Protocol for the Examination of Resection Specimens From Patients with Phyllodes Tumor of the Breast

Version: 1.1.0.0
Protocol Posting Date: June 2022
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

This protocol may be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes excision, segmental resection, lumpectomy, quadrantectomy, and partial or total mastectomy
Tumor Type	**Description**
Phyllodes tumor	

The following should NOT be reported using this protocol:

Procedure
Biopsy
Cytologic specimens

Important Note
The American Joint Committee on Cancer (AJCC) eighth edition and the World Health Organization (WHO) recommend staging malignant phyllodes tumors according to guidelines established for soft tissue sarcomas – extremity and trunk. T category, N category and stage group assignments do not apply to benign or borderline tumors. An abbreviated stage group table that only applies to malignant phyllodes tumors is included in the Explanatory Notes.

Authors
Stuart J. Schnitt, MD*; James L. Connolly, MD; Patrick L. Fitzgibbons, MD, FCAP; Laura H. Rosenberger, MD; Puay Hoon Tan, MD.
With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
* Denotes primary author.

Accreditation Requirements
The use of this case summary is recommended for clinical care purposes but is not required for accreditation purposes. The core and conditional data elements are routinely reported. Non-core data elements are indicated with a plus sign (+) to allow for reporting information that may be of clinical value.

Summary of Changes

v 1.1.0.0

- Updated pN0 to remove text "or unknown lymph node status"

Reporting Template

Protocol Posting Date: June 2022
Select a single response unless otherwise indicated.

CASE SUMMARY: (PHYLLODES OF THE BREAST: Resection)
Standard(s): AJCC-UICC 8
Note: Use of this reporting template is optional and is not required for accreditation purposes. The template can be used for benign and borderline phyllodes tumors, but pathologic stage classification should only be done for those tumors classified as malignant.

SPECIMEN

Procedure
___ Excision (less than total mastectomy)
___ Total mastectomy (including nipple-sparing and skin-sparing mastectomy)
___ Other (specify): _____
___ Not specified

Specimen Laterality
___ Right
___ Left
___ Not specified

TUMOR

+Tumor Site (select all that apply)
___ Upper outer quadrant
___ Lower outer quadrant
___ Upper inner quadrant
___ Lower inner quadrant
___ Central
___ Nipple
___ Clock position
Specify Clock Position (select all that apply)
___ 1 o'clock
___ 2 o'clock
___ 3 o'clock
___ 4 o'clock
___ 5 o'clock
___ 6 o'clock
___ 7 o'clock
___ 8 o'clock
___ 9 o'clock
___ 10 o'clock
___ 11 o'clock
___ 12 o'clock
___ Specify distance from nipple in Centimeters (cm): _____ cm
___ Other (specify): _____

___ Not specified

Tumor Size

___ Greatest dimension in Millimeters (mm): _____ mm

+Additional Dimension in Millimeters (mm): ____ x ____ mm

___ Cannot be determined (explain): _____

Histologic Type (Note A)

A diagnosis of malignant phyllodes tumor requires the presence of all five of the following features: marked stromal cellularity, marked stromal atypia, stromal overgrowth, an infiltrative tumor border and greater than or equal to 10 mitoses per 10 high power fields (HPFs). Tumors should be classified as borderline when some but not all of these changes are present. Malignant phyllodes tumor is also diagnosed when malignant heterologous elements other than pure well differentiated liposarcoma are present, even if not all of the other histologic features of malignancy are observed.

___ Phyllodes tumor, benign

___ Phyllodes tumor, borderline

___ Phyllodes tumor, malignant

Stromal Cellularity (Note B)

___ Mild (stromal nuclei are non-overlapping)

___ Moderate (some overlapping stromal nuclei)

___ Marked (many overlapping stromal nuclei)

Stromal Atypia (Note C)

___ None

___ Mild (minimal variation in nuclear size, even chromatin, and smooth nuclear contours)

___ Moderate (more variation in nuclear size and irregular nuclear membranes)

___ Marked (marked nuclear pleomorphism, hyperchromasia, and irregular nuclear contours)

Stromal Overgrowth (Note D)

Stromal overgrowth is present when there is at least one low-power microscopic field (4x objective and 10x eyepiece or 22.9 mm2) that contains stroma only without epithelial elements.

___ Absent

___ Present

___ Cannot be determined

Mitotic Rate (Note E)

Malignant phyllodes tumors have greater than or equal to 10 mitoses per 10 high-power fields (40x objective and 10x eyepiece) or greater than or equal to 5 mitoses / mm2. Benign phyllodes tumors have less than 5 mitoses per 10 HPFs (less than 2.5 mitoses / mm2).

___ None identified: _____

___ Specify number of mitoses per 10 high power fields: _____ mitoses per 10 High Power Fields (HPFs)

OR

___ Specify number of mitoses per square Millimeter (mm): _____ mitoses per mm2

___ Cannot be determined

Histologic Tumor Border

A circumscribed border is smooth and well-defined or shows a minimally irregular tumor interface with adjacent stroma. Infiltrative (permeative) tumor borders can be focally infiltrative (unequivocal invasion into adjacent stroma in one low power field) or extensively infiltrative (unequivocal invasion in a wide area or in multiple foci along the tumor periphery).

___ Circumscribed (well-defined; pushing)

___ Infiltrative (permeative)
+___ Focal
+___ Extensive
___ Cannot be determined

Malignant Heterologous Elements (Note F)

A phyllodes tumor is regarded as malignant when there are malignant heterologous elements, even when not all of the other histological features of malignancy are present. This rule does not apply if the only heterologous element is well differentiated liposarcoma. In the breast, those tumors usually lack MDM2 and CDK4 amplifications and have a low metastatic risk. A diagnosis of malignant phyllodes tumor should therefore not be based solely on the presence of well-differentiated liposarcoma without all of the other histologic features of malignancy.

___ Not identified
___ Liposarcoma (excluding well-differentiated liposarcoma)
___ Osteosarcoma
___ Chondrosarcoma
___ Other (specify): _____

MARGINS

Margin Status for Phyllodes Tumor

Margin status is listed as positive if there is ink on phyllodes tumor (i.e., the distance is 0 mm)

___ All margins negative for phyllodes tumor

Closest Margin(s) to Phyllodes Tumor (select all that apply)

___ Anterior
___ Posterior
___ Superior
___ Inferior
___ Medial
___ Lateral
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Distance from Phyllodes Tumor to Closest Margin

Specify in Millimeters (mm)

___ Exact distance: _____ mm
___ Less than: _____ mm
___ Greater than: _____ mm
___ Other (specify): _____
___ Cannot be determined (explain): _____

___ Phyllodes tumor present at margin

Margin(s) Involved by Phyllodes Tumor (select all that apply)

___ Anterior
___ Posterior
___ Superior
___ Inferior
___ Medial
___ Lateral
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Margin Comment: _____

REGIONAL LYMPH NODES

Regional Lymph Node Status
___ Not applicable (no regional lymph nodes submitted or found)
___ Regional lymph nodes present
___ All regional lymph nodes negative for tumor
___ Tumor present in regional lymph nodes
Number of Lymph Nodes with Tumor
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
Number of Lymph Nodes Examined
___ Exact number (specify): _____
___ At least (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Regional Lymph Node Comment: _____

DISTANT METASTASIS

Distant Site(s) Involved, if applicable
___ Not applicable
___ Other (specify): _____
___ Cannot be determined

PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th Edition) (Note G)
Staging applies only to malignant phyllodes tumors. pT and pN categories should not be assigned for benign and borderline tumors.

Pathologic Stage Classification (pTNM, AJCC 8th Edition) (required only if the tumor is malignant)
Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. As per the AJCC (Chapter 1, 8th Ed.) it is the managing physician's responsibility to establish the final pathologic stage based upon all pertinent information, including but potentially not limited to this pathology report.
___ Not applicable (tumor is not graded as malignant)
___ Tumor is malignant
The following section applies only if the tumor is malignant. Do not assign pT and pN stage categories for benign or borderline tumors.
TNM Descriptors (select all that apply)
___ Not applicable
___ m (multiple)
___ r (recurrent)
___ y (post treatment)

pT Category

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor
___ pT1: Tumor 5 cm or less in greatest dimension
___ pT2: Tumor more than 5 cm but not more than 10 cm
___ pT3: Tumor more than 10 cm but not more than 15 cm
___ pT4: Tumor more than 15 cm in greatest dimension

pN Category

When no lymph nodes are present, the pathologic 'N' category is not assigned (pNX is not used and should not be reported)

___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)
___ pN0: No regional lymph node metastasis
___ pN1: Regional lymph node metastasis

pM Category (required only if confirmed pathologically)

___ Not applicable - pM cannot be determined from the submitted specimen(s)
___ pM1: Distant metastasis

ADDITIONAL FINDINGS

+Additional Findings (select all that apply)

___ Fibroepithelial proliferation (coexisting fibroadenoma or fibroadenomatoid change in the tissue surrounding the phyllodes tumor)
___ Atypical ductal hyperplasia
___ Atypical lobular hyperplasia
___ Other (specify): _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Histologic Type / Grade

Phyllodes tumors are classified as malignant when all five of the following histological features are present: marked stromal hypercellularity; marked stromal atypia; stromal overgrowth; an infiltrative (permeative) tumor border; and greater than or equal to 10 mitotic figures in 10 high power fields (see Table 1). Tumors should be classified as borderline if some but not all of these changes are present.

There are rare phyllodes tumors that do not have all five histologic features but display malignant behavior. When a tumor lacks one or two features but shows severe abnormalities in others, the pathologist should consider adding a comment that such tumors may exhibit aggressive behavior.

Benign phyllodes tumors have mild stromal hypercellularity, minimal to no stromal atypia, no stromal overgrowth, circumscribed (pushing) tumor borders and less than or equal to 4 mitoses per 10 high-power fields (HPFs).[1]

The distinction between benign and borderline phyllodes tumors is not well-defined and there is no universal agreement which histologic features should be given greater emphasis. When the distinction between a benign and borderline tumor is unclear, it may be helpful to include a comment about this in the pathology report.

A phyllodes tumor is also categorized as malignant if there is a malignant heterologous mesenchymal component (e.g. liposarcoma, chondrosarcoma, osteosarcoma) even if the other histological parameters are not present, or if only some are present. An exception to this rule is if the heterologous element is atypical lipomatous tumor/well-differentiated liposarcoma. Well-differentiated liposarcomas in the breast usually lack MDM2 and CDK4 amplifications and appear to have a low metastatic risk. Hence, a diagnosis of malignant phyllodes tumor should not be based solely on the presence of well-differentiated liposarcoma without the other histologic features that support malignancy.[1]

Table 1. Histologic features of phyllodes tumors (adapted from Tse G, et al[2])

Histologic feature	Benign	Borderline	Malignant
Stromal cellularity	Mild	Moderate	Marked
Stromal atypia	Mild or none	Mild or moderate	Marked
Stromal overgrowth	Absent	Absent or very focal	Present
Mitotic rate	≤4 mitoses per 10 HPFs or <2.5 mitoses per mm^2	5 - 9 mitoses per 10 HPFs or 2.5 - 5 mitoses/mm^2	≥10 mitoses per 10 HPFs or ≥5 mitoses/mm^2
Tumor border	Circumscribed	Usually circumscribed but may be focally infiltrative	Focally or extensively infiltrative (permeative)
Malignant heterologous stromal elements	Absent	Absent	Sometimes present

HPF: High power field (40x objective and 10x eyepiece)

References

1. Tan BY, Apple SK, Badve S, et al. Phyllodes tumours of the breast: a consensus review. *Histopathology*. 2016;68:5-21.
2. Tse G, Koo JS, Thike AA. Phyllodes tumour. In: WHO Classification of Tumours Editorial Board. Breast Tumours, 5th ed, vol 2. Lyon (France): *International Agency for Research on Cancer*; 2019:172-176.

B. Stromal Cellularity

Mild hypercellularity is characterized by a slight increase in stromal cells as compared with normal perilobular stroma, with evenly spaced nuclei that are not touching or overlapping, while marked stromal cellularity shows confluent areas of densely overlapping nuclei. Moderate stromal cellularity has findings that are intermediate between the two, with some overlapping stromal nuclei.[1,2]

References

1. Tan BY, Apple SK, Badve S, et al. Phyllodes tumours of the breast: a consensus review. *Histopathology*. 2016;68:5-21.
2. Jara-Lazaro AR, Akhilesh M, Thike AA, et al. Predictors of phyllodes tumours on core biopsy specimens of fibroepithelial neoplasms. *Histopathology*. 2010; 57:220–232.

C. Stromal Atypia

Mild stromal atypia is reported when there is little variation in nuclear size and the nuclear contours are smooth. Cases with moderate atypia show some variation in the size of stromal nuclei and some wrinkling of nuclear membranes. Marked stromal atypia is identified when there is marked variation in nuclear size, coarse chromatin and irregular nuclear membranes with discernible nucleoli.[1,2]

References

1. Tan BY, Apple SK, Badve S, et al. Phyllodes tumours of the breast: a consensus review. *Histopathology*. 2016;68:5-21.
2. Jara-Lazaro AR, Akhilesh M, Thike AA, et al. Predictors of phyllodes tumours on core biopsy specimens of fibroepithelial neoplasms. *Histopathology*. 2010; 57:220–232.

D. Stromal Overgrowth

Stromal overgrowth is defined by the absence of epithelial elements in at least one low-power microscopic field containing only stroma. A low-power field can be defined either as a 4x objective and 10x eyepiece or as 22.9 mm^2.[1,2,3]

References

1. Tan BY, Apple SK, Badve S, et al. Phyllodes tumours of the breast: a consensus review. *Histopathology*. 2016;68:5-21.
2. Jara-Lazaro AR, Akhilesh M, Thike AA, et al. Predictors of phyllodes tumours on core biopsy specimens of fibroepithelial neoplasms. *Histopathology*. 2010; 57:220–232.
3. Tan PH, Thike AA, Tan WJ, et al. Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins. *J Clin Pathol* 2012;65:69-76.

E. Mitotic Rate

A diagnosis of malignant phyllodes tumor requires at least 10 mitoses per 10 high power fields (40x objective and 10x eyepiece) or at least 5 mitoses/mm^2. Mitotic activity in benign phyllodes tumor is usually low (less than or equal to 4 mitoses per 10 HPFs or less than 2.5 mitoses per mm^2). Borderline phyllodes tumors usually have 5 to 9 mitoses per 10 HPF (2.5 to 5 mitoses/mm^2).[1]

To report the number of mitoses per square millimeter, the area of the high power field must be known, but microscopes vary in field size so the area must be determined for each microscope. The diameter of an HPF can be determined using a micrometer or calculated by using the method below:

Using a clear ruler, measure the diameter of a low-power field. This number can be used to calculate a constant based on the following formula:

Eyepiece Magnification x Objective Magnification x Microscopic Field Diameter = A Constant

Once the value of the constant is known, the diameter of the high power field can be calculated by using the following formula:

High Power Field Diameter = Constant / (Eyepiece Magnification x Objective Magnification)

Half of the field diameter is the radius of the field (r), which can then be used to calculate the area of the HPF:

Area of High Power Field = r^2 x 3.1415

References

1. Tse G, Koo JS, Thike AA. Phyllodes tumour. In: *WHO Classification of Tumours Editorial Board. Breast Tumours, 5th ed*, vol 2. Lyon (France): International Agency for Research on Cancer; 2019:172-176.

F. Malignant Heterologous Elements

Malignant heterologous elements include osteosarcoma, chondrosarcoma, rhabdomyosarcoma, and rarely other types of sarcoma. The presence of well differentiated liposarcoma alone is not used to categorize a phyllodes tumor as malignant.[1,2]

References

1. Tan BY, Apple SK, Badve S, et al. Phyllodes tumours of the breast: a consensus review. *Histopathology*. 2016;68:5-21.
2. Jara-Lazaro AR, Akhilesh M, Thike AA, et al. Predictors of phyllodes tumours on core biopsy specimens of fibroepithelial neoplasms. *Histopathology*. 2010; 57:220–232.

G. Pathologic Stage Classification

The American Joint Committee on Cancer (AJCC) eighth edition[1] and the World Health Organization (WHO)[2] recommend staging malignant phyllodes tumors according to guidelines established for soft tissue sarcomas – extremity and trunk. T category, N category and stage group assignments do not apply to benign or borderline phyllodes tumors and should only be reported if the tumor is malignant.

AJCC Prognostic Stage Groups

T	N	M	Stage group
T1	N0	M0	II
T2	N0	M0	IIIA
T3, T4	N0	M0	IIIB
Any T	N1	M0	IV
Any T	Any N	M1	IV

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y” and “r” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The “m” suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or after initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor before multimodality therapy (ie, before initiation of neoadjuvant therapy).

The “r” prefix indicates a recurrent tumor when staged after a documented disease-free interval and is identified by the “r” prefix: rTNM.

T Category Considerations

Only malignant phyllodes tumors are staged according to AJCC staging rules. The pathologic 'T' category (pT) is not assigned for benign and borderline phyllodes tumors.

N Category Considerations

Regional nodal metastasis is uncommon in phyllodes tumor and lymph nodes may not be sampled. When no lymph nodes are resected or present in the specimen, the pathologic ‘N’ category is not assigned; pNX should not be used.

References

1. Maki RG, Folpe AL, Guadagnolo BA, et al. Chapter 45. Soft tissue sarcoma – Unusual histologies and sites. In: Amin MB, ed. *AJCC Cancer Staging Manual. 8th ed.* New York: Springer; 2017:539-544.
2. Tse G, Koo JS, Thike AA. Phyllodes tumour. In: *WHO Classification of Tumours Editorial Board. Breast Tumours, 5th ed, vol 2*. Lyon (France): International Agency for Research on Cancer; 2019:172-176.