MAURIE MARKMAN, MD, EDITOR

An update on breast cancer: evolving treatments and persistent questions

JOSEPH P. CROWE JR, MD

SUMMARY This review describes recent advances in imaging technology and treatment options, and discusses the persistent questions about the best strategies for preventing, diagnosing and treating breast cancer. Possible clinical implications of new research on the causes of breast cancer are also examined. The evolution of breast cancer management over the past century is summarized.

KEY POINTS The incidence of breast cancer has increased 1% to 2% per year over the past decade. The reason for this increase is not understood and cannot be explained solely by earlier detection of disease. Epidemiologic evidence points toward enviromental factors, particularly diet, as causes of breast cancer, but such links are difficult to confirm. A mutation in the *BRCA1* gene is implicated in 5% of all breast cancers, but its discovery poses enormous ethical questions: should women be screened for this abnormality? If it is found, how should such women be followed up? Breast-conserving surgery leads to outcomes similar to those for mastectomy in patients with early-stage breast cancer. Whether all patients who undergo this surgery should also receive radiation therapy is a topic of debate. Conservative surgery without radiation therapy should be considered investigational. Two types of breast reconstruction are available to women during or after mastectomy: implant reconstruction and use of autologous tissue. Physicians should provide educational information at appropriate points in the patient's care.

INDEX TERMS: BREAST NEOPLASMS CLEVE CLIN J MED 1996; 63:48–56

From the Breast Center, The Cleveland Clinic Foundation.
Address reprint requests to J.P.C., Director, Breast Services, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.

SURGERY, RADIATION therapy, and systemic therapy have each been the focus of breast cancer management at various times during the past century; today, breast cancer treatment should be multimodal, with a dual focus on both local and systemic therapy. Although early diagnosis remains important to breast cancer outcome and must not be underestimated, today's advanced imaging technology leads to many clinical dilemmas that make the diagnosis of breast cancer as challenging as the treatment. The most satisfactory outcomes start with a diagnostic approach that includes the primary physician, the surgeon, the radiologist, and the pathologist. Furthermore, the vast amount of breast cancer information available to the public makes it imperative that the physician involve and educate the patient.

The research and clinical experience that brought advances in breast cancer management in recent decades also gave rise to controversies and treatment dilemmas yet unresolved. This re-

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.

view examines these key issues: breast cancer screening recommendations, biopsy options, indications for breast-conserving surgery and radiation therapy after breast-conserving surgery, and options for breast reconstruction after mastectomy.

Recent research findings and their implications are reviewed, including dietary and endocrine factors as possible causes of breast cancer, genetic factors underlying breast cancer, and the ethical dilemmas genetic research poses.

CURRENT TRENDS

In 1994, 184 000 new cases of breast cancer were diagnosed in the United States, and the incidence has increased 1% to 2% per year over the past decade. The reason for this increase is not understood and cannot be explained solely by earlier detection.

Deaths from breast cancer are expected to reach 46 000 this year in the United States, making it the second leading cause of cancer deaths among women and the leading overall cause of deaths among women younger than age 50. The rate of mortality due to breast cancer in the general population has not changed over the past 60 years, in spite of apparent advances in both diagnosis and treatment. However, there is definite evidence to suggest that screening for breast cancer reduces mortality,[1] and as more women undergo annual screening, an overall reduction should become apparent.

SEARCHING FOR CAUSES

The cause of breast cancer remains elusive. Environmental and hormonal explanations have been proposed.[2] Epidemiologic evidence point toward environmental factors, particularly diet.

A link with dietary fat?

Breast cancer is less common in countries such as Japan, where people consume less dietary fat. When women of one ethnic group immigrate from areas of low fat consumption to an area of high fat consumption, such as the United States, that group's risk of breast cancer will increase within one or two generations. However, case-control and cohort studies have not shown a consistent correlation between fat consumption and breast cancer risk. The Harvard Nurses' Health Study monitored the diet of 120 000 women for over 10 years and found that fat consumption correlated with the risk of colon cancer but not breast cancer.[3]

If there is a relationship between diet and breast cancer, it may be difficult to demonstrate. Perhaps diet has an effect only during early phases of breast tissue development, a possibility the studies did not take into account. Another possibility is that diets did not vary sufficiently among the populations studied to demonstrate any difference. Large, prospective diet-intervention trials may be necessary to demonstrate any effect of diet on either the development or the progression of breast cancer.[4] Although compliance has been an issue in the design of such trials, results from a large, randomized controlled trial indicate that dietary interventions are feasible, and dietary changes persist after completion of the intervention.[5]

Endocrine factors

It has been difficult to link endocrine factors to breast cancer development. Early menarche, late menopause, nulliparity, and late childbearing are associated with higher risk, whereas early oophorectomy and early childbearing are associated with lower risk. Menarche occurs earlier in countries with better nutrition and higher fat consumption, possibly providing a link between environmental and endogenous endocrine factors. Together, these observations suggest that, for some women, uninterrupted estrogen cycling during a certain period of maturation may lead to breast cancer years later.

A postulated relationship between exogenous hormones and breast cancer risk has been difficult to validate, because of several factors. Over the past several decades, the type and amount of estrogen and progesterone used for birth control and estrogen replacement therapy have varied considerably. Prolonged oral contraceptive use is associated with a slightly increased risk of breast cancer (relative risk 1.4).[6] Whether progesterone (alone or in combination with estrogen) lowers the risk is not known. Hormone replacement therapy may be associated with breast cancer development, but the risk appears to depend on the amount, duration, and combination of hormones.[6]

The evidence for an endocrine link is sufficiently persuasive to justify several trials of tamoxifen to prevent breast cancer. Tamoxifen blocks the effects of estrogen by binding to estrogen receptors in breast tissue. The mechanism by which tamoxifen

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.

might prevent breast cancer is unknown; however, women who take tamoxifen for breast cancer treatment have a lower incidence of contralateral breast cancer than those who do not take it. Although prevention trials are clearly important, they are unlikely to provide solutions that will reduce the incidence of breast cancer in the near future.

Advances in molecular biology

Recent advances in molecular biology are illuminating how breast cancer develops and may have clinical application in the future. Areas of investigation include DNA content (ploidy), *HER-2/neu*-oncogene amplification,[7] growth factors, epidermal growth factor receptor, collagenases, cathepsins,

A historical perspective: breast cancer surgery and radiation therapy

Breast cancer treatment reached an important milestone in 1882, at New York Roosevelt Hospital, when William Stewart Halsted performed the first radical mastectomy. Surgeons in the United States and Europe had performed mastectomies previously, but the results had been poor and the rate of local failure was as high as 80%.

The development of the radical mastectomy

Halsted had concluded that the high mastectomy failure rate resulted from inadequate resection of the pectoralis major muscle, an insight based on research by German surgeon Richard von Volkman, who had found microscopic involvement of breast cancer in the pectoralis major muscle. Because Halsted believed that breast cancer spread in an orderly manner from the breast to the regional lymph nodes, he devised a procedure that included removal of the entire breast with a wide skin margin, the pectoralis major muscle, and the axillary lymph nodes.

Halsted published his clinical experience with radical mastectomy in the *Johns Hopkins Hospital Reports* in 1894. The local recurrence rate was only 6% in this series, even though 27 of 50 patients were labeled as having a "hopeless" or "unfavorable" prognosis on the basis of the extent of disease at initial presentation. Ten days after Halsted's series was published, Willie Meyer of the New York Graduate School of Medicine described a similar operation that he had developed independently of Halsted. Meyer's operation involved removal of the pectoralis minor, use of an oblique incision, and delayed skin grafting of the chest wall. However, as early as 1898, the theory of orderly local cancer progression, Halsted's rationale for radical mastectomy, was challenged. At a meeting of the American Surgical Association, Rudolph Matas, a professor of surgery at Tulane, argued that breast cancer could spread systemically, essentially negating any benefit of radical resection.

Discovery of x-rays transforms treatment

The discovery of x-rays in 1895 profoundly changed local breast cancer treatment. Within 2 months, Emile Grubbe, a second-year medical student in Chicago, performed the first radiation therapy for breast cancer. Eight years later, Georg Clemens Perthes, Professor of Surgery in Leipzig, suggested that x-rays affect cells by inhibiting cell division. W.S. Handley of Middlesex, England, suggested inserting radon tubes into intercostal spaces to treat internal mammary node metastases. In 1917, H.H. Janeway of Memorial Hospital in New York described using interstitial irradiation. This approach was developed further by Geoffrey Keynes of St. Bartholomew's Hospital in London, who used radium needles to treat breast cancer and, by 1932, was combining local excision with interstitial implantation of radium needles. Super-voltage x-rays eventually replaced radium needles for postoperative breast cancer treatment. In 1948, Robert McWhirter from Edinburgh reported results for simple mastectomy and postoperative radiation that were superior to radical mastectomy results.[1,2]

Surgical techniques progress

Surgical procedures continued to evolve. In England, R.S. Handley developed a procedure that included routine internal mammary node dissection. Haagensen and Cooley at Columbia in New York and Wangensteen in Minnesota extended the Halsted radical operation to include division of the clavicle, resection of the first rib, and dissection of the internal mammary,

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.

and alterations in the *p53* tumor-suppressor gene.[8,9] Nevertheless, prognostic factors such as tumor size, nuclear grade, histologic differentiation, lymphatic and vascular invasion, lymph node involvement, and hormone receptor status continue to be the criteria that determine whether to offer systemic therapy for early-stage breast cancers.[10]

The *BRCA1* gene: New findings present clinical dilemmas

Some of the most exciting research involves the quest for genes related to breast cancer. Skolnick et al[11] have cloned the *BRCA1* gene, located on the long arm of chromosome 17. Although inheritance of a mutated form of this gene is estimated to ac-

supraclavicular, and upper mediastinal nodes. Patey and Dyson at Middlesex Hospital took a different approach. In 1948 they reported the technique of modified radical mastectomy, which involved resecting the pectoralis minor but leaving the pectoralis major muscle intact.

Use of less radical approaches was not limited to Europe. At the Cleveland Clinic during the 1920s and 1930s, George W. Crile used a mastectomy technique that was similar to the modified radical mastectomy of today. His son, George H. "Barney" Crile, did not immediately adopt his father's departure from standard radical surgery when he graduated from Harvard Medical School in the 1930s. Instead, Barney Crile used both the radical and the extended radical mastectomy. However, in the 1950s, after comparing his father's results and those of Keynes in London, neither of whom performed radical mastectomies, with the results of surgeons who routinely did so, Crile became convinced that there was no advantage to radical mastectomy and adopted the more conservative surgical approach. By the late 1950s, the radical mastectomy was no longer a standard procedure at the Cleveland Clinic.[3]

Conservative approach accepted slowly

Surgeons in the United States were slow to accept this more conservative approach. As late as the early 1970s, the Halsted radical mastectomy was still being performed more frequently than the modified radical mastectomy. To resolve the controversy, prospective randomized trials were undertaken in the United States and Europe to compare radical mastectomy, modified radical mastectomy, and total mastectomy with and without radiation therapy. The largest such trial (B-04), initiated in 1971 by the National Surgical Adjuvant Breast and Bowel Project (NSABP), included 1655 patients from 34 institutions and compared radical mastectomy and total mastectomy (simple mastectomy without node removal) with and without radiation therapy. Patients had similar recurrence and survival rates, irrespective of which local treatment they received.[4] Even among patients with cancer in their axillary lymph nodes, the radical surgery conferred no advantage over a less radical approach. Finally, modified radical mastectomy had virtually replaced radical mastectomy in the United States by the late 1970s.

During the decades-long era when the focus of treatment was radical surgery, there had been little interest in any other approach, such as partial mastectomy. As early as the 1930s Keynes had demonstrated that partial mastectomy with interstitial radiation could be used effectively, and in the 1950s Barney Crile had used partial mastectomy for patients with small tumors.[3] However, high local recurrence rates for partial mastectomy without radiation therapy was a concern. Pierquin and Baclese in France, Mustakallia in Finland, Peters in Canada, and Porritt in England found excellent results when radiation was added to partial mastectomy. More recently, the work of Montegue at M.D. Anderson Cancer Center, Harris and Hellman at the Joint Center for Radiation Therapy at Harvard University, Prosnitz at Duke University, and Fowble at the University of Pennsylvania has helped to refine the technique of radiation therapy and to allow for appropriate selection of patients for breast-conserving surgery.

References

1. **Robinson JO.** Treatment of breast cancer through the ages. Am J Surg 1986; **151**:317–333.
2. **Leffall LD Jr.** 100 years of breast cancer. Halsted to Fisher. Bull American College of Surgeons 1994; **79(8)**:12–20.
3. **Crile G Jr.** Evolution of thought about pathology, clinical behavior and treatment of cancer of the breast. Surv Synth Pathol Res 1984; **3**:547–551.
4. **Fisher B, Redmond C, and others for the National Surgical Adjuvant Breast and Bowel Project.** Lumpectomy for breast cancer: an update of the NSABP experience. J Natl Cancer Inst Monogr 1992; **11**:7–13.

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.

count for only 5% of all breast cancers, a woman with this gene who has multiple relatives with early-onset breast cancer or breast and ovarian cancer may have a risk of breast cancer of greater than 95%. The impact of screening for this gene will be enormous. Issues concerning who should be screened and at what age are already being raised. A woman found to have a mutation in the *BRCA1* gene, and the physician who treats her, will face more hard questions: When will she develop breast cancer? How should she be monitored? Should she wait and participate in prevention trials or should she immediately seek out a surgeon willing to perform bilateral mastectomies to prevent breast cancer?

A second gene, *BRCA2*, has been mapped to a specific region on chromosome 13. However, since 95% of breast cancer patients have no mutations in either gene, absence of mutations in these genes should not lead to complacency in screening or surveillance. When genetic screening becomes available, physicians should consider referring patients who have genetic risk markers for genetic counseling.

DIAGNOSING BREAST CANCER

Screening and early detection

Screening offers the best chance for early detection and improved survival. The American Cancer Society recommends that women without symptoms perform breast self-examination every month beginning at age 20 and undergo physician breast examination every 3 years between ages 20 and 40 and every year thereafter and mammography every 1 to 2 years between ages 40 and 49 and every year thereafter.[12] This entails a considerable number of tests: 16 million screening mammograms each year in the United States. About 1.5 million of these studies require additional special views for better evaluation, adding another 8 to 9 million imaging and other diagnostic procedures each year.

Recently, the value of screening mammography for the 40-to-49-year-old age group has been questioned. None of the trials that could be evaluated had sufficient numbers of patients in this group to allow for reliable subgroup analysis. In spite of these limitations, five of the eight randomized trials did show a mortality reduction of between 22% and 49% in this group.[1]

In theory, an algorithm could provide reasonable guidelines for screening and diagnosis. The inherent problem with any such attempt is that breast cancer screening is based on examination and mammography, both of which rely entirely on subjective interpretation. For the breast mass or mammographic abnormality with a very high or low probability of being cancerous, either biopsy or follow-up decisions are straightforward. For abnormalities with intermediate probability, additional imaging and tissue sampling procedures can be used to further characterize the lesion and thereby select the most appropriate patients for surgical biopsy.

What type of biopsy?

The decisions about what type of biopsy to perform and how to follow up an identified lesion are not always straightforward. Twenty years ago, these decisions were less complex: a woman presented with a palpable lump, an excisional biopsy was performed, and, if cancer was found, definitive treatment, usually mastectomy, was the next step. Today, there are more options. Approximately 50% of all excisional biopsies are now done for nonpalpable lesions identified on mammography, including masses, asymmetric areas, and microcalcifications. Patients with nonpalpable lesions can undergo stereotactic biopsy (a procedure usually done by a radiologist) or excisional biopsy with wire localization. A patient with a palpable mass might benefit from a fine-needle aspiration cytologic study or core tissue biopsy performed in the office. Fine-needle aspiration cytologic study or possible core tissue biopsy can provide useful information in the evaluation of palpable masses, but any persistent, dominant, palpable mass should be excised for definite diagnosis regardless of the results of these sampling procedures. New imaging techniques are also available, such as ultrasonography, cone-down and compression mammography, magnetic resonance imaging, computed tomography, and positron-emission tomography, each of which has advantages and limitations. The different options for imaging and performing a biopsy should be discussed with the patient, so that she can understand the risks and benefits of each.

Excisional biopsy

Excisional (or "open") biopsy is the standard for breast cancer diagnosis. Overall, this technique reveals one cancer for every three or four benign findings; in some practices, the ratio may be as low as one in 10. Between 750 000 and 1 000 000 exci-

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.

sional breast biopsies are performed each year, of which approximately 180 000 detect cancer.

An excisional breast biopsy, by definition, removes a palpable or nonpalpable lesion entirely. The technique has improved considerably over the past decade. In the past, general anesthesia was required. If frozen-section analysis revealed cancer, a radical mastectomy was performed immediately, and even when the biopsy result was benign, the patient often required hospitalization for several days. A drain was frequently placed in the biopsy cavity, and the cosmetic result tended to be poor.

Today, in most situations, open breast biopsy is relatively simple and is performed as a single outpatient procedure. General anesthesia is usually unnecessary. A small, superficial lesion can be removed under local anesthesia; a combination of an intravenous sedative and a local anesthetic is very effective for a larger or deeper lesion. The patient is discharged shortly after the procedure, and usually has minimal postoperative discomfort.

Pathology reporting

Cytologic analysis of samples obtained by fine-needle aspiration, which is not as accurate as histologic analysis of tissue samples, has a false-negative rate as high as 30% to 40%, depending on the experience of the surgeon and cytologist.[13] Although false-positive cytology results are infrequent, a histologic diagnosis must accompany any cytologic diagnosis before surgical treatment is undertaken if there is any possibility of a benign diagnosis. However, if the clinical findings are compatible with breast cancer, a positive aspiration cytologic study may be all that is required to proceed with treatment. To proceed with a definitive surgical procedure such as mastectomy on the basis of a cytologic diagnosis alone is inappropriate and could have disastrous consequences.

Local, regional, and systemic therapy is contingent upon detailed analysis of tissue obtained by excisional biopsy. It is often beneficial for the surgeon to note the orientation of the specimen when it is removed from the patient and for the pathologist to report the findings relative to this orientation. Resection margins should be marked with ink or dye before the specimen is sectioned. Obvious lesions should be described and measured, and their relationship to the specimen margins as the specimen is sectioned should be noted. The pathologist must be made aware of the type of abnormality that was identified on mammography, because frequently there are no grossly identifiable lesions. The specimen mammogram is the only means available to locate the area of concern.

TABLE 1
PATHOLOGIC ANALYSIS OF BREAST BIOPSY SPECIMENS

Quantitation of relevant histology
Invasive duct and lobular
Duct carcinoma in situ
Premalignant changes
Lobular carcinoma in situ
Atypical duct and lobular hyperplasia
Tumor grade
Histologic
Nuclear
Vascular and lymphatic involvement
Tissue samples for:
Hormone receptor analysis
DNA flow cytometry (S-phase, index, ploidy)

The pathologist and the surgeon should decide together, on a patient-by-patient basis, if frozen-section analysis is necessary. This procedure may be appropriate for larger lesions but could prohibit a complete description of smaller cancers.

Processing of the specimen for permanent-section microscopic analysis is also critical. Tissue blocks are submitted in such a manner that the amount of precancer, noninvasive cancer, and invasive cancer can be determined and then related to the resection margins. Tissue from invasive cancers should be submitted for hormone receptor analysis (quantitative cytosol receptors or immunohistochemical analysis), and DNA analysis (S-phase, index, and ploidy). Information that should be included in a pathology report for any cancer or precancer finding is shown in *Table 1*.

BREAST CANCER TREATMENT

Breast-conserving surgery

Breast-conserving surgery has increased gradually in popularity over the last decade. Four prospective randomized trials have demonstrated similar outcomes with breast-conserving surgery or mastectomy in patients with early-stage breast cancer.[14–16]

Who should receive breast-conserving surgery?

Two issues need to be addressed before proceeding with breast-conserving surgery: the cosmetic re-

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.

TABLE 2
OPTIMAL FACTORS
FOR BREAST-CONSERVING SURGERY

Small, unicentric tumor
Specimen margins free of tumor
Low nuclear grade
Intraductal component of tumor < 25%
Age > 40 years
Good cosmetic result after surgery and radiation therapy

sult and the chance of local recurrence. Studies suggest that patients with tumors measuring up to 4 cm are candidates for this approach. However, large tumors (larger than 3 cm), may make histologically clear margins impossible to obtain while simultaneously achieving a good cosmetic result. The relative size of the lesion compared with the breast is a more significant determinant of the cosmetic result than is the absolute lesion size. Patients with more than one tumor within the same breast will likely need more breast tissue removed than would allow for a good cosmetic result. Patients who have centrally located lesions that require resection of the nipple-areolar complex may not be the best candidates for breast conservation. However, for certain patients, central breast resection that includes the nipple-areolar complex may be preferable to mastectomy. The expectations and wishes of the patient must be foremost at all times.

Several factors have been linked to a high chance of local recurrence after breast-conserving surgery.[17] Tumors that cannot be removed completely (in which the resection margin is "involved with tumor") have a high chance of recurring. Studies from the Joint Center for Radiation Therapy suggest that microscopic margin involvement does not lead to a higher rate of local recurrence if the tumor bed receives a radiation therapy "boost."[18] However, in a recent study, Spivack and colleagues[19] found a higher local recurrence rate with microscopically positive margins regardless of boost radiation.

Tumors with a high nuclear grade or those with an extensive intraductal component (> 25%) are also reported to have a higher recurrence rate.[18] Younger age has also been considered a relative contraindication to breast-conserving surgery. Several studies suggest a high recurrence rate in patients younger than 40 years.[20] Generally, young age is not an absolute contraindication, and the patient's motivation may be particularly important in this age group. Patients who have collagen-vascular disease (discoid or systemic lupus erythematosus or scleroderma) often have complications with radiation therapy and are not good candidates for breast-conserving surgery. Patients who have large, pendulous breasts frequently experience swelling, fibrosis, or breast discomfort and may also not be good candidates.

Too often, breast-conserving surgery is considered "simpler," "easier" or "less" treatment than mastectomy. It is not. The patient's decision to proceed with this procedure demands a long-term commitment. Patients must have access to a radiation facility and be followed closely. There is a small but definite chance of local recurrence every year, which does not diminish with time. Patients need to understand that they will require subsequent mammograms, possibly biopsies, and possibly mastectomy if the cancer recurs in the breast. Careful planning and appropriate patient selection are very important. All patients should have the chance to discuss radiation therapy with the radiation oncologist before proceeding to breast-conserving surgery. Factors that help define good candidates are outlined in *Table 2*.

Is radiation therapy always necessary after breast-conserving surgery?

A current debate is whether all patients who undergo breast-conserving surgery should also receive radiation therapy. Four randomized trials evaluated this question, and in each, radiation therapy significantly reduced the incidence of local recurrence: from 43% to 13% in the NSABP B-06 trial,[14] from 5% to 0% in an Italian trial,[21] from 11% to 3% in a Swedish trial,[22] and from 26% to 6% in a Canadian trial.[23] The NSABP and Swedish trial found radiation therapy beneficial even for patients with small tumors (T1; ≤ 2 cm).

On the other hand, several retrospective, nonrandomized series have not found radiation therapy definitely beneficial for some patients with small lesions.[24,25] In a recent review of the Cleveland Clinic experience, Hermann and colleagues[25] reported on 2020 patients with stage 0, I, or II breast cancer who were followed up for 14 years. Radiation therapy after partial mastectomy appeared to benefit the stage II patients, who had a 5-year local recurrence rate of 4.0% and a 10-year local recurrence rate of 10.3%, compared with 11.3% and 21.6%, respectively, for similar patients treated by partial

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.

mastectomy alone ($P = .01$). At 10 years, the actuarial local recurrence rate for stage 0 patients treated by segmental mastectomy with and without radiation therapy was 7.7% vs 8.6%, respectively; for stage I patients, it was 18.3% vs 14.1%. These data suggest that partial mastectomy alone may be appropriate for selected patients who have small tumors with clear margins, negative axillary nodes, and no evidence of multifocality.

In an effort to identify a group of patients who might not need radiation therapy, Pierce et al[26] performed a prospective study of 87 patients who had tumors 2 cm or smaller and no vascular or lymphatic invasion or axillary node involvement. The primary tumors were resected with a margin of at least 1 cm of uninvolved tissue. The study was terminated when a 7.3% rate of local recurrence was found at 30 months.[26] It is possible that patients with even smaller and histologically more favorable tumors resected with wider margins (> 1 cm) may not experience this unacceptable relapse rate. At present, however, conservative surgery without radiation therapy should be considered investigational.

Mastectomy and breast reconstruction

Many mastectomy patients are interested in breast reconstruction. Two distinct types of breast reconstruction have evolved and can be implemented either during mastectomy (immediate reconstruction) or afterward (delayed reconstruction). Implant reconstruction involves placing a prosthesis filled with saline under the pectoralis major muscle. During the past several years, expandable implant prostheses have been developed, in which saline is injected into the prosthesis over several weeks following the insertion. Prosthesis reconstructions can be performed quickly and easily, particularly when combined with mastectomy. However, they have the long-term disadvantage of potential capsular contracture.

The second type of reconstruction involves autologous tissue, which gives a result more like the normal breast. Tissue from the patient's lower abdomen is usually used and is transferred to the mastectomy site as a pedicle flap attached to the rectus abdominis muscle (transverse rectus myocutaneous flap, or TRAM), or as a free-flap reconstruction with microvascular anastomosis to regional vessels, most often the thoracodorsal artery and vein. TRAM reconstruction is an excellent procedure that can have good results when performed at the time of the mastectomy and when a technique that spares the entire breast skin envelope is employed. TRAM reconstruction is not a simple procedure, and patients need to understand its risks and benefits. Yet, properly performed, the advantages of TRAM reconstruction outweigh its disadvantages.

PATIENT EDUCATION

The increasing complexity of breast cancer diagnosis and treatment, coupled with the vast amount of information available to the public, can be overwhelming to patients. A successful approach requires that all physicians participating in the patient's care take time to provide sufficient information at the appropriate opportunity.

ACKNOWLEDGMENT

Rebecca Patrick provided editorial assistance in the preparation of this manuscript.

REFERENCES

1. **Kopans DB.** Screening for breast cancer and mortality reduction among women 40-49 years of age. Cancer 1994; **74(1 Suppl):**311–322.
2. **Marshall E.** The politics of breast cancer. Science 1993; **259:**616–617.
3. **Giovannucci E, Stamfer M, Colditz G, et al.** A comparison of prospective and retrospective assessments of diet in the study of breast cancer. Am J Epidemiol 1993; **137:**502–511.
4. **Chlebowski RT, Grosvenor M.** The scope of nutrition intervention trials with cancer-related endpoints. Cancer 1994; **74(9 Suppl):**2734–2738.
5. **White E, Shattuck AL, Kristal AR, et al.** Maintenance of a low-fat diet: follow-up of the Women's Health Trial. Cancer Epidemiol Biomarkers Prev 1992; **1(4):**315–323.
6. **Fentiman IS.** The endocrine dimension. In: Fentiman IS. Prevention of breast cancer. Austin, Tex: RG Landes Company; 1993:32–52.
7. **Borgan PI, Tiwari RK, Rossi J, Wong GY, Osborne MP.** Amplification of Her2/neu oncogene is associated with early metastasis in human breast cancer. Proc Annu Meet Am Assoc Cancer Res 1990; **31:**A1858. Abstract.
8. **Vogelstein B, Kinsler KW.** p53 function and dysfunction. Cell 1992; **70:**523–526.
9. **Isola J, Visakorp T, Holli K, Kallioniemi OP.** Association of over expression of tumor suppressor protein p53 with rapid cell proliferation and poor prognosis in node negative breast cancer patients. J Natl Cancer Inst 1992; **84:**1109–1114.
10. **Mansour EG, Ravoin PM, Dressler L.** Prognostic factors in early breast cancer. Cancer 1994; **74:**381–400.
11. **Miki Y, Swensen J, Shattuck-Eidens D, et al.** A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. Science Oct 7 1994; **266:**66–71.
12. **Mettlin C, Smart C.** Breast cancer detection guidelines for women aged 40 to 49 years: rationale for the American Cancer Society reaffirmation of recommendations. CA Cancer J Clin 1994; **44:**248–255.
13. **Layfield LJ, Glasgow BJ, Cramer H.** Fine-needle aspiration in the management of breast masses. Pathol Annu 1989; **24 (part 2):**23–62.

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.

CLEVELAND CLINIC JOURNAL OF MEDICINE

INTERNAL MEDICINE BOARD REVIEW

Clinical vignettes and questions on the differential diagnosis and treatment of medical conditions likely to be encountered on the Qualifying Examination in Medicine – as well as in practice. Take the challenge.

IN THIS ISSUE
Page 8

14. **Fisher B, Redmond C, and others for the National Surgical Adjuvant Breast and Bowel Project.** Lumpectomy for breast cancer: an update of the NSABP experience. J Natl Cancer Inst Monogr 1992; **11**:7–13.
15. **Sarrazin D, Le MG, Arriagada R, et al.** Ten-year results of a randomized trial comparing a conservative treatment to mastectomy in early breast cancer. Radiother Oncol 1994; **14**:177–184.
16. **Bader J, Lippman M, Swain S, et al.** Preliminary report of the comparison of lumpectomy (L) and radiation (XRT) to mastectomy (M) for stage I and II BC. Int J Radiat Oncol Biol Phys 1987; **13 (Suppl 1)**:160. Abstract.
17. **Balch CM, Singletary SE, Bland KI.** Clinical decision-making in early breast cancer. Ann Surg 1993; **3**:207–225.
18. **Schnitt SJ, Abner A, Gelman R, et al.** The relationship between microscopic margins of resection and the risk of local recurrence in patients with breast cancer treated with breast-conserving surgery and radiation therapy. Cancer 1994; **74(6)**:1746–1751.
19. **Spivack B, Khanna M, Tafra L, Juillard G, Giuliano A.** Margin status and local recurrence after breast-conserving surgery. Arch Surg 1994; **129**:952–957.
20. **Matthews RH, McNeese MD, Montague ED, et al.** Prognostic implications of age in breast cancer patients treated with tumorectomy and irradiation or with mastectomy. Int J Radiat Oncol Biol Phys 1988; **14**:659–663.
21. **Veronesi U, Luini A, Del Vecchio M.** Radiotherapy after breast preserving surgery in women with localized cancer of the breast. N Engl J Med 1993; **328**:1587–1591.
22. **Uppsala-Orebro Breast Cancer Study Group.** Sector resection with or without postoperative radiotherapy for stage I breast cancer: a randomized trial. J Natl Cancer Inst 1990; **82**:277.
23. **Clark RM, McCulloch PB, Levine MN, et al.** Randomized clinical trial to assess the effectiveness of breast irradiation following lumpectomy and axillary dissection for node negative breast cancer. J Natl Cancer Inst 1992; **84**:683–689.
24. **Moffat FL, Ketcham AS, Robinson DS, et al.** Segmental mastectomy without radiotherapy for T1 and small T2 breast carcinomas. Arch Surg 1990; **125**:364–369.
25. **Hermann RE, Esselstyn CB, Grundfest-Broniatowski S, et al.** Partial mastectomy without radiation is adequate treatment for patients with stages O and I carcinoma of the breast. Surg Gynecol Obstet 1993; **177**:247–253.
26. **Pierce SM, Schnitt S, Gelman R, Love S, Eberlein T, Harris, JR.** Wide excision without radiation therapy in selected patients with early stage breast cancer. Proc Am Soc Clin Oncol 1993; **12**:70. Abstract.

Downloaded from www.ccjm.org on August 10, 2025. For personal use only. All other uses require permission.