Breast Cancer Surgery

Historical Evolution, Current Status and Future Perspectives

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The diagnosis and management of breast cancer have changed dramatically over the past two decades in response not only to new technologies but also to cultural and social aspects of the disease. Mastectomy (either radical or modified radical) was the historical mainstay of the treatment of breast cancer for decades. Although mastectomy continues to be appropriate for some patients, breast conservation has become the preferred method of treatment for many patients. Meeting the dual goal of optimum cosmesis and minimal rates of in-breast recurrences after breast-conservation therapy requires the selection and integration of appropriate diagnostic methods (including breast imaging techniques and breast biopsy techniques) as well as therapeutic methods (breast irradiation techniques, and systemic cytotoxic and hormonal therapy). To achieve optimal breast-conservation treatment, a multidisciplinary approach is necessary. Mastectomy followed by breast reconstruction is a valuable alternative for patients who require or choose mastectomy. After tumor downstaging with induction chemotherapy, a large percentage of patients with large or locally advanced tumors will be able to undergo breast-conservation therapy. Partial (levels I and II) axillary lymph node dissection remains the standard of care in the surgical management of patients with invasive breast cancer. Recently, there has been intense interest in selective axillary lymph node dissection, focused mainly on the identification of patients who are likely to benefit from axillary lymph node dissection, using sentinel lymph node biopsy.

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> *The glory of Medicine is that it is constantly moving forward, that there is always more to learn.* (William J. Mayo, MD)

Breast cancer is the most common malignancy among women in the Western world. The incidence has been increasing for several decades and by the year 2000 breast cancer will affect close to one million per year and cause the death of over 400000 women worldwide (1–3).

Over the past two decades, the management of breast cancer has dramatically changed. Current emphasis is on less invasive diagnostic methods, less radical surgical procedures, more liberal use of aggressive systemic therapies and alternative strategies (4). This paper reviews the current status of surgical management of breast cancer, alternative treatment strategies and future perspectives.

HISTORICAL ASPECTS

Cases of breast cancer have been recorded in medical writings for more than 5000 years. In documents from the ancient word, they appear with perhaps greater frequency than any other form of cancer. This suggests that the frequency of breast cancer was significant, particularly considering that life expectancy in the ancient world was probably no more than 40 years. The first written evidence suggestive of breast cancer is from ancient Egypt and is found in the Edwin Smith and Ebers Papyrus, dating back from 3000 to 2500 BC (5). While cauterization was used to treat certain breast problems at the time, it is unclear whether these included breast malignancies. In Ancient Greece, Hippocrates referred to malignancies that were either 'deep-seated' or 'hidden'. Hippocrates recognized the poor prognosis of these tumors and did not consider surgery to be beneficial: 'It is better to give no treatment in cases of hidden cancer; treatment causes speedy death, but to omit treatment is to prolong life' (6, 7). Theophilus, commenting on Hippocrates, remarked that 'even if the disease is eradicated by cutting or burning, many untoward symptoms follow' (7, 8). Throughout most of the pre-Christian era, the treatment of breast cancer was surveillance, with invocations for help from the gods. Breast amputation was used as punishment and breast surgery played no role as a definitive treatment during this period.

The dawn of the Christian era witnessed the beginning of the surgical treatment of breast cancer. In the first century AD, Leonides (7) described the operative technique of breast cancer. Galen proposed excision of breast cancer discovered at an early stage (8).

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The Roman writer Celsus in his work 'De re medicina in libri octo' presented a full clinical description of cancer, and his work 'De re medicina'' was the first printed classical medical work (Florentia, 1478). Anatomical paradigms for breast cancer arose with the Renaissance and the study of the anatomy. The critical person in the development of scientific anatomy based on observation and dissection was Andreas Vesalius (1514–1564). Andreas Vesalius treated breast cancer by wide local excision. Hemostasis was achieved by ligating blood vessels rather than by the brutal cauterization in common use during this era (9). Ambroise Pare (1510–1590) advocated local excision for small tumors; however, for most patients he would compress the base of the breast between lead plates to try to induce ischemia and arrest the progression of the disease (10). He also described the swelling of axillary lymph nodes that is observed in patients with breast cancer (9). Johannes Scultetus (1595–1645) excised the breast after traction had been applied by heavy leather thongs threaded through its base, hemostasis being induced by applying a hot iron to the chest wall (11). Goullaume de Houppeville incorporated the subjacent pectoralis major muscle in his mastectomies and Marcus Aurelius Severino (1560–1634) first removed enlarged axillary lymph nodes (12). Fabry von Hilden observed that excising axillary tumors may be difficult and dangerous; he also recognized the futility of incomplete resection of fixed lesions and he deferred treating ulcerating lesions.

In 1757 in France, Henri Francois Le Dran reasoned that because axillary nodal involvement in a patient with a cancer of the breast was indicative of a poor prognosis, the disease must spread through the lymphatics and then into the general circulation after its origin in the breast. At its earliest phase of development, therefore, breast cancer was a local disease and could be eliminated by surgery. If 'cancer lymph' passed beyond the adjacent lymph nodes, the entire lymphatic system would become contaminated (13). Jean Louis Petit (1674–1750) of Paris, a leading founder of the French Academy of Surgery, proposed en bloc resection of the breast, palpable lymph nodes and the underlying pectoralis major muscle if attached to the tumor (14). Samuel Sharpe in England and Benjamin Bell (1749–1806) in Scotland also promoted mastectomy and the excision of palpable axillary lymph nodes (14). However, the limitations of surgery in the pre-anesthetic and pre-antiseptic era restricted the application of these radical procedures except as a treatment of desperation.

In the 19th century most surgeons apparently treated breast cancers by limited resections, with local recurrence being the rule. Alexander Monro (1773–1859) found only 4 out of 60 patients treated by local resection to be free of disease at 2 years. Such eminent English surgeons as James Syme (1799–1878), Sir James Paget (1814–1899), and Robert Liston (1794–1847) all wrote with skepticism on the possibility of effecting a cure for breast cancer through surgery (15–17). Sir James Paget operated on 235 patients and in 1853 he wrote: 'In deciding for or against the removal of a cancerous growth, in any single case, we may, I think, dismiss all hope that the operation will be a final remedy for the disease' (15). In 1856 he again wrote: 'We have to ask ourselves whether it is probable that the operation will add to the length and comfort of life enough to justify incurring the risk for its own consequences' (16). Charles Moore (1821–1870) of England, a surgeon at the Middlesex Hospital, in 1867, elaborated basic principles of breast cancer surgery that by the 20th century became widely accepted. He wrote: 'It is desirable to avoid not only cutting into the tumor but also seeing it...lest the active microscopic elements in it should be set free and lodge in the wound. Diseased axillary glands should be taken away at the same direction as the breast itself' (18). He urged wide resection of the tumor and directed surgeons to remove the entire breast as well as adjacent diseased tissue, including generous margins of skin, the pectoralis muscles if necessary, and axillary lymph nodes (18). This approach was advocated in the United States by Samuel Gross (1837–1889). The surgical revolution brought about by general anesthesia, introduced in 1846, and antiseptic practice, proposed by Lister in 1867, led to an escalated effort to surgically treat breast cancer. Routine axillary dissection in the treatment of breast cancer was practiced as early as 1871 by Ernst Kuster (1838–1922) in Germany and by W. Mitchell Banks in England (19). Richard von Volkmann (1830–1889) in 1875 and Lothar Heidenheim (1860–1940) in 1889 proposed the removal of the pectoralis major muscle fascia *en bloc* with the breast and the axillary lymph nodes (14).

William Stewart Halsted (1852–1922) extended the operation devised by von Volkmann. In 1894 he reported his experience with the radical treatment of breast cancer in 50 patients (20, 21). He removed all breast tissue, the pectoralis major muscle, and the axillary lymphatics. In his report of 1898 he described removal of the pectoralis minor as well (22). This procedure became known as the classic Halsted radical mastectomy. In this procedure, the breast tissue was removed first, followed by the pectoralis muscles, and then, beginning at the apex of the axilla, the axillary lymphatics. Wily Meyer (1858–1932) in 1894 proposed an alternative method of performing the radical mastectomy (23). In this procedure, the axillary lymphatics were dissected first, followed by the breast tissue and pectoral muscles. Halsted's publications in 1894, 1898 and 1907 (20–22, 24) contributed to wide acceptance of radical mastectomy during the first three-quarters of the 20th century. Most patients in Halsted's era had advanced disease, and about three-quarters of Halsted's patients had axillary lymph node metastases. Whereas prior surgical treatment of breast cancer was associated with local recurrence rates of 60 to 82% and a 3-year survival rate of 9 to 39%, Halsted reported a 6% local recurrence rate and

3-year survival rate of 38 to 42% (20, 24). The 10-year survival rate for Halsted's patients was 12% (25). Throughout the first three-quarters of the 20th century there was continuous improvement in results from radical mastectomy, not because of significant changes in surgical technique, but because of a combination of patients presenting with earlier stages of disease and surgeons having stricter criteria for selection of operable cases.

In 1948, Patey proposed that removal of the pectoralis major did not add to the value of surgical treatment with radical mastectomy (26). He described a modified radical mastectomy, in which all the breast tissue is removed in conjunction with the pectoralis minor and the axillary contents, while preserving the pectoralis major. Both Auchincloss and Madden further modified this procedure by preserving both the pectoralis major and the pectoralis minor muscles (27, 28). Subsequently, large retrospective series by many surgeons and two prospective randomized trials confirmed that local control and survival rates achieved with modified radical mastectomy were comparable to those for the Halsted radical mastectomy (29, 30). As a result of this experience, by 1982, 72.3% of all radical mastectomies were of the modified variety (see Table 1) (31).

CURRENT STATUS; ACHIEVEMENTS, LIMITATIONS AND FUTURE PERSPECTIVES

Breast-conservation therapy vs. radical mastectomy

Radical or modified radical mastectomy, although both effective, were accompanied by the psychological trauma of breast amputation. This promoted the evaluation of more conservative procedures, in which the major portion of the breast tissue was preserved. Because it was clear even to Halsted's predecessors that partial mastectomy alone was followed by significant local recurrence rates, some form of adjuvant therapy for the remaining breast tissue was needed. Although scientists have been recommending breast-conservation treatment since the 1920s (32–36), this type of therapy was associated with an increased rate of cancer recurrence and poorer survival. However, results in the 1980s and 1990s have demonstrated that overall and disease-free survival from breast cancer are equivalent for mastectomy compared to breast-conserving surgery with postoperative radiotherapy for women with early breast cancer (37–45). Several other studies, of retrospect design, support these data and survival differences were not significantly different between breast-conserving surgery with radiotherapy and mastectomy (46–52). Recurrence of cancer in the breast following breast-conservation therapy has been seen in 3% to 17% of the patients in the randomized studies, compared with 2% to 10% chest wall recurrences in the mastectomy patients (45). The majority of patients with recurrence after breast-conservation therapy can be salvaged with a mastectomy. Additional local failures after salvage mastectomy have been reported in approximately 5% of patients (45). The National Institutes of Health recognized the equivalency of medical outcomes for these procedures in a Consensus Development Conference Statement in 1990 and recommended breast-conservation therapy as the appropriate method of primary therapy for most women with early breast cancer (53).

Table 1

Use of the Halsted radical mastectomy and modified radical mastectomy by year in the treatment of breast cancer [1]

Year	Radical mastectomy (%)	Modified radical mastectomy (%)
1972	47.9	27.7
1976	25.5	51.9
1977	20.9	55.4
1981	3.4	72.3

[1] *Source*: American College of Surgeons, Commission on Cancer, Chicago, 1982 (31).

Breast-conservation therapy as an alternative to mastectomy is especially important today; nowadays, because of widespread screening mammography, the average size of invasive tumors has decreased, and the incidence of non-invasive breast carcinoma has increased. Therefore, breast-conservation therapy may be appropriate for most (50%–75%) of patients with clinical stage I or II breast cancer (54, 55). Breast-conserving surgery is an important part of breast-conserving therapy, which may be defined as a combination of conservative surgery for resection of the primary tumor with or without surgical staging of the axilla, followed by radiotherapy for the eradication of residual microscopic disease of the breast with or without adjuvant systemic therapy. The goal of this technique is to provide satisfactory cosmetic results without compromising local tumor control or survival compared with modified radical mastectomy (56). Meeting the dual goals of optimum cosmesis and minimal rates of in-breast recurrence after breast-conservation therapy requires the selection and integration of appropriate breast imaging techniques, breast biopsy techniques, breast irradiation techniques, and systemic cytotoxic and hormonal therapy.

Clearly, the most important issue in the decision to proceed with breast-conservation therapy is assessing the risk for local recurrence. Many series have reported an association between young age (< 35 years) and an increased risk of locoregional recurrence following breast-conservation therapy (40, 57–63), but other series have not corroborated these findings (64–67). Harris has pointed out that young age is a risk factor for local recurrence after both breast preservation and mastectomy, and is also associated with distant relapse after any local therapy (62). It therefore appears that, with such conflicting data, it would not be reasonable to deny a young patient breast-

conservation therapy based on age alone. This is particularly important, since breast-conservation therapy is a particularly attractive alternative for the younger patient. The importance of microscopically negative margins has been repeatedly shown (68–77). However, opinion differs on the necessary extent of the margin. Solin et al. (78) defined negative margins as 2 mm, while Borger et al. (57) required excision of the tumor with 1–2 cm of macroscopically uninvolved tissue. It appears that–with the breast irradiation as a part of the breast conservation treatment–wide tumor-free margins have little practical importance. In Solin's study, the radiation dose was escalated depending on the margin status, with the primary site boosted to 65 Gy when the margins were positive. Using this tactic, no differences between groups with negative, close, or positive margins concerning locoregional control were observed (37, 79–81). Other factors associated with an increased risk of locoregional recurrence following breast-conserving surgery include tumor necrosis, intralymphatic extension, vascular invasion, high tumor grade and extensive intraductal component (57, 76, 82–86). However, none of these factors is predictive and therefore they would not generally be used to exclude patients from the option of breast-conservation surgery.

Although it is clear that breast-conservation therapy is equivalent to mastectomy for patients with stage I or II disease, the decision to embark on a treatment strategy involving breast conservation should be individualized for each patient. Numerous factors contribute to this decision (56, 87, 88). The patient's motivation and commitment to breast conservation must be strong, as daily outpatient radiation treatments over 5–6 weeks to a total dose of 50 Gy are required. Size of the breast is another important factor in selecting patients for breast-conservation therapy. For extremely small breasts, the cosmetic result may be unacceptable following local excision, especially for larger lesions. These patients may benefit from a strategy of mastectomy followed by breast reconstruction, occasionally coupled with surgical augmentation or reduction of the contralateral breast. Concerning tumor size, there is some disagreement over the relative importance of the various proposed criteria. Although some institutions restrict breast-conservation therapy to patients with small tumors (< 2.5 cm) (68, 89, 90), most authors believe that breast-conservation therapy should not be limited in patients with small tumors. For tumors < 5 cm, the likelihood of residual cancer is not dependent on tumor size, which is consistent with the relative lack of significance of tumor size as a risk factor for local recurrence following breast-conservation therapy (90–95). Patients are considered candidates for breast-conserving surgery if excision of the tumor can be performed without a resultant major cosmetic deformity (56). This is based on the relative size of tumor and the breast and on the location of the tumor. Minor degrees of breast deformity are corrected by transportation of local flaps, wide undermining, and cornization of residual breast tissue (96–98). However, when the tumor is large (> 5 cm) or the breast is small, local excision rarely results in a cosmetically acceptable result and it may be difficult to correct the breast deformity using such minor procedures; volume reduction and deformation of the shape of the breast are the primary reasons for a poor cosmetic outcome. Deformities can be corrected by immediate transposition of adipose tissue with a vascular pedicle of the latissimus dorsi muscle (99, 100). Nowadays, these procedures can be performed endoscopically (101, 102). However, for those patients, mastectomy followed by breast reconstruction is a valuable alternative. The ability of preoperative chemotherapy to downstage these tumors to the point where breast conservation may be undertaken remains an intriguing approach (see below).

For a few patients, breast-conservation therapy may be absolutely or relatively contraindicated because of concerns for toxicity or a heightened risk of local failure (103). Pregnancy in the first or second trimester is an absolute contraindication to treatment with radiation therapy because of the teratogenic and carcinogenic effects on the fetus (103, 104). Clearly, in patients with multifocal disease (two or more gross lesions in different quadrants, or diffuse microcalcifications on mammography) breast-conservation therapy is contraindicated (103, 104). Prior radiation therapy and rheumatologic disorders are relative contraindications to breast-conservation therapy (104–107). Although patients with subareolar lesions often have extensive spread of disease along the ducts (108, 109), these patients are acceptable candidates for breast-conservation therapy; the resection may need to include the nipple-areola complex but, with preservation of most of the breast volume, good cosmesis can be achieved. Moreover, the option of plastic surgery is available for those who desire a reconstruction of the nipple-areola complex (103).

The results of prospective randomized clinical trials demonstrated that breast irradiation significantly reduces the rate of ipsilateral breast cancer recurrence after breast-conserving surgery (37, 38, 61, 90, 110–112). The rates of local breast relapse after breast-conserving surgery without radiation therapy that are reported in the literature vary from 6% to 43% (37, 38, 61, 90, 93, 113–115). The identification, however, of a subset of patients who can be safely spared radiation therapy after breast-conserving surgery is an important goal. Although some factors associated with a decreased local relapse have been identified (such as older age, negative nodes, small tumor size [< 2.5 cm], positive estrogen receptor status, absence of tumor emboli, etc.), radiation therapy remains at present a part of breast-conservation therapy for patients with invasive breast carcinoma (116). Conservative surgery without radiotherapy remains an investigatory approach (53, 116).

It should be noted that although consensus conferences and randomized clinical trials showed that breast-conservation therapy is appropriate for the majority of women diagnosed with early breast cancer, large geographic differences in rates of breast-conservation therapy have persisted over time (117). In a recent study from the United States, breast-conservation therapy was performed in 34% of 80 887 women with breast cancer treated surgically from 1983 through 1992 (ranging from 19% in Iowa to 41% in Connecticut) (118). Additional efforts by health-care professionals are needed to provide patients with adequate information on treatment options for early breast cancer (118).

Breast-conservation therapy after tumor downstaging with induction chemotherapy

Patients with large or locally advanced breast cancers (skin or chest wall involvement [T4], large fixed or matted axillary lymph nodes [N2], or evidence of infra- or supraclavicular nodal disease) have traditionally been treated with mastectomy as a part of a multimodality therapy (combination of surgery, radiation therapy and chemotherapy) (119). These patients are at high risk for harboring micrometastatic disease that ultimately leads to distant failure and death. Induction (or 'primary', 'neoadjuvant', or 'preoperative') chemotherapy has been used in an attempt to improve survival of these patients and to convert patients first thought to have inoperable disease to candidates for surgery. High overall response rates (70–90%) have been observed following primary chemotherapy (120–124). Frequently, there will be enough shrinkage of the primary tumor for cosmetically acceptable breast-conserving surgery to become possible (125–130). The percentage of patients who were able to undergo breast-conservation therapy following induction chemotherapy varies in the literature (from 25% to 90%) (125–130). Early initiation of systemic therapy and the ability to assess tumor response to induction chemotherapy regimens are additional benefits of induction chemotherapy. On the other hand primary chemotherapy may modify other prognostic factors, such as tumor size, histologic and nuclear grade, steroid hormone receptor status, lymphatic and/or vascular invasion, etc. (131, 132). Many ongoing clinical trials have been designed to assess controversial areas, such as timing of chemotherapy, choice of drug regimens, role of axillary staging and extent of surgical resection.

Breast reconstruction following mastectomy: an alternative to breast-conservation therapy

Renneker & Cutler, in a 1952 report, were the first to show that two psychological issues face breast cancer patients: anxiety, brought about by the life-threatening nature of the illness, and anxiety, caused by the disfigurement from surgical therapy (133). Quality of life has since become an important issue in the treatment of breast cancer patients, and efforts have been made to develop local therapy that is less disfiguring. Breast-conservation therapy is an effort directed toward this end. However, despite this advance in therapy, a significant number of patients still require or choose modified radical mastectomy. For those patients, breast reconstruction should be considered a standard component of cancer therapy. Reconstruction may involve autologous tissue, synthetic implants, or a combination of both. During the early days of breast reconstruction it was believed that reconstruction should be delayed for a minimum of two years following mastectomy. The rationale for this belief was that the added surgical trauma and risk were unwarranted in the breast cancer patient and might induce recurrence of the disease. During the 1980s investigators started performing immediate reconstruction using breast implants, without any increase in complication or local recurrence rates (134). The safety of this tactic has been repeatedly demonstrated during the past two decades (135–137). Moreover, immediate reconstruction carries a substantial psychological benefit for many women and often facilitates a better cosmetic result. The use of adjuvant chemotherapy is not a contraindication for immediate reconstruction, but does mandate that the reconstructive surgery should be performed with a minimum of complications so the adjuvant therapy does not have to be delayed. There are two relative contraindications for immediate reconstruction following mastectomy: (a) advanced-stage breast cancer and (b) postoperative radiation therapy, especially for patients undergoing implant-based reconstruction, since irradiation increases the risk of capsular contracture (in patients with breast implants) and of atrophy and hardening of the reconstructed breast (in patients undergoing breast reconstruction with autogenous tissue).

Two materials can be used to simulate the breast mound: alloplastic material, in the form of silicone or saline implants, and autogenous tissue, primarily in the form of a transversus abdominus myocutaneous (TRAM) flaps or the latissimus dorsi flap. Each method has its own advantages and disadvantages (138–141). When there is no local tissue or a pedicled flap is unavailable or problematic (i.e. in patients who have several risk factors for pedicled tissue transfer, such as smoking, obesity, multiple abdominal scars, etc.), a microvascular tissue transfer, or a free flap, is sometimes the only means for breast reconstruction using autogenous tissue. In this case, a free TRAM or a free gluteus maximus muocutaneous flap can be used with good results (142–145).

While breast mass reconstruction may be undertaken immediately following mastectomy, nipple reconstruction is usually delayed 6–12 weeks to allow time for the reconstructed breast to remodel and attain its final shape and position. The nipple-areola complex can then be reconstructed using local skin flaps developed under local

anesthesia, while pigment is provided using tattooing techniques (146, 147).

Breast-conserving surgery: the role of endoscopy

For optimal cosmetic results in breast cancer surgery, an alternative endoscopic procedure has recently been proposed to remove tumors through a small, single incision remote from the breast itself (148–150). With this technique, the tumor is endoscopically resected by electrocautery through a short incision in the axilla, after which axillary dissection can be performed through the same wound, as usual. Therefore, the surgical wounds are not visible from the front and the breasts have a cosmetically satisfactory shape postoperatively. The same advantages of minimally invasive surgery (i.e., smaller incision, less pain and earlier recovery) have been the rationale for performing axillary exploration and/or dissection and sentinel lymphadenectomy through an endoscopic approach (151–153).

Moreover, breast reconstruction can be performed endoscopically through small incisions placed in the axillary line or through the umbilical approach (99–102, 154–157). Harvested endoscopically, a portion of the latissimus muscle can be rotated to fill the lumpectomy defect, with the advantage of no additional scar on the back (99, 100). The endoscopic approach can also be used for the insertion of saline-filled breast implants (155), while there is the potential for using the rectus abdominis myofascial flap through this approach (156).

Proponents of endoscopic surgery in breast cancer maintained that this approach has the same therapeutic oncological effect as the standard open surgery and, in addition, offers a greater cosmetic advantage. However, experience with this technique is still limited and long-term follow-up is necessary.

In situ destruction of the primary breast cancer

Recently, there has been increased interest in extending the local treatment of breast cancer to 'incision-less surgery'. This can be accomplished using different approaches, but the idea is to destroy all the tissue in a radius around the tumor while leaving the remaining breast unaltered, using different energy sources (such as laser, ultrasound or microwave) for interstitial hyperthermia or cryosurgery (158–164). This approach has been used in a small number of patients (161, 163, 164) and is currently under investigation. The goal is to treat small breast cancers (≤ 10 mm) following stereotactic biopsy with a probe placed through a 2-mm entrance site and no other visible surface change. This step should be followed by a course of radiation therapy to the remaining breast. Although this approach addresses neither regional metastases nor the concern of distant disease, it may have a role in the management of patients with a small, single focus of infiltrating ductal breast carcinoma. With an even greater increase in the rate of discovery of small, often early, breast cancers that have an excellent prognosis, the disease in these patients may be regarded as a local problem that may be approached by minimal 'incision-less surgery'. However, the role of this approach remains to be determined in the future.

Diagnostic procedures

Meeting the dual goals of optimum cosmesis and minimal rates of in-breast recurrence after breast-conservation therapy requires the selection and integration of appropriate diagnostic methods (including breast imaging techniques and breast biopsy techniques) as well as therapeutic methods (breast irradiation techniques, and systemic cytotoxic and hormonal therapy). Breast lesions have traditionally been diagnosed by examining excisional breast biopsy specimens. However, histologic examinations of these biopsy specimens show benign tissue in 70–80% of cases (4, 55, 165, 166). Several methods have been introduced to establish a more selective use of excisional breast biopsy in the management of patients with palpable and occult breast lesions. These methods include fine-needle aspiration biopsy (FNA), core needle biopsy (CNB) (for palpable lesions), and stereotactic or ultrasound-guided FNA or core needle biopsy (for non-palpable lesions). However, open (surgical) biopsy remains the standard of care and should be considered when the results from these less invasive techniques are non-diagnostic or when the diagnosis is discordant with the clinical picture and mammographic findings (4, 165).

Palpable lesions

FNA is widely used in the evaluation of palpable breast lesions to ascertain whether a mass is solid or cystic; and if solid, whether it is benign or malignant (4, 165, 166). FNA has several advantages, in that it is highly sensitive, inexpensive, and quick. It can be performed in the outpatient setting with minimal discomfort and low morbidity while allowing the patient and surgeon an opportunity to plan definitive treatment. However, the accuracy of FNA correlates directly with the competency and experience of the cytopathologist. Accurate interpretation therefore requires and excellent FNA specimen from the lesion in question and evaluation by a certified cytopathologist (167–169). Newer immunohistochemical techniques have made it possible to analyze cytologic material for steroid receptor status, ploidy analysis or proliferation index. However, this requires additional smears and a special fixative must be immediately available. Coordination with the cytopathologist is essential (169, 170). The major problem with FNA is the potential for false-negative results. Sampling errors are more likely in small masses (missed by the needle) or in very large lesions with a significant necrotic component (165). In these cases and when the suspicious lesion is visible on ultrasonography, ultrasound-guided FNA can be helpful in placing the needle and confirming

that the appropriate area has been sampled. FNA may also be falsely negative in invasive lobular carcinomas (because the cancer cells may resemble lymphocytes), or in scirrhous and lobular carcinomas because they often contain only a few cancer cells and the yield of cells may be insufficient to make the diagnosis. Moreover, the presence of blood in the aspirate makes the cytology difficult to read (165–172). Therefore, a negative or indeterminate result never excludes the presence of malignancy. The clinical impression, mammographic interpretation and histologic evaluation must conform to one another (4, 165). Should there be any doubt about the precise diagnosis, an open excisional biopsy should be performed. Open biopsy is also indicated when atypia is found, since in this case it is important to ensure that ductal carcinoma in situ (DCIS) or invasive cancer are not adjacent to the atypical area that has been sampled. Because FNA results provide a cytologic diagnosis, that is evaluation of single cells, the technique cannot be used to distinguish between in situ and invasive carcinomas (172). It appears that the accuracy of the diagnosis made from FNA results improves when the cytopathologist performs the biopsy and immediately interprets the material to assess for the quality of the specimen. The experienced cytopathologist can achieve low false-negative rates (which in the literature range between 1% and 31%) and avoid false-positive results (0–4.1%) (169). False-positive results usually occur when a malignant cystosarcoma phylloides is mistakenly interpreted as an invasive carcinoma (165).

Complications are very uncommon (165, 171). However, hematoma, ecchymosis, wound infection and even pneumothorax have been reported. This potentially lethal complication of pneumothorax–albeit very rare–is more likely to occur in an anesthetized patient with a peripheral and/or deep-seated lesion (171). Pneumothorax is decidedly more common when positive-pressure ventilation is applied (165). Concern is occasionally expressed about the spread of malignant cells by FNA, but this concern appears unfounded.

The main advantage of using FNA is that when malignant cells are found, the patient can discuss the options for definitive treatment with the surgeon before any intervention is undertaken (4, 165). Moreover, this tactic allows efficient preoperative staging work-up, and has been associated with lower rates of tumor at the margins of resection, because the surgeon's mindset at the time of surgery is toward assuring a complete resection (173). However, surgeons should remain cautious about basing definitive and often radical procedures purely on the findings of FNA. Mature surgical judgement remains prudent and the clinical, radiological and cytologic findings should all support operative decisions (165).

With CNB, a larger sample of tissue is obtained and therefore can be used either to confirm the benign nature of an indeterminate and likely benign lesion, thus avoiding surgical biopsy, or to confirm the diagnosis of cancer with the intent to expedite treatment (174, 175). The confirmed preoperative diagnosis of cancer allows the surgeon to perform definitive surgical therapy in one setting and makes CNB a cost-effective procedure. Moreover, larger tissue sampling allows analysis of estrogen and progesterone receptor status. The major advantage of CNB over FNA is that it provides more tissue, allowing a histologic diagnosis based on tissue architecture to be performed (4, 165, 171–175). The disadvantages of CNB include technical difficulty and more pain for the patient. Such features may hamper the overall ability to achieve accurate tissue sampling. CNB can be safely performed as an outpatient procedure. False-negative results, albeit less common than with FNA, remain problematic in small, mobile masses as these lesions often 'bounce' away from the Tru-cut needle. Therefore, CNBs seem especially helpful in large or fixed lesions (165). However, since CNB is a sampling technique, it, like FNA, should be performed with careful correlation of the clinical, mammographic and pathologic interpretation. Discordance of these findings should prompt open excisional biopsy (4, 165). Many lesions do not yield definitive results with a CNB, including papillary lesions, phylloides tumors, suspicious architectural distortion (suspect radial scar), and so on. If these lesions are suspected, an excisional biopsy should be performed. Moreover, CNB may fail to identify small areas of invasion in cases of DCIS with microinvasion or focal areas of invasion (165, 171, 172). Complications include ecchymosis, hematoma, infection and pneumothorax. Since the needle is longer and the required pressure greater, the risk of pneumothorax is greater than after FNA (165). Therefore CNB should be performed carefully and the needle always passed in parallel to the chest wall/rib cage.

Since establishing the diagnosis preoperatively using these minimally invasive methods has many advantages, all palpable breast masses should undergo preliminary needle biopsy, except in young women and in cases where the mass has clinical and imaging characteristics that virtually assure the surgeon that it is benign (165, 173).

Non-palpable lesions

Non-palpable breast lesions (either very small tumors or deeply seated ones) are detected initially radiographically, most commonly by mammography. Non-palpable lesions are now seen in an increasing proportion of primary breast cancer patients and are in direct relationship to the mammographic application in a given population. As the proportion of women who have a mammography at yearly intervals increases, the proportion of non-palpable breast cancers is expected to exceed 50 or 60% (55, 173). In these cases, diagnostic procedures will require ultrasound or mammographic guidance. These procedures include ultrasound-guided or stereotactic (mammographically guided) FNA, ultrasound-guided or stereotactic (mammographi-

cally guided) CNA, and needle-localization open (surgical) biopsy (4, 165, 176–179).

The advanced breast biopsy instrumentation (ABBI®) was introduced in April 1996. This minimally invasive technique uses digital stereotactic imaging to perform excisional biopsies of suspicious, non-palpable mammographic lesions and has been proposed as a significant advance in the diagnosis and perhaps even in the treatment of breast malignancy. Initial experience showed that ABBI® is a safe accurate and cost-effective method for performing breast biopsies (180). However, other investigators reported some problems, in terms of both patient unsuitability and mechanical failure (181). The role of the ABBI® system in the management of breast cancer has not yet been defined (180, 181).

Despite these newer sophisticated techniques, in most centers excisional breast biopsy following a localization technique remains the evaluation of choice for non-palpable lesions identified by screening mammography (165). Several localization techniques have been proposed (182–187), the most common being to introduce a hooked wire into the suspicious lesion under radiographic guidance. Various localization wire systems are available, including curved wires and various hook wires, with or without thickened wire segments to enable palpation (165). The surgeon and the mammographer should be familiar with the system used. Recently, radio-guided surgery of occult breast cancers has been proposed as an alternative to guide-wire (needle) localization biopsy (186, 187). Excisional biopsy following localization of the suspicious lesion is indicated when the minimally invasive biopsy techniques previously reported (i.e. FNA or CNB) are not appropriate or are not available or when there is discordance between the histologic findings from guided FNA/CNB and the clinical impression and mammographic interpretation (165). The goal of this technique is to excise the suspicious lesion without removing a large amount of normal tissue. Therefore, the localization should be precise (ideally within 5 mm of the lesion) (165). Excisional biopsy of clinically occult breast lesions after image-guided needle localization or using radio-guided surgery remains the standard of care for making a tissue diagnosis, since it gives the pathologist the opportunity to examine the histologic features of the entire lesion. Moreover, if the lesion proves to be malignant and the margins of excision are negative, then breast-conserving surgery may be finished with this single procedure (165). It should be borne in mind that, in non-palpable breast lesions, establishing the diagnosis of malignancy preoperatively (using radiographically guided minimally invasive methods, such as FNA or CNB) has been associated with lower rates of tumor at the margins of resection because again the surgeon's mindset at the time of surgery is toward assuring a complete resection during open (excisional) biopsy. Moreover, success rates for sentinel lymph node biopsy are higher when this study is performed at the time of excision of the suspicious lesion rather than after excisional biopsies (188).

Role of lymph node dissection and lymphatic mapping

Traditionally, axillary lymph node dissection (ALND) has been considered as a standard part of the surgical management of patients with breast cancer. In general, ALND has three goals:

1. To provide accurate prognostic information.
2. To maintain local control of disease in the axilla.
3. To provide a rational basis for decisions about adjuvant therapy.

However, just as the need for radiation therapy after breast-conserving therapy has been questioned for patients with early breast cancer, the necessity for ALND for every patient with invasive cancer is the subject of ongoing debate in the literature (189–196).

Currently, the approach of selective ALND in breast cancer patients is focused on:

- *the identification of patients with a low risk for nodal involvement*, i.e. patients with DCIS of pure tubular carcinoma or patients with tumors < 1 cm (197–201)
- *the identification of patients whose treatment will not be affected by axillary status*. For example, adjuvant systemic therapy is recommended for patients with tumors measuring 1 cm or larger or with unfavorable characteristics of the primary biopsy, regardless of nodal status (202–204). Moreover, for most elderly patients, lumpectomy and tamoxifen will be more appropriate alternatives (54), since mastectomy under general anesthesia in frail elderly patients may give rise to mortality rates of up to 2% (205–207).
- *the sentinel lymph node biopsy*: The sentinel lymph node (SLN) concept is based on the orderly progression of tumor cells within the lymphatic system (208, 209). It is possible to identify (by visual inspection at surgery or with a handheld gamma probe) the SLN by injection of a marker, such as a blue dye or a radionuclide, into the breast at the site of the tumor (4, 165, 188, 210–220). Although some surgeons, mainly in the United States, are begging that SLN biopsy be accepted as an adequate staging procedure of the axilla, this method should be considered only as an investigational approach and further study with longer patient follow-up is necessary.

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