

Protocol for the Examination of Specimens from Patients with Ductal Carcinoma in Situ (DCIS) of the Breast

Protocol applies to DCIS without invasive carcinoma or microinvasion and Paget disease of the nipple not associated with invasive breast carcinoma. This protocol does not apply to any tumor with invasive carcinoma, including DCIS with microinvasion only.

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AJCC/UICC TNM, 8th edition
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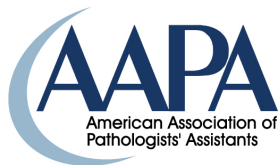
This protocol is revised to the 8th edition of the AJCC Cancer Staging Manual and the current version of the CAP Cancer Protocol Breast DCIS 4.1.0.0.

Procedures Covered in this Protocol:

- Biopsies
- Excisions
 - Localized excision
 - Excisions without localization
- Re-excision specimens
 - Complete
 - Select
- Total mastectomy
 - Simple mastectomy
 - Skin-sparing mastectomy
 - Nipple-sparing mastectomy
 - Modified radical mastectomy
 - Radical mastectomy
- Lymph Node Sampling

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**AAPA Macroscopic Examination Guidelines:
Utilization of the *CAP Cancer Protocols* at the Surgical Gross Bench**

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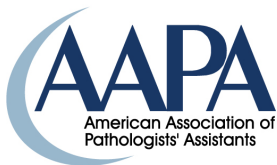
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The purpose of the Protocols is to support Laboratory Personnel engaged in the macroscopic examination of cancer resection specimens. The Protocols are based on specified relevant source documents, drafted by pathologists' assistant experts, and supported by information provided by the College of American Pathologists (CAP) and the American Joint Committee on Cancer (AJCC). These Protocols are intended to serve patients by ensuring that the macroscopic examination of cancer resection specimens is compliant with CAP Cancer Protocols, the AJCC Cancer Staging Manual, and provide optimization of the pre-analytic steps necessary to promote appropriate molecular studies.

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Ambiguous Terminology:

Axillary tail ≠ Axillary dissection

The axillary tail (aka. tail of Spence or axillary process) is an extension of the tissue of the breast that extends into the axilla and is included in all total mastectomies. This would include simple mastectomies which do not include an “axillary dissection” containing lymph nodes as in a modified radical mastectomy. Generally, in a simple mastectomy, the surgeon will mark the axillary tail with a suture for orientation purposes.¹ An axillary dissection (aka. axillary contents) is a surgical procedure that incises the axilla to identify, examine, or remove lymph nodes. Axillary dissection has been the standard technique used in the staging and treatment of the axilla in breast cancer.^{2, 3}

Radiographically Identifiable Markers

There is variation in the use of descriptive terms for markers deployed at the time of a core biopsy procedure (“clips”, “markers”, etc.). We recommend the term “radiographic identified marker;” which may be simplified to marker (NCCN guideline uses the term “radiographic identified marker”). Precise description of the marker (e.g. coiled or ribbon) should be dependent on the institution. Be aware of possible marker migration; be sure to reference the patient’s imaging.^{8,9}

Multifocal and Multicentric Disease

The presence of two or more foci of cancer within the same breast quadrant is defined as multifocal, while the presence of two or more foci of cancer in different quadrants of the same breast is defined as multicentric.³² Multicentric breast cancers typically exhibit cancer foci >5 cm apart and are frequently associated with extensive intraductal carcinoma (EIC).³³ Because *in situ* carcinoma is a precursor of invasive carcinoma, the presence of *in situ* disease in multiple separate cancer foci has led investigators to view such foci as polyclonal tumors versus those of monoclonal origin.³⁴ However, unless clonal analysis is performed on each cancer focus, whether the tumors are of polyclonal or monoclonal origin, the disease cannot be assessed by spatial presentation alone.

Breast Specific Molecular Considerations:

- ER and PgR levels should have 6 to 72 hours of formalin fixation (fixation time should be documented – a CAP checklist requirement).⁴
- *HER2* testing should have 6 to 72 hours of formalin fixation (fixation time should be documented - a CAP checklist requirement).⁴
- The cold ischemic time between breast tissue removal and the initiation of fixation should be documented to be less than or equal to one hour (cold ischemic time should be documented – a CAP checklist requirement).⁴
- Preliminary sectioning may be required to facilitate adequate fixation. If delivery of a resection specimen is delayed (e.g., from a remote site), the tumor should be bisected prior to immersion in fixative. The identity of the margins needs to be retained or the margins separately submitted.⁴
- Tissue taken for research studies or assays that do not involve the histologic examination of the tissue (e.g., reverse transcriptase polymerase chain reaction [RT-PCR]) should be taken in such a way to be able to evaluate the tissue for small areas of invasion. For example, a thin slice of

tissue taken for research studies should be matched with an adjacent slice of tissue that will be examined microscopically.

- DCIS has shown a heterogenous distribution of estrogen, progesterone and *HER2* antigenicity. Negative results on core needle biopsies may necessitate repeat studies on excisional surgical specimens, especially in larger areas of DCIS, making it critical that all breast specimens follow the guidelines for regulated cold ischemic time and fixation.^{5,6,7}

PROCEDURES AND GENERAL ANATOMIC CONSIDERATIONS:

■ **Procedures Covered by this Protocol:**

- Biopsy*
- Excision (less than total mastectomy)
Excisions include specimen types:
 - With or without localization (wire-guided, radioactive seed, other)
 - Lumpectomy with or without localization
 - Quadrantectomy
 - Segmental or partial mastectomy
- Re-excision specimens: Additional excision of a positive or close margin following an excision.
 - Complete (all margins re-excised)
 - Select (targeted margin(s) re-excised)
- Total Mastectomy: encompasses the removal of all breast tissue, usually including the nipple and areola. While the extent of disease should be documented, the overarching goal of macroscopic examination for DCIS is to rule out the presence of invasive breast carcinoma, and to ensure that surgical margins are clear.

There are several different types of total mastectomy specimens:

- Simple mastectomy (without removal of axillary lymph nodes)
- Skin-sparing mastectomy (with removal of the nipple and only a narrow surrounding rim of skin)
- Nipple sparing mastectomy (with no attached skin or nipple)
- Modified radical mastectomy (with an axillary dissection)
- Radical mastectomy (with an axillary dissection, and removal of the pectoralis muscles)

*With the exception of molecular considerations, this protocol does not address very small incisional biopsies (including core needle biopsies) and excisions containing only DCIS after a core needle biopsy or other specimen showing invasive carcinoma or DCIS with microinvasion.

- Lymph Node Sampling
 - Sentinel lymph node(s)
 - Axillary dissection (partial or complete dissection)
 - Lymph nodes present within the breast specimen (i.e., intramammary lymph nodes)
 - Other lymph nodes (e.g., supraclavicular or location not identified)

■ **Specimen Laterality:**

- Specify Right or Left

■ **Specimen Size and Extent of Resection:**

- Provide specimen weight.

- Provide three dimensions; include anatomic orientation of the three planes of dimension, if provided (anterior - posterior / medial – lateral / superior – inferior).
- Provide two dimensions of attached skin and include location (anterior, medial, lateral, inferior), if present.
- Document nipple / areola, if present. Document if nipple is inverted, everted, retracted, or ulcerated.
- If unoriented, provide two surface dimensions and thickness.
- Lymph node sampling (Refer to the Lymph Node Section on page 21.)

■ **Specimen Integrity and Adequacy:**

- Document defects with location as part of integrity assessment. Differential application of ink to the margins in areas affected by defects or disruptions can be done to help clarify identifiable true margins from the defect. A gross photograph of any defect may be taken for future documentation.
- For any specimens with a defect or disruption, statements should include, with as much clarity as can be provided, the anatomic location of the defects or disruptions, and should also incorporate statements which assess the relationship of any defects or disruptions to the tumor. If defects or disruptions involve the targeted area/prior biopsy site and serve to hinder assessment of the final surgical margin this must be stated. Consultation with the surgeon for clarification should be considered, as this may assist in creating a post-surgery treatment plan.
- Consult surgeon as necessary / feasible to identify true margins when they are unclear.
 - If the specimen is an incisional biopsy, margins do not need to be evaluated. However, one should exercise caution in assuming what constitutes an incisional biopsy and err on the side of marking the surgical margins with ink.
- Maintaining in-vivo orientation:
 - Specimen compression during radiographic imaging should be minimized or avoided (i.e., TranSpec compression device).¹⁰
 - The surgeon should indicate the true orientation of the mastectomy specimen with sutures. If not, clarify orientation with operating surgeon.
 - One should not assume that the skin surfacing an excision specimen represents the anterior surface (the surgical approach may not necessarily originate anteriorly).
 - One should not assume that the skin surfacing a mastectomy specimen always represents a transverse/horizontal incision by the surgeon. The surgical incision can be transverse or oblique (pointing to the axilla) at the discretion of the operating surgeon taking into account the position of the tumor and possible scar encroachment into the cleavage area. The surgeon should indicate the true orientation of the mastectomy specimen with sutures. If not, clarify orientation with operating surgeon.

■ **Specimen Radiography:**

- Specimen radiography is important to assess the adequacy of excision.
- Compression of the specimen should be minimized, as it can compromise the ability to assess the distance of the DCIS from the surgical margin.

- Compression devices can provide assistance to radiologists and, if used, should be reserved for nonpalpable lesions that require this technique for imaging (e.g., microcalcifications).
 - DCIS found in biopsies performed for microcalcifications will almost always be at the site of the calcification or in close proximity.
 - The presence of microcalcifications in the specimen should be confirmed by specimen radiography.
 - The relationship of the radiologic calcifications to the DCIS should be indicated.

■ **Specimen Sampling Goals:**

- The clinical or radiographic lesion for which the surgery was performed must be examined microscopically.
 - A specimen radiograph or other radiologic imaging study may be necessary to identify a nonpalpable imaging finding.
 - When practical, the entire specimen should be submitted sequentially for microscopic examination. If this is not possible, at least the entire region of the targeted lesion should be submitted in a sequential fashion for microscopic examination.
 - If DCIS, lobular carcinoma in situ (LCIS), or atypical hyperplasia is identified, all fibrous tissue should be examined (if feasible).
- Sample all other macroscopically identified lesions.
- Each designated margin must be evaluated for involvement by DCIS.
- State if the specimen is received sectioned or fragmented as this could limit the ability to evaluate the size of the lesion and/or the status of margins.
 - Note the approximate percentage of the specimen or lesion that has been examined microscopically if the entire specimen or macroscopically evident lesion has not been examined.

■ **Clinical Information**

The Joint Commission requires that clinical information be provided for pathology specimens. Relevant clinical information is necessary for the accurate evaluation of breast specimens and includes:

- Patient information
- Specimen information
- Type of specimen

TUMOR ("T" of TNM)

TNM Descriptors (required only if applicable)

____r (recurrent)

____y (post treatment)

Definition of Primary Tumor (pT)

pT Category	pT Criteria
pTis (DCIS) *	Ductal carcinoma <i>in situ</i>
pTis (Paget)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma <i>in situ</i> (DCIS) in the underlying breast parenchyma *. 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.

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**Note: Lobular carcinoma in situ (LCIS) is removed from TNM staging in the AJCC Cancer Staging Manual, 8th Edition.*

Note: Paget disease with underlying DCIS is classified as Tis (DCIS). If there has been a prior core needle biopsy, the pathologic findings from the core, if available, should be incorporated in the T classification. If invasive carcinoma or microinvasion were present on the core, the protocol for invasive carcinomas of the breast should be used and should incorporate this information.

■ **Size (Extent) of DCIS:**

Although the size is not required for pT classification or stage, the size (extent) of DCIS is an important factor in patient management. A precise measurement of the extent of DCIS is very difficult because in most cases, there is no identifiable macroscopic lesion other than the usual changes associated with a prior biopsy. The radiographic assessment of DCIS is usually based on distribution of calcifications which can both underestimate and overestimate the extent of DCIS.

Notes:

- The size (extent) of DCIS is an estimation of the volume of breast tissue occupied by DCIS.
- If possible, a specimen radiograph should be obtained and can be an invaluable adjunct to gross examination, especially in those cases where the targeted lesion and/or area of prior biopsy cannot be identified grossly.^{14,15}
- When macroscopic findings are present (e.g., areas of tissue thickening and/or punctate necrosis), they often do not correspond to the entire area of involvement.
- If no discrete mass, biopsy site, or radiographic marker can be identified, it is recommended the breast tissue located in the general region of the biopsy proven DCIS be submitted in its entirety for microscopic examination. Any firm or fibrous tissue in this area should be measured, with a note stating no biopsy site is macroscopically identifiable.¹² If possible, additional radiographic imaging of the sectioned specimen could be obtained to aid in tissue selection/submission. Specimen orientation should be maintained at all times.

- If there are multiple biopsy sites, the varying appearance of the radiographic markers (if applicable) may also be described in the report. There are many types of marker designs including ribbon, wing, coil and cylinder. The prosector should be aware that clips do move, sometimes significantly, after placement.³¹

■ **Methods for Estimating the Size (Extent) of DCIS:**

There are several methods for estimating the extent of DCIS in a specimen. The pathologist can measure/calculate the extent of DCIS by the manner in which the prosector submits sections. The methods for this process and the manner in which orientation is maintained may vary from institution to institution, however within a given institution there should be a consistent approach to handling and submitting these specimens.

- **DCIS in 1 block:** If the area involved by DCIS is limited to a single slide, the pathologist can measure this area from the slide and report the slide.
- **Serial Sequential Sampling (SSS):** The entire specimen is submitted sequentially such that the location of each block can be determined. The extent of DCIS can be calculated by using a specimen diagram, the thickness of the individual slices (CAP recommends 4 mm), and the location of the involved blocks. This method is recommended for all excisions performed for suspected DCIS or with previously diagnosed DCIS (e.g., by diagnosis on a prior core needle biopsy). (*See Figure 1, page 13*)
- **Nonsequential sampling:** This method is utilized when the entire specimen is not submitted for microscopic examination. Multiplying the number of blocks involved by DCIS by the approximate width of a tissue section (4 mm) gives an estimate of the extent. This method may underestimate extent if all areas of DCIS are not sampled. Therefore, it is recommended that all tissue likely to be involved by DCIS be sampled (e.g., all grossly abnormal tissue and all tissue with radiologically suspicious calcifications).
- **Margins:** If DCIS involves or is close to two opposing margins, the distance between the margins can be used as the extent of the DCIS within the specimen.
- **Gross lesions:** In some cases of high-grade DCIS, there may be a gross lesion that can be measured. Accuracy of the gross size must be confirmed by microscopic examination.

■ **Tumor Site(s):**

- Specify tumor site
 - Upper outer quadrant
 - Lower outer quadrant
 - Upper inner quadrant
 - Lower inner quadrant
 - Central
 - Nipple
 - Position: ____ o'clock
 - Other (specify)

- **Specimen Management including Management of Surgical Margins:**
 - **Unoriented incisional biopsies (generally small samples):**
 - Even though margins do not need to be evaluated for incisional biopsies, exercise caution in assuming what constitutes an incisional biopsy and err on the side of marking the surgical margins with ink.
 - Describe all macroscopically abnormal tissue and/or areas of radiographic concern, and submit the entire specimen doing so using the serial sequential method.
 - **Excisions:**
 - Oriented wide local excision with macroscopically evident DCIS:
 - Differentially ink the margins according to your institution's protocol.
 - Provide measurement of lesional tissue and measurements of lesional tissue to all 6 margins.
 - Submit sections using the serial sequential method showing the relationship of the lesional tissue to the closest margins. This should be done for all margins where lesional tissue and margin can be seen on one slide. (*Figure 1*)
 - Perpendicular sections should be submitted to assess the macroscopically negative margins.
 - State how the specimen was submitted, e.g., "sectioned from medial to lateral".
 - No macroscopic evidence of DCIS (radiographic evidence only):
 - Differentially ink the margins according to your institution's protocol.
 - Identify the area of radiographic concern (area with image detectable marker, area of microcalcifications, or changes of prior core biopsy if grossly evident).
 - If possible, provide the measurement of the area of radiographic concern relative to all margins.
 - Submit sections using the serial sequential method showing the relationship of the area of radiographic concern to the closest margins. This should be done for all margins where the tumor and margin can be seen on one slide.
 - Perpendicular sections should be submitted to assess the macroscopically negative margins.
 - State how the specimen was submitted, e.g., "sectioned from medial to lateral".

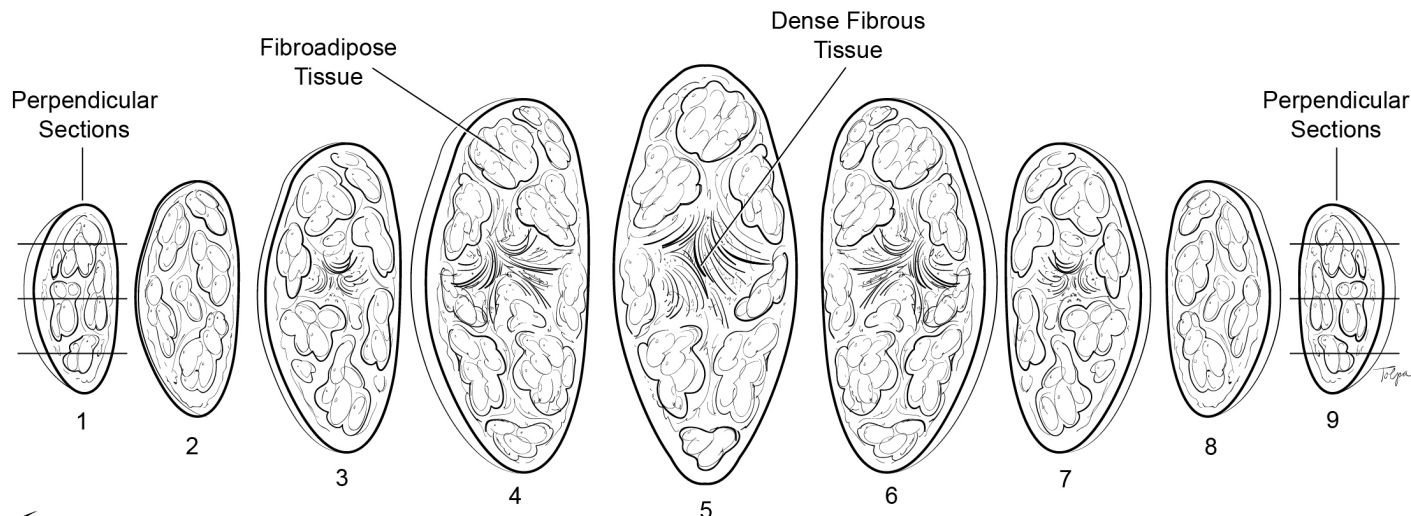


Figure 1: Excisional Biopsy - Serial Sequential Sectioning with Number Designation

When serially sectioning an excisional specimen, number each slice and record which slice(s) the tumor, biopsy site, or clip is located.

- Large excisional specimens in which specimen is not entirely submitted (e.g., large oriented excisions/lumpectomy, partial mastectomy):
 - Differentially ink the margins according to your institution's protocol.
 - Identify the area of radiographic concern (area with radiographic marker, area of microcalcifications, or changes of prior core biopsy if grossly evident).
 - Submit sections using the nonsequential sampling method. If possible submit the entire area of radiographic concern.
 - Sections for microscopic examination can be mapped by means of dictation, directly on the radiograph, on a printed image, or other methods deemed appropriate.
 - These sections should be taken with preference for fibrous areas at intervals which would serve to alter the patient's prognostic status. (22,23,24,25,26)
 - Sample all other macroscopically identified lesions.
 - If an entire excisional specimen or grossly evident lesion is not examined microscopically, it is helpful to note the approximate percentage of the specimen or lesion that has been examined.
- Unoriented wide local excision:
 - Same as above except the measurement will be to the closest unoriented margin.

• **Re-Excisions:**

- Complete Re-excision (six margin re-excision):
 - Differentially ink the margins according to your institution's protocol.
 - Provide a measurement of the cavity in three dimensions, including anatomic planes of orientation.
 - Provide measurement of margin clearance for each of the six margins.

- Submit sequential perpendicular sections (spanning between the biopsy cavity surface and true margin) for any margin in which the prior resection has a clearance of 0.1 cm or less.
- Submit nonsequential representative perpendicular sections for previously negative margins, giving preference to fibrous areas or areas of narrow clearance. ^(27,28,29)
- Select re-excision (less than six margin re-excision):
 - Differentially ink the margins according to your institution's protocol.
 - Sequentially submit all tissue or, for larger specimens, sequentially submit all areas where thickness is less than 1.0 cm, or where biopsy changes are less than 1.0 cm from true margin.
 - For other thicker areas (greater than 1.0 cm), non-sequential sections at regular intervals with preference given to fibrous areas is acceptable.
- **Total Mastectomy (simple, skin sparing, modified radical or radical mastectomies):** ^{30,25}
 - Mastectomy encompasses the removal of all breast tissue, thus, while the extent of disease should be documented, the overarching goal of macroscopic examination is to ensure that surgical margins are clear.
 - The specimen should be oriented by the surgeon.
 - Ascertain the integrity of the margins, including the pectoralis fascia. Document size of any attached skeletal muscle. If defects are present, clarification of the defects from the surgeon should be obtained before inking.
 - Differentially ink the margins according to your institution's protocol.
 - Serially section the specimen perpendicular to the medial-lateral axis at 0.5 cm intervals. This is best done from the deep to the superficial surface. If skin is present, keep the skin intact, unless specimen radiography is needed.
 - Locate and orient by quadrant or o'clock position the site(s) of prior biopsy or prior lumpectomy and note the distance from the deep margin and superficial/other margin when close.
 - Indicate whether or not the radiographic marker was identified on examination. In cases with more than one biopsy site indicate the type of radiographic marker at each site.
 - Submit the entire area of prior biopsy in a serial sequential manner when possible. If area is large utilize nonsequential sampling. In cases with prior lumpectomy submit representative sections from lumpectomy site including closest margin(s) when possible.
 - If there are two or more prior biopsy sites within the specimen, measure the distance between the sites, and submit intervening breast tissue between the sites.
 - Submit margin sections from the non-closest margin if fibrous tissue spans between the prior biopsy site/tumor and these margins.
 - Submit additional sections for any macroscopically evident non-biopsied lesion(s).
 - Submit additional sections to assess any quadrant which was not previously biopsied, with preference given to fibrous tissue and areas where fibrous tissue approaches the margins.
 - Submit at least one perpendicular section of the nipple unless the nipple is macroscopically abnormal or there is a clinical history of Paget's disease.
 - If the deep margin is not involved by tumor, submit one perpendicular section at the site of the biopsy cavity/lesion. If skeletal muscle is present it should also be sampled.

- **Nipple Sparing Mastectomy:**

- For nipple-sparing mastectomies the specimen should be oriented by the surgeon with two perpendicular sutures with additional suture orientation indicating the undersurface of nipple. If the undersurface of nipple is not oriented by the surgeon and cannot be identified by the prosector, the surgeon should be notified for clarification.
- The remaining specimen handling will be the same as above for total mastectomy.

- **Posttherapy or Postneoadjuvant Therapy Classification (y) (Figure 2)**

Cases where systemic and/or radiation therapy are given before surgery (neoadjuvant) or where no surgery is performed may have the extent of disease assessed at the conclusion of the therapy by clinical or pathologic means (if resection is 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.

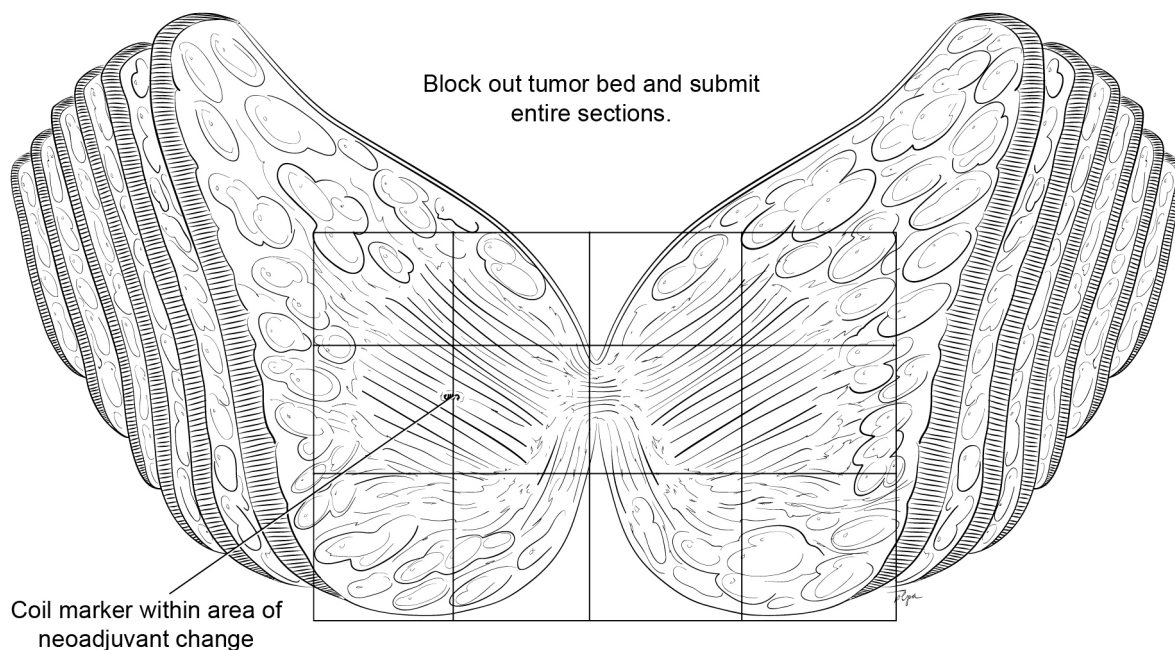


Figure 2: DCIS Treated with Neoadjuvant Chemotherapy
Posterior Portion of Mastectomy

This illustration demonstrates a method to block out tissue that has undergone a full treatment response to neoadjuvant chemotherapy.

■ **DCIS and Skin:**

Signs of DCIS involving nipple skin (Paget's Disease) may not be visible after resection. DCIS can spread from a ductal system into the skin of the breast. The normal squamous barrier is disrupted, and extracellular fluid can seep onto the surface, resulting in a scale crust. The crust is removed when the skin is cleaned prior to surgery, and the involved nipple usually has a normal appearance in the specimen. If not grossly apparent, one may have to rely on a clinical history of Paget's Disease (Lester 2006)

Sampling Nipple with Paget's Disease (Figure 3)

- The nipple is amputated in a plane parallel to the skin surface.
- A second, deeper section is taken in the same plane. This section will demonstrate all the major ducts as they approach the nipple.
- The more superficial section is serially sectioned perpendicular to the skin surface and all these slices are submitted. This section will demonstrate all of the nipple ducts as they empty onto the skin surface. (Lester 2006)

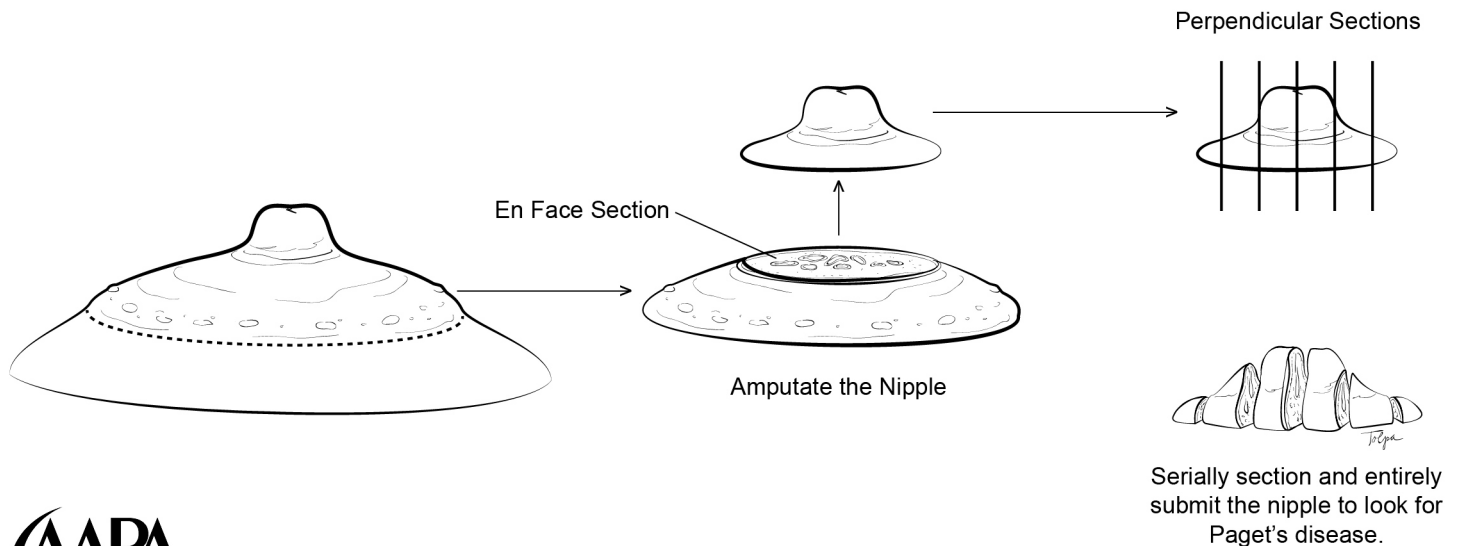


Figure 3: Paget's Breast - Nipple Sectioning

TNM Descriptors

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

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

“y” prefix: indicates those cases in which classification is performed during or following initial multimodality therapy. The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor prior to multimodality therapy.

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

“a” prefix: designates the stage determined after autopsy: aTNM.

Residual Tumor (R) Category

The absence or presence of residual tumor after treatment is described by the symbol R. In some cases treated with surgery and/or with neoadjuvant therapy there will be residual tumor at the primary site after treatment because of incomplete resection or local and regional disease that extends beyond the limit of ability of resection.

The absence or presence of residual tumor at the primary tumor site after treatment is denoted by the symbol R. The R categories for the primary tumor site are as follows:

R	R Definition
RX	Presence of residual tumor cannot be assessed
R0	No residual tumor
R1	Microscopic residual tumor
R2	Macroscopic residual tumor at the primary cancer site or regional nodal sites

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■ **Margins (Figure 4)**

The current NCCN guidelines for DCIS state that “Margins less than 2 mm are considered inadequate.” Surgical margins greater than 2 mm are generally associated with lower local recurrence rates. However, close surgical margins (<1 mm) at the fibroglandular boundary of the breast (chest wall or skin) do not mandate surgical re-excision but can be an indication for higher dose radiation to the involved lumpectomy site”.^{16,17} A positive margin requires ink on DCIS.

- The specimen should be oriented in order to identify specific margins.
 - Margins may be identified by sutures or clips placed on the specimen surface or by means of communication between the surgeon and pathologist and should be documented in the pathology report.
 - The prosector can identify the margins for microscopic evaluation by:
 - the use of multiple colored inks
 - by submitting the margins in specific cassettes
 - by the surgeon submitting each margin as a separately excised specimen.

Inks should be applied to the surface of the specimen, taking care to avoid penetration into the specimen.

In most cases of DCIS there is no macroscopically identified lesion. In these cases, the distance from all margins of the prior biopsy site or targeted area is noted.

- Specify if margins are involved or uninvolved by DCIS.
 - If margin is uninvolved by DCIS, specify the distance from the closest margin in mm.
 - Specify distance of tumor from the superior, inferior, medial, lateral, anterior, and posterior margin, or other specified margin in mm.
- Specify which margin is positive for DCIS (if applicable).
 - For positive margins, specify extent (focal, minimal / moderate / extensive).

• **Deep margin**

The likelihood of breast tissue beyond this margin (and therefore possible involvement by DCIS) is very small. A deep muscle fascial margin (e.g., on a mastectomy specimen) is unlikely to have clinical significance.

• **Superficial margin (generally anterior)**

This margin may be immediately below the skin, and there may not be additional breast tissue beyond this margin. However, breast tissue can be left in skin flaps, and the likelihood of residual breast tissue is related to the thickness of the flap.³⁶

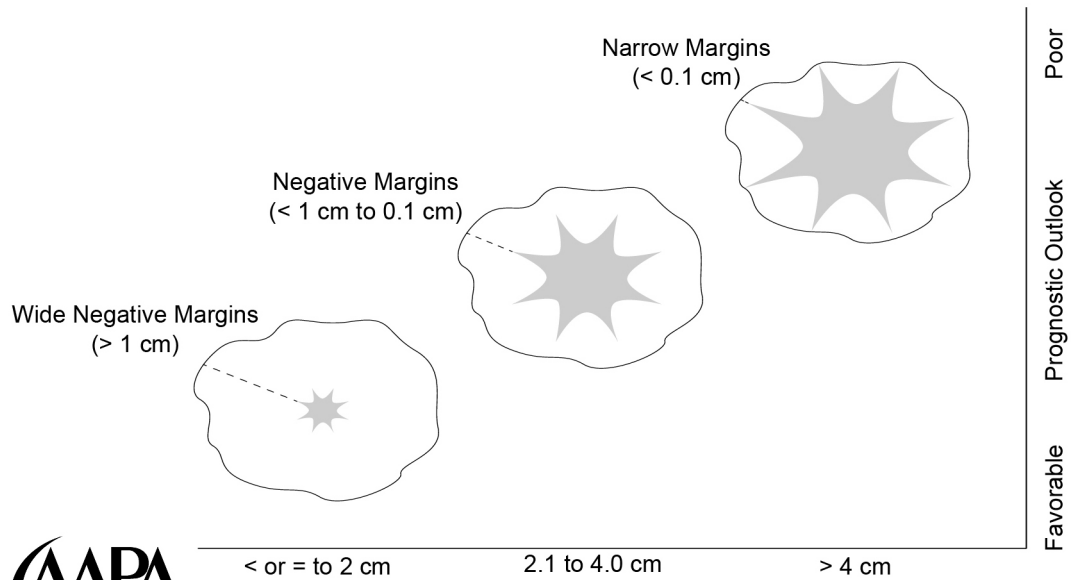


Figure 4: Extent of DCIS and Margin Status

LYMPH NODES ("N" of TNM)

The pathology report should state the total number of lymph nodes examined (including the number of sentinel nodes), the number of nodes with metastases, and the greatest dimension of the largest metastatic focus. If there is at least one lymph node with macrometastasis, only lymph nodes with micro or macrometastasis are included in the total number of involved nodes for N classification. Lymph nodes with isolated tumor cells would not be included in this count. At least 1 lymph node with or without metastatic cancer documented by pathologic examination is required for pathologic N classification.

■ Regional Lymph Nodes include:

- Axillary (ipsilateral): interpectoral (Rotter's) nodes and lymph nodes along the axillary vein and its tributaries that may be (but are not required to be) divided into the following levels:
 - Level I (low-axilla): lymph nodes lateral to the lateral border of the pectoralis minor muscle.
 - Level II (mid-axilla): lymph nodes between the medial and lateral borders of the pectoralis minor muscle and the interpectoral (Rotter's) lymph nodes.
 - Level III (apical axilla): lymph nodes medial to the medial margin of the pectoralis minor muscle and inferior to the clavicle. Also known as apical or infraclavicular nodes.
- Internal mammary (ipsilateral): lymph nodes in the intercostal spaces along the edge of the sternum in the endothoracic fascia.
- Supraclavicular: lymph nodes in the supraclavicular fossa, a triangle defined by the omohyoid muscle and tendon (lateral and superior border), the internal jugular vein (medial border), and the clavicle and subclavian vein (lower border). Adjacent lymph nodes outside of this triangle are considered lower cervical nodes (M1).
- Intramammary: lymph nodes within the breast; these are considered axillary lymph nodes for purposes of classification and staging.

■ Sentinel lymph nodes:

- The sentinel node is usually the first involved lymph node. In the unusual situation in which a sentinel node is not involved by metastatic carcinoma, but a nonsentinel node is involved, this information must be included in the pathology report.
- The sentinel node is identified by the surgeon by uptake of radiotracer or dye or both.
- Adjacent palpable nonsentinel nodes may also be removed.

Regional Lymph Nodes (pN)

Modifier (required only if 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.

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Note: 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.

Definition of Regional Lymph Nodes – Pathological (pN)

N Category	N Criteria
pNX	Regional lymph nodes cannot be assessed (e.g., not removed for pathologic study or previously removed)
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
pN1	Micrometastases; or metastases in 1 to 3 axillary lymph nodes; and/or clinically negative internal mammary nodes with micrometastases or macrometastases by sentinel lymph node biopsy
pN1mi	Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm)
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
pN2	Metastases in 4 - 9 axillary lymph nodes; or positive ipsilateral internal mammary lymph nodes by imaging in the absence of axillary lymph node metastases
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
pN3	Metastases in 10 or more axillary lymph nodes; or in infraclavicular (Level III axillary) lymph nodes; or positive ipsilateral internal mammary lymph nodes by imaging in the presence of one or more positive Level I, II axillary lymph nodes; or in more than three axillary lymph nodes and micrometastases or macrometastases by sentinel lymph node biopsy in clinically negative ipsilateral internal mammary lymph nodes; or in ipsilateral supraclavicular lymph 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

Note: (sn) and (f) suffixes should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or FNA/core needle biopsy respectively, with NO further resection of nodes.

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Isolated tumor cell clusters (ITC) 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 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.

The classification is based on axillary lymph node dissection with or without sentinel lymph node dissection.

Note:

Current guidelines suggest that at least 10 lymph nodes should be examined for optimal prognostic staging. The descriptor for “Regional Lymph Nodes” (pN) extends the number to pN3 if metastasis is found in 10 or more lymph nodes.

The presence of nodal involvement indicates the presence of invasive breast carcinoma. (18,19,20,21)

Lymph node sampling:

- Sampling must be adequate to detect all macrometastases, as they are known to have prognostic importance (i.e., all metastatic deposits >2 mm).
- Specify site of lymph nodes identified.
- Specify the total number of lymph nodes examined (sentinel and nonsentinel).
- Measure lymph nodes in three dimensions or provide a range in size of greatest dimension if multiple.
- Specify the number of lymph nodes with macroscopic metastases. *
- Specify the greatest dimension of the largest metastatic focus.
- State if there is or is not macroscopic evidence of extranodal tumor extension. **

*An accurate assessment of the number of positive lymph nodes is a critical prognostic indicator.

**The presence of extranodal extension may be associated with a higher frequency of axillary recurrence.

Sentinel Nodes:

Each node is serially sectioned at 2 mm intervals and in the absence of macroscopic evidence of metastatic tumor, entirely submitted.

For macroscopically positive lymph nodes:

- Describe the cut surface of the identified lymph nodes and the macroscopic appearance of tumor metastasis including the size and location within the node.
 - State if the metastatic focus is subcapsular and/or intramedullary.
- Give a precise size of the lymph node and tumor implant.
- Representative sampling of these lymph nodes is adequate.
- Sample areas where extranodal tumor extension is seen or cannot be excluded.
- If possible, submit lymph node sections so that the long axis of the lymph node is demonstrated.
- Take steps to ensure that an accurate lymph node count can be rendered.

For small lymph nodes or macroscopically negative larger lymph nodes:

- Submit small lymph nodes (2-3 mm) in toto.
- Thinly section larger lymph nodes at 2 mm intervals and entirely submit.
- Submit the entire capsule of the lymph node for possible extranodal extension.
- If the lymph node is large but macroscopically negative, submit sequentially so that a size calculation can be established.
- If possible, submit lymph node sections so that the long axis of the lymph node is demonstrated.
- Take steps to ensure that an accurate lymph node count can be rendered.



AAPA Macroscopic Examination Guidelines: Utilization of the *CAP Cancer Protocols* at the Surgical Gross Bench

Note:

At least one lymph node with the presence or absence of cancer documented by pathologic examination is required for pathologic staging N. A tumor nodule with a smooth contour 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.

METASTASIS ("M" of TNM)

■ Distant Metastasis

Definition of Distant Metastasis (pM) (required only if confirmed pathologically)

pM Category	pM Criteria
pM1	Histologically proven metastases larger than 0.2 mm

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Note: The presence of distant metastases in a case of DCIS would be very unusual. Additional sampling to identify invasive carcinoma in the breast or additional history to document a prior or synchronous invasive carcinoma is advised in the evaluation of such cases.

The pathologic assignment of the presence of metastases (pM1) requires a biopsy positive for cancer at the metastatic site. Pathologic classification of the absence of distant metastases can only be made at autopsy.

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