy nor axillary node dissection are considered standard care in the surgical management of the clinically node-negative patient with phyllodes tumors.

Treatment

- Surgical Management
- Adjuvant Radiation Therapy
- Combine Therapy
- Adjuvant Endocrine Therapy
- Systemic Therapy
• The role of radiation therapy for phyllodes tumors remains unclear.

• benign phyllodes tumors
  - manage conservatively with surgery alone

• borderline and malignant phyllodes tumors
  - mastectomy alone yields excellent local control rates

A prospective, multi-institutional study of borderline and malignant phyllodes tumors evaluated 46 patients who underwent breast conserving surgery with negative surgical margins, revealing that adjuvant radiotherapy improved local control with no recurrences reported at 56 months of median follow-up.


Adjuvant radiation therapy may be considered appropriate treatment for selected locally recurrent phyllodes tumors, such as following mastectomy.
Treatment

- Surgical Management
- Adjuvant Radiation Therapy
- Combine Therapy
- Adjuvant Endocrine Therapy
- Systemic Therapy
• Some reports have supported the use of combined chemoradiation following phyllodes tumor recurrence.

• neoadjuvant hyperfractionated radiotherapy, superficial hyperthermia, and ifosfamide were administered after the second local recurrence of this tumor. Resection of the tumor bed revealed a pathologically complete response with an actual disease free follow-up of 48 months.

Treatment

- Surgical Management
- Adjuvant Radiation Therapy
- Combine Therapy
- Adjuvant Endocrine Therapy
- Systemic Therapy
• Phyllodes tumors variably express steroid receptors, but there is no known value to adjuvant endocrine therapy with tamoxifen or aromatase inhibitors.


• There would be little rationale for using these drugs because steroid receptor protein expression decreases with increasing malignancy, they are primarily expressed by the epithelial component of phyllodes tumors, and only the stromal component of phyllodes tumors metastasizes.
Treatment

- Surgical Management
- Adjuvant Radiation Therapy
- Combine Therapy
- Adjuvant Endocrine Therapy
- Systemic Therapy
• The systemic treatment principles of phyllodes tumors are driven by similar principles to those governing the management of soft tissue sarcoma.
Clinical suspicion of phyllodes tumor:
- Palpable mass
- Rapid growth
- Large size (>3 cm)
- Imaging with ultrasound suggestive of fibroadenoma except for size and/or history of growth
- History and physical exam
- Ultrasound
- Mammogram for women ≥30 y

Fibroadenoma
- Observe

Excisional biopsy
- Phyllodes tumor includes benign, borderline, and malignant
  - Wide excision without axillary staging

Invasive or in situ cancer
- See appropriate guidelines

Fibroadenoma or indeterminate
- Excisional biopsy
  - See findings above

Core needle biopsy
- Phyllodes tumor includes benign, borderline, and malignant
  - Wide excision without axillary staging

Invasive or in situ cancer
- See appropriate guidelines

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Footnotes:

- Excisional biopsy includes complete mass removal, but without the intent of obtaining surgical margins.
- FNA or core biopsy may not distinguish a fibroadenoma from a phyllodes tumor in some cases. The sensitivity of core biopsy for the diagnosis of phyllodes tumor is greater than that of FNA biopsy, but neither core biopsy nor FNA biopsy can always differentiate phyllodes tumors from fibroadenomas. In cases with clinical suspicion for phyllodes tumor, excision of the lesion may be needed for definitive pathologic classification.
- Wide excision means excision with the intention of obtaining surgical margins ≥1 cm. Narrow surgical margins are associated with heightened local recurrence risk, but are not an absolute indication for mastectomy when partial mastectomy fails to achieve margin width ≥1 cm.
- There are no prospective randomized data supporting the use of radiation treatment with phyllodes tumors. However, in the setting where additional recurrence would create significant morbidity (e.g., chest wall recurrence following mastectomy), radiation therapy may be considered following the same principles that are applied to the treatment of soft tissue sarcoma.

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Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.
Risk Factors for Recurrence

- Local Recurrence
- Distant Metastases
Risk Factors for Recurrence

- Local Recurrence
- Distant Metastases
• Recurrence of phyllodes tumors is possible for all lesions with recurrence rates as high as 46%.

Factors Associated with Risk of Local Recurrence

<table>
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<th>Study</th>
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<th>Necrosis</th>
<th>Fibroproliferation</th>
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• recur after lumpectomy
  - wide re-excision is performed if possible
  - sometimes requires mastectomy

• recur after mastectomy
  - full thickness soft tissue excision from skin to rib cage
  - soft tissue advancement flap closure is typically necessary to close the defect and, in some cases, skin grafting or more complex reconstructive approaches are needed.
Risk Factors for Recurrence

- Local Recurrence
- Distant Metastases
Primary Treatment of Cystosarcoma Phyllodes of the Breast

BACKGROUND. Cystosarcoma phyllodes is a rare sarcoma of the breast. Although surgical removal is the mainstay of treatment, the extent of surgery required (enucleation vs. mastectomy) and the need for adjuvant therapy, such as radiotherapy, are unclear. The current study evaluated the role of local and distant failure, as well as potential prognostic factors, to better define appropriate treatment strategies.

METHODS. One hundred one patients treated primarily for cystosarcoma phyllodes of the breast were evaluated. These tumors were classified histologically into benign (58%), indeterminate (12%), and malignant (30%) based on well-defined criteria. Distant metastasis was considered separately. Surgery was comprised of local excision with breast conservation (47%) or mastectomy (53%). Microscopic surgical margins were negative in 95% of cases. All adjuvant radiotherapy was performed in patients with a tumor size > 5 cm, as determined by imaging studies.

RESULTS. Overall survival for the 101 patients was 88%, 79%, and 62% at 5, 10, and 15 years, respectively. For patients with nonmalignant (benign or indeterminate) and malignant cystosarcoma phyllodes, the overall survival was 91% and 82%, respectively, at 5, 79% and 42%, respectively, at 10 years. Local recurrence occurred in 4 patients, with an actuarial 10-year rate of 8%. Eight patients developed distant metastases, with an actuarial 10-year rate of 13%. Multivariate analysis using Cox proportional hazards revealed that the only independent predictor of distant failure was a positive surgical margin.

CONCLUSIONS. Local failure in this group of largely margin-negative cystosarcoma phyllodes of the breast was low, showing that surgery with appropriate margins is the preferred primary therapy. The current data do not support the use of adjuvant radiotherapy for adequately resected disease. Patients with a tumor size > 5 cm were found to have a higher rate of distant failure.

Cystosarcoma phyllodes is an uncommon fibroepithelial breast neoplasm that accounts for 0.5–1% of female breast carcinoma cases. These tumors occur in women of all ages, including adolescents and the elderly. The majority arise in women between ages 35–65 years. Surgery has been the primary mode of treatment to date. However, the setting in which mastectomy might be preferred over local excision, and those in which adjuvant radiotherapy might prove beneficial, are unclear. The ability to predict the behavior of these tumors based on histopathologic features such as margin status.

KEYWORDS: phyllodes tumor, breast sarcoma, surgery, radiotherapy.

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### Factors Associated with Risk of Metastatic Recurrence

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<td>Telli</td>
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<td>Yes</td>
<td>Yes</td>
<td>N/A</td>
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</table>

• The lung is the most common site of phyllodes tumor metastases.


• Other metastatic sites can include bone, liver, heart, distant lymph nodes, distant soft tissue locations such as the forearm, the thyroid, and the pancreas.

### Phyllodes Tumor Recurrence

**Clinical Presentation**
- Locally recurrent breast mass following excision of phyllodes tumor

**Workup**
- History and physical exam
- Ultrasound
- Mammogram
- Tissue sampling\(^b\) (histology preferred)
- Consider chest imaging (x-ray or CT, CT contrast optional)

**Findings**
- No metastatic disease
- Metastatic disease

**Treatment**
- Re-excision with wide margins without axillary staging
- Consider post-operative radiation (category 2B)\(^e\)
- Metastatic disease management following principles of soft tissue sarcoma
  (See NCCN Guidelines for Soft Tissue Sarcoma)

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\(^b\)FNA or core biopsy may not distinguish a fibroadenoma from a phyllodes tumor in some cases. The sensitivity of core biopsy for the diagnosis of phyllodes tumor is greater than that of FNA biopsy, but neither core biopsy nor FNA biopsy can always differentiate phyllodes tumors from fibroadenomas. In cases with clinical suspicion for phyllodes tumor, excision of the lesion may be needed for definitive pathologic classification.

\(^e\)There are no prospective randomized data supporting the use of radiation treatment with phyllodes tumors. However, in the setting where additional recurrence would create significant morbidity (e.g., chest wall recurrence following mastectomy), radiation therapy may be considered following the same principles that are applied to the treatment of soft tissue sarcoma.

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Summary (1)

• Surgical management consists of excision to achieve widely negative surgical margins to decrease the likelihood of local breast recurrence. The majority of studies indicate a margin of more than 1 cm is preferable, with some actually advocating for more than 2 cm.

• When phyllodes tumors are excised with positive or close margins, re-excision should be performed.

• The role of adjuvant radiation is controversial, with some studies indicating improved local control but no increased survival when used in patients with borderline or malignant tumors.
Summary (2)

• Locally recurrent tumors may warrant adjuvant chest wall radiation following re-excision.

• Routine adjuvant systemic therapy following initial excision is not recommended. Chemotherapy for locally recurrent tumors remains questionable. When used for treatment of metastatic disease, guidelines for treating sarcoma, rather than breast carcinoma, should be followed.
Thank you for your attention.