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

Version: 1.1.1.2
Protocol Posting Date: September 2022
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

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

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

The following should NOT be reported using this protocol:

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

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

Summary of Changes

v 1.1.1.2

- Updated Explanatory Note A

Reporting Template
Protocol Posting Date: September 2022
Select a single response unless otherwise indicated.

CASE SUMMARY: (INVASIVE CARCINOMA OF THE BREAST: Biopsy)
This template is recommended for reporting biopsy specimens, but is not required for accreditation purposes.

SPECIMEN

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

Specimen Laterality
___ Right
___ Left
___ Not specified

TUMOR

+Tumor Site (select all that apply)
___ Upper outer quadrant
___ Lower outer quadrant
___ Upper inner quadrant
___ Lower inner quadrant
___ Central
___ Nipple
___ Clock position
Specify Clock Position (select all that apply)
___ 1 o'clock
___ 2 o'clock
___ 3 o'clock
___ 4 o'clock
___ 5 o'clock
___ 6 o'clock
___ 7 o'clock
___ 8 o'clock
___ 9 o'clock
___ 10 o'clock
___ 11 o'clock
___ 12 o'clock
___ Specify distance from nipple in Centimeters (cm): _____ cm
___ Other (specify): _____
___ Not specified

Histologic Type (Note A)
___ No residual invasive carcinoma
___ Invasive carcinoma of no special type (ductal)
___ Micro-invasive carcinoma
___ Invasive lobular carcinoma
___ Invasive carcinoma with mixed ductal and lobular features
___ Invasive carcinoma with features of (specify): _____
___ Tubular carcinoma
___ Invasive cribriform carcinoma
___ Mucinous carcinoma
___ Invasive micropapillary carcinoma
___ Apocrine adenocarcinoma
___ Metaplastic carcinoma
___ Encapsulated papillary carcinoma with invasion
___ Solid papillary carcinoma with invasion
___ Intraductal papillary adenocarcinoma with invasion
___ Adenoid cystic carcinoma
___ Neuroendocrine tumor
___ Neuroendocrine carcinoma
___ Invasive carcinoma, type cannot be determined: _____
___ Other histologic type not listed (specify): _____
+Histologic Type Comment: _____

Histologic Grade (Nottingham Histologic Score) (Note B)
___ Not applicable (no residual carcinoma or microinvasion only)
___ Nottingham Score
Glandular (Acinar) / Tubular Differentiation
___ 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)
___ Score cannot be determined: _____
Nuclear Pleomorphism
___ Score 1 (Nuclei small with little increase in size in comparison with normal breast epithelial cells, regular outlines, uniform nuclear chromatin, little variation in size)
___ Score 2 (Cells larger than normal with open vesicular nuclei, visible nucleoli, and moderate variability in both size and shape)
___ Score 3 (Vesicular nuclei, often with prominent nucleoli, exhibiting marked variation in size and shape, occasionally with very large and bizarre forms)
___ Score cannot be determined: _____
Mitotic Rate
See Table 1 in CAP Protocol.
___ Score 1
___ Score 2
___ Score 3
___ Score cannot be determined: _____
Overall Grade
___ Grade 1 (scores of 3, 4 or 5)

___ Grade 2 (scores of 6 or 7)
___ Grade 3 (scores of 8 or 9)
___ Score cannot be determined (explain): _____

+Tumor Size
___ Microinvasion only (less than or equal to 1 mm)
___ Greatest dimension of largest invasive focus greater than 1 mm (specify exact measurement in Millimeters (mm)): _____ mm
+Additional Dimension in Millimeters (mm): ____ x ____ mm
___ Tumor size cannot be determined (explain): _____

Ductal Carcinoma In Situ (DCIS) (Note C)
___ Not identified
___ Present
Architectural Patterns (select all that apply)
___ Comedo
___ Paget disease (DCIS involving nipple skin)
___ Cribriform
___ Micropapillary
___ Papillary
___ Solid
___ Other (specify): _____
Nuclear Grade
___ Grade I (low)
___ Grade II (intermediate)
___ Grade III (high)
___ Other (specify): _____
___ Cannot be determined: _____
Necrosis
___ Not identified
___ Present, focal (small foci or single cell necrosis)
___ Present, central (expansive "comedo" necrosis)
___ Other (specify): _____
___ Cannot be determined: _____
___ Cannot be excluded

+Lymphovascular Invasion
___ Not identified
___ Present
___ Cannot be determined: _____

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

ADDITIONAL FINDINGS (Note E)

+Additional Findings (specify): _____

SPECIAL STUDIES

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

+Breast Biomarker Studies (specify pending studies): _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. Histologic Type

This protocol applies to all invasive carcinomas of the breast. The World Health Organization (WHO)[1] classification of breast carcinoma is recommended, although the protocol does not preclude the use of other classifications or histologic types. Carcinomas may be classified based on the H&E appearance without the use of immunohistochemical studies.

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." Choices are added for tumors with mixed features and those with some but not all features of specific histologic types.

WHO Classification of Invasive Carcinoma of the Breast[1]
___ No residual invasive carcinoma
___ Invasive carcinoma of no special type (ductal)
___ Micro-invasive carcinoma
___ Invasive lobular carcinoma
___ Invasive carcinoma with mixed ductal and lobular features
___ Invasive carcinoma with mixed features (specify): _____
___ Tubular carcinoma
___ Invasive cribriform carcinoma
___ Mucinous carcinoma
___ Invasive micropapillary carcinoma
___ Apocrine adenocarcinoma

Metaplastic Carcinoma
___ Metaplastic carcinoma NOS
___ Low grade adenosquamous carcinoma
___ Fibromatosis-like metaplastic carcinoma
___ Spindle cell carcinoma
___ Squamous cell carcinoma
___ Metaplastic carcinoma with mesenchymal differentiation

Neuroendocrine Tumor
___ Neuroendocrine tumor NOS
___ Neuroendocrine tumor, grade 1
___ Neuroendocrine tumor, grade 2

Neuroendocrine Carcinoma
___ Neuroendocrine carcinoma NOS
___ Neuroendocrine carcinoma, small cell
___ Neuroendocrine carcinoma, large cell
___ Invasive carcinoma, type cannot be determined
___ Other histologic type (specify): _____
    ___ Invasive papillary carcinoma
    ___ Encapsulated papillary carcinoma with invasion

___ Solid papillary carcinoma with invasion
___ Intraductal papillary adenocarcinoma with invasion
___ Oncocytic carcinoma
___ Lipid-rich carcinoma
___ Glycogen-rich carcinoma
___ Sebaceous carcinoma
___ Mucinous cystadenocarcinoma NOS
___ Acinar cell carcinoma
___ Classic adenoid cystic carcinoma
___ Solid-basaloid adenoid cystic carcinoma
___ Adenoid cystic carcinoma with high-grade transformation
___ Secretory carcinoma
___ Mucoepidermoid carcinoma
___ Polymorphous adenocarcinoma
___ Tall cell carcinoma with reversed polarity
___ Adenomyoepithelioma with carcinoma
___ Epithelial-myoepithelial carcinoma
___ Other type not listed (specify): _____

References

1. WHO Classification of Tumours Editorial Board. Breast tumours. Lyon (France): International Agency for Research on Cancer; 2019. (WHO classification of tumours series, 5th ed.; vol. 2)

B. Histologic Grade

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

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

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

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

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

When the value of the constant is known, the diameter of an HPF can be calculated for other objectives by using the following formula:

Unknown Field Diameter = Constant/(Eyepiece Magnification x Objective Magnification)

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

3.1415 x r^2= Area of Microscopic Field

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

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

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

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

References
1. Ellis IO, Elston CW. Histologic grade. In: O'Malley FP, Pinder SE, eds. *Breast Pathology.* Philadelphia, PA: Elsevier; 2006:225-233.
2. *Pathology Reporting of Breast Disease***.** A Joint Document Incorporating the Third Edition of the NHS Breast Screening Programme's *Guidelines for Pathology Reporting in Breast Cancer Screening* and the Second Edition of The Royal College of Pathologists' *Minimum Dataset for Breast Cancer Histopathology* Published by the NHS Cancer Screening Programmes jointly with The Royal College of Pathologists. NHSBSP Publication No 58. January 2005. http://www.cancerscreening.nhs.uk/ breastscreen/publications/nhsbsp58.html. Accessed April 8, 2009.

C. Ductal Carcinoma In Situ

Nuclear Grade of DCIS

The nuclear grade of DCIS is determined using 6 morphologic features (Table 1).[1]

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. Schwartz GF, Lagios MD, Carter D, et al. Consensus conference on the classification of ductal carcinoma in situ. *Cancer.* 1997;80:1798-1802.

D. Microcalcifications

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

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

E. Additional Findings

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