COLLEGE of AMERICAN PATHOLOGISTS

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

Version: 4.11.0.0

Protocol Posting Date: June 2026

CAP Laboratory Accreditation Program Protocol Required Use Date: March 2027

The changes included in this current protocol version affect accreditation requirements. The new deadline for implementing this protocol version is reflected in the above accreditation date.

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Excision less than total mastectomy	Includes specimens designated excision, segmental resection, lumpectomy, quadrantectomy, and segmental or partial mastectomy, with or without axillary contents
Total Mastectomy	Includes skin-sparing and nipple-sparing mastectomy, with or without axillary contents
Tumor Type	**Description**
Invasive breast carcinoma of any type, with or without ductal carcinoma in situ (DCIS)	Includes invasive and microinvasive carcinomas

This protocol is NOT required for accreditation purposes for the following:

Procedure
Needle or skin biopsies
Primary resection specimen with no residual cancer (e.g., following neoadjuvant therapy)
Additional excision performed after the definitive resection (e.g., re-excision of surgical margins)
Cytologic specimens

The following specimen types should NOT be reported using this protocol:

Specimen
Very small incisional biopsies (including core needle biopsies)
Re-excision of a biopsy site after removal of most of the carcinoma (including completion mastectomy) if there are no additional findings relevant to the original pT, pN stage

The following tumor types should NOT be reported using this protocol:

Tumor Type
Ductal carcinoma in situ (DCIS) without invasive carcinoma (consider the Breast DCIS Resection protocol)
Paget disease of the nipple without invasive carcinoma (consider the Breast DCIS Resection protocol)
Encapsulated or solid papillary carcinoma without invasion (consider the Breast DCIS Resection protocol)
Phyllodes tumor (consider the Phyllodes tumor protocol)
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

Synoptic reporting with core and conditional data elements for designated specimen types* is required for accreditation.

- Data elements designated as core must be reported.
- Data elements designated as conditional only need to be reported if applicable.
- Data elements designated as optional are identified with "+". Although not required for accreditation, they may be considered for reporting.

This protocol is not required for recurrent or metastatic tumors resected at a different time than the primary tumor. This protocol is also not required for pathology reviews performed at a second institution (i.e., second opinion and referrals to another institution).

Full accreditation requirements can be found on the CAP website under Accreditation Checklists.
A list of core and conditional data elements can be found in the Summary of Required Elements under Resources on the CAP Cancer Protocols website.
**Includes definitive primary cancer resection and pediatric biopsy tumor types.*

Synoptic Reporting

All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired Data element: Response format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
    - Anatomic site or specimen, laterality, and procedure
    - Pathologic Stage Classification (pTNM) elements
    - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location
- Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e., all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

v 4.11.0.0

- WHO 6th Edition updates to content and explanatory notes
- Cover page update
- Tumor Site, Histologic Type, Histologic Grade, Nuclear Pleomorphism, Tumor Size, Tumor Extent, Lymphatic and / or Vascular Invasion, Treatment Effect in Lymph Nodes, and Residual Cancer Burden (RCB) Parameters question updates
- Tumor Focality question updated and made required (core)
- Ductal Carcinoma In Situ question modifications to include updates to Architectural Pattern question
- Added repeating Tumor Characteristic section, Additional Lesion(s), and Extent of LCIS questions
- MARGIN, REGIONAL LYMPH NODE, SPECIAL STUDIES section updates
- Minor pTNM Classification updates to include pT4 staging display item and pM Category Special Case Number(s) with Metastasis question terminology

Reporting Template

Protocol Posting Date: June 2026
Select a single response unless otherwise indicated.
CASE SUMMARY: (INVASIVE CARCINOMA OF THE BREAST: Resection)
Standard(s): AJCC 8

SPECIMEN

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

Specimen Laterality
___ Right
___ Left
___ Not specified

TUMOR

Tumor Focality (Note B)
___ Unifocal
___ Multifocal
  ___ Multiple foci of invasive carcinoma with similar features (e.g., satellites or post-treatment foci of the same histologic type, grade, and biomarkers) (complete only one Tumor Characteristics section)
  ___ Multiple foci of invasive carcinoma with different features (complete a separate Tumor Characteristics section for each distinct invasive carcinoma)
  ___ Other (specify): _____
  ___ Cannot be determined (explain): _____
  +Number of Foci
  ___ Specify number: _____
  ___ At least: _____
  ___ Cannot be determined: _____
___ No residual invasive carcinoma
___ Cannot be determined (explain): _____

Tumor Characteristics

Separate invasive cancers in the same breast should be included in a single cancer summary protocol using the option to report multiple separate foci. The American Joint Committee on Cancer (AJCC) pT stage is assigned based on the largest focus (and the "m" modifier is used only if they are also macroscopically distinct). If a patient has bilateral breast carcinomas, the cancers are reported in separate case summaries.

For multifocal tumors with different features, one may choose to repeat the following 4 elements (Tumor Site, Histologic Type, Histologic Grade, and Tumor Size). For this scenario, assign a unique Tumor Identifier to each invasive cancer you want to report the additional features for (e.g., "Lesion 1" or other more specific descriptor). May be repeated up to 5 times for invasive carcinomas.

Tumor Identifier (required only for cases with multiple tumors): _____

+Tumor Site (Note C)

Tumor Site descriptor should specify the location of the invasive cancer based on correlation with radiology designation and / or gross findings (e.g., "R1, 3:00, 2 cm from nipple" or "upper outer quadrant").

___ Specify tumor site / location: _____

___ Not specified

Histologic Type (Note D)

The latest WHO Breast Tumours criteria should be used to classify histologic type. Pure special type favorable carcinomas (e.g., pure tubular, mucinous, and cribriform) should be at least 90% special type histology (or classified as Mixed). Invasive cancers with histology that is considered a "specific morphologic pattern" of invasive breast cancer 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 tumors not otherwise listed, use "Other histologic type" and specify / describe.

___ No residual invasive carcinoma
___ 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, pure or greater than 90%
___ Invasive cribriform carcinoma, pure or greater than 90%
___ Mucinous carcinoma, pure or greater than 90%
___ Invasive micropapillary carcinoma, pure or greater than 90%
___ 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 E)

___ 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 E

___ 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: _____

Tumor Size (Note F)

The size of the invasive carcinoma should take into consideration the gross and imaging findings correlated with the microscopic examination and be based on the tissue sampling strategy and cassette map. The size does not include adjacent ductal carcinoma in situ (DCIS) or separate satellites of invasion (greater than 5 mm apart). If multifocal, use the largest contiguous focus for pT category.

If there has been a prior core needle biopsy or incisional biopsy showing a larger area of invasion than in the excisional specimen, the largest dimension of the invasive carcinoma in the prior specimen, if known, should be used for determining the T category. This also applies if the entire tumor has been removed by prior biopsy. The size of the largest foci in the two specimens should not be added together.

If there has been prior neoadjuvant treatment and no invasive carcinoma is present, the cancer is classified as ypTis if there is residual DCIS and ypT0 if there is no remaining carcinoma. A cancer protocol is recommended (but not required) in this scenario.

___ No residual invasive carcinoma
___ Microinvasion only (less than or equal to 1 mm)
___ Largest contiguous focus of invasive carcinoma (specify exact measurement in Millimeters (mm)): _____ mm
___ Size of largest invasive focus cannot be determined (explain): _____

+Size(s) and Location(s) of Additional Foci in Millimeters (mm) (if additional invasive foci have similar features)#

 # Values may be recorded on a single line using units (mm) and semicolons (;) as separators

___ Specify size(s) and location(s): _____
___ Cannot be determined: _____

___ Not applicable
+Tumor Size Comment: _____

Ductal Carcinoma In Situ (DCIS) (Note G)

___ Not identified
___ Present

Extent of DCIS (select all that apply)

Extent of DCIS can be reported in a number of ways depending on its relationship to the invasive cancer. This information may be helpful for correlation with the size of imaging findings and describing the relative proportions of invasive disease vs DCIS. Any of the below options can be used (including using multiple options). For example, when DCIS is a minor admixed component of a larger invasive cancer, DCIS extent can be included as a percentage of the entire tumor volume rather than a span in mm. If DCIS extends beyond the invasive cancer, reporting the estimated size of DCIS can be useful for imaging correlation.

___ Admixed with invasive carcinoma
+Specify DCIS as a Percentage of Entire Tumor: _____ %
___ Extends beyond the invasive carcinoma
___ Separate from the invasive carcinoma
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Estimated Size of DCIS

___ Largest dimension of DCIS in Millimeters (mm): _____ mm
___ Other (specify): _____

+Architectural Pattern(s) (select all that apply)

Reporting all architectural patterns present may not always be clinically relevant. The dominant pattern can also be selected. Solid papillary carcinoma in situ and Encapsulated papillary carcinoma patterns ideally should be reported if present in association with invasive cancers. These forms of papillary DCIS / encapsulated carcinoma may lack myoepithelial staining but if they meet criteria otherwise for these diagnoses they are not considered a part of the invasive cancer size (note that invasive forms of solid papillary carcinoma also exist).

___ 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)

+Necrosis

___ Not identified
___ Present, focal (small foci or single cell necrosis)
___ Present, central (expansive "comedo" necrosis)

___ Cannot be excluded (explain): _____

+DCIS Comment: _____

+Additional Lesion(s) (select all that apply)

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 variant (describe in "Other (specify)").

___ Not 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): _____

+Extent of LCIS: _____
+Additional Lesion(s) Comment: _____

Tumor Extent (required only if nipple, skin, or skeletal muscle are present and involved) (Note H)

___ Not applicable (skin, nipple, and skeletal muscle are absent OR are uninvolved and it is not necessary to document their presence)
___ Applicable (nipple, skin or skeletal muscle involved or are uninvolved and want to document their presence)

Nipple Status (select all that apply)

___ Not present in specimen
___ Present and not involved
___ Paget's disease present
___ Involved by invasive carcinoma
___ DCIS in major lactiferous ducts present
___ Other (specify): _____
___ Cannot be determined (explain): _____

Skin Status

___ Not present in specimen
___ Present and not involved
___ Carcinoma directly invades into the dermis or epidermis without macroscopic skin ulceration (this does not change the T classification)
___ Carcinoma directly invades into the dermis or epidermis with macroscopic skin ulceration (classified as T4b)
___ Other (specify): _____
___ Cannot be determined (explain): _____

Macroscopic Skin Satellite Foci

Satellite skin nodules must be separate from the primary tumor and macroscopically identified to assign a category as T4b. Skin nodules identified only on microscopic examination and in the absence of epidermal ulceration or skin edema (clinical peau d'orange) do not qualify as T4b. Such tumors should be categorized based on tumor size.

___ Not identified
___ Present (T4b)
___ Cannot be determined (explain): _____

Skeletal Muscle

Invasion into pectoralis muscle is not considered chest wall invasion, and cancers are not classified as T4a unless

there is invasion deeper than this muscle which typically requires surgical / clinical correlation.
___ Not present in specimen
___ Present and not involved
___ Carcinoma invades skeletal muscle
___ Carcinoma invades into the chest wall deep to pectoralis muscle (classified as T4a)
___ Other (specify): _____
___ Cannot be determined (explain): _____
+Tumor Extent Comment: _____

Lymphatic and / or Vascular Invasion (Note I)
___ Not identified
___ Present, focal (limited to one to two vessels in one block)
___ Present, extensive (greater than two vessels in one block or present in two or more blocks)
___ Other (specify): _____
___ Cannot be determined (explain): _____
+Lymphatic and / or Vascular Invasion Comment: _____

Dermal Lymphatic and / or Vascular Invasion (required only if applicable)
___ Not applicable (no skin present)
___ Not identified
___ Present
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Microcalcifications (Note J) (select all that apply)
___ Not identified
___ Present in DCIS
___ Present in invasive carcinoma
___ Present in non-neoplastic tissue
___ Other (specify): _____

Treatment Effect in Breast (Note K)
The largest contiguous focus of residual tumor, if present, is used to determine ypT category. Treatment-related fibrosis in the tumor bed adjacent to foci of residual invasive carcinoma is not included in determining ypT dimension.
___ No known presurgical therapy
___ No definite response to presurgical therapy in the invasive carcinoma
___ Evidence of response to presurgical therapy in the invasive carcinoma (specify in Treatment Effect in Breast Comment if need to clarify extent of response)
___ No residual invasive carcinoma is present in the breast after presurgical therapy
___ Other (specify): _____
___ Cannot be determined (explain): _____
+Treatment Effect in Breast Comment: _____

Treatment Effect in Lymph Node(s) (required if nodes are submitted and it is known that the patient had presurgical therapy)
The largest contiguous focus of residual tumor in the lymph nodes, if present, is used to determine ypN category. Treatment-related fibrosis adjacent to residual nodal deposits is not included in determining ypN dimension.

___ Not applicable
___ No definite response to presurgical therapy in metastatic carcinoma
___ Metastatic carcinoma present with evidence of response to presurgical therapy (specify in Treatment Effect in Lymph Node(s) Comment if need to clarify extent of response)
___ No lymph node metastases. Fibrous scarring or histiocytic aggregates, possibly related to prior lymph node metastases with pathologic complete response
___ No lymph node metastases and no fibrous scarring or histiocytic aggregates in the nodes
___ Cannot be determined (explain): _____

+Treatment Effect in Lymph Node(s) Comment: _____

Residual Cancer Burden (RCB) Parameters (NCCN recommends reporting RCB parameters in all post-neoadjuvant chemotherapy cases (category 2B) and cancer registries currently collect the RCB Score and Class)# (Note K)

 # The RCB calculator can be found at the MD Anderson website: http://www3.mdanderson.org/app/medcalc/index.cfm?pagename=jsconvert3

Primary Tumor Bed. Note that RCB score and class in the pathology report is the only treatment response parameter that can be collected by most cancer registries (if you report only the individual RCB parameters without calculating and reporting the RCB score and class, the parameters are not used by registries to calculate RCB). If you need to report more than one RCB score (when more than one biologically distinct invasive cancer is / was present), use the "RCB Comment" to describe additional details.

+Greatest Dimension of Primary Tumor Bed Area in Millimeters (mm) (involved by residual invasive carcinoma): _____ mm

+Second Greatest Dimension of Primary Tumor Bed Area in Millimeters (mm): _____ mm

+Percentage of Overall Cancer Cellularity (in the area measured above): _____ %

+Percentage of Cancer that is In Situ Disease: _____ %

Lymph Nodes

+Number of Positive Lymph Nodes: _____

+Diameter of Largest Nodal Metastasis in Millimeters (mm): _____ mm

RCB Calculations

+Residual Cancer Burden Score: _____

+Residual Cancer Burden Class
___ RCB-0 (pCR)
___ RCB-I
___ RCB-II
___ RCB-III

+RCB Comment: _____

MARGINS (Note L)

Final Margin Status for Invasive Carcinoma (required only if residual invasive carcinoma is present in specimen)#

 # Final margin status should be determined based on findings in any additional separately submitted final margins, as well as margins that are considered final in the primary resection specimen (i.e., a final margin status summary). If the final margin status is not clear based on the specimens received (i.e., additional margins without a clear relationship to initial margins), the distances to each can be stated in the "Other (specify)" reporting section with a recommendation for surgical correlation.

___ Not applicable (no residual invasive carcinoma in specimen)
___ All final margins greater than 2 mm from invasive carcinoma
___ Invasive carcinoma present within 0-2 mm of final margins
Margin(s) Involved by Invasive Carcinoma (at ink)
___ None identified
___ Specify involved margins: _____
+Margin(s) Less than 1 mm from Invasive Carcinoma (but not at ink)
___ None identified
___ Specify: _____
+Margin(s) 1 to 2 mm from Invasive Carcinoma
___ None identified
___ Specify: _____
+Margin(s) Greater than 2 mm from Invasive Carcinoma
___ None identified
___ Specify: _____
___ Other (specify): _____
___ Cannot be determined (explain): _____
+Margin Comment for Invasive Carcinoma: _____

Final Margin Status for DCIS (required only if DCIS is present in specimen)#

 # Final margin status should be determined based on findings in any additional separately submitted final margins, as well as margins that are considered final in the primary resection specimen (i.e., a final margin status summary). If the final margin status is not clear based on the specimen(s) received (i.e., additional margins without a clear relationship to initial margins), the distances to each can be stated in the "Other (specify)" reporting section with a recommendation for surgical correlation.

___ Not applicable (no residual DCIS in specimen)
___ All final margins greater than 2 mm from DCIS
___ DCIS present within 0-2 mm of final margins (specify specific margins below)
Margin(s) Involved by DCIS (at ink)
___ None identified
___ Specify involved margins: _____
Margin(s) Less than 1 mm from DCIS (but not at ink)
___ None identified
___ Specify: _____
Margin(s) 1 to 2 mm from DCIS
___ None identified
___ Specify: _____
+Margin(s) Greater than 2 mm from DCIS
___ None identified

___ Specify: _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Margin Comment for DCIS (consider using for pleiomorphic or florid LCIS):

_____

REGIONAL LYMPH NODES (Note M)

For multiple separate primary cancers with different features, it may be relevant to describe the histologic features of the lymph node metastases in the "Regional Lymph Node Comment"

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 node(s)

Number of Lymph Nodes with Macrometastases (greater than 2 mm)

___ Exact number (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

Number of Lymph Nodes with Micrometastases (greater than 0.2 mm to 2 mm and / or greater than 200 cells)

___ Exact number (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

Number of Lymph Nodes with Isolated Tumor Cells (0.2 mm or less OR 200 cells or less) (required only if applicable)#

 # Reporting the number of lymph nodes with isolated tumor cells is required only in the absence of macrometastasis or micrometastasis in other lymph nodes.

___ Not applicable
___ Exact number (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Total Number of Positive Macroscopic and Microscopic Lymph Nodes Counted Towards pN Category#

 # If only micrometastasis is present, count them as pN1mi regardless of how many are present

___ Exact number (specify): _____
___ Other (specify): _____
___ Cannot be determined: _____

Size of Largest Nodal Metastatic Deposit#

 # The size of a tumor deposit is determined by measuring the largest dimension of any group of cells that are touching one another (confluent or contiguous tumor cells), regardless of whether the deposit is confined to the lymph node, extends outside the node (extranodal extension), is totally present outside the lymph node and invading adipose tissue, or is present within a lymphatic channel adjacent to the node.
Specify in Millimeters (mm)

___ Exact size: _____ mm
___ Other (specify): _____
___ Cannot be determined (explain): _____

Extranodal Extension (ENE)#

 # The measurement of extranodal extent can be performed either perpendicular to the lymph node capsule or in another dimension. As a general principle, the larger measurement can be preferentially used but there is no evidence to support a specific method. It is optional to report the specific measurement of extranodal extension, which may not be feasible when extensive (details of extranodal extension can also be described in the "Regional Lymph Node Comment" or the "Other (specify)" sections).

___ Not identified
___ Present

+Largest Measurement of Extranodal Extension
Specify in Millimeters (mm)
___ Exact measurement: _____ mm
___ Other (specify): _____
___ Cannot be determined: _____

+Number of Lymph Nodes with Extranodal Extension
___ Exact number (specify): _____
___ Other (specify): _____
___ Cannot be determined: _____

___ Other (specify): _____
___ Cannot be determined (explain): _____

___ Other (specify): _____
___ Cannot be determined (explain): _____

Total Number of Lymph Nodes Examined (sentinel and non-sentinel)
___ Exact number (specify): _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Regional Lymph Node Comment: _____

DISTANT METASTASIS

Distant Site(s) Involved, if applicable (select all that apply)
___ Not applicable
___ Non-regional lymph node(s) (specify, if possible): _____
___ Lung: _____
___ Liver: _____
___ Bone: _____
___ Brain: _____
___ Other (specify): _____
___ Cannot be determined (explain): _____

pTNM CLASSIFICATION (AJCC 8th Edition) (Note N)
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.

Modified Classification (required only if applicable) (select all that apply)
___ Not applicable
___ y (post-neoadjuvant therapy)

___ r (recurrence)

pT Category

 # For the purposes of this checklist, these categories should only be used in the setting of preoperative (neoadjuvant) therapy for which a previously diagnosed invasive carcinoma is no longer present after treatment. Patients with pathological complete response (absence of residual invasive carcinoma in both the breast and lymph nodes) should be categorized as ypT0N0 or ypTisN0, not ypTX.

___ pT not assigned (cannot be determined based on available pathological information)
___ pT0: No evidence of primary tumor#
___ pTis (DCIS): Ductal carcinoma in situ#

Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.

___ pTis (Paget): Paget disease of the nipple NOT associated with invasive carcinoma and / or carcinoma in situ (DCIS) in the underlying breast parenchyma##

pT1: Tumor less than or equal to 20 mm in greatest dimension

___ pT1mi: Tumor less than or equal to 1 mm in greatest dimension

Round any measurement greater than 1.0-1.9 mm to 2 mm

___ pT1a: Tumor greater than 1 mm but less than or equal to 5 mm in greatest dimension###
___ pT1b: Tumor greater than 5 mm but less than or equal to 10 mm in greatest dimension
___ pT1c: Tumor greater than 10 mm but less than or equal to 20 mm in greatest dimension
___ pT1 (subcategory cannot be determined)
___ pT2: Tumor greater than 20 mm but less than or equal to 50 mm in greatest dimension
___ pT3: Tumor greater than 50 mm in greatest dimension

Invasion of the dermis alone does not qualify as pT4.

pT4: Tumor of any size with direct extension to the chest wall and / or to the skin (ulceration or macroscopic nodules)####

___ pT4a: Extension to the chest wall; invasion or adherence to pectoralis muscle in the absence of invasion of chest wall structures does not qualify as T4
___ pT4b: Ulceration and / or ipsilateral satellite nodules and / or edema (including peau d'orange) of the skin which do not meet the criteria for inflammatory carcinoma
___ pT4c: Both T4a and T4b are present

Inflammatory carcinoma requires the presence of clinical findings of erythema and edema involving at least one-third or more of the skin of the breast. (Note N)

___ pT4d: Inflammatory carcinoma#####
___ pT4 (subcategory cannot be determined)

T Suffix (required only if applicable)

___ Not applicable
___ (m) multiple primary synchronous tumors in a single organ

pN Category

Choose a category based on lymph nodes received with the specimen; immunohistochemistry and / or molecular studies are not required.

If internal mammary lymph nodes, infraclavicular nodes, or supraclavicular lymph nodes are included in the specimen, consult the AJCC Cancer Staging Manual for additional lymph node categories.

___ pN not assigned (no nodes submitted or found)
___ pN not assigned (cannot be determined based on available pathological information)

 # Isolated tumor cells (ITCs) are defined as small clusters of cells not greater than 0.2 mm or single tumor cells, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by immunohistochemical (IHC) methods. Nodes containing only ITCs are excluded from the total positive node count when determining the N category but should be included in the total number of nodes evaluated.

___ pN0: No regional lymph node metastasis identified or ITCs only#
___ pN0 (i+): ITCs only (malignant cell clusters no larger than 0.2 mm) in regional lymph node(s)
___ pN0 (mol+): Positive molecular findings by reverse transcriptase polymerase chain reaction (RT-PCR); no ITCs detected
___ pN1mi: Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
Approximately 1000 tumor cells are contained in a 3-dimensional 0.2 mm cluster. Thus, if more than 200 individual tumor cells are identified as single dispersed tumor cells or as a nearly confluent elliptical or spherical focus in a single histologic section of a lymph node, there is a high probability that more than 1000 cells are present in the lymph node. In these situations, the node should be classified as containing a micrometastasis (pN1mi). Cells in different lymph node cross-sections or longitudinal sections or levels of the block are not added together; the 200 cells must be in a single node profile even if the node has been thinly sectioned into multiple slices. It is recognized that there is substantial overlap between the upper limit of the ITC and the lower limit of the micrometastasis categories due to inherent limitations in pathologic nodal evaluation and detection of minimal tumor burden in lymph nodes. Thus, the threshold of 200 cells in a single cross-section is a guideline to help pathologists distinguish between these 2 categories. The pathologist should use judgment regarding whether it is likely that the cluster of cells represents a true micrometastasis or is simply a small group of isolated tumor cells.
___ pN1a: Metastases in 1-3 axillary lymph nodes, at least one metastasis larger than 2.0 mm##
___ pN1b: Metastases in ipsilateral internal mammary sentinel nodes, excluding ITCs
___ pN1c: pN1a and pN1b combined
___ pN2a: Metastases in 4-9 axillary lymph nodes (at least one tumor deposit larger than 2.0 mm)##
___ pN2b: Metastases in clinically detected internal mammary lymph nodes with or without microscopic confirmation; with pathologically negative axillary nodes
___ pN3a: Metastases in 10 or more axillary lymph nodes (at least one tumor deposit larger than 2.0 mm)##; or metastases to the infraclavicular (Level III axillary lymph) nodes
___ pN3b: pN1a or pN2a in the presence of cN2b (positive internal mammary nodes by imaging); or pN2a in the presence of pN1b
___ pN3c: Metastases in ipsilateral supraclavicular lymph nodes

N Suffix (required only if applicable) (select all that apply)
The (sn) modifier is added to the N category when a sentinel node biopsy is performed (using either dye or tracer) and fewer than six lymph nodes are removed (sentinel and nonsentinel). The (f) modifier is added to the N category to denote confirmation of metastasis by fine needle aspiration / core needle biopsy with NO further resection of nodes.
___ Not applicable
___ (sn): Sentinel node(s) evaluated. If 6 or more nodes (sentinel or nonsentinel) are removed, this modifier should not be used
___ (f): Nodal metastasis confirmed by fine needle aspiration or core needle biopsy

pM Category (required only if confirmed pathologically)
___ Not applicable - pM cannot be determined from the submitted specimen(s)
___ pM1: Histologically proven metastases larger than 0.2 mm
+Specify Case Number(s) with Metastasis (if from a previous procedure): _____

ADDITIONAL FINDINGS (Note O)

+Additional Findings (specify): _____

SPECIAL STUDIES

This section is available to include prior breast cancer biomarker results on the invasive cancer in the resection, typically as reported on the initial core biopsy specimen(s). Specify the case number, tumor identifier (if relevant), and the available biomarker results. The CAP Breast Biomarker Template should be used for reporting biomarkers performed on samples from this resection specimen. Pending biomarker studies can be listed in the "Comments" section of this report.
If information from other specimens is included in completing the case summary (e.g., the results of biomarkers from a prior core needle biopsy or relevant diagnoses on prior specimens), then this must be clearly stated in the "Comments" section, and the accession numbers of the other cases should be provided.

+Biomarker Testing Performed on Prior Case (specify): _____

Specify Tumor Identifier (if multiple tumors are present): _____

+Breast Biomarker Testing Performed on Previous Biopsy (select all that apply)
___ Estrogen Receptor (ER)
Estrogen Receptor (ER) Status
___ Positive (greater than 10% of cells demonstrate nuclear positivity)
+Percentage of Cells with Nuclear Positivity for ER
___ Specify percentage: _____ %
OR
Select range below:
___ 11-20%
___ 21-30%
___ 31-40%
___ 41-50%
___ 51-60%
___ 61-70%
___ 71-80%
___ 81-90%
___ 91-100%
___ Low Positive (1-10% of cells with nuclear positivity)
___ Negative
___ Cannot be determined (explain): _____
___ Progesterone Receptor (PgR)
Progesterone Receptor (PgR) Status
___ Positive
+Percentage of Cells with Nuclear Positivity for PgR
___ Specify percentage: _____ %
OR
Select range below:
___ 1-10%
___ 11-20%
___ 21-30%
___ 31-40%
___ 41-50%
___ 51-60%
___ 61-70%

___ 71-80%
___ 81-90%
___ 91-100%
___ Negative
___ Cannot be determined (explain): _____
___ HER2 (by immunohistochemistry)

HER2 Status (by immunohistochemistry)
 # Breast cancers with HER2 IHC scores of 0+, 1+, or 2+ (ISH negative) may be eligible for treatment targeting non-amplified levels of HER2 expression in the metastatic setting. Currently, patients with no membrane staining by IHC (0) are ineligible / excluded.
___ Negative (Score 0): no membrane staining detected (0 / absent membrane staining)#
___ Negative (Score 0+): membrane staining that is incomplete and is faint / barely perceptible and in less than or equal to 10% of tumor cells (0+ / with membrane staining)#
___ Negative (Score 1+)#
___ Equivocal (Score 2+)#
___ Positive (Score 3+)
+HER2 Clustered Heterogeneity
___ Not identified
___ Present
Percentage of Cells with Uniform Intense Complete Membrane Staining
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined (explain): _____
___ Other (specify): _____
___ Not applicable
___ Cannot be determined (explain): _____
___ HER2 (by in situ hybridization)
HER2 Status (by in situ hybridization)
___ Negative (not amplified)
___ Positive (amplified)
___ Cannot be determined (explain): _____
___ Ki-67
Percentage of Ki-67 Positive Nuclei (select all that apply)
___ Specify percentage: _____ %
___ Specify range: _____
___ Cannot be determined (explain): _____
+Specify Prior Biomarkers on Additional Foci of Invasion (if relevant; i.e., if foci differ in histologic type, grade, or biomarker status; specify tumor identifier for each; may repeat up to 10X): _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Procedures

The following types of breast specimens and procedures may be reported with the case summary:

Excisions: These procedures resect breast tissue without the intent of removing the entire breast. The nipple is usually not included with excisions. Excisions include specimens designated "partial mastectomies," "lumpectomies," and "quadrantectomies."

Total Mastectomy: Removal of all breast tissue, generally including the nipple and areola.

- Simple mastectomy: This procedure consists of a total mastectomy without removal of axillary lymph nodes.
- Skin-sparing mastectomy: This is a total mastectomy with removal of the nipple and only a narrow surrounding rim of skin.
- Nipple sparing mastectomy: This is a total mastectomy without removal of skin or nipple. The subareolar tissue is examined and the nipple later removed if involved by carcinoma.
- Modified radical mastectomy: This procedure consists of a total mastectomy with an axillary dissection. In the case summary, the breast and lymph node specimens are documented separately. A small portion of pectoralis muscle is sometimes removed.
- Radical mastectomy: This procedure consists of a total mastectomy with removal of the pectoralis major and pectoralis minor muscles as well as axillary contents. This type of specimen and procedure can be indicated on the case summary as "Other."

B. Tumor Focality (Single or Multiple Foci of Invasive Carcinoma)

If a single focus of invasive cancer is present, Unifocal is selected and the specific tumor characteristics are reported in the subsequent sections.

If multiple invasive carcinomas are present in the same breast, Multifocal should be selected and the specific scenario clarified using the reporting options (or other). Foci of invasion can be considered separate if they are at least 5 mm apart (with some judgment involved for exceptions like post-neoadjuvant treatment, microinvasion, etc.). For pT categorization purposes, the "(m)" modifier is used to indicate multiple foci are present that are macroscopically distinct, and the size of the largest focus is used for the pT category (the "(m)" modifier is not used when there are only microscopic satellites). If there are bilateral invasive cancers, separate reporting protocols for each breast are utilized.

If there are multiple foci of invasive carcinoma with similar features (same histologic type, grade and biomarkers) only one Tumour Characteristics section is needed, but the number of foci present can be estimated and reported here, and the in the Tumor Size section the sizes of additional foci can be reported.

When there are multiple foci of invasive carcinoma that are considered separate and biologically distinct, a separate Tumor Characteristics section for each invasive cancer can be reported. A unique **Tumor Identifier** is required (e.g., "L1 invasive lobular carcinoma", "Lesion 2" or "Larger invasive focus", etc.) to distinguish each cancer that will have a separately reported Tumor Site, Histologic Type, Histologic Grade, and Tumor Size.

Breast cancer biomarker status (ER, PR, HER2, and/or Ki67) for different cancers on prior biopsies can be reported in the Special Studies section if relevant. If being performed on the surgical specimen samples,

separate Breast Cancer Biomarker protocols should be used to report on separate invasive cancers with the appropriate Tumor Identifier included for each.

In Figure B1, examples of multiple foci of invasive carcinoma include the following:

- **Extensive carcinoma in situ (CIS) with multiple foci of invasion (Figure B1, A).** Extensive DCIS is sometimes associated with multiple areas of invasion. The invasive carcinomas are usually similar in histologic appearance and immunophenotype, unless the DCIS is heterogeneous.
- **Invasive carcinoma with smaller satellite foci of invasion (Figure B1, B).** A large carcinoma is sometimes surrounded by smaller adjacent foci of invasion. They are usually identical in histologic appearance and immunophenotype to the dominant carcinoma. If foci are more than 5 mm away from the main tumor, they can be considered separate satellites (multifocal, similar histologic features).
- **Invasive carcinoma with extensive lymphovascular invasion (LVI) (Figure B1, C).** Additional foci of invasion may arise from areas of LVI (i.e., an intramammary metastasis). The multiple carcinomas are usually identical in histologic appearance and immunophenotype. The origin of satellite skin nodules classified as T4b is generally due to invasion arising from foci of dermal lymphovascular invasion.
- **#Multiple biologically separate invasive carcinomas is illustrated in Panel D.** Some patients have multiple, synchronous, biologically independent carcinomas. If invasive carcinomas differ in histologic type, grade, or biomarker status, then these details may be reported using separate Tumor Characteristics sections in the same protocol.
- **Invasive carcinomas after neoadjuvant therapy (Figure B1, E).** Cancers with a significant response to chemotherapy typically present as multiple residual foci within a fibrotic tumor bed (see Note K). The foci of invasion are usually identical in appearance and immunophenotype.
- **Transection of a single carcinoma into multiple fragments (Figure B1, F).** If invasive carcinoma is present in multiple fragments of a fragmented specimen, transection of 1 carcinoma should be considered. Correlation with clinical and imaging findings can sometimes be helpful to determine the best size for T classification and to determine whether or not multiple foci were present.

 # Multiple biologically separate invasive carcinomas may now be reported using separate Tumor Characteristics sections in the same protocol.

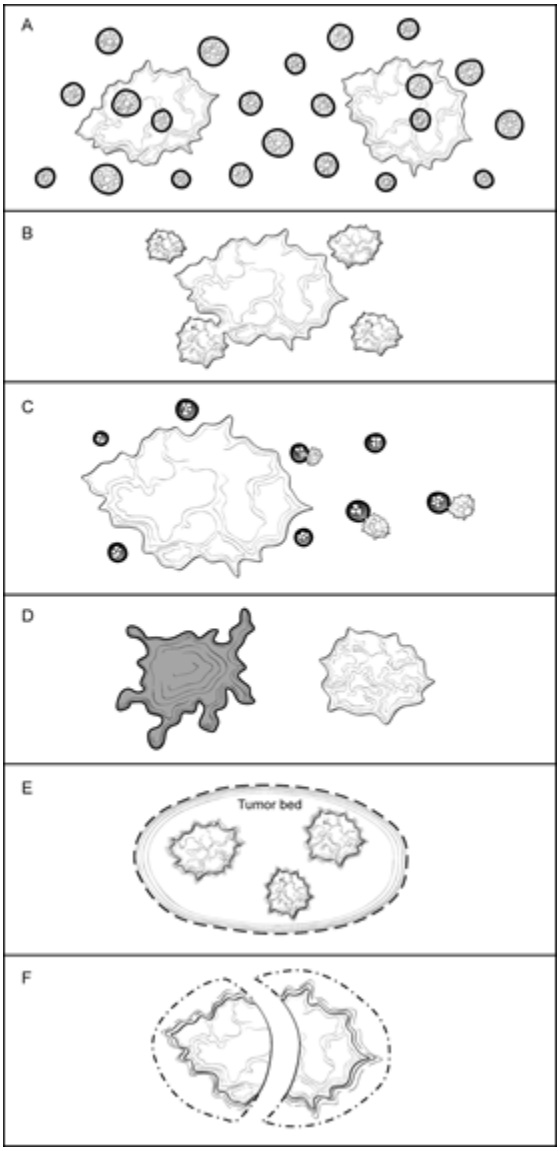

Figure B1. Multiple Invasive Carcinomas. A. Extensive carcinoma in situ with multiple foci of invasion. **B**. Invasive carcinoma with smaller satellite foci. **C**. Invasive carcinoma with extensive lymphovascular invasion. Areas of lymphovascular invasion can give rise to additional foci of invasive carcinoma (i.e., intramammary metastasis). **D.** Multiple biologically separate invasive carcinomas. These carcinomas are usually widely separated and may be histologically and immunophenotypically distinct. **E.** Invasive carcinomas after presurgical (neoadjuvant) therapy. If there is a marked response to treatment, multiple foci of carcinoma may be scattered over a fibrotic tumor bed. **F**. Transection of a single carcinoma into multiple fragments. If a carcinoma is transected during excision, it may be difficult to determine if 1 or multiple carcinomas are present.

C. Tumor Identifier and Tumor Site

A unique Tumor Identifier is required only when reporting Tumor Characteristics for multiple separate ipsilateral invasive cancers. This unique identifier should help distinguish each invasive focus and can be terms used clinically, in the imaging reports, gross exam or as designated by the pathologist (e.g., “R1 focus,” “Lesion 2,” etc.). The site of an invasive carcinoma is also helpful to document, when provided by the surgeon, breast imaging, or previous pathology report, to correlate with prior studies (e.g., a core needle biopsy) or with future biopsies or cancer events. The site is often indicated by a clock position and distance from the nipple or by involved quadrant(s) when large.

The approximate tumor site can be determined in a mastectomy. However, it is sometimes difficult to correlate exactly with the position as determined in vivo because of differences in how the specimen would be positioned on the chest wall (i.e., the skin ellipse may be horizontal or point to the axilla). It is helpful to locate the carcinoma with respect to the clinical site or imaging site, when possible.

If the patient has undergone presurgical (neoadjuvant) therapy and there is no residual invasive carcinoma, the tumor site refers to the location of the prior invasive carcinoma.

D. 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; however, the ER and HER2 status can sometimes help inform histologic type.

Pure special type favorable histologic type carcinomas of luminal/ER positive biology (ex. pure tubular, mucinous and cribriform) should be at least 90% special type histology (or classify as Mixed).

For metaplastic carcinomas, the specific subtype should ideally be reported since these can have very different outcomes. Subtypes of metaplastic carcinoma recognized by the WHO include spindle cell, heterologous differentiation/matrix production, squamous cell and mixed forms as well as two favorable types: low-grade adenosquamous carcinoma and fibromatosis-like.

Invasive cancers with histology that is considered a “specific morphologic pattern” of invasive breast cancer no special type/ductal include: invasive carcinoma with neuroendocrine differentiation, medullary pattern, and other rare patterns such as osteoclast-like stromal giant cell rich.

A modified list is presented in the case summary based on the most frequent types of invasive carcinomas and terminology that is in widespread usage. The modified list is intended to capture the majority of tumors and reduce the frequency of tumors being reported as “other.”

Very rare types, such as invasive papillary carcinoma, neuroendocrine tumor, acinic-cell like, mucoepidermoid carcinoma, mucinous cystadenocarcinoma and tall cell carcinoma with reversed polarity should be indicated by their WHO terminology in the “other” category. For carcinomas with some features of a specific type that are not definitive, the features can be described in the “other” category.

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

E. 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 or by digital image measurements. 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:

$3.1416 \times r^2 =$ 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*. 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.

F. Tumor Size (Size of Invasive Carcinoma)

The size of an invasive carcinoma is an important prognostic factor. The single greatest dimension of the largest invasive carcinoma is used to determine T classification (Figure E1, A through F). The best size for AJCC pT classification should use information from imaging, gross examination, and microscopic evaluation.[1] Sizes should be measured to the nearest millimeter.

The clinical information, gross evaluation and tissue submission strategy are essential to determining an accurate pT category. Knowing the following clinical/radiographic information when deciding the tissue

sampling strategy is helpful: 1. Expected number and size of lesions in the resection (and location for mastectomy specimens). 2. Prior biopsies and/or clips (and specific diagnoses). 3. If patient had neoadjuvant treatment for the current cancer.

Visual determination of size is often unreliable, especially for invasive lobular carcinoma, post-neoadjuvant invasive cancers, and carcinoma in situ. The size by palpation of a hard mass correlates with invasion of tumor cells into stroma when there is a robust desmoplastic response. Frequently, there is not a palpable hard mass or invasion may extend beyond a palpable abnormality. Therefore, it is helpful to use serial sequential sampling, focusing on the area around the biopsy site. A schematic diagram indicating where blocks have been submitted, slice thickness, and the location of blocks involved by invasive carcinoma will aid in determining tumor size. Specimen slices, especially of the peripheral slices submitted should be thinned to 3-4 mm to avoid overestimating tumor size.

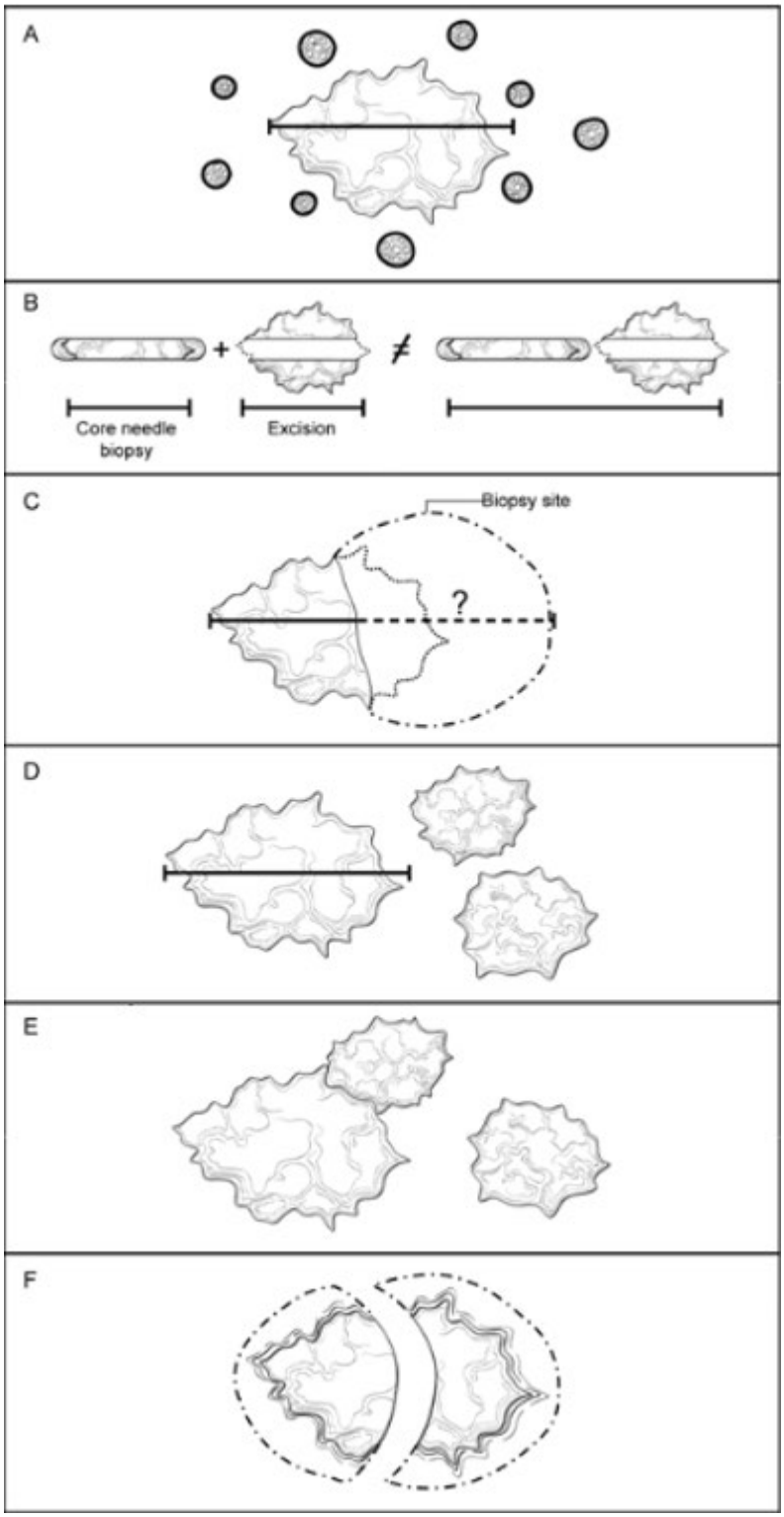
A
B
Core needle biopsy
Excision
C
Biopsy site
?
D
E
F

Figure F1. Determining the size of an invasive carcinoma. A. Invasive carcinoma with surrounding ductal carcinoma in situ (DCIS). The size only includes the area of the invasive carcinoma and does not include the adjacent DCIS. The size should be measured to the closest 1 mm. **B.** Small invasive carcinoma with prior core needle biopsy. The size of the carcinoma in the core needle biopsy should not be added to the size of the carcinoma in the excisional specimen, as this will generally overestimate the true size. The best size for classification must take into consideration the largest dimension of the carcinoma in both specimens as well as the size by imaging before the core needle biopsy. **C.** Small invasive carcinomas with adjacent biopsy site changes. In some excisional specimens, a small carcinoma will be present adjacent to a relatively large area of biopsy site changes. The actual size cannot be determined with certainty. The size in the core needle biopsy, in the excisional specimen, and by imaging should be considered to determine the best size for classification. **D.** Multiple invasive carcinomas. If multiple carcinomas are present, the size of the largest invasive carcinoma is used for pT classification. The modifier "(m)" is used to indicate that multiple invasive carcinomas are present. **E**. Multiple invasive carcinomas in close proximity. It may be difficult to distinguish multiple adjacent carcinomas from one large invasive carcinoma. Careful examination of the specimen with submission of tissue between grossly evident carcinomas is recommended. Correlation with imaging findings can be helpful. Generally, microscopic size confirmation of the largest grossly identified invasive carcinoma is used for pT classification. As a pragmatic approach, if two histologically similar carcinomas are within 5.0 mm of each other, measure from outer edges of the two but if they are 5 mm or more apart they can be considered separate foci. **F**. Invasive carcinomas that have been transected. If an invasive carcinoma has been transected and is present in more than 1 tissue fragment, the sizes in each fragment should not be added together, as this may overestimate the true size. In many cases, correlation with the size on breast imaging will be helpful to choose the best size for classification. In other cases, the pathologist will need to use his or her judgment in assigning an AJCC T category.

Microinvasion: Microinvasion is defined by the AJCC as invasion measuring 1 mm or less in size.[1] Invasive tumors that are larger than 1.0 mm but less than 2.0 mm are rounded up to 2.0 mm and are not considered microinvasive. In some cases, immunoperoxidase studies for myoepithelial cells may be helpful to document areas of invasion and the size of the invasive foci. Microinvasion is not a histologic type.

If more than 1 focus of microinvasion is present, the number of foci present, an estimate of the number, or a note that the number of foci is too numerous to quantify should be reported.

Per the WHO, "if there are multiple foci of microinvasion in close proximity, a pragmatic approach would be to apply the same recommendation used for staging multifocal established invasive carcinomas and regard deposits <5 mm apart as parts of a single invasive tumour deposit. Although there is only limited evidence, this is a practical approach which would classify close proximity multifocal microinvasion (<5mm apart) as an established invasive carcinoma, base the invasive tumour size measurement on the maximum dimension of the region with 2 or more microinvasive foci, and stage accordingly. There should be caution in applying this rule if there is very minimal infiltration and examination of further deeper sections should be considered".[2]

References

1. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017.

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

G. Ductal Carcinoma In Situ

Ductal carcinoma in situ[1,2,3,4] associated with invasive carcinoma increases the risk of local recurrence for women undergoing breast-conserving surgery. It is more important to report the features of DCIS when in situ disease is predominant (e.g., cases of DCIS with microinvasion or extensive DCIS associated with T1a carcinoma). If DCIS is a minimal component of the invasive carcinoma, the features of the DCIS have less clinical relevance. The extent of DCIS and its relative proportions to the invasive cancer can be useful for imaging correlation, to justify the indications for the extent of the surgery and to reflect the risk of possible occult invasion or margin involvement when very extensive.

The pathology report should include an estimate of the extent of the DCIS present. It can be reported in multiple ways depending on its relationship to the invasive cancer present: 1. As an estimated percentage of the entire tumor when admixed intimately with invasion. 2. As an estimated size or span of DCIS by correlation of gross sampling and microscopic involvement (this is useful to report when the DCIS is larger than the invasion). The College of American Pathologists (CAP) DCIS protocol provides additional information on determining the extent of DCIS.

Architectural Pattern of DCIS

The architectural pattern has traditionally been reported for DCIS but reporting all patterns present may not always be clinically relevant. The dominant pattern can also be selected. Solid papillary carcinoma in situ and Encapsulated papillary carcinoma patterns ideally should be reported if present in association with invasive cancers. These forms of papillary DCIS/encapsulated carcinoma may lack myoepithelial staining but if they meet criteria otherwise for these diagnoses, they are not considered a part of the invasive cancer size (note that invasive forms of solid papillary carcinoma also exist).

Nuclear grade and the presence of necrosis are more predictive of clinical outcome than architectural pattern.

Nuclear Grade of DCIS

The nuclear grade of DCIS is determined using 6 morphologic features (Table 2).

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.

H. Macroscopic and Microscopic Extent of Tumor
The extent of an invasive breast cancer involving local structures such as the skin and chest wall can alter the AJCC pT stage. If skin or muscle are part of a specimen, their presence should always be included in the gross description and the relationship of these structures to the carcinoma reported in the final diagnosis. The gross extent of skin involvement if present should be clearly documented since macroscopic skin ulceration or macroscopic skin satellites are required for a change in pT category (microscopic findings can support this but without gross findings there is no change in pT category).

If a surgical specimen includes the nipple this can be documented and specified whether it is not involved, contains Paget's disease (extension of cancer into the nipple epidermis), DCIS in the major lactiferous ducts or stromal involvement by invasive carcinoma. While nipple involvement may be relevant to surgical planning or local recurrence risk, it does not change the overall pT stage.

Figure H1 illustrates multiple ways that breast carcinoma can involve the skin:

- DCIS involving nipple epidermis (Paget disease of the nipple) (Figure H1, A): DCIS can extend from the lactiferous sinuses into the contiguous skin without crossing the basement membrane. This finding does not change the T classification of the invasive carcinoma.

- Invasive carcinoma invading into dermis or epidermis, without ulceration (Figure H1, B): Skin invasion correlates with the clinical finding of a carcinoma fixed to the skin and may be associated with skin or nipple retraction. This finding does not change the T classification.
- Invasive carcinoma invading into dermis and epidermis with gross skin ulceration (Figure H1, C): In the past, skin ulceration was associated with very large, locally advanced carcinomas. However, skin ulceration can also be associated with superficially located small carcinomas. It is unknown if skin involvement confers a worse prognosis as compared to carcinomas of similar size without skin invasion. Carcinomas with grossly evident skin ulceration are classified as T4b.
- Ipsilateral satellite skin nodules (Figure H1, D): An area of invasive carcinoma within the dermis, separate from the main carcinoma, is usually associated with lymphovascular invasion. The satellite nodules should be macroscopically evident and confirmed microscopically. This finding is classified as T4b. The clinical significance of incidental microscopic satellite nodules in the dermis has not been investigated.
- Dermal lymphovascular invasion (Figure H1, E): Carcinoma present within lymphatic spaces in the dermis is often correlated with the clinical features of inflammatory carcinoma (diffuse erythema and edema involving one-third or more of the breast), and such cases would be classified as T4d. In the absence of the clinical features of inflammatory carcinoma, this finding remains a poor prognostic factor but is insufficient to classify a cancer as T4d. This finding is separately documented under “Dermal Lymphovascular Invasion.”

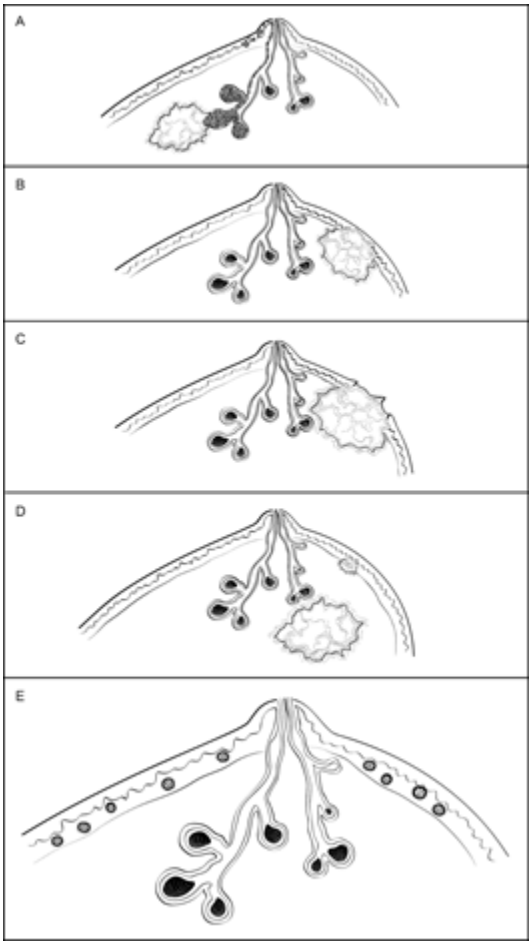

Figure H1. Invasive Carcinoma: Skin Involvement. A. Ductal carcinoma in situ (DCIS) involving nipple epidermis (Paget disease of the nipple) associated with an invasive carcinoma. DCIS can traverse the lactiferous sinuses into the epidermis without crossing a basement membrane. This finding does not change the T classification of an underlying invasive carcinoma. **B**. Invasive carcinoma invading into dermis or epidermis, without ulceration. This finding does not change the T classification of the invasive carcinoma. **C**. Invasive carcinoma invading into dermis and epidermis with gross skin ulceration. This carcinoma would be classified as T4b, unless additional features warrant classification as T4c (chest wall invasion) or T4d (inflammatory carcinoma). **D.** Ipsilateral satellite skin nodules. An area of invasive carcinoma in the skin, separate from the main carcinoma, is usually associated with lymphovascular invasion. This finding is classified as T4b if the skin nodules are grossly/clinically apparent, unless additional features warrant classification as T4c (chest wall invasion) or T4d (inflammatory carcinoma). **E.** Dermal lymphovascular invasion. If carcinoma within lymphatic spaces in the dermis is correlated with the clinical features of inflammatory carcinoma (diffuse erythema and edema involving one-third or more of the breast), the carcinoma is classified as T4d. If clinical signs are not present, this finding does not change the T classification, but is an indicator of a poor prognosis.

Muscle
Skeletal muscle may be present at the deep/posterior margin. The presence of muscle documents that the excision has extended to the deep fascia. Invasion into skeletal muscle should be reported, as this finding may be used as an indication for postmastectomy radiation therapy.

The skeletal muscle present is generally pectoralis muscle. Invasion into this muscle is not included as T4a. Invasion must extend through this muscle into the chest wall (intercostal muscles or deeper) in order to be classified as T4a. However, chest wall muscles are rarely removed in mastectomy specimens. The T4a classification is generally established with imaging of locally advanced carcinomas.

I. Lymphatic and/or Vascular Invasion
Lymphatic and/or vascular invasion (LVI) is associated with local recurrence and reduced survival.[1,2,3] Distinguishing lymphatic channels from blood vessels is unnecessary. Documenting the presence of dermal lymphatic and/or vascular invasion is particularly important because of its strong association with the clinical findings of inflammatory breast carcinoma. Reporting the LVI status for stage IIA and IIB patients who have an axillary lymph node dissection (ALND) may influence the use of radiotherapy.[4]

Strict criteria have been proposed for the diagnosis of LVI (Table 3).[5] Lymphatic and/or vascular invasion may be seen in stroma between uninvolved lobules and can sometimes be mistaken for DCIS if the cells completely fill the lymphatic space.

Guidelines issued by the St. Gallen International Expert Consensus Conference[6] include recommendations based on the presence of “extensive” LVI but do not define the term “extensive”. There are conflicting results on the significance of the number of foci of LVI.[2,3] There is no agreed definition of extensive LVI and sub categorization of LVI as extensive or focal is subjective. Pathologists may report the number of foci and/or the number of blocks with LVI as a measure of extent. 1-2 vessels involved in one block maybe considered focal and more than 2 vessels involved in two or more blocks may be considered extensive.

Table 3. Criteria for Lymphatic and/or Vascular Invasion (LVI)

1.	LVI must be diagnosed outside the border of the invasive carcinoma. The most common area to find LVI is within 1 mm of the edge of the carcinoma.
2.	The tumor emboli usually do not conform exactly to the contours of the space in which they are found. In contrast, invasive carcinoma with retraction artifact mimicking LVI will have exactly the same shape.
3.	Endothelial cell nuclei should be seen in the cells lining the space.
4.	Lymphatics are often found adjacent to blood vessels and often partially encircle a blood vessel.

Data derived from Rosen.[5]

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J. 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, ink from margin evaluation, and hemosiderin).

K. Treatment Effect

Patients may be treated with endocrine therapy or chemotherapy before surgical excision (neoadjuvant therapy). A y prefix is added when assigning AJCC T and N categories after neoadjuvant treatment (ypT and ypN). The y prefix does apply to neoadjuvant endocrine therapy if it was a formal, planned course of neoadjuvant systemic treatment done for several months. The y prefix should not be reported if endocrine treatment was just a short course (a few days or weeks). The response of the invasive carcinoma to neoadjuvant therapy is a strong predictor of disease-free and overall survival. Special attention to finding the tumor bed grossly so it can be sampled and examined microscopically is necessary for these specimens.[1,2,3,4,5,6]

The NCCN recommends that post neoadjuvant chemotherapy treatment response be included in breast pathology reports using the Residual Cancer Burden (RCB) system (category 2B recommendation). The RCB protocol instructions and calculator can be found at the MD Anderson website: http://www3.mdanderson.org/app/medcalc/index.cfm?pagename=jsconvert3. This site also includes materials and guides that explain the system. Pathologists should be aware that, while the individual RCB parameters as well as the RCB Score and Class are each optional reporting elements, cancer registries can only collect the RCB Score and Class from the pathology report.

The RCB was not validated or designed for neoadjuvant endocrine treatment and an RCB Score and Class should not be reported. However, individual RCB parameters such as cellularity might be helpful in describing residual disease burden; reporting these parameters may be of interest but is optional.

RCB Assessment of Primary Tumor Bed

The size (area) of the primary tumor bed with residual viable invasive carcinoma and the cellularity of residual carcinoma in the tumor bed provide a reproducible estimate of the volume of residual invasive carcinoma. The "tumor bed" size for RCB parameters of a treated cancer is measured as the span of residual invasive carcinoma (contiguous or discontiguous foci) in two dimensions, which requires gross tissue sampling methods that can provide this information (see RCB website for protocol). See figure below for an example of the tumor bed parameter measurements.

The residual invasive carcinoma cellularity is estimated by determining the overall cancer cellularity (invasive and in situ) and the percentage of residual in situ carcinoma. The RCB calculation subtracts the amount of in situ disease to obtain the estimate of residual invasive carcinoma cellularity used to determine the RCB. If only LVI remains after therapy, the area with LVI is used as the primary tumor bed area and the cellularity of the LVI is used as the residual cancer cellularity.

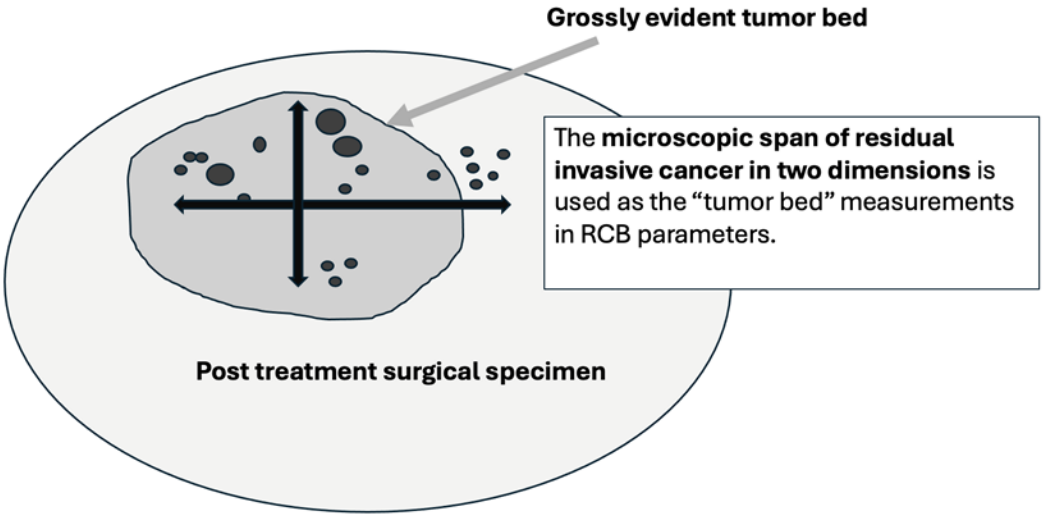

Figure K1. Tumor bed measurements for RCB parameters

If reporting RCB parameters, the "tumor bed" dimensions should be the largest two-dimensional span of residual invasive carcinoma confirmed on microscopic examination. The gross fibrous tumor bed (shown as grey area) is not always the same measurements as the span of residual invasion (shown as multiple smaller solid circles in this example). The two-dimensional span of residual invasion may include foci that are not contiguous and present across multiple slices/sections. Only the largest span of invasion (not DCIS) is included in the overall tumor bed measurements.

RCB Assessment of Regional Lymph Nodes

According to the AJCC 8th edition staging system, the size of the largest contiguous focus of residual metastatic carcinoma present in the lymph nodes is used to assign the pN category; intervening therapy-

related fibrosis is not included in this measurement. However, when measuring the diameter of the largest lymph node metastasis for the RCB calculation, foci of residual metastatic carcinoma with intervening therapy-related fibrosis and any extracapsular extension are included in the measurement.

Lymph nodes containing only isolated tumor cells (ITCs) are not included in the number of positive lymph nodes when determining the AJCC pN category, but nodes containing only ITCs detected by routine stains are included in the RCB calculation. A size smaller than 0.2 mm (e.g., 0.05 mm) can be entered in the RCB calculator.

If there are separate metastases within the node with intervening normal nodal tissue, then these should be considered as separate foci and the largest single focus is used as the size of the largest metastatic deposit for both AJCC Staging and RCB calculation.

Post Neoadjuvant Treatment Staging, Grading and Biomarkers

Invasive carcinomas with a minor response may show little or no change in size. With greater degrees of response, the carcinoma shows decreased cellularity and may be present as multiple foci of invasion scattered over a larger tumor bed. The post-neoadjuvant therapy pathologic T-category (ypT) is based on the largest single focus of residual tumor, if present. Treatment-related fibrosis adjacent to residual invasive carcinoma is not included in the ypT maximum dimension. The “m” modifier is used to indicate that multiple foci of invasive carcinoma are present. The inclusion of additional information, such as the distance over which invasive carcinoma is present, the number of foci of invasive carcinoma, or the number of slides or blocks with invasive carcinoma, may be helpful in estimating the extent of residual disease. If no residual invasive carcinoma is present in the breast, the case summary can be used to report residual DCIS and/or metastatic carcinoma in lymph nodes. If there is no residual carcinoma in the breast or in the lymph nodes, then a CAP protocol case summary need not be used for reporting. Cases with no residual invasive carcinoma after neoadjuvant therapy are categorized as ypTis if there is residual DCIS or ypT0 if there is no residual cancer (not ypTX). It can be categorized as ypTx if there is only LVI in the breast resection specimen. Cases categorized as M1 before neoadjuvant therapy stay that way (i.e., they remain Stage IV even if there is complete pathologic response).

Most carcinomas are of the same grade after treatment. In a few cases, the grade will be higher because of marked nuclear pleomorphism. In very rare cases, the carcinoma will be of lower grade. The prognostic significance of a change in grade after treatment has not been determined.

If negative prior to treatment, it is recommended that ER, PgR, and HER2 be repeated on invasive carcinomas after treatment, as significant changes may occur in a subset of carcinomas, sometimes due to tumor heterogeneity and limited sampling prior to treatment.

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L. Margins

Whenever feasible, the specimen should be oriented in order for the pathologist to identify specific margins. This is particularly important for excisions less than total mastectomy, where it may be necessary for the surgeon to excise residual tumor at a specific margin (e.g., superior, inferior, medial, lateral, anterior, or deep). Identification of surgical margins also allows measurement of the distance between the carcinoma and specific margins. All identifiable margins should be evaluated for involvement by carcinoma both grossly and microscopically. Final margin status should be based on additional separately submitted margins as well as those that are considered final in the main resection specimen.[1]

Orientation may be done by sutures or clips placed on the specimen surface or by other means of communication between surgeon and pathologist and should be documented in the pathology report. Margins can be identified in several ways, including the use of multiple-colored inks, by submitting the margins in specific cassettes, or by the surgeon submitting each margin as a separately excised specimen. Inks should be applied carefully to avoid penetration deep into the specimen.

The final margin status should be reported for both invasive carcinoma and the DCIS when present (cancer in angiolymphatic spaces is not included in the final margin status). Margin status is considered Involved if the final margins have invasive cancer or DCIS at ink (inclusive of any additional margins removed). If the specimen is oriented, the specific site(s) of involvement should also be reported. Additionally, margins less than 1 mm to cancer (but not at ink), margins 1-2 mm from cancer and margins greater than 2 mm from cancer can be specified if considered relevant. For ease of reporting, an option for “all final margins greater than 2 mm” is also available in the protocol. “Other” can be used for complex scenarios (such as description of the margin status of multiple specimens that require surgical correlation) and “Cannot be determined” for other uncommon scenarios with explanation. The Margin comment section can be used to clarify any additional margin details.

The deep margin may be at muscle fascia. If so, the likelihood of additional breast tissue beyond this margin (and therefore possible involvement by DCIS) is extremely small. A deep muscle fascial margin (e.g., on a mastectomy specimen) positive for DCIS is unlikely to have clinical significance. However, invasive carcinoma at the deep margin, especially if associated with muscle invasion, is often an indication for postmastectomy radiation.

A superficial (generally anterior) margin may be immediately below the skin, and there may not be additional breast tissue beyond this margin. However, some breast tissue can be left in skin flaps, and the likelihood of residual breast tissue is related to the thickness of the flap.[2]

Specimen radiography is important to assess the adequacy of excision. Compression of the specimen should be minimized, as it can severely compromise the ability to assess the distance of the DCIS from the surgical margin. Mechanical compression devices should be used with caution and preferably reserved for nonpalpable lesions that require this technique for imaging (e.g., microcalcifications).

It is helpful to report the approximate extent of margin involvement (e.g. linear extent of invasion at margin and/or number of foci/blocks involved).

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M. Lymph Node Sampling and Reporting

Most patients with invasive carcinoma will have lymph nodes sampled.

Types of lymph nodes:

- **Sentinel lymph nodes** are identified by the surgeon by uptake of radiotracer or dye or both. They are considered sentinel lymph nodes if less than six nodes are removed. Adjacent palpable non-sentinel nodes may also be removed.
- **Axillary lymph nodes** are removed by en bloc resection of axillary tissue. The nodes are divided into levels: I (low-axilla: lateral to the lateral border of the pectoralis minor muscle); II (mid-axilla: between the medial and lateral borders of the pectoralis minor muscle and the interpectoral [Rotter's] lymph nodes); and III (apical axilla or infraclavicular nodes: medial to the medial margin of the pectoralis minor muscle and inferior to the clavicle). A surgeon may choose to remove 1 or more of these levels. Levels I and II are typically removed in the axillary dissection, with level III nodes only removed if considered suspicious by the surgeon intraoperatively. Level III nodes must be specifically identified, as there are additional AJCC N categories for these nodes.
- **Intramammary nodes** are present within breast tissue and are most commonly found in the upper outer quadrant. Intramammary nodes may rarely be sentinel lymph nodes. These nodes are included with axillary nodes for AJCC N classification.
- **Internal mammary nodes, supraclavicular nodes, and infraclavicular nodes** are rarely removed for breast cancer staging. If metastases are present in these nodes, there are specific AJCC N categories (see *AJCC Cancer Staging Manual*).[1]

Lymph node sampling:

- **Grossly positive nodes:** The size of grossly positive nodes should be recorded. One section to include any areas suggestive of extranodal invasion is sufficient. Cancerous nodules in the axillary

fat adjacent to the breast, without histologic evidence of residual lymph node tissue or surrounding breast tissue or ductal carcinoma in situ, are classified as regional lymph node metastasis.

- **Grossly negative nodes:** Sampling must be adequate to detect all macrometastases, as they are known to have prognostic importance (i.e., all metastatic deposits >2 mm). Thus, each node should be thinly sliced along the long axis of the node at 2 mm, and all slices should be submitted for microscopic examination. At least 1 representative hematoxylin-and-eosin (H&E) level must be examined. Additional methods of sampling, such as additional H&E levels or immunohistochemical studies, may detect isolated tumor cells or micrometastases. However, the clinical impact on outcome of these small metastases is minimal.[2]

The nodes must be submitted in such a way that every node can be evaluated and counted separately.
Reverse transcriptase polymerase chain reaction has been developed as an alternative method for examining lymph nodes.[3,4] The tissue used for this assay cannot be examined microscopically. All macrometastases must be identified histologically. Therefore, nodal tissue can only be used for other assays if all macrometastases can be identified by H&E examination. False-positive and false-negative results can occur with RT-PCR. The significance of a positive RT-PCR result for a histologically negative lymph node is unknown.

Reporting lymph nodes:

- **Number of nodes examined:** The total number of nodes includes sentinel nodes, nonsentinel nodes, nodes from axillary dissections, and intramammary nodes. When the number of sentinel and nonsentinel nodes removed is less than 6 nodes, the AJCC “sn” modifier is used.
- **Size of metastases:** The size of a tumor deposit is determined by measuring the largest dimension of any group of cells that are touching one another (confluent or contiguous tumor cells), regardless of whether the deposit is confined to the lymph node, extends outside the node (extranodal extension), is totally present outside the lymph node and invading adipose tissue, or is present within a lymphatic channel adjacent to the node or in the capsule.
- Metastases are classified into 3 groups:
    - Isolated tumor cell clusters (ITCs) are defined as small clusters of cells not larger than 0.2 mm, or single cells, or fewer than 200 cells in a single cross-section. ITCs may be detected by routine histology or by immunohistochemical (IHC) methods. Nodes containing only ITCs are not included in the total number of positive nodes when determining the N category.
    - Micrometastases measure more than 0.2 mm, but not more than 2 mm, and/or comprise more than 200 cells in a single cross-section. If only micrometastases are present, the N category is pN1mi. If at least 1 macrometastasis is present, nodes with micrometastases are included in the total number of positive nodes when determining the N category.
    - Macrometastases measure more than 2 mm.

In most cases, if metastases are present, the sentinel node will be involved. In rare cases, only nonsentinel nodes contain metastases. These cases can occur if the true sentinel node is completely replaced by tumor (and therefore is not detected by radioactive tracer or dye), if there is unusual lymphatic drainage, or if there is failure of the technique to identify the node. This finding should be included in the report.

Details of Lymph node metastases from one or more biologically distinct tumors may be added in the comment section of the Regional Lymph node section.

In some cases, the best N category can be difficult to determine (Figure M1).

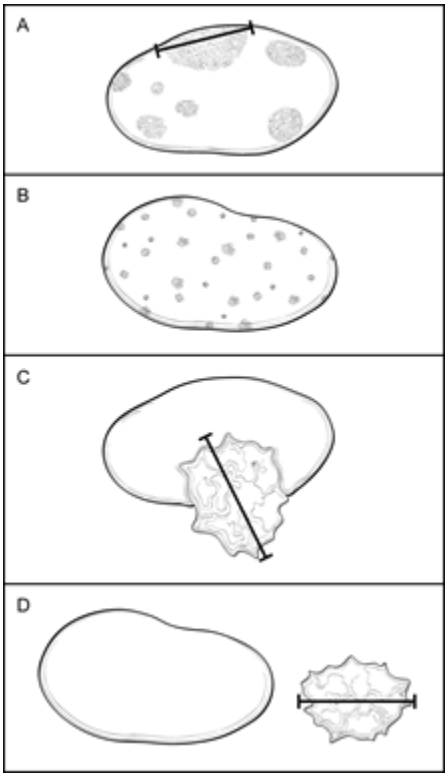

Figure M1. Classification of Lymph Node Metastases. A. Multiple clusters of tumor cells. Classification is based on the size of the largest contiguous cluster of tumor cells. The distance between clusters should not be included in the size measurement. However, if the overall volume of tumor is similar to the next highest nodal category, it is recommended that the pathologist use his or her judgment to assign the best N category and to include the reasoning in a note. **B**. Dispersed pattern of lymph node metastasis. Some carcinomas, in particular lobular carcinomas, metastasize as single cells and do not form cohesive clusters. In such cases, the "size" of the metastasis is difficult to determine. If more than 200 tumor cells are present in 1 cross-section of the node, then the category of isolated tumor cells should not be used. If there is difficulty in assigning the N category, it is recommended that the reason be provided in a note. **C**. Extranodal invasion. The area of invasion outside the lymph node capsule is included in the overall size of the lymph node metastasis. The size of the metastasis includes the tumor cells and the desmoplastic response (i.e., the cells do not need to be contiguous, but the cells plus fibrosis should be contiguous). The finding of extranodal invasion is also reported. **D.** Cancerous nodules in axillary fat. Areas of carcinoma invading into the stroma in axillary adipose tissue, without residual nodal tissue, are considered to be positive lymph nodes. However, if there is surrounding breast tissue or ductal carcinoma in situ, then the invasive carcinoma should be classified as an invasive carcinoma and not as a lymph node metastasis.

- **Nodes after neoadjuvant therapy:** The response of metastatic carcinoma in lymph nodes after treatment is an important prognostic factor. In addition to the information described above, evidence of treatment response (e.g., small tumor deposits within an area of fibrosis) should also be reported (see Note K). Only the largest contiguous focus of residual tumor in the node evaluation is used for classification; any treatment-associated fibrosis is not included.

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N. pTNM Classification

The tumor-node-metastasis (TNM) staging system maintained collaboratively by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended.[1] Assignment of Pathologic Prognostic Stage Group is the responsibility of the managing physician and not the pathologist.[1]

Pathologic Classification

The pathologic classification of a cancer is based on information acquired before treatment supplemented and modified by the additional evidence acquired during and from surgery, particularly from pathologic examination of resected tissues. The pathologic classification provides additional precise and objective data. Classification of T, N, and M by pathologic means is denoted by use of a lower case "p" prefix (pT, pN, pM).

Pathologic T (pT): The pathologic assessment of the primary tumor (pT) generally is based on resection of the primary tumor generally from a single specimen. Resection of the tumor with several partial removals at the same or separate operations necessitates an effort at reasonable estimates of the size and extension of the tumor to assign the correct or highest pT category. In this situation, imaging findings can be used for determination of the pathologic size (pT). On rare occasions, the tumor size is obtained from a previous core needle biopsy specimen, as the tumor in the core may be larger than the tumor in the excision specimen.

AJCC/UICC definition of inflammatory carcinoma (T4d): Inflammatory carcinoma is a clinical-pathologic entity characterized by diffuse erythema and edema (peau d'orange) involving one-third or more of the skin of the breast. The skin changes are due to lymphedema caused by tumor emboli within dermal lymphatics, which may or may not be obvious in a small skin biopsy. However, a tissue diagnosis is still necessary to demonstrate an invasive carcinoma in the underlying breast parenchyma or at least in the dermal lymphatics, as well as to determine biological markers, such as ER, PgR, and HER2 status. Tumor emboli in dermal lymphatics without the clinical skin changes described above do not qualify as inflammatory carcinoma. Locally advanced breast cancers directly invading the dermis or ulcerating the skin without the clinical skin changes also do not qualify as inflammatory carcinoma. Thus, the term inflammatory carcinoma should not be applied to neglected locally advanced cancer of the breast presenting late in the course of a patient's disease. The rare case that exhibits all the features of inflammatory carcinoma, but in which skin

changes involve less than one-third of the skin, should be classified by the size and extent of the underlying carcinoma.

Pathologic N (pN): The pathologic assessment of regional lymph nodes (pN) ideally requires resection of a minimum number of lymph nodes to assure that there is sufficient sampling to identify positive nodes if present. The recommended number generally does not apply in cases where sentinel node has been accepted as accurate for defining regional node involvement and a sentinel node procedure has been performed. At least 1 node with *presence or absence* of cancer documented by pathologic examination is required for pathologic N classification.

Direct extension of primary tumor into a regional node is classified as node positive. A tumor nodule in a regional node area is classified as a positive node. The size of the metastasis, not the size of the node, is used for the criterion for the N category.

Specialized pathologic techniques such as immunohistochemistry or molecular techniques may identify limited metastases in lymph nodes that may not have been identified without the use of the special diagnostic techniques. Single tumor cells or small clusters of cells are classified as isolated tumor cells (ITCs). The standard definition for ITCs is a cluster of cells not more than 0.2 mm in greatest diameter. Cases with ITCs only in lymph nodes are classified as pN0. This rule also generally applies to cases with findings of tumor cells or their components by nonmorphologic techniques such as flow cytometry or DNA analysis.

AJCC/UICC definition of isolated tumor cells: Isolated tumor cell clusters (ITC) are defined as small clusters of cells not greater than 0.2 mm or single tumor cells, or fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by immunohistochemical (IHC) methods. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.

Approximately 1000 tumor cells are contained in a 3-dimensional 0.2-mm cluster. Thus, if more than 200 individual tumor cells are identified as single dispersed tumor cells or as a nearly confluent elliptical or spherical focus in a single histologic section of a lymph node, there is a high probability that more than 1000 cells are present in the lymph node. In these situations, the node should be classified as containing a micrometastasis (pN1mi). Cells in different lymph node cross-sections or longitudinal sections or levels of the block are not added together; the 200 cells must be in a single node profile even if the node has been thinly sectioned into multiple slices. It is recognized that there is substantial overlap between the upper limit of the ITC and the lower limit of the micrometastasis categories due to inherent limitations in pathologic nodal evaluation and detection of minimal tumor burden in lymph nodes. Thus, the threshold of 200 cells in a single cross-section is a guideline to help pathologists distinguish between these 2 categories. The pathologist should use judgment regarding whether it is likely that the cluster of cells represents a true micrometastasis or is simply a small group of isolated tumor cells.

Pathologic M (pM): The pathologic assignment of the presence of metastases (pM1) requires histologic confirmation of cancer at the metastatic site. The designation MX has been eliminated from the AJCC/UICC TNM system. Pathologic M0 is an undefined concept, and the category “pM0” may not be used. Pathologic classification of the absence of distant metastases can only be made at autopsy. Cases with a biopsy of a possible metastatic site that shows ITCs such as circulating tumor cells (CTCs) or disseminated tumor cells

(DTCs), or bone marrow micrometastases detected by IHC or molecular techniques, are classified as M0(i+) to denote the uncertain prognostic significance of these findings, and to classify the stage group according to the T and N and M0.

Posttherapy or post-neoadjuvant therapy classification (yTNM): Cases for which systemic and/or radiation therapy are given before surgery ("neoadjuvant") or for which no surgery is performed may have the extent of disease assessed at the conclusion of the therapy by clinical or pathologic means (if resection performed). This classification is useful to clinicians because the extent of response to therapy may provide important prognostic information to patients and help direct the extent of surgery or subsequent systemic and/or radiation therapy. T and N are classified by using the same categories as for clinical or pathologic staging for the disease type, and the findings are recorded by using the prefix designator "y" (e.g., ycT; ycN; ypT; ypN). The "yc" prefix is used for the clinical stage after therapy, and the "yp" prefix is used for the pathologic stage for those cases that have surgical resection after neoadjuvant therapy. The M component should be classified by the M status defined pathologically prior to therapy.

Recurrence classification (rTNM): This classification is assigned when further treatment is planned for a cancer that recurs after a disease-free interval. Second or subsequent primary cancers detected outside the staging window (generally 4 months) are known as metachronous primary tumors and are not staged with the 'y' prefix. The original stage assigned at the time of initial diagnosis and treatment does not change when the cancer recurs or progresses. The use of this staging for retreatment or recurrence is denoted with the 'r' prefix (rTNM). All information available at the time of retreatment should be used in determining the rTNM stage.

Multiple tumors: For patients with multiple ipsilateral invasive carcinomas, the T category assignment is based on the largest tumor. The "(m)" modifier is used to distinguish these cases from those with only a single invasive focus. For patients with simultaneous bilateral invasive carcinomas, each carcinoma is staged as a separate primary tumor, with independent determination of T and N categories and biomarker status.

Metachronous primaries: Second or subsequent primary cancers occurring in the same organ or in different organs are staged as a new cancer with the TNM system. Second cancers are not staged using the "y" prefix unless the treatment of the second cancer warrants this use.

References

1. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.

O. Additional Findings

In some cases, additional pathologic findings are important for the clinical management of patients.

If the biopsy was performed for a benign lesion and the invasive carcinoma is an incidental finding, this should be documented. An example would be the finding of DCIS with microinvasion in an excision for a large palpable fibroadenoma.

If there has been a prior core needle biopsy or excisional biopsy, the biopsy site should be sampled and documented in the report. If the intention was to completely re-excise a prior surgical site, the report should

document biopsy changes at the margin that could indicate an incomplete excision. This protocol should not be used if the main area of carcinoma has been previously removed and the current specimen is a re-excision of the margins.

Special Studies/Biomarker[1,2,3]
Reporting the results of biomarkers previously performed on a biopsy is helpful for a complete cancer summary. If there are multiple separate primary cancers, indicate which you are reporting the biomarkers on using the unique Tumor Identifier used in the protocol for each tumor to distinguish them. The Biomarker comment section can be used to report the profiles of the additional foci.

It may be useful to perform the breast cancer biomarkers on the invasive cancer(s) in the surgical specimen in some scenarios. If biomarkers are being performed or repeated, they can be reported separately using the Breast Cancer Biomarkers protocol.[1]

References

1. Allison K, Krishnamurti, U. Template for Reporting Results of Biomarker Testing of Specimens from Patients with Carcinoma of the Breast. 2025; www.cap.org/cancerprotocols., accessed March 3, 2026.
2. Allison KH, Hammond EH, Dowsett M: Estrogen and Progesterone Receptor Testing in Breast Cancer: ASCO/CAP Guideline Update. *J Clin Oncol* 2020; 38 (12): 1346-66; DOI: 10.1200/JCO.19.02309.
3. Wolff AC, Somerfield MR, Dowsett M: Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: ASCO–College of American Pathologists Guideline Update. *J Clin Oncol* 2023: 41 (22): 3867-3872; DOI: 10.1200/JCO.22.02864.