1. Ductal Carcinoma In Situ

Qingqing Ding, MD, PhD; Fang Fan, MD, PhD

Lumpectomy (also called partial or segmental mastectomy) is a breast-conserving surgery defined as complete surgical resection of a primary tumor as well as some surrounding normal breast tissue, with a goal of achieving negative margins. Lumpectomy may be performed with image guidance, which includes wire-guided localization and radioactive (or magnetic) seed localization.

Total mastectomy or simple mastectomy is defined as complete removal of all breast tissue, which may be performed in conjunction with a sentinel node biopsy. Two types of total mastectomy—the skin-sparing mastectomy and the nipple-sparing mastectomy—are usually performed for patients with ductal carcinoma in situ (DCIS) who wish to undergo immediate breast reconstruction.

Accurate pathologic reporting of DCIS is essential to guide postsurgical treatment, such as radiation therapy, and provide information to predict prognosis. Adequate tumor sampling and thorough examination of essential margins are of utmost importance in processing surgical specimens with DCIS. Careful review of radiologic imaging (mammography, ultrasound, and magnetic resonance imaging [MRI]), clinical history, and preoperative biopsy is necessary before grossing any breast resection specimen.

I. Indications for lumpectomy or mastectomy for DCIS

Lumpectomy

- Lesion should be limited to one quadrant or section of the breast.
- Cosmetically acceptable resection is achievable given the extent of disease relative to the size of the breast.
- Histologically negative margins are obtainable with lumpectomy.

Mastectomy

- DCIS lesion does not meet the above criteria, usually due to large size (>5 cm) or multicentric disease.

II. What do we expect to see in the lumpectomy and mastectomy specimens macroscopically and microscopically?

Based on the degree of nuclear atypia, DCIS is classified into low, intermediate, and high grade. It can show multiple growth patterns, such as solid, cribriform, papillary, and micropapillary patterns. Microcalcifications are usually seen in association with DCIS. High-grade DCIS can form a mass-like lesion, but low- and intermediate-grade DCIS usually does not.

In cases of biopsy-confirmed DCIS, comprehensive evaluation of the involved breast tissue is critical to rule out possible microinvasion or focal invasive carcinoma, especially for those with high nuclear grade. Another important element in pathologic reporting of DCIS is the status of margins. According to the current consensus guideline by the Society of Surgical Oncology, the American Society for Radiation Oncology, and the American Society of Clinical Oncology, a margin greater than 2 mm is considered as the standard for an adequate margin for DCIS.¹

III. Photo documentation of lumpectomy and total mastectomy specimens

Once received, the lumpectomy specimen should be radiographed immediately to confirm the presence/number of the biopsy clip and/or seed in order to ensure removal of the targeted lesion. It is not necessary to radiograph a total mastectomy specimen immediately, but taking one image to localize the biopsy clip and calcification is encouraged. Then, the specimen should be grossly examined to correlate the size and location of lesion tissue with preoperative radiologic imaging. The total mastectomy specimen should also be examined for any skin and/or nipple change.

IV. Dissection technique: step-by-step description

1. Orient and ink specimen.

The orientation of lumpectomy or total mastectomy specimen is usually designated by the surgeon (such as long stitch-lateral and short stitch-superior, as shown in Figures 1-1A and 1-2A). If there is any question about the orientation, the surgeon should be contacted immediately. The specimen is measured in three dimensions, including the attached skin on total mastectomy specimen, and inked. Inking should be careful as the ink may penetrate deep into tissue cleft and cause a false-positive margin. Different hospitals may have different ink codes. Generally, five or six colors are used for the lumpectomy specimen, whereas three colors are adequate for the total mastectomy specimen. See the following ink code examples.

Ink code for lumpectomy
Superior: blue
Inferior: green
Anterior: yellow
Posterior: black
Medial and lateral: orange

Ink code for total mastectomy
Superior/anterior: blue
Inferior/anterior: orange
Posterior: black
Nipple areola complex (for nipple-sparing mastectomy, Figure 1-3); yellow

2. Serially section the specimen.

After inking, the specimen is serially sectioned along the lateral-medial axis (from lateral to medial for left breast and from medial to lateral for right breast). If the lumpectomy specimen is wire guided, the wire should be carefully removed before slicing the specimen. The specimen should be sectioned at the same intervals (approximately 0.5-1.0 cm) throughout, which will be helpful to evaluate the tumor size after microscopic examination. For the lumpectomy specimen, except the lateral and medial tips, each slice should have four color-inked margins (Figures 1-1C). For the total mastectomy specimen, we suggest that the specimen be placed on the gross table with anterior surface down and then cut from the posterior surface to make sure every slice contains posterior margin. After sectioning, all the slices are placed on a plastic plate in order (from lateral to medial if left breast, from medial to lateral if right breast; Figures 1-1C and 1-2C). Then each slice is carefully examined to determine the size and location of lesion, number of involved slices, and distance of lesion to different margins. If there are multiple lesions, the location of each lesion and the distance between them should be documented. In addition, the specimen should be palpated to detect any possible intramammary lymph node.

With the wide usage of radioactive (or magnetic) seed localization in lumpectomy surgery, specimen radiographing is usually required to document the presence/number of the seeds and biopsy clips (Figure 1-1D). If a radioactive seed is located, it should be

---

carefully removed and placed in a designated container per institutional radioactive safety regulations. If adequate margin status is questioned, radiographing the sliced lumpectomy specimen will contribute greatly in the determination of margin distance and delineation of lesional tissue/microcalcification in the specimen.

For a total mastectomy specimen, when multiple lesions/areas of suspicious calcifications are present or when the lesion is ill defined, an x-ray film of the sliced specimen can be used to determine the size and distribution of microcalcifications, which helps to sample the specimen accurately in correlation with the gross examination. Moreover, if the lesion is close to the margin but the specific distance is difficult to evaluate grossly, an x-ray film of the sliced specimen will make the intraoperative margin evaluation more accurate. For example, in Figure 1-2D, the microcalcifications approach anterior/superior and deep margins focally, which is difficult to appreciate grossly.

After successful examination of the specimen, the surgeon should be informed intraoperatively about the presence and number of biopsy clips and/or radioactive seed, as well as the distance between the lesion and margins. If the lesion or microcalcifications approach a certain margin, re-excision of that margin is recommended intraoperatively to avoid a potential subsequent second surgery for re-excision.

3. Properly and adequately sample specimen.

If the lesion has been previously biopsied, the area with biopsy clip is the targeted area for sampling. Other suspicious areas (microcalcifications) without previous biopsy also need to be sampled.

For small lumpectomy specimens, the entire specimen with all six margins is submitted. For the two end margins, perpendicular sections of the margins should be submitted (Figure 1-1E).

For larger lumpectomy specimens, adequate representative sections of the tumor with adjacent margin should be submitted. If submitting representative sections, the cross-section of the tumor...
or microcalcification in each involved slice with closest margins must be submitted, followed by adjacent normal-appearing breast tissue in adjacent slices, as well as the two end margins.

For lumpectomy, additional shave margins may be taken and designated by the surgeon (Figure 1-1F). Ink the true margin in black and the opposite side with another color, such as blue; then serially section the entire margin (perpendicularly to show black-inked true margin) and submit all sequentially.

For mastectomy, if there is a large tumor or large area of microcalcification, adequate representative sections should be submitted to search for possible microinvasion or small foci of invasive carcinoma, especially in cases of DCIS with high nuclear grade (Figure 1-2E). First, the cross-section of the tumor or microcalcification area in each involved slice with closest margins are submitted. Next, adjacent normal-appearing breast tissue in the adjacent slices is submitted. If there are multiple tumors or areas of microcalcification, the tissue between the adjacent two lesions should be submitted in order to document if the two lesions represent a single contiguous lesion or two separate lesions. In addition, entire nipple, nipple base, and representative skin section should be submitted. For the nipple-sparing mastectomy, the nipple areola complex will be submitted. If the tumor is close to the nipple, frozen
diagnosis may be already performed on nipple areola complex. For the quadrant that is not involved by tumor/microcalcification, representative sections of each quadrant should be submitted. Finally, the representative lateral and medial slices, as well as any grossly identified intramammary lymph node, are also submitted.

The clearly documented gross description must include radiographic findings, ink code, and section code.

V. Sample gross description

Lumpectomy

Right breast, radioactive seed–localized lumpectomy: A lumpectomy specimen labeled “short stitch superior and long stitch lateral” measures 4.0 cm (from medial to lateral) x 3.5 cm (from superior to inferior) x 2.6 cm (from anterior to posterior). Radiography of the specimen reveals two biopsy clips and a radioactive seed. After inking, the specimen is serially sectioned from medial to lateral into six slices, with biopsy clips and radioactive seed in slice #3. The biopsy clips and radioactive seed are removed, and the radioactive seed is put in the specific container.

There is an ill-defined fibrotic nodule in slice #3, measuring 1.1 x 0.8 x 0.5 cm, which is 0.5 cm to the anterior, 0.9 cm to the posterior, 0.6 cm to the superior, 1.5 cm to the inferior, 1.5 cm to the lateral, and 2.1 cm to the medial margins. No other mass lesion or suspicious microcalcification is identified in other slices.

Ink code
Superior: blue
Inferior: green
Anterior: yellow
Posterior: black
Medial and lateral: orange

Section code (Figure 1-2E)
A1–2: Lateral margin, perpendicular sections of slice #1
A3: Superior 1/2 of slice #2
A4: Inferior 1/2 of slice #2
A5: Tumor with superior 1/2 of slice #3 (with biopsy clip)
A6: Inferior 1/2 of slice #3
A7: Anterior/superior 1/4 of slice #4
A8: Anterior/inferior 1/4 of slice #4
A9: Posterior/superior 1/4 of slice #4
A10: Posterior/inferior 1/4 of slice #4
A11: Superior 1/3 of slice #5
A12: Middle 1/3 of slice #5
A13: Inferior 1/3 of slice #5
A14-15: Medial margin, perpendicular sections of slice #6

Lumpectomy with additional shave margins

B. Right breast, additional superior margin, excision: An additional superior margin specimen measures 3.2 x 2.7 x 0.7 cm, with clips designating true margin. The true margin is inked black, the opposite side is inked blue. The specimen is serially sectioned perpendicularly and submitted entirely in B1-B3.

C. Right breast, additional inferior margin, excision: An additional inferior margin specimen measures 2.8 x 1.7 x 0.6 cm, with clips designating true margin. The true margin is inked black, the opposite side is inked blue. The specimen is serially sectioned perpendicularly and submitted entirely in C1-C2.

D. Right breast, additional lateral margin, excision: An additional lateral margin specimen measures 3.7 x 2.6 x 0.8 cm, with clips designating true margin. The true margin is inked black, the opposite side is inked blue. The specimen is serially sectioned perpendicularly and submitted entirely in D1-D3.

E. Right breast, additional medial margin, excision: An additional medial margin specimen measures 3.6 x 2.6 x 1.0 cm, with clips designating true margin. The true margin is inked black, the opposite side is inked blue. The specimen is serially sectioned perpendicularly and submitted entirely in E1-E3.

F. Right breast, additional posterior margin, excision: An additional posterior margin specimen measures 2.2 x 1.4 x 0.5 cm, with clips designating true margin. The true margin is inked black, the opposite side is inked blue. The specimen is serially sectioned perpendicularly and submitted entirely in F1-F3.

G. Right breast, additional anterior margin, excision: An additional anterior margin specimen measures 3.4 x 1.6 x 0.8 cm, with clips designating true margin. The true margin is inked black, the opposite side is inked blue. The specimen is serially sectioned perpendicularly and submitted entirely in G1-G3.

Total mastectomy

Right breast, total mastectomy: A total mastectomy specimen labeled “short stitch superior and long stitch lateral” measures 18.6 cm (from lateral to medial) x 17.4 cm (from superior to inferior) x 3.8 cm (from anterior to posterior), with attached 18.1 x 8.3 cm elliptical tan-white skin and 1.2 x 1.1 x 0.6 cm everted nipple. Radiography of the specimen reveals two biopsy clips in an area with approximately 6 x 5 cm microcalcifications. After inking, the specimen is serially sectioned from medial to lateral into 15 slices, with biopsy clips in slice #7 and nipple in slice #10 and #11.

There is an ill-defined, firm nodule in slices #5 to #9, measuring approximately 6.0 x 5.0 x 2.5 cm. The nodule is located in the upper outer quadrant 10-11 o’clock, with 1.8 cm to the nipple, 1.2 cm to the closest superior skin margin, 4.2 cm to the closest inferior skin margin, 0.2 cm to the anterior/superior, 0.6 cm to the posterior, 5.2 cm to the superior, 6.3 cm to the inferior, 4.8 cm to the lateral, and 7.2 cm to the medial margins. Radiography of the specimen shows two biopsy clips in slice #7 and extensive microcalcifications associated with nodule in slices #5 to #11. The microcalcifications approach the anterior/superior and posterior margins and extend to the dermis and nipple base. No other mass lesion or suspicious microcalcification is identified in other slices. No skin lesion or induration/reaction is identified. The remaining breast tissue is composed of 30% fibrotic tissue and 70% adipose tissue.

Ink code
Anterior/superior: blue
Anterior/inferior: orange
Posterior: black

Section code (Figure 1-2E)
A1: Entire nipple, serially sectioned (for nipple-sparing mastectomy, submit the nipple areola complex)
A2: Nipple base
A3: Representative lateral edge, perpendicular sections of slice #1
A4: Representative section of upper outer quadrant in slice #3
A5: Representative section of lower outer quadrant in slice #3
A6-7: Adjacent tissue to tumor in slice #4
A8-10: Tumor in slice #5 (from superior to inferior)
A11-13: Posterior portion of tumor with posterior margins in slice #6 (from superior to inferior)
A14-16: Anterior portion of tumor in slice #6 (from superior to inferior)
A17: Representative inferior/anterior margin with skin in slice #6
A18: Representative superior margin in slice #7
A19: Tumor with closest anterior/superior margin in slice #7
A20: Tumor with closest superior skin margin in slice #7
A21-22: Anterior portion of tumor in slice #7 (from superior to inferior)
A23-25: Posterior portion of tumor with posterior margins in slice #7 (from superior to inferior, with two clips in A23)
A26-28: Posterior portion of tumor with posterior margins in slice #8 (from superior to inferior)
A29-31: Anterior portion of tumor in slice #8 (from superior to inferior)
A32: Tissue with microcalcifications below A28 and A31 in slice #8
A33-34: Posterior portion of tumor with posterior margins in slice #9 (from superior to inferior)
A35-36: Anterior portion of tumor with skin in slice #9 (from superior to inferior)
A37-38: Adjacent tissue to tumor in slice #10
A39: Representative section of upper inner quadrant in slice #12
A40: Representative section of lower inner quadrant in slice #12
A41: Representative medial edge, perpendicular sections of slice #15

VI. Common pathologic findings in lumpectomy and mastectomy for DCIS
- DCIS, low nuclear grade, solid pattern (Figure 1-4A)
- DCIS, high nuclear grade, solid pattern with comedonecrosis (Figure 1-4B)
- DCIS with microinvasion (Figure 1-4C)
- DCIS with invasive carcinoma (Figure 1-4D)

VII. Common potential staging pitfalls and solutions
Missing the microinvasive carcinoma (≤1 mm) or small focus of invasive carcinoma (>1 mm but ≤5 mm) is the most common pitfall in staging. For every high-grade DCIS, it is important to think about the potential microinvasion or even invasive carcinoma. It is critical and required to review all the clinical information, such as clinical examination and radiologic results, before grossing the specimen. Knowing all the information about the current DCIS lesion—such as tumor size, location, microcalcification area and extent—is necessary for accurate sampling. For small tumors, the entire lesion should be submitted. If the tumor is large and submission of the entire tumor is not practical, adequate representative sections from each slice with tumor/microcalcifications are still required. In addition, areas with suspicious microcalcifications should not be missed. If the tumor is not easy to identify grossly, radiography of the specimen slices will help to detect the area with microcalcifications.

Occasionally, isolated tumor cells (ITCs) can be identified in the axillary sentinel lymph nodes, especially in DCIS with papillary and/or micropapillary growth patterns, which may be due to drainage of detached tumor cells to the axillary lymph node after previous biopsy. However, it also may indicate the potential presence of true invasive carcinoma associated with DCIS. Therefore, when ITCs are identified, careful reviewing of the record of grossing procedure and re-reviewing of the slides microscopically is required to determine if additional tissue sampling is needed. If micrometastasis is identified without microinvasive or invasive carcinoma identified in the breast specimen, submission of all remaining tumor is recommended if the entire tumor has not been submitted previously.

VIII. What should be included in the pathology report?
- Description of specimen and procedure
- Description of the type of tumor (DCIS), nuclear grade, architectural pattern, presence or absence of necrosis and associated microcalcifications

Per the current College of American Pathologists (CAP) cancer protocol for DCIS, additional information needs to be supplied, as listed below:
- Description of the DCIS site and position
- Tumor size and extent
- Status of margins (positive or negative, the closest margin)
- For positive or close margins (<2 mm), specify extent (local, minimal/moderate, or extensive) of the DCIS near the positive/close margin
- Status of regional lymph nodes
- pTNM stage
If there is microinvasive carcinoma or invasive carcinoma, it is necessary to give the invasive tumor type and Nottingham histologic score, as well as detailed information, by following the CAP protocol for invasive carcinoma (see chapter 2, Invasive Breast Carcinoma).

**Sample final diagnosis**
Right breast, total mastectomy:
Ductal carcinoma in situ (DCIS), high nuclear grade, solid and cribriform patterns with comedonecrosis and associated microcalcifications

See tumor checklist.

**DCIS checklist:**
- Procedure: Total mastectomy
- Specimen Laterality: Right
- Tumor Site: Upper outer quadrant
- Position: 10-11 o’clock
- Size (Extent) of DCIS
  - Estimated size (extent) of DCIS: approximately 6.0 cm
  - Additional dimensions: 5.0 x 2.5 cm
- Histologic Type: Ductal carcinoma in situ
- Architectural Patterns: Solid and cribriform
- Nuclear Grade: Grade III (high)
- Necrosis: Present, central (expansive “comedo” necrosis)
- Microcalcifications: Present in DCIS

- Margins
  - Uninvolved by DCIS
    - Distance from closest margin (millimeters): 2.1 mm
    - Specify closest margin: Anterior/Superior
- Regional Lymph Nodes: 3 axillary sentinel nodes, negative for carcinoma
- Pathologic Stage Classification: pTis (sn)N0 Mn/a
- Primary Tumor (pT)
  - pTis (DCIS): Ductal carcinoma in situ.
- Regional Lymph Nodes (pN)
  - (sn): Sentinel node(s) evaluated.
  - pN0: No regional lymph node metastasis identified or ITCs only
- Distant Metastasis (pM)
  - Not applicable

**References**