Protocol for the Examination of Biopsy Specimens from Patients with Invasive Carcinoma of the Breast

Version: 1.3.0.0
Protocol Posting Date: June 2026

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
Biopsy	Includes specimens designated needle biopsy, fine needle aspiration and others (for excisional biopsy, see below)
Tumor Type	**Description**
Invasive breast carcinoma of any type, with or without ductal carcinoma in situ (DCIS)	Includes microinvasive carcinoma and carcinoma with neuroendocrine features

The following should NOT be reported using this protocol:

Procedure
Resection (consider Breast Invasive Carcinoma Resection protocol)
Excisional biopsy (consider Breast Invasive Carcinoma Resection protocol)
Tumor Type
Ductal carcinoma in situ (DCIS) without invasive carcinoma (consider the DCIS Biopsy protocol)
Paget disease of the nipple without invasive carcinoma (consider the DCIS Biopsy protocol)
Encapsulated or solid papillary carcinoma without invasion (consider the Breast DCIS Biopsy protocol)
Phyllodes tumor
Lymphoma (consider the Precursor and Mature Lymphoid Malignancies protocol)
Sarcoma (consider the Soft Tissue protocol)

Version Contributors

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Glossary:
Author: Expert who is a current member of the Cancer Committee, or an expert designated by the chair of the Cancer Committee.
Expert Contributors: Includes members of other CAP committees or external subject matter experts who contribute to the current version of the protocol.

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 1.3.0.0

- WHO 6th Edition updates to content and explanatory notes
- Cover page update
- Tumor Site, Histologic Type, Histologic Grade, Nuclear Pleomorphism, Mitotic Rate, and Overall Grade question updates
- Largest Invasive Focus in this Limited Biopsy Sample in Millimeters (mm) question made required (core)
- Ductal Carcinoma In Situ question modifications to include addition of Extent of DCIS (relative to invasion) question and updates to Architectural Pattern question, previously required
- Added Additional Lesion(s) question

Reporting Template

Protocol Posting Date: June 2026
Select a single response unless otherwise indicated.
CASE SUMMARY: (INVASIVE CARCINOMA OF THE BREAST: Biopsy)
Standard(s):
This template is recommended for reporting biopsy specimens, but is not required for accreditation purposes.

SPECIMEN

Procedure
___ Needle biopsy
___ Fine needle aspiration
___ Other (specify): _____
___ Not specified

Specimen Laterality
___ Right
___ Left
___ Not specified

TUMOR

+Tumor Site
Tumor Site descriptor should specify the location of the biopsy site as designated by radiology or clinical note (e.g., "R1, 3:00, 2 cm from nipple" or "upper outer quadrant").
___ Specify tumor site / location: _____
___ Not specified

Histologic Type (Note A)
The latest WHO Breast Tumours criteria should be used to classify histologic type. For favorable histologic types that require greater than 90% for the diagnosis of the pure / non-mixed form (such as mucinous, tubular and cribriform), these histologic types should only be used if the material in the biopsy sample would be consistent with this diagnosis if it all looked similar on surgical excision (e.g., not high-grade and not mixed with non-special type cancer histology). Invasive cancers with histology that is considered a "specific morphologic pattern" of invasive breast cancer of no special type / ductal include: invasive carcinoma with neuroendocrine differentiation, medullary pattern, and other rare patterns such as osteoclast-like stromal giant cell rich. For carcinomas with some features of a specific type that are not definitive, or rare tumor types not otherwise listed, use "Other histologic type" and specify / describe. Microinvasion is not considered a histologic type.
___ Invasive carcinoma of no special type (ductal)
___ Invasive carcinoma of no special type (ductal) with specific morphologic pattern (specify, e.g., with neuroendocrine differentiation, with medullary pattern, etc.): _____
___ Invasive lobular carcinoma, classic
___ Invasive lobular carcinoma, variant pattern (specify, e.g., pleomorphic, histiocytoid, etc.): _____
___ Mixed histologic types (specify types and percentages): _____
___ Tubular carcinoma, features of pure type
___ Invasive cribriform carcinoma, features of pure type
___ Mucinous carcinoma, features of pure type
___ Invasive micropapillary carcinoma
___ Invasive apocrine carcinoma
___ Metaplastic carcinoma, spindle cell
___ Metaplastic carcinoma, with heterologous differentiation / matrix production

___ Metaplastic carcinoma, squamous cell
___ Metaplastic carcinoma, mixed (specify types and percentages): _____
___ Metaplastic carcinoma, favorable type, low-grade adenosquamous
___ Metaplastic carcinoma, favorable type, low-grade fibromatosis-like
___ Metaplastic carcinoma, other type (specify): _____
___ Invasive solid papillary carcinoma
___ Adenoid cystic carcinoma, classic
___ Secretory carcinoma
___ Other histologic type not listed (specify): _____
+Histologic Type Comment: _____

Histologic Grade (Nottingham Histologic Score) (required only if applicable) (Note B)
___ Not applicable (no residual carcinoma or microinvasion only)
___ Nottingham Score

Tubule Formation
___ Score 1 (greater than 75% of tumor area forming glandular / tubular structures)
___ Score 2 (10% to 75% of tumor area forming glandular / tubular structures)
___ Score 3 (less than 10% of tumor area forming glandular / tubular structures)
___ Only microinvasion present (not graded)
___ Score cannot be determined (explain): _____

Nuclear Pleomorphism
___ Score 1 (similar / less than 1.5 times the size of benign epithelial cell nuclei, minimal pleomorphism, even chromatin pattern, nucleoli either not visible or very inconspicuous)
___ Score 2 (larger / 1.5–2 times the size of benign epithelial cell nuclei, mild to moderate pleomorphism and visible but small and inconspicuous nucleoli)
___ Score 3 (larger / greater than 2 times the size of benign epithelial cell nuclei, vesicular chromatin, marked variation in size and shape of nuclei, often prominent nucleoli)
___ Only microinvasion present (not graded)
___ Score cannot be determined (explain): _____

Mitotic Rate
See Table 1 in Note B
___ Score 1
___ Score 2
___ Score 3
___ Only microinvasion present (not graded)
___ Score cannot be determined (explain): _____

Overall Grade
___ Grade 1 (scores of 3, 4 or 5)
___ Grade 2 (scores of 6 or 7)
___ Grade 3 (scores of 8 or 9)
___ Only microinvasion present (not graded)
___ Score cannot be determined (explain): _____
+Histologic Grade Comment: _____

Largest Invasive Focus in this Limited Biopsy Sample in Millimeters (mm)
Measure the largest invasive focus based on span in a single core (using judgement to determine if small discontinuous foci are more likely to be separate vs contiguous). Do not add up extent in multiple separate cores since this may overestimate size. Note that the largest invasive focus in a core biopsy sample may be used for future pT stage if invasive cancer is more limited or absent in the final surgical specimen (non-neoadjuvant treatment setting only).

___ Exact measurement: _____ mm
___ At least: _____ mm
___ Other (specify): _____
___ Cannot be determined (explain): _____

Ductal Carcinoma In Situ (DCIS) (Note C)
___ Not identified
___ Present
+Extent of DCIS (relative to invasion)
___ DCIS is more extensive than invasive carcinoma
___ DCIS is similar in extent to invasive carcinoma
___ DCIS is focal or a minor component relative to invasive carcinoma
___ Other (specify): _____
+Architectural Pattern(s) (select all that apply)
___ Comedo
___ Cribriform
___ Micropapillary
___ Papillary
___ Solid
___ Solid papillary carcinoma in situ
___ Encapsulated papillary carcinoma in situ
___ Paget disease (DCIS involving nipple skin)
___ Other (specify): _____
Nuclear Grade
___ Grade I (low)
___ Grade II (intermediate)
___ Grade III (high)
___ Other (specify): _____
___ Cannot be determined (explain): _____
Necrosis
___ Not identified
___ Present, focal (small foci or single cell necrosis)
___ Present, central (expansive "comedo" necrosis)
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Cannot be excluded (explain): _____
+DCIS Comment: _____

+Lymphatic and / or Vascular Invasion
___ Not identified
___ Present
___ Cannot be determined: _____
+Lymphatic and / or Vascular Invasion Comment: _____
+Microcalcifications (Note D) (select all that apply)
___ Not identified
___ Present in DCIS
___ Present in invasive carcinoma
___ Present in non-neoplastic tissue
___ Other (specify): _____

+Additional Lesion(s) (select all that apply)
Non-classic / variant subtypes of LCIS include: Pleomorphic LCIS (pleomorphic nuclei greater than 4 times the size of a lymphocyte or equivalent to nuclei of high-grade DCIS) and Florid LCIS (proliferation of cells cytologically similar to those of classic LCIS but expanding the acini of the involved TDLUs so that little to no residual intervening intra-lobular stroma is present, and / or an expanded acinus or duct spans approximately 40–50 cells in diameter). Comedonecrosis in classic LCIS may also be considered non-classic / variant (describe in "Other (specify)").

___ None identified
___ Lobular carcinoma in situ, classic
___ Lobular carcinoma in situ, pleomorphic
___ Lobular carcinoma in situ (specify): _____
___ Atypical lobular hyperplasia
___ Atypical ductal hyperplasia
___ Flat epithelial atypia
___ Other (specify): _____

+Additional Lesion(s) Comment: _____

ADDITIONAL FINDINGS (Note E)

+Additional Findings (specify): _____

SPECIAL STUDIES
For hormone receptor and HER2 reporting, the CAP Breast Biomarker Template should be used. www.cap.org/cancerprotocols

+Breast Biomarker Studies (specify pending studies): _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Histologic Type

This protocol applies to all invasive carcinomas of the breast. The World Health Organization (WHO)[1] classification of breast carcinoma is recommended, although the protocol does not preclude the use of other classifications or histologic types. Carcinomas may be classified based on the H&E appearance without the use of immunohistochemical studies. The most common histologic types are listed. Uncommon types can be added as free text in the "other" category. Carcinomas may be classified based on the H&E appearance without the use of immunohistochemical studies.

Since biopsy samples are usually only a small representative sample of a larger invasive cancer, the histologic type is preliminary and may be modified upon examination of a subsequent surgical specimen. However, since initial treatment decisions are made based on initial biopsy samples, the preliminary histologic type (and other characteristics) should be based on standardized criteria using the findings in the sample.

For favorable histologic types that require > 90% for the diagnosis of the pure/non-mixed form (such as mucinous, tubular and cribriform), these histologic types should only be used if the material in the sample would be consistent with this diagnosis if it all looked similar on surgical excision (e.g., not high grade and not mixed with non-special type cancer histology). For example, if high-grade or mixed features are present in a mucin producing carcinoma, it should NOT be categorized as "Mucinous carcinoma, features of pure type" since this diagnosis would be excluded per the WHO diagnostic criteria. Consider reporting notable features like mucin production, neuroendocrine differentiation or special patterns using the "Invasive carcinoma of no special type (ductal) with specific morphologic pattern" reporting option. Additional comments can also be added in the optional Histologic Type Comment section to clarify details or modify the type with additional findings such as variant features (e.g., Invasive lobular carcinoma with pleomorphic features, etc.).

References

1. WHO Classification of Tumours Editorial Board. *Breast Tumors*. Lyon (France): International Agency for Research on Cancer; 2026. (WHO classification of tumours series, 6th ed).

B. Histologic Grade

All invasive breast carcinomas should be graded.[1,2,3,4] The Nottingham combined histologic grade (Elston-Ellis modification of Scarff-Bloom-Richardson grading system) should be used for reporting. Within each stage grouping, there is a relation between histologic grade and outcome.

The Nottingham combined histologic grade evaluates the amount of tubule formation, the extent of nuclear pleomorphism, and the mitotic count (or mitotic rate). Each variable is given a score of 1, 2, or 3, and the scores are added to produce a grade. The mitotic score is determined by the number of mitotic figures found in 10 consecutive high-power fields (HPF) in the most mitotically active part of the tumor. Only clearly identifiable mitotic figures should be counted; hyperchromatic, karyorrhectic, or apoptotic nuclei are excluded. Because of variations in field size, the HPF size must be determined for each microscope and the appropriate point score determined accordingly. It is recommended that the size be measured by using a micrometer. However, the diameter of an HPF can also be calculated by using the method below.

Measuring the Size of a High-Power Field (HPF) with a Ruler

Use a clear ruler to 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

When the value of the constant is known, the diameter of an HPF can be calculated for other objectives by using the following formula:
Unknown 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:
3.1415 x r^2= Area of Microscopic Field

If the microscopic field diameter or the area of the field is known, Table 1 can be used to determine the number of mitoses corresponding to different scores.

Table 1. Score Categories According to Field Diameter and Mitotic Count

Scoring Categories of Mitotic Counts				
		Number of mitoses per 10 fields corresponding to:		
Field diameter (mm)	Area (mm^2)	Score 1	Score 2	Score 3
0.40	0.125	≤4	5 to 9	≥10
0.41	0.132	≤4	5 to 9	≥10
0.42	0.139	≤5	6 to 10	≥11
0.43	0.145	≤5	6 to 10	≥11
0.44	0.152	≤5	6 to 11	≥12
0.45	0.159	≤5	6 to 11	≥12
0.46	0.166	≤6	7 to 12	≥13
0.47	0.173	≤6	7 to 12	≥13
0.48	0.181	≤6	7 to 13	≥14
0.49	0.189	≤6	7 to13	≥14
0.50	0.196	≤7	8 to 14	≥15
0.51	0.204	≤7	8 to 14	≥15
0.52	0.212	≤7	8 to 15	≥16
0.53	0.221	≤8	9 to 16	≥17
0.54	0.229	≤8	9 to 16	≥17
0.55	0.238	≤8	9 to 17	≥18
0.56	0.246	≤8	9 to 17	≥18
0.57	0.255	≤9	10 to 18	≥19
0.58	0.264	≤9	10 to 19	≥20
0.59	0.273	≤9	10 to 19	≥20
0.60	0.283	≤10	11 to 20	≥21
0.61	0.292	≤10	11 to 21	≥22
0.62	0.302	≤11	12 to 22	≥23
0.63	0.312	≤11	12 to22	≥23
0.64	0.322	≤11	12 to 23	≥24
0.65	0.332	≤12	13 to 24	≥25
0.66	0.342	≤12	13 to 24	≥25
0.67	0.353	≤12	13 to 25	≥26
0.68	0.363	≤13	14 to 26	≥27
0.69	0.374	≤13	14 to 27	≥ 28

From Pathology Reporting of Breast Disease.[2] *Copyright 2005 National Health Service Cancer Screening Programme and The Royal College of Pathologists. Adapted with permission.*

References

1. Ellis IO, Elston CW. Histologic grade. In: O'Malley FP, Pinder SE, eds. *Breast Pathology.* Philadelphia, PA: Elsevier; 2006:225-233.
2. Ellis I, Webster F, Allison KH et al.: Dataset for reporting of the invasive carcinoma of the breast: recommendations from the International Collaboration on Cancer Reporting (ICCR).(2024) *Histopathology* 85, 418–436. https://doi.org/10.1111/his.15191

3. Schwartz AM, Henson DE, Chen D, Rajamarthandan S: Histologic grade remains a prognostic factor for breast cancer regardless of the number of positive lymph nodes and tumor size: a study of 161 708 cases of breast cancer from the SEER Program. *Arch Pathol Lab Med.* 2014;138(8):1048-52. doi: 10.5858/arpa.2013-0435-OA.
4. Royal College of Pathologists. Dataset for histopathological reporting of breast disease in surgical excision specimens of breast cancer, November 2024 https://www.rcpath.org/static/d255f34c-176a-490d-9b5a7d58ac85f3a6/b4cf9184-33ff-4662-b33990b3701c3d87/G148-Dataset-for-histopathological-reporting-of-breast-disease-in-surgical-excision-specimens-of-breast-cancer.pdf Accessed February 6, 2026.

C. Ductal Carcinoma In Situ
Nuclear Grade of DCIS
The nuclear grade of DCIS is determined using 6 morphologic features (Table 1).[1,2,3,4]

Table 2. Nuclear Grade of Ductal Carcinoma in Situ

Feature	Grade I (Low)	Grade II (Intermediate)	Grade III (High)
Pleomorphism	Monotonous (monomorphic)	Intermediate	Markedly pleomorphic
Size	1.5 to 2 x the size of a normal red blood cell or a normal duct epithelial cell nucleus	Intermediate	>2.5 x the size of a normal red blood cell or a normal duct epithelial cell nucleus
Chromatin	Usually diffuse, finely dispersed chromatin	Intermediate	Usually vesicular with irregular chromatin distribution
Nucleoli	Only occasional	Intermediate	Prominent, often multiple
Mitoses	Only occasional	Intermediate	May be frequent
Orientation	Polarized toward luminal spaces	Intermediate	Usually not polarized toward the luminal space

Necrosis
The presence of necrosis is correlated with the finding of mammographic calcifications (i.e., most areas of necrosis will calcify). Ductal carcinoma in situ that presents as mammographic calcifications often recurs as calcifications. Necrosis can be classified as follows:

- Central ("comedo"): The central portion of an involved ductal space is replaced by an area of expansive necrosis that is easily detected at low magnification. Ghost cells and karyorrhectic debris are generally present. Although central necrosis is generally associated with high-grade nuclei (i.e., comedo DCIS), it can also occur with DCIS of low or intermediate nuclear grade.
- Focal: Small foci, indistinct at low magnification, or single cell necrosis.

Necrosis should be distinguished from secretory material, which can also be associated with calcifications, but does not include nuclear debris.

References
1. Morrow M, Harris JR. Local management of invasive breast cancer (chapter 33). In: Harris JR, Lippman ME, Morrow M, Osborne KE, eds. *Diseases of the Breast*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:522-523.
2. Bane A.: Ductal Carcinoma In Situ: What the Pathologist Needs to Know and Why. *Int J Breast Cancer* 2013:914053. doi: 10.1155/2013/914053.
3. Hanna WM, Parra-Herran C, Lu FI et al. Ductal carcinoma in situ of the breast: an update for the pathologist in the era of individualized risk assessment and tailored therapies. *Mod Pathol.* 2019 32 (7): 896-915.

4. Fitzgibbons PL, Connelly, JL. Protocol for the Examination of Specimens from Patients with Ductal Carcinoma In Situ (DCIS) of the Breast. 2021; www.cap.org/cancerprotocols., accessed March 3, 2026.

D. Microcalcifications

Cancer found in biopsies performed for microcalcifications will almost always be at the site of the calcifications or in close proximity. The presence of the targeted calcifications in the specimen should be confirmed by specimen radiography. The pathologist must be satisfied that the specimen has been sampled in such a way that the lesion responsible for the calcifications has been examined microscopically. The relationship of the radiologic calcifications to the invasive carcinoma and the DCIS should be indicated.

If calcifications can be seen in the specimen radiograph but not in the initial histologic sections, deeper levels should be examined. If needed, radiographs of the paraffin block(s) may be obtained to detect calcifications remaining in the block(s). If microcalcifications cannot be confirmed by routine microscopic evaluation, polarized light may be helpful, since calcium oxalate crystals are refractile and polarizable but usually clear or tinged yellow in H&E sections. On rare occasions, calcifications do not survive tissue processing or prolonged fixation in formalin. Foreign material can sometimes simulate calcifications (e.g., metallic fragments after surgery or trauma).

E. Additional Findings

In some cases, additional pathologic findings are important for the clinical management of patients. If multiple invasive carcinomas are present and differ in histologic type, grade, or the expression of ER, PgR, or HER2, this information should be included as text in this section.