

25 Breast

Pedram Argani, M.D.

General Comments

A wide variety of surgical techniques are employed to biopsy or resect breast tissue. In general, these specimens can be divided into several groups: (1) needle core biopsies performed by radiologists; (2) small biopsies performed for mammographic abnormalities; (3) “lumpectomies” for grossly benign palpable tumors and grossly malignant palpable tumors; (4) mastectomies with or without a lymph node dissection, performed for carcinoma; and (5) reduction mammoplasties.

The processing of these specimens can be difficult and labor-intensive for a number of reasons. Breast specimens are fatty tissues that require meticulous attention to proper fixation to ensure adequate microscopic and immunohistochemical evaluation. Breast specimens often harbor subtle mammographic abnormalities that may not be apparent on gross examination. Detection of these lesions relies on careful dissection coupled with ample tissue sectioning. Breast specimens usually do not contain useful anatomic landmarks, yet important treatment decisions ultimately rest on your ability to assess the status of the specimen margins accurately. Detailed attention to specimen orientation and margin designation is therefore critical. Chapter 1 covers many of the fundamental issues of tissue processing and sampling; but when it comes to handling breast specimens, a few points warrant special emphasis.

Examination of the Specimen

All breast tissue, even if removed for cosmetic reasons, should be examined fresh. It is much

easier to appreciate subtle scirrhous areas that could correspond to small invasive carcinomas in the background of fresh tissue. After formalin fixation, all of the tissue is firm, making this distinction more difficult.

Inking

Breast specimens (with the exception of needle core biopsies) should be inked prior to immersion in formalin. Before the ink is applied, blot the surface of the specimen dry so the ink better adheres to the surface of the specimen. After the ink is applied, again blot the surface of the specimen dry. This step helps prevent the ink from penetrating the tissues as the specimen is sectioned. Immersion for 20 seconds in Bouin’s fixative immediately after inking may help fix the ink to the specimen, but remember to rinse the Bouin’s solution from the specimen before sectioning. Always be certain that the ink is completely dry before cutting into the specimen. Be patient; you may have to wait 5 to 10 minutes or so for the ink to dry completely.

Sometimes the surgeon designates (e.g., using sutures) the anatomic orientation of a specimen. The easiest way to maintain this orientation is to use inks of different colors to designate each of the six specimen margins (superior, inferior, medial, lateral, anterior, posterior). If only one color is used, you must keep track of and dictate which inked surfaces are represented in each of the cassettes. Also, if the specimen is not submitted in its entirety, it must be stored so one can go “back to the bucket” and take more sections from a specific area as needed.

Fixation

Breast tissue that has not been properly fixed compromises the ability of the histopathology laboratory to cut high quality sections for microscopic examination, limits the ability of the pathologist to interpret difficult “borderline” lesions (e.g., atypical duct hyperplasia), and diminishes the reliability of immunohistochemical assays (e.g., Ki-67 proliferation index, estrogen and progesterone receptors) for predicting tumor behavior. If the specimen is to be fixed prior to complete processing and sampling, take the time to “bread-loaf” the specimen at 1-cm intervals before submerging it in formalin. This step allows the formalin to penetrate all of the tissue. Keep in mind that formalin penetrates tissue at a rate of approximately 4 mm in 24 hours. If the specimen is not bread-loafed prior to submersion in formalin, much of the tissue will remain unfixed, particularly in the center of the specimen. If you are not sure that the specimen is adequately fixed when it is time to submit it for processing at the end of the day, it is better *not* to submit it that day. Allow the specimen cassettes to fix overnight in formalin; then submit them for processing the next day.

Needle Core Biopsy

Record the number, size, and color of the tissue cores. All of the cores should be entirely submitted to the histopathology laboratory for further processing. Each tissue block should be sectioned at three levels.

As part of the microscopic evaluation of these specimens, the histopathologic findings must be correlated with the clinical and mammographic findings. For example, if the biopsy specimen is from a mass lesion, your report should indicate whether the microscopic findings account for a breast mass. If, on the other hand, the biopsy was performed because of worrisome calcifications, your report should document the presence of these calcifications when they are found. Discrepancies between the microscopic findings and the clinical/mammographic findings may necessitate additional work on your part. If you cannot find calcifications when they were seen by mammography, additional levels of the tissue block should be cut. It may be nec-

essary to confirm the presence of calcifications by obtaining radiographs of the paraffin blocks. However, you should be aware that calcifications that were present in the tissue submitted to pathology (as documented in radiology by specimen radiographs) sometimes chip out of the block when it is sectioned by the histotechnologist. The presence of tissue tears in the hematoxylin and eosin (H&E) section is a good clue that this has occurred.

Biopsies for Mammographic Abnormalities

Nonpalpable lesions detected mammographically are often biopsied by the surgeon and the specimen then sent to radiology, where a specimen radiograph is obtained to confirm that the surgeon has indeed biopsied or excised the lesion detected on the clinical mammogram. In these cases the radiologist frequently marks the lesion with a needle or dye, and both the biopsy and the specimen mammogram are then sent to the surgical pathology laboratory.

Once received in pathology, the specimen should be measured, inked, and serially sectioned (Figure 25-1). Take care to slice the breast thinly (2 mm). Take advantage of the specimen radiograph; the gross findings can be correlated with the lesion seen radiographically. If a lesion is seen, note the largest dimension of the lesion and carefully note the relationship of the lesion to the inked margins as well as the circumscription and nature of the border of the lesion.

Sequentially submit the entire specimen, up to 20 blocks of tissue, for histologic examination. Sequential sectioning allows one to better reconstruct the distribution of the lesion from the slides. When taking these sections, be sure that the sections demonstrate the relation of the lesion to the closest inked margin. Be sure also to designate which block contains the area marked by the radiologist’s needle as containing calcification.

For large biopsy specimens that cannot be completely submitted in 20 or fewer sections, the extent of tissue sampling is not clear. Owings et al.¹⁰ suggested a method for selective tissue sampling in these large specimens. According to their method, initial sampling should include the submission of all tissue corresponding to

radiographic calcifications and all surrounding fibrous tissue. If carcinoma or atypical duct hyperplasia is identified in these initial sections, the remaining tissue should be submitted in its entirety to determine the extent of the lesion and the status of the margins and to exclude invasion in cases of ductal carcinoma *in situ*.

Lumpectomy

Lumpectomy for a Grossly Benign Palpable Mass

A lumpectomy specimen from a palpable mass that is grossly benign should be measured, inked, and serially sectioned perpendicular to the closest palpable margin. Inspect the cut surface and record the size and appearance of the lesion as well as its distance from the margins. Sequentially submit the entire lumpectomy specimen in up to 10 cassettes. Be sure that your sections show the border of the lesion with the surrounding breast tissue (important for distinguishing fibroadenoma from phyllodes tumors), and take perpendicular sections from the lesion to the margins. If the margins are designated, be sure to obtain a section perpendicular to each of the six margins. Cost-effective strategies for handling large lumpectomy specimens have also been proposed. Schnitt et al.^{11,12} suggested submitting a maximum of 10 initial sections of the fibrous tissue in these cases, as carcinoma and atypical hyperplasia are unlikely to be found in the fatty tissue alone.

Lumpectomy for Grossly Identifiable Cancers

Lumpectomy biopsies for grossly identifiable cancers are usually brought to the surgical pathology laboratory with some indication of orientation provided by the surgeon. Frequently, but not universally, a short stitch is used to designate the superior aspect of the specimen and a long stitch to designate the lateral aspect of the specimen. From these two landmarks you can then determine the inferior, medial, anterior, and posterior margins. As illustrated, these margins are easier to conceptualize if you think of the specimen as a cube. After orienting the speci-

men, measure it, ink it, and obtain one or two perpendicular sections from each of the six margins (superior, inferior, medial, lateral, superficial, deep). Serially section the specimen at 2- to 3-mm intervals. Note the size of the tumor and the distance to each of the margins. Obtain two to five sections of the tumor. If a portion of skin is present, it should also be sampled for histologic examination. If the lumpectomy specimen is relatively small, submit it entirely (Figure 25-2). For large lumpectomy specimens, where the entire specimen cannot be submitted in 20 cassettes, submit representative sections (Figure 25-3).

Additional (Revised) Margins Submitted by the Surgeon

Sometimes the surgeon separately submits additional (revised) margins for one or all six of the lumpectomy surfaces. Usually these specimens appear as a strip of tissue with a stitch on one face marking the new margin. The opposite surface, which would face the lumpectomy specimen, often contains fresh blood and is not a true margin. Ink the surface containing the stitch, obtain serial sections perpendicular to the ink, and submit all of the sections for microscopic examination (Figure 25-4). Do not ink the opposite surface; otherwise, it may be impossible to tell which is the true margin.

Re-excision Lumpectomy

Re-excision lumpectomies are generally performed because a positive margin was identified during a prior excision. Therefore, specimen sampling should focus on the biopsy cavity to document the presence of residual disease and on the new specimen margins to ensure the adequacy of tumor removal during the re-excision. Try to submit re-excision specimens in their entirety if they can be submitted in fewer than 10 cassettes. If the biopsy cavity appears grossly benign, two sections per centimeter of greatest specimen diameter is probably adequate.

Mastectomy

True radical mastectomies are seldom performed anymore. The procedure includes complete axillary dissection including removal of the

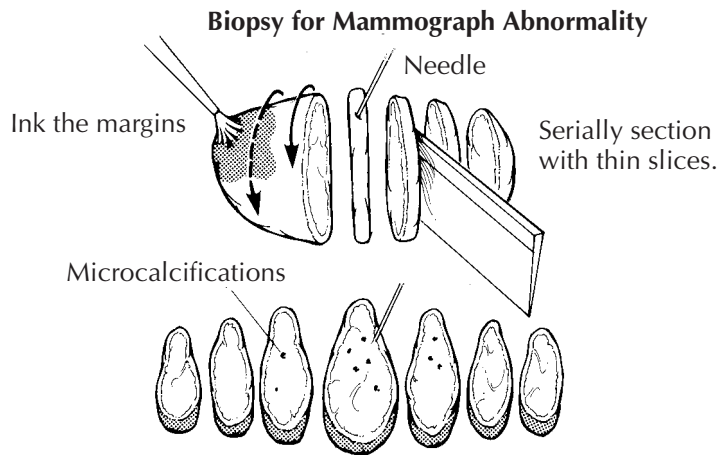


Fig. 25-1. Biopsy for Mammographic Abnormality

1. Ink the specimen in different colors to main orientation (if provided).
2. Serially section the specimen into thin slices.
3. Describe any lesions and distance to the margins.
4. Submit entire specimen sequentially (if under 20 cassettes); indicate which cassettes contain the lesion and the site of the needle.

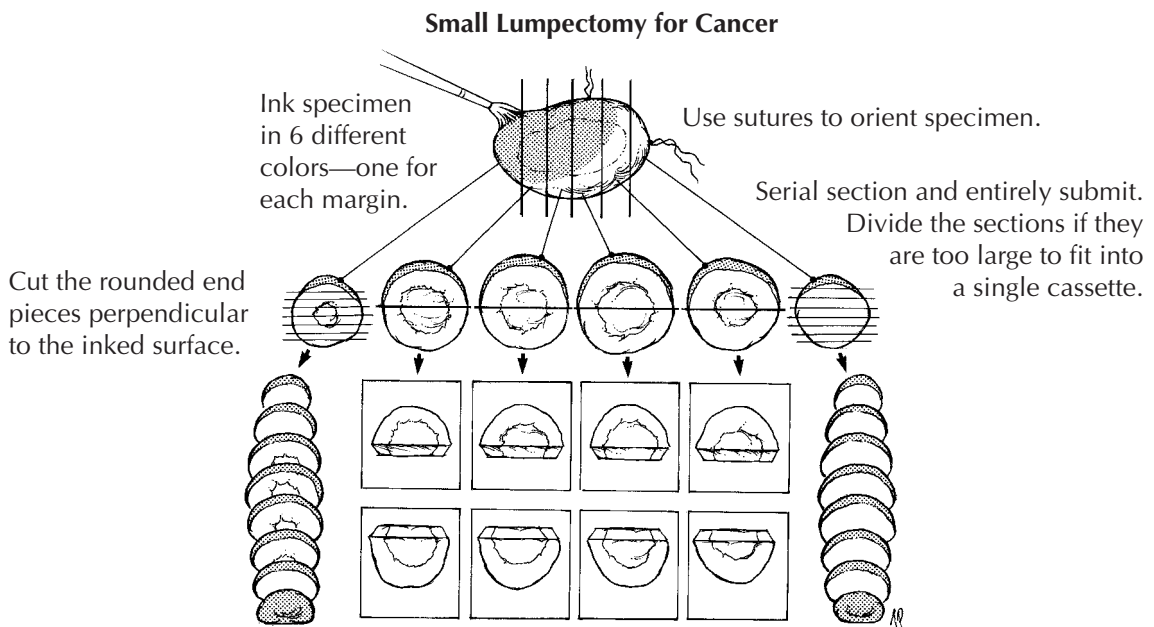


Fig. 25-2. Small Lumpectomy for Breast Cancer

1. Orient the specimen using the attached sutures, and record its dimensions.
2. Ink the specimen borders using 6 ink colors, one for each specific margin.
3. Serially section the specimen perpendicular to the largest dimension. Record the size of the tumor and its distance to each margin.
4. Serially section the round end pieces perpendicular to demonstrate their margins.
5. Submit the specimen in entirety in sequential cassettes. Some slices may be too large to fit comfortably in one cassette, and should be bisected.

Large Lumpectomy for Cancer

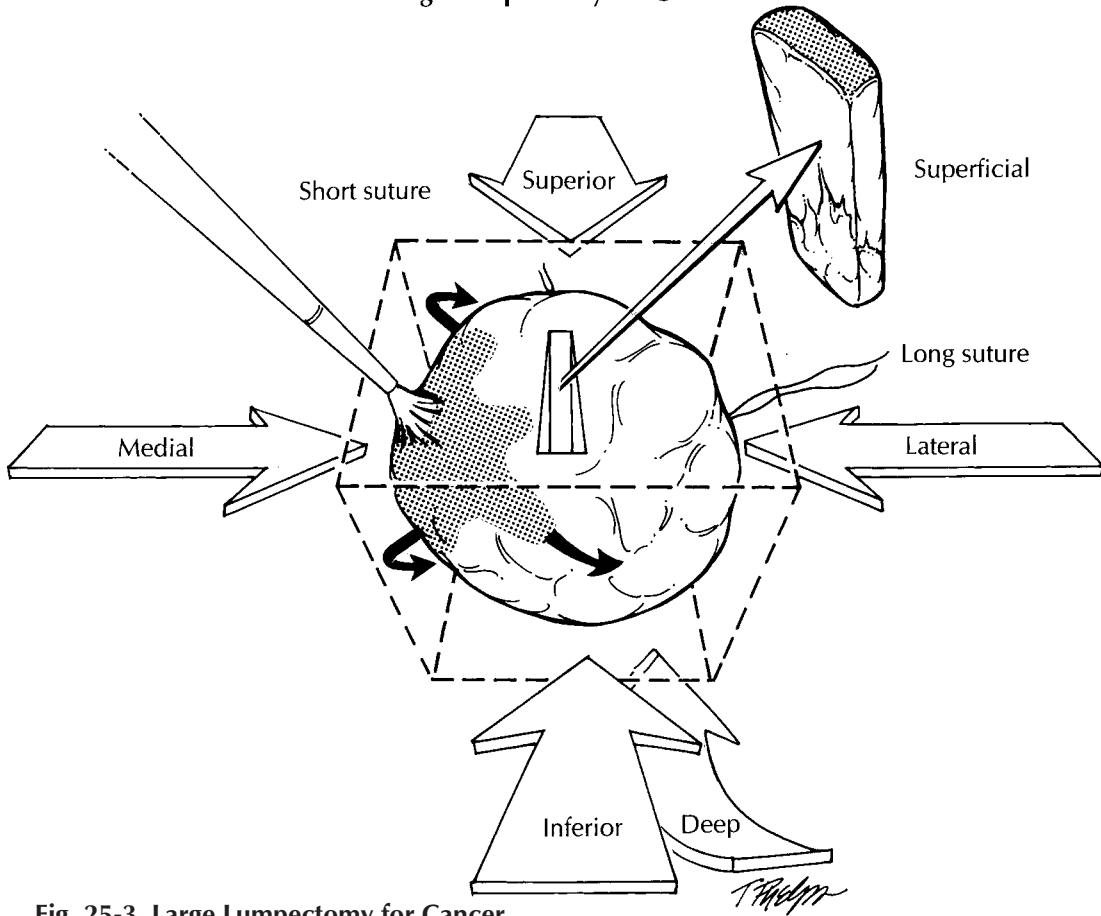


Fig. 25-3. Large Lumpectomy for Cancer

1. Ink the specimen in different colors to maintain orientation.
2. Serially section the specimen into thin slices.
3. Describe the size of the tumor, and distance to the margins.
4. Submit 1–2 perpendicular sections from each of the six margins.
5. Submit sections from tumor (2–5 sections).

Additional (Revised) Margin of Lumpectomy

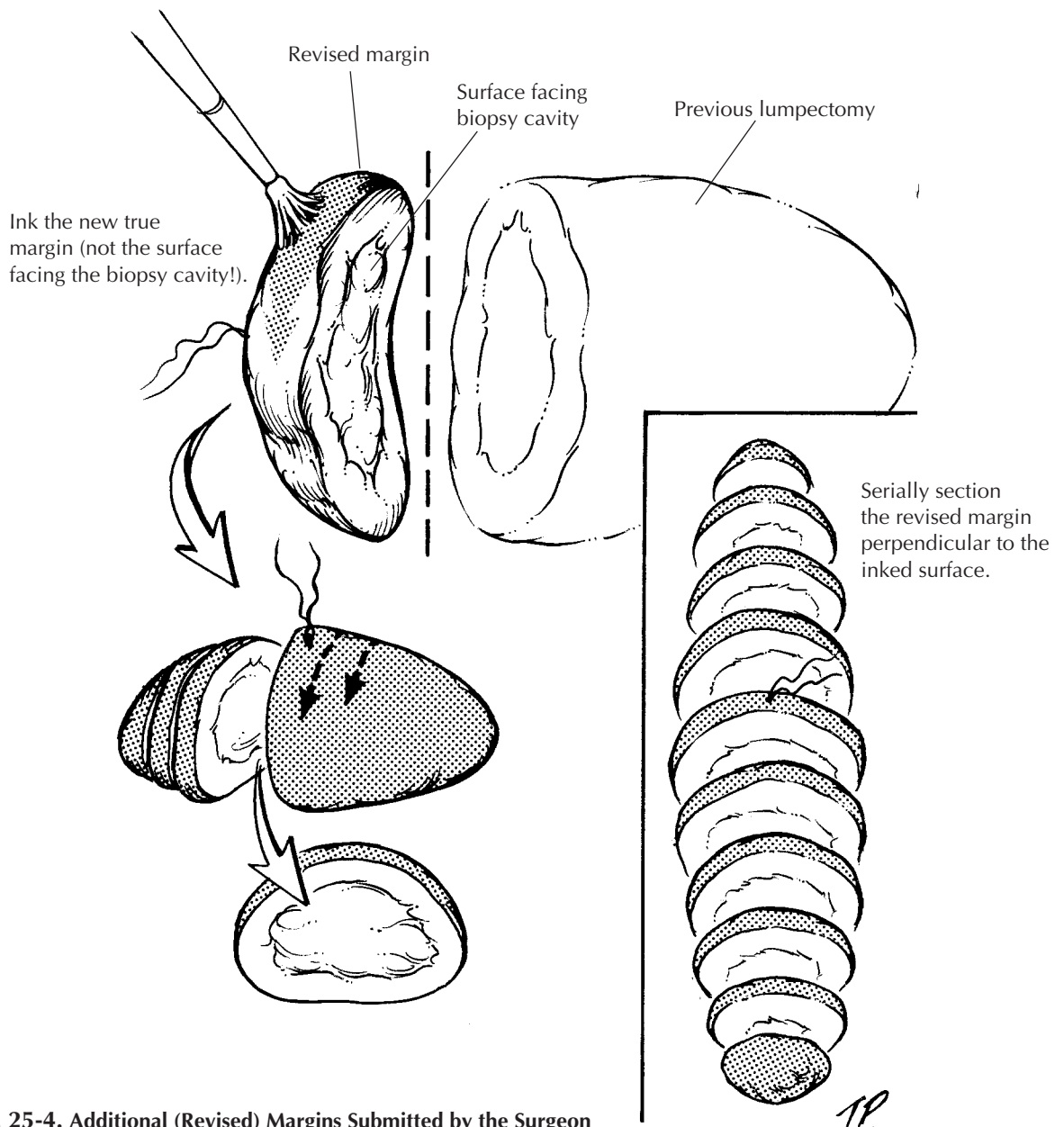


Fig. 25-4. Additional (Revised) Margins Submitted by the Surgeon

1. Measure the specimen, and orient it by identifying the new true margin (usually designated by a suture) and the opposite surface, which faces the biopsy cavity from the earlier lumpectomy specimen.
2. Place the specimen on the cutting board so that the true margin (designated by the suture) is facing up.
3. Ink only the true margin (not the surface facing the biopsy cavity!)
4. Serially section the specimen perpendicular to the inked surface and submit it in entirety.

modified radical mastectomy is more common. With this procedure the undersurface of the specimen is composed only of fascial planes with occasional shreds of pectoralis major muscles attached. The anterior surface usually contains an island of skin and nipple with the subcutaneous tissue extending beyond it. Nevertheless, complete axillary dissection typically is included within the specimen, forming an elongated tail at one end of the otherwise elliptical specimen. Most mastectomies are performed after a core needle biopsy has established a diagnosis of invasive carcinoma or after a lumpectomy has not been successful in completely removing an *in situ* and/or invasive carcinoma.

First, orient the specimen to localize the four quadrants of the breast correctly. This step should not be difficult if you use the axillary contents, the sidedness of the breast, and the surgeon's description of the location of the tumor. Once the specimen has been oriented, place a safety pin in the corner of the upper outer quadrant. This practice helps you to reorient the specimen quickly in case you have to return to the specimen. Weigh and measure the specimen; then describe the skin, nipple, and any biopsy sites seen. The axillary tail can be removed now for later examination. Next, take the time to palpate the specimen. Localize the biopsy scar, the biopsy cavity, and any masses. Examine the deep surface of the specimen for attached fragments of skeletal muscle, and ink it so perpendicular sections can be obtained to evaluate the deep soft tissue margin. Also ink the exposed breast tissue lateral to the skin ellipse on the anterior surface of the specimen (preferably with ink of a different color). These constitute the anterior margins. Hence, all surfaces except for the skin and axillary tail should be inked.

The breast can then be placed skin surface down on a cutting board and sectioned. As illustrated (Figure 25-5), use the nipple to center the specimen; then with two long perpendicular cuts section the breast into four quadrants. Each quadrant can be further sectioned, each in its own direction. These cuts should not go all the way through the specimen but, instead, should leave the pieces attached together by a rim of unsectioned breast or skin. This procedure not only helps orient the specimen in a clinically relevant way, it helps remind you to document in which quadrant(s) the lesion lies.

The gross dictation should include (1) the overall dimensions and the weight of the specimen; (2) the overall dimensions of the skin surface; (3) the presence or absence of a biopsy scar and biopsy cavity and their relation to the nipple; (4) the presence of any retraction or ulceration of the nipple and/or surrounding skin; (5) the presence or absence of muscle on the undersurface of the specimen; (6) *the size and gross appearance of the tumor including the quadrant of the breast in which it is localized*; and (7) the distance of the tumor to the deep and anterior margins. At least two and ideally five sections of the primary lesion should be submitted for histologic examination. Two sections can then be submitted from each of the remaining breast quadrants. If the mastectomy was performed as a prophylactic procedure in a patient with an *in situ* carcinoma, submit at least three sections from each quadrant; also submit any suspicious lesions in their entirety. Submit a section of the nipple and one of the skin in the area of the prior biopsy site.

Finally, dissect all lymph nodes from the axillary contents. If lymph nodes are separated into levels I, II, and III by their relationship to the pectoralis minor muscle (lateral, below, and medial to it, respectively), maintain this orientation. Chapter 5 details the procedures for processing sentinel and nonsentinel lymph nodes for metastatic tumors. When dealing with axillary lymph nodes in patients with carcinoma of the breast, it is particularly important to identify and evaluate each lymph node and to submit lymph nodes that are grossly negative for tumor in their entirety. Grossly positive nodes do not need to be submitted in their entirety. The size of the tumor in the grossly involved lymph node should be documented in your gross report.

Reduction Mammoplasty

There are no rigid criteria that dictate the number of sections to submit from reduction mammoplasty. In the absence of such criteria, a few considerations provide some helpful guidelines for specimen sampling. First, thorough gross examination of the thinly sliced specimen is the key to identifying clinically significant lesions. Second, because the risk of breast cancer increases with age, submit relatively more sections from specimens removed from older patients.

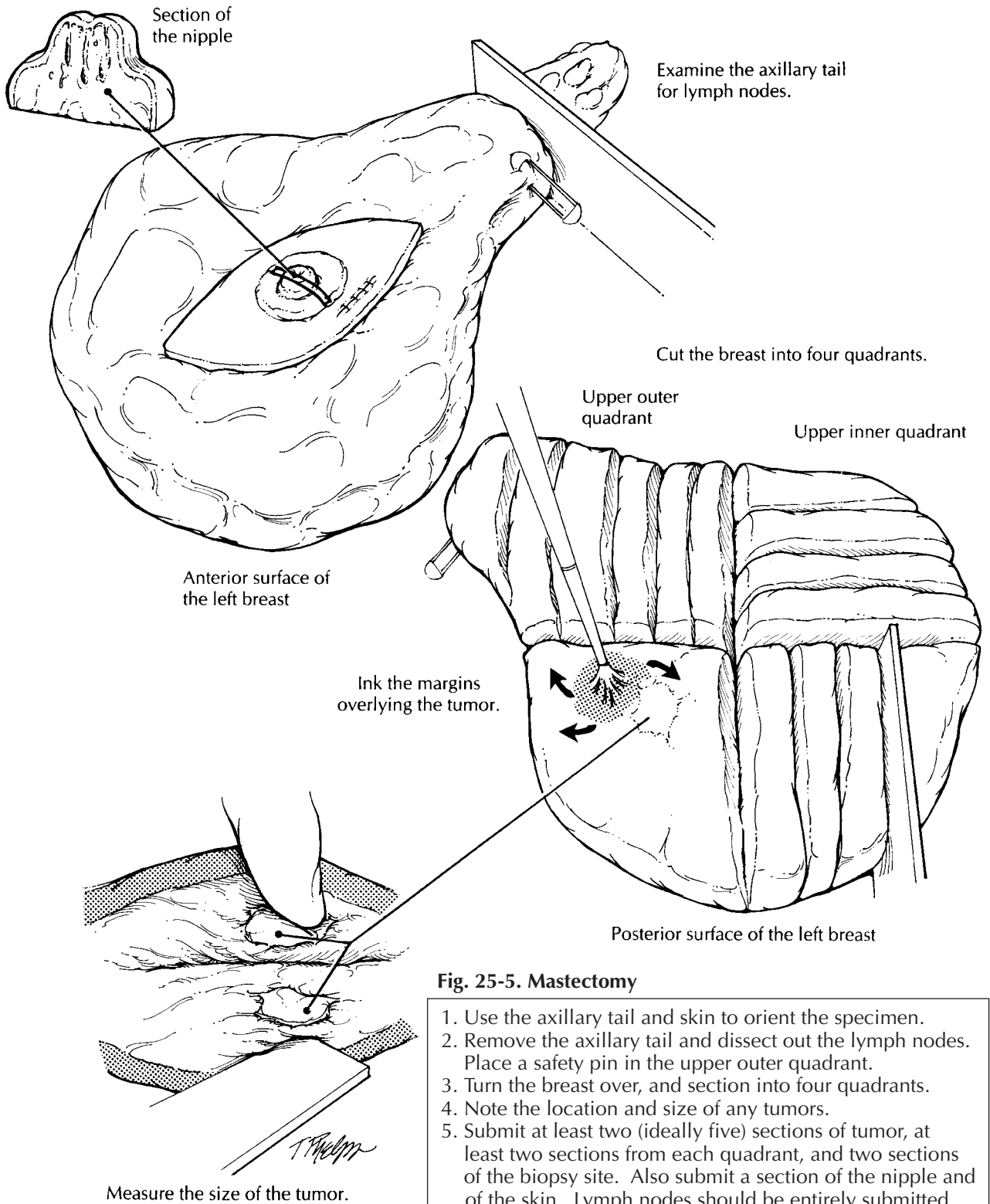


Fig. 25-5. Mastectomy

1. Use the axillary tail and skin to orient the specimen.
2. Remove the axillary tail and dissect out the lymph nodes. Place a safety pin in the upper outer quadrant.
3. Turn the breast over, and section into four quadrants.
4. Note the location and size of any tumors.
5. Submit at least two (ideally five) sections of tumor, at least two sections from each quadrant, and two sections of the biopsy site. Also submit a section of the nipple and of the skin. Lymph nodes should be entirely submitted for histologic evaluation.

We suggest submitting three sections from patients under 30 years of age and five sections from patients over 50 years of age. Third, because carcinomas and atypical hyperplasias are much more likely to involve fibrous breast tissue than fatty breast tissue, sections should selectively target dense and fibrotic breast parenchyma. The identification of atypical lesions or carcinoma on these initial sections indicates the need to go back to the specimen to obtain additional sections.

Important Issues to Address in Your Microscopic Surgical Pathology Report

- What procedure was performed and what structures/organs are present?
- What are the gross size and location (nipple, central portion, upper inner quadrant, upper outer quadrant, lower inner quadrant, lower outer quadrant, axillary tail) of any tumors identified? What is the microscopic size of the tumor? Are these measurements concordant?
- Are the tumors *in situ* or infiltrating? If the lesion contains both *in situ* and infiltrating carcinoma, what proportion of the lesion is *in situ*, and what proportion is infiltrating? Does *in situ* carcinoma extend away from the main tumor mass?
- What are the histologic type and grade of the *in situ* or infiltrating carcinoma?
- Is vascular/lymphatic invasion present?
- Is there skin or nipple involvement?
- Does the tumor involve the margins of resection? If it is close to a margin (i.e., less than 10 mm), record in millimeters the exact distance of the tumor from each of the margins.
- Does the tumor directly extend into the chest wall or the skin?
- Are microcalcifications present?
- Record the location and number of nodes examined and the presence or absence of metastatic carcinoma in these nodes. What is the size of the largest metastasis? Does the metastasis extend beyond the lymph node capsule into the surrounding perinodal fat?

Breast Implants

The handling of prosthetic breast implants deserves a special note. We suggest that you follow The College of American Pathologists (CAP) recommendations.¹³ Briefly, they suggest that you first weigh the implant and describe its external surface (e.g., smooth, textured), its contents (clear gel, oil, watery fluid), and its condition (intact or ruptured). Next, document any inscriptions printed on the implant and *photograph the implant*, particularly if it is ruptured. You can then turn your attention to the tissue capsule—the wall of fibroconnective tissue that forms around the breast implant. Weigh and measure the capsule, describe its inner surface, and submit one or two tissue cassettes of the capsule for histologic examination. If any nodules are present in the capsule, they should be sampled more extensively. Finally, store the implants. With the current flood of litigation, the implants should probably be stored indefinitely.