Protocol for the Examination of Biopsy Specimens From Patients With Invasive Carcinoma of the Breast

Version: Breast Invasive Biopsy 1.0.0.1  Protocol Posting Date: August 2019

Accreditation Requirements
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:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy</td>
<td>Includes specimens designated needle biopsy, fine needle aspiration and others (for excisional biopsy, see below)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive breast carcinoma of any type, with or without ductal carcinoma in situ (DCIS)</td>
<td>Includes microinvasive carcinoma and carcinoma with neuroendocrine features</td>
</tr>
</tbody>
</table>

The following should NOT be reported using this protocol:

<table>
<thead>
<tr>
<th>Procedure</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection (consider Breast Invasive Carcinoma Resection protocol)</td>
<td></td>
</tr>
<tr>
<td>Excisional biopsy (consider Breast Invasive Carcinoma Resection protocol)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ductal carcinoma in situ (DCIS) without invasive carcinoma (consider the DCIS Biopsy protocol)</td>
</tr>
<tr>
<td>Paget disease of the nipple without invasive carcinoma (consider the DCIS Biopsy protocol)</td>
</tr>
<tr>
<td>Encapsulated or solid papillary carcinoma without invasion (consider the Breast DCIS Biopsy protocol)</td>
</tr>
<tr>
<td>Phyllodes tumor</td>
</tr>
<tr>
<td>Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)</td>
</tr>
<tr>
<td>Sarcoma (consider the Soft Tissue protocol)</td>
</tr>
</tbody>
</table>

Authors
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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.

* Denotes primary author. All other contributing authors are listed alphabetically.

Accreditation Requirements
The use of this biopsy case summary is recommended for clinical care purposes, but is not required for accreditation purposes. The core and conditional data elements are routinely reported for biopsy specimens. Non-core data elements are included to allow for reporting information that may be of clinical value.

Summary of Changes
1.0.0.1 – Edits to DCIS Explanatory Notes
Surgical Pathology Cancer Case Summary

Protocol posting date: August 2019

INVASIVE CARCINOMA OF THE BREAST: Biopsy

Notes:
This case summary is recommended for reporting biopsy specimens but is NOT REQUIRED for accreditation purposes. Core data elements are bolded to help identify routinely reported elements.

Select a single response unless otherwise indicated.

Procedure, Laterality, and Site may be listed separately or on 1 line.

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

Specimen Laterality
___ Right
___ Left
___ Not specified

Tumor Site (select all that apply)
___ Upper outer quadrant
___ Lower outer quadrant
___ Upper inner quadrant
___ Lower inner quadrant
___ Central
___ Nipple
___ Clock position (specify): _____o’clock
___ Distance from nipple (centimeters):______cm
___ Other (specify): _____________________
___ Not specified

Histologic Type (Note A)
___ Invasive carcinoma of no special type (invasive ductal carcinoma, not otherwise specified)
___ Micro-invasive carcinoma
___ Invasive lobular carcinoma
___ Invasive carcinoma with lobular features
___ Invasive carcinoma with ductal and lobular features (“mixed type carcinoma”)
___ Mucinous carcinoma
___ Tubular carcinoma
___ Invasive carcinoma, tubulo-lobular variant
___ Invasive cribriform carcinoma
___ Invasive micropapillary carcinoma
___ Invasive papillary carcinoma
___ Invasive carcinoma with medullary features
___ Metaplastic carcinoma
___ Low-grade adenosquamous carcinoma
___ Fibromatosis-like metaplastic carcinoma
___ Metaplastic carcinoma, spindle cell type

The routinely reported core data elements are bolded.
___ Metaplastic carcinoma, mixed epithelial and mesenchymal type
___ Invasive carcinoma with metaplastic features
___ Squamous cell carcinoma
___ Adenoid cystic carcinoma
___ Invasive carcinoma with apocrine features
___ Invasive carcinoma with clear cell (glycogen rich) features
___ Invasive carcinoma with neuroendocrine features
___ Invasive carcinoma, with signet-ring cell features
___ Secretory carcinoma
___ Invasive carcinoma, type cannot be determined
___ Other histologic type not listed (specify): ____________________________

Histologic Grade (Nottingham Histologic Score) (Note B)
___ Not applicable (microinvasion only)

Glandular (Acinar)/Tubular Differentiation
___ Score 1 (>75% of tumor area forming glandular/tubular structures)
___ Score 2 (10% to 75% of tumor area forming glandular/tubular structures)
___ Score 3 (<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)
___ 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: ___________________)

Ductal Carcinoma In Situ (DCIS) (Note C)
___ Not identified
___ Present
___ Cannot be excluded

Architectural Patterns (if DCIS is present select all that apply)
___ Comedo
___ Paget disease (DCIS involving nipple skin)
___ Cribriform
___ Micropapillary
___ Papillary
___ Solid
___ Other (specify): ____________________________
Nuclear Grade (if DCIS is present)
___ Grade I (low)
___ Grade II (intermediate)
___ Grade III (high)

Necrosis (if DCIS is present)
___ Not identified
___ Present, focal (small foci or single cell necrosis)
___ Present, central (expansive “comedo” necrosis)

Lymphovascular Invasion
___ Not identified
___ Present
___ Cannot be determined

Additional Pathologic Findings (Note D)
Specify: ____________________________

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

Ancillary Studies

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

Biomarker Studies
___ Pending

Comment(s)
A. Histologic Type
This protocol applies to all invasive carcinomas of the breast. The World Health Organization (WHO) classification of breast carcinoma is presented below, 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 protocol, 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 classification of tumors being reported as “other.” The WHO classification is presented for completeness.

WHO Classification of Invasive Carcinoma of the Breast

Microinvasive carcinoma
Invasive carcinoma of no special type (NST)
  Pleomorphic carcinoma
  Carcinoma with osteoclast-like stromal giant cells
  Carcinoma with choriocarcinomatous features
  Carcinoma with melanotic features
Invasive lobular carcinoma
  Classic lobular carcinoma
  Solid lobular carcinoma
  Alveolar lobular carcinoma
  Pleomorphic lobular carcinoma
  Tubulolobular carcinoma
  Mixed lobular carcinoma
Tubular carcinoma
Cribriform carcinoma
Mucinous carcinoma
Carcinoma with medullary features
  Medullary carcinoma
  Atypical medullary carcinoma
  Invasive carcinoma NST with medullary features
Carcinoma with apocrine differentiation
Carcinoma with signet-ring-cell differentiation
Invasive micropapillary carcinoma
Metaplastic carcinoma of no special type
  Low-grade adenosquamous carcinoma
  Fibromatosis-like metaplastic carcinoma
  Squamous cell carcinoma
  Spindle cell carcinoma
  Metaplastic carcinoma with mesenchymal differentiation
    Chondroid differentiation
    Osseous differentiation
    Other types of mesenchymal differentiation
  Mixed metaplastic carcinoma
  Myoepithelial carcinoma
Papillary carcinoma
  Encapsulated papillary carcinoma with invasion
  Solid papillary carcinoma, invasive
Epithelial-myoeiithelial tumors
Adenomyoeiithelioma with carcinoma
Adenoid cystic carcinoma

Rare types
Carcinoma with neuroendocrine features
Neuroendocrine tumor, well-differentiated
Neuroendocrine carcinoma poorly differentiated (small cell carcinoma)
Carcinoma with neuroendocrine differentiation
Secretory carcinoma
Invasive papillary carcinoma
Acinic cell carcinoma
Mucoepidermoid carcinoma
Polymorphous carcinoma
Oncocytic carcinoma
Lipid-rich carcinoma
Glycogen-rich clear cell carcinoma
Sebaceous carcinoma

References

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 r² = 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

<table>
<thead>
<tr>
<th>Scoring Categories of Mitotic Counts</th>
<th>Number of mitoses per 10 fields corresponding to:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score 1</td>
</tr>
<tr>
<td>Field diameter (mm)</td>
<td>Area (mm²)</td>
</tr>
<tr>
<td>0.40</td>
<td>0.125</td>
</tr>
<tr>
<td>0.41</td>
<td>0.132</td>
</tr>
<tr>
<td>0.42</td>
<td>0.139</td>
</tr>
<tr>
<td>0.43</td>
<td>0.145</td>
</tr>
<tr>
<td>0.44</td>
<td>0.152</td>
</tr>
<tr>
<td>0.45</td>
<td>0.159</td>
</tr>
<tr>
<td>0.46</td>
<td>0.166</td>
</tr>
<tr>
<td>0.47</td>
<td>0.173</td>
</tr>
<tr>
<td>0.48</td>
<td>0.181</td>
</tr>
<tr>
<td>0.49</td>
<td>0.189</td>
</tr>
<tr>
<td>0.50</td>
<td>0.196</td>
</tr>
<tr>
<td>0.51</td>
<td>0.204</td>
</tr>
<tr>
<td>0.52</td>
<td>0.212</td>
</tr>
<tr>
<td>0.53</td>
<td>0.221</td>
</tr>
<tr>
<td>0.54</td>
<td>0.229</td>
</tr>
<tr>
<td>0.55</td>
<td>0.238</td>
</tr>
<tr>
<td>0.56</td>
<td>0.246</td>
</tr>
<tr>
<td>0.57</td>
<td>0.255</td>
</tr>
<tr>
<td>0.58</td>
<td>0.264</td>
</tr>
<tr>
<td>0.59</td>
<td>0.273</td>
</tr>
<tr>
<td>0.60</td>
<td>0.283</td>
</tr>
<tr>
<td>0.61</td>
<td>0.292</td>
</tr>
<tr>
<td>0.62</td>
<td>0.302</td>
</tr>
<tr>
<td>0.63</td>
<td>0.312</td>
</tr>
<tr>
<td>0.64</td>
<td>0.322</td>
</tr>
<tr>
<td>0.65</td>
<td>0.332</td>
</tr>
<tr>
<td>0.66</td>
<td>0.342</td>
</tr>
<tr>
<td>0.67</td>
<td>0.353</td>
</tr>
<tr>
<td>0.68</td>
<td>0.363</td>
</tr>
<tr>
<td>0.69</td>
<td>0.374</td>
</tr>
</tbody>
</table>

From Pathology Reporting of Breast Disease.² Copyright 2005 National Health Service Cancer Screening Programme and The Royal College of Pathologists. Adapted with permission.
C. Ductal Carcinoma In Situ

Architectural Pattern of DCIS

The architectural pattern has traditionally been reported for DCIS. However, nuclear grade and the presence of necrosis are more predictive of clinical outcome.

Nuclear Grade of DCIS

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

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

Necrosis

The presence of necrosis is correlated with the finding of mammographic calcifications (ie, 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 (ie, 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

D. Additional Pathologic 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.

E. 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 (eg, metallic fragments after surgery or trauma).