Breast Imaging and Interventional Procedures – the Basis for Oncoplastic Breast Surgery

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Key Words

Breast cancer · Breast imaging · Mammography · Breast ultrasound · Magnetic resonance mammography · Oncoplastic surgery · Interventional breast procedures

Summary

Preoperative staging of breast cancer based on breast imaging is mandatory. Breast imaging is a general term that encompasses mammography, breast sonography, and magnetic resonance tomography (MRT) of the breast (magnetic resonance mammography, MRM). It is known that earlier diagnosis of breast cancer is more likely to result in a favorable oncological outcome. In this context, use and limitations of MRM in diagnosis and staging of breast cancer as well as its influence on surgical procedures have to be discussed. Different interventional procedures have been developed. The histological results of interventional procedures guided by ultrasound, stereotactic mammography or MRT have to be integrated in planning surgical resection margins in oncoplastic breast-conserving surgery. Image-guided wire markings are an important tool for planning these surgical resection margins. This paper gives an overview on the importance of breast imaging, interventional procedures, and wire markings for breast-conserving surgical therapy.

Schlüsselwörter

Mammakarzinom · Mammadiagnostik · Mammografie · Mammasonografie · Magnetresonanztomografie · Onkoplastische Chirurgie · Interventionelle Mammadiagnostik

Zusammenfassung

Die komplementäre Mammadiagnostik bildet die Grundlage für das präoperative Staging beim Mammakarzinom. Zur komplementären Mammadiagnostik gehören im Speziellen die Mammografie, die Mammasonografie und die Magnetresonanztomografie (MRT) der Mamma (Magnetresonanztomografie, MRM). Je früher die Diagnose eines Mammakarzinoms erfolgt, desto besser ist die Prognose. In diesem Zusammenhang müssen besonders Stellenwert, Einsatz und Limitationen der MRM bei Diagnose und Staging des Mammakarzinoms sowie ihre Auswirkungen auf das operative Vorgehen diskutiert werden. Die histologischen Ergebnisse nach sonografisch, stereotaktisch oder MRT-gesteuerter interventioneller Diagnostik sollten in die Planung der Resektionsgrenzen im Rahmen der brusterhaltenden, onkoplastischen Mammachirurgie integriert werden. Für die Planung der Resektionsgrenzen stellen die unterschiedlichsten bildgebend gesteuerten Markierungstechniken wichtige Instrumente dar. Diese Arbeit gibt einen aktuellen Überblick über die Bedeutung der bildgebenden Mammadiagnostik, der interventionellen Diagnostik und der Markierungstechniken für die Planung und Durchführung der brusterhaltenden, operativen Therapie des Mammakarzinoms.

Breast Imaging

It is known that earlier diagnosis of breast cancer is more likely to result in a favorable outcome. Tumor size at diagnosis and lymph node stage are the best predictors of outcome. Regardless of tumor type or grade, the smaller a breast cancer is at the time of diagnosis, the more likely it is that it has not spread beyond the breast. As a result the current strategy for reducing breast cancer mortality is to seek diagnosis as early as possible. Early diagnosis is achieved by encouraging women to present as early as possible to breast clinics when they develop breast symptoms and through breast cancer screening. Breast imaging is fundamental to both.

Breast imaging is a more general term that encompasses mammography, breast sonography, breast magnetic resonance imaging (MRI) and other emerging technologies (fig. 1). To provide uniformity in the assessment of breast imaging findings, the American College of Radiologists (ACR) established final assessment classifications (Breast Imaging Reporting and Data System, BI-RADS) [1–3]. The final assessment categories are as follows: category 1: negative; category 2: benign; category 3: probably benign (risk of malignancy < 2%); category 4: suspicious abnormality (biopsy should be considered); category 5: highly suggestive of malignancy; category 6: histologically proven cancer before neoadjuvant chemotherapy.

Category 4 and 5 assessments indicate abnormalities that require tissue biopsy for diagnosis. These categories represent a broad range (3–100%) of risk of cancer.

Mammography

X-ray mammography has been the basis of breast imaging for more than 30 years. The sensitivity of mammography for breast cancer is age dependent. The denser the breast, the less effective this method is for detecting early signs of breast cancer. Breast density tends to be higher in younger women, and increased density obscures early signs of breast cancer [4]. The sensitivity of mammography for breast cancer in women over 60 years of age approaches 95%, while mammography can be expected to detect less than 50% of breast cancers in women under 40 years of age [5]. Mammography uses ionizing radiation to obtain an image and therefore should only be used where there is likely to be a clinical benefit. Consensus is that the benefits of mammography in women over the age of 40 years are likely to far outweigh any oncogenic effects of repeated exposure. Screening of women over the age of 40 by mammography is accepted practice. However, in symptomatic practice there is rarely an indication for performing mammography in women under the age of 35 unless there is a strong clinical suspicion of malignancy. Practice is changing, and ultrasound is being increasingly used for the assessment of women with focal breast symptoms in this age range. Mammography is routine in all women in the screening age group

attending symptomatic clinics who have not had a screening mammogram in the past year. Film/screen mammography has been refined over the years and has now reached the limits of this technology [6]. It is a difficult technique to maintain at the quality levels required for optimal diagnosis because labor-intensive quality-control measures are necessary to sustain the diagnostic standards. The future of mammography lies in digital acquisition of the image. Major benefits have been predicted from acquiring mammograms in direct digital format [7]. Compared with conventional mammography, the predicted benefits of full-field digital mammography include better imaging of the dense breast, the application of computer-aided detection, and a number of logistical advantages providing potential for more efficient mammography services. The much wider dynamic range of digital mammography means that visualization of the entire breast density range on a single image is easily achievable. In the clinical setting, comparative studies have shown that digital mammography performs as well as film/screen mammography [8–11].

Recent preoperative mammographic evaluation is necessary to determine a patient's eligibility for breast-conserving therapy. Mammographic evaluation defines the extent of a patient's disease, the presence or absence of multicentricity and other factors that might influence the treatment decision, and evaluates the contralateral breast. The size of the tumor should be included in the mammographic report. If the mass is associated with microcalcifications, an assessment of the extent of the calcifications within and outside the mass should be made. Magnification mammography is important for characterizing microcalcifications.

Mammography is the basis of stereotactic breast biopsy. Stereotactic biopsy can be carried out using a dedicated prone biopsy table or by using an add-on device to a conventional upright mammography unit. This technique is used for biopsy of unpalpable lesions that are not clearly visible on ultrasound, e.g. microcalcifications [12].

Ultrasound

High-frequency (≥ 7.5 MHz) ultrasound is a very effective diagnostic tool for the investigation of focal breast symptoms. Ultrasound does not involve ionizing radiation and is a very safe imaging technique. It has a high sensitivity for breast pathology and also a very high negative predictive value. High-resolution ultrasound easily distinguishes between most solid and cystic lesions and can differentiate benign from malignant lesions with a high degree of accuracy. Ultrasound is the technique of choice for the further investigation of focal symptomatic breast problems at all ages. Under 35 years of age, when the risk of breast cancer is very low, it is usually the only imaging technique required. Over 35, when the risk of breast cancer begins to increase, it is often used in conjunction with mammography. Ultrasound is less sensitive than mam-

Fig. 1. Complementary breast imaging.

mammography for the early signs of breast cancer and is therefore not used for population screening. However, ultrasound does increase the detection of small breast cancer in women who have a dense background pattern on mammography [13–15]. In the screening setting, there is currently insufficient evidence of any mortality benefit and insufficient resources to allow for routine ultrasound screening of women with dense mammograms. Ultrasound is the technique of first choice for biopsy of both palpable and impalpable breast lesions visible on scanning [16]. Ultrasound is being increasingly used to assess the axilla in women with breast cancer. Axillary nodes that show abnormal morphology can be accurately sampled by needle core biopsy.

Doppler ultrasound adds little to breast diagnosis and is not widely used. Three-dimensional ultrasound of the breast is said to increase the accuracy of biopsy and the detection of multifocal disease, but again is not widely available [17, 18]. Elastography is a new application of ultrasound technology that allows the accurate assessment of the stiffness of breast tissue. It is being evaluated at present and may prove to be a useful tool in excluding significant abnormalities, for instance in assessment of asymptomatic abnormalities detected by ultrasound screening.

Magnetic Resonance Mammography

Magnetic resonance imaging is now widely available. However, magnetic resonance mammography (MRM) of the breast requires dedicated breast coils, and these are much less widely available. In order to image the breast the patient is scanned prone, and injection of intravenous contrast (Gd-DTPA) is required. A variety of possible clinical indications for contrast-enhanced MRI of the breast have been reported. These include screening for breast cancer, determining the local extent of malignant disease, identifying an occult primary, assessing

response to neoadjuvant chemotherapy, identifying local recurrences after breast-conserving therapy, breast imaging after implant reconstruction or breast augmentation, and the detection of ipsilateral breast cancer in patients presenting with axillary lymph node metastases (carcinoma of unknown primary, CUP syndrome) [19–23].

MRM is the most sensitive technique for detection of breast cancer, approaching 100% for invasive cancer and 60–70% for ductal carcinoma in situ (DCIS), but it has a high false-positive rate [24–28]. Rapid acquisition of images facilitates assessment of signal enhancement curves that can be helpful in distinguishing benign and malignant disease. However, significant overlap in the enhancement patterns usually means that needle sampling is required. Breast lesions seen on MRM that are larger than 10 mm can be seen on ultrasound if they are clinically significant. MRM is likely to prove the best method for screening younger women (under 40 years) at increased risk of breast cancer but, because of cost, it is unlikely to be used for general population screening. MRM is the best technique for imaging women with breast implants. It is also of benefit in identifying recurrent disease where conventional imaging and biopsy have failed to exclude recurrence. Provided it is carried out more than 18 months after surgery, MRI will accurately distinguish between scarring and tumor recurrence [29, 30]. MRI is being increasingly used to examine women for multifocal disease prior to conservation surgery, although the lack of evidence of efficacy means that it is not routine in this clinical setting. MRI of the axilla will demonstrate axillary metastatic disease, but its sensitivity is not sufficient for it to replace surgical staging of the axilla.

Many questions surrounding the use of MRI of the breast in patients with breast cancer remain unanswered. Just because MRI can detect additional areas of cancer, does it really matter clinically? Should surgical treatment be altered because MRI detects additional foci of cancer, especially in those cases when these areas represent tiny foci of DCIS? Would

Fig. 2. Ultrasound-guided breast core biopsy (14-gauge).

these additional areas of cancer identified on MRI be successfully treated with postoperative radiation therapy? The rate of MRI-detected multifocal disease, which ranges from 16% to 37%, is clearly much higher than the rate of in-breast recurrence after breast-conserving therapy, with reported rates in two studies with a 20-year follow-up of 8.8% and 14.3%, respectively [31, 32]. This strongly suggests that in some, and perhaps many cases, the additional foci of cancer identified only on MRI, especially those that prove to be in situ disease, would likely be successfully treated with postoperative radiation. Which MRI-detected multifocal or multicentric cancer would be successfully treated with postoperative radiation and which would not, later presenting as a local ‘recurrence’? This question will not likely be answered because once these lesions are detected, they are usually localized and excised. In those cases when MRI detects an invasive cancer that is clearly separate from the primary cancer, either in the same or a different quadrant, should mastectomy be recommended, based on the historical treatment of clinically or mammographically detected multifocal or multicentric cancer, or is the patient still eligible for breast-conserving therapy if the lesion can be successfully excised with negative margins [33]? The answer will likely differ from patient to patient. Treatment decisions must be made on a case-by-case basis, with careful review of the imaging, pathologic, and surgical findings [34]. There are additional questions concerning patient selection. Which are the patients at highest risk for having multifocal or multicentric cancer who would benefit most from MRI (palpable cancer, young patients, patients with dense breasts, patients with lobular cancer)? Based on the current success of breast-conserving surgery, it is unlikely that MRI of the breast is warranted in all patients with newly diagnosed breast cancer [20, 34]. Clinical investigation continues in an effort to find answers to these questions.

Breast Cancer Screening

The aim of breast cancer screening is to reduce mortality through early detection. Randomized controlled trials and case-control studies demonstrated that population screening

by mammography can be expected to reduce overall breast cancer mortality by around 25% and by 35–40% in those who participate [35, 36]. The validity of these trials was questioned in 2000–2002, but subsequent reviews by the Swedish combined trials group and a WHO International Agency of Research on Cancer committee of experts have reaffirmed the mortality benefit of mammographic screening and determined that criticisms of the mammographic screening trials were unjustified [37, 38]. The mortality benefit of screening is greatest in women aged 55–70 years. The mortality benefit of screening women aged between 40 and 55 is approximately 20%. Screening women under the age of 40 has not been shown to provide any mortality benefit [39–41].

The screening method is two-view mammography. Clinical examination of the breast and breast self-examination have not been shown to contribute to mortality reduction through early detection and so are not included.

Women at increased risk of developing breast cancer due to a proven inherited predisposing genetic mutation, family history, previous radiotherapy or benign risk lesions may be selected for screening at young age [42, 43]. There is evidence that MRM is the most sensitive method of imaging young women, but has significant resource implications [44]. The specificity of MRM has been a concern, although with second-look recall, targeted ultrasound, and the slowly increasing availability of MRI-guided biopsy this may be less of a problem than initially thought.

Image-Guided Breast Biopsy

Needle biopsy is highly accurate in determining the nature of most breast lesions classified as BI-RADS 4 or 5. Patients with benign conditions avoid unnecessary surgery. Carrying out open surgical biopsy for diagnosis should be regarded as a failure of the diagnostic process. For patients who prove to have breast cancer, needle biopsy provides accurate understanding of the type and extent of disease, so ensuring that patients and the doctors treating them are able to make an informed treatment choice. Needle biopsy not only provides accurate information on the nature of malignant disease, such as histological type and grade, but also facilitates pretreatment assessment of

Fig. 3. Vacuum-assisted core biopsy (11-gauge).

tumor biology (hormone receptors, HER-2/neu receptor, genetic profiling etc.) [45, 46].

Breast needle biopsies of nonpalpable lesions require imaging to guide needle placement. Imaging guidance can be performed with ultrasonography, stereotactic mammography or MRI. Ultrasound guidance is the technique of choice; it is less costly and easy to perform. Ultrasound provides real-time visualization of the biopsy procedure and visual confirmation of adequate sampling. Between 80 and 90% of breast abnormalities will be clearly visible on ultrasound and amenable to biopsy using this technique [47]. For impalpable abnormalities not visible on ultrasound, stereotactic X-ray-guided biopsy is

required. A few lesions are only visible on MRI and require magnetic resonance-guided biopsy.

Most lesions selected for ultrasound-guided biopsy are solid masses that can be sampled with 14-gauge core needles. The technical aspects involved in performing ultrasound-guided procedures with a free-hand approach have been described previously [48]. The technique used consists of the following steps: imaging the lesion, finding the needle in the longitudinal plane through the breast, maximally visualizing the needle tip, and placing the needle in the lesion (fig. 2). Development of good hand-eye coordination is crucial to a successful lesion sampling [49].

Using the 14-gauge needle, multiple core biopsy samples are necessary to ensure accurate sampling of different areas of the lesion. In most cases, accurate lesion sampling can be achieved by obtaining 5 core samples for masses and 10 core samples for microcalcifications [50, 51].

To improve sampling of microcalcifications using digital, stereotactic mammography guidance, the vacuum-assisted biopsy instrument with probes coming in 11-gauge size has been developed [12] (fig. 3). In contrast to the automated biopsy gun devices the directional, vacuum-assisted biopsy instrument is inserted once and rotated while in the breast to obtain samples from different areas of the lesion. By avoiding the need for needle reinsertion, the biopsy time is markedly reduced. A vacuum is used to pull tissue samples into the sample notch, where it is cut and transported back through the needle and out to the collection chamber. Multiple tissue samples are collected without removing the needle from the breast.

Studies have shown improved sampling of microcalcifications with the vacuum-assisted biopsy instrument [52, 53]. For calcifications it is imperative that there is proof of representative sampling with specimen radiography. If calcification is not demonstrated on the specimen radiography and the histology is benign, then management cannot be based on this result as there is a high risk of sampling error; the procedure must either be repeated or open surgical biopsy carried out [54–60]. An 8-gauge vacuum-assisted biopsy probe is preferred for therapeutic removal of breast lesions such as fibroadenomas [61–63].

A device called the Advanced Breast Biopsy Instrumentation (ABBI) system has been developed to perform automated stereotactic volume biopsy and was granted FDA approval in 1996. This device offers cannula sizes of 0.5–2.0 cm in diameter, which remove cylinders of tissue of the selected size. It is more expensive and more invasive than core needle or vacuum-assisted biopsy and involves cautery and wound suturing. In theory, the potential advantage of this diagnostic system may be the ability to remove an entire small lesion in a single specimen rather than multiple fragments and avoid the need for follow-up studies. Although not approved by the FDA for this function, in certain cases the ABBI biopsy could serve as an excisional biopsy and obviate the need for additional

surgery [64]. If, after the ABBI procedure, patients also require surgical biopsy, the procedure is then, in effect, a more expensive and more invasive core biopsy method for obtaining diagnosis.

The low specificity of MRI requires the ability to perform MRI-guided biopsies, which require an additional specialized MRI biopsy coil and MRI-compatible wires and needles for localization and core biopsies [65–67]. Centers that cannot perform MRI-guided localization and biopsy lack the ability to manage lesions visible only with MRI and are at a clear disadvantage.

The technical aspects of MRI-guided localization and biopsy are similar to those for stereotactic biopsies in that the patient is prone during the procedure, the breast is held in compression, and the needle plane is guided into the tissue parallel to the chest wall. Needle placement is performed with the patient outside the bore of the magnet using an MRI-compatible needle, often made of titanium. The patient is then returned to the magnet, and confirmation of adequate needle placement is obtained. After sufficient core samples are obtained outside of the bore of the magnet, a clip is deployed marking the biopsy cavity. MRI-guided procedures are more time consuming and uncomfortable for patients than ultrasound-guided procedures. In our practice, patients with MRI-detected indeterminate or suspect lesions are first scheduled for targeted ultrasonography because often these lesions can be visualized after discovery on MRI. The same principles of quality assurance and pathologic correlation apply to MRI-guided biopsies as they do to ultrasound-guided and stereotactic biopsies. The optimal rate of positive biopsies resulting from MRI-guided procedures will depend on the patient selection criteria used to image patients with MRI.

In cases of complete radiological removal of small occult breast lesions with needle biopsies, clip marking with the possibility for re-localization in cases of necessary therapeutic open surgical resection is mandatory. Core needle and vacuum-assisted biopsy is extremely useful in the evaluation of patients with multiple suspect lesions. Tissue samples can be obtained without having to perform multiple surgical biopsies. Establishing the extent of a patient's cancer allows surgical mapping. Optimal resection can help determine the most appropriate surgical therapy, e.g. oncoplastic breast-conserving surgery.

It is important that the result of needle breast biopsy is always correlated with the clinical and imaging findings before clinical management is discussed with the patient. This is best achieved by reviewing each case at prospective multidisciplinary meetings.

Wire-Guided Surgical Excision

The number of impalpable, clinically occult breast lesions is increasing. Accurate localization techniques are required to

facilitate their surgical excision as the therapeutic part of a planned oncoplastic breast-conserving procedure [68]. The hooked wire is the most commonly employed technique and has proved very reliable, but does have inherent associated problems. There are various designs of localization wire in common use. All have some form of anchoring device such as a hook with a splayed or barbed tip. The wire is deployed under ultrasound or stereotactic guidance (for mammographic lesions only) within a rigid over-sheath cannula, which is then removed once positioning is satisfactory. Most wires are very flexible, and when the cannula is removed, the wire may assume a quite circuitous course, especially after stereotactic insertion when the breast is released from compression. In a very fatty breast in which there is no solid lesion or the wire has not transfixed the lesion, care must be taken to avoid displacing the wire. Accurate wire placement is essential, and ideally the shortest possible length of wire should be within the breast. Procedures that can be surgically more challenging are wide local excisions (segmental resection) for DCIS with no mass lesion. In such cases, where the distribution of disease is often more eccentric, careful three-dimensional excision planning especially in oncoplastic procedures is necessary. Inserting more than one wire and even bracketing the lesion with three or four wires can occasionally be useful.

If the procedure is being performed to establish a diagnosis (diagnostic segmentectomy), a representative portion of the lesion is excised through a small incision, thus leaving a satisfactory cosmetic result if the lesion proves to be benign (fig. 4). The European surgical quality assurance guidelines require such diagnostic surgical excision specimens to weigh less than 30 g. Protocols vary for therapeutic excisions, but in general the lesion should be excised with a 10-mm macroscopic margin of normal tissue. Intraoperative specimen radiography is essential, both to check that the lesion has been removed and, if cancer has been diagnosed, to ensure that adequate radiological resection margins have been achieved. We have to consider that especially in DCIS the proved radiological resection margin (specimen radiography) sometimes differs from the histological resection margin [68–70].

Breast Imaging in the Preoperative Setting

Advances in breast imaging have led some authors to question whether whole-breast ultrasound or MRI should be part of the standard preoperative evaluation of a patient with breast cancer [71]. Golshan et al. [72] reviewed the impact of ipsilateral whole-breast ultrasound on the surgical management of 426 patients with clinical stage I and II cancer. The ultrasound identification of tumor not evident by mammogram or physical examination at a distance of more than 1 cm from the primary tumor or in a separate quadrant of the breast was scored as a finding that changed therapy. Seventy-five of the 426 patients (18%) had additional lesions identified by ultrasound,

Fig. 4. Wire-guided (mammography and MRI) segmental excision.

but only 12 were malignant. The role of ultrasound as a diagnostic tool for the evaluation of breast masses is well established – as is its role in defining lesions that are poorly seen on mammogram or are mammographically occult – and the available data support its use as a routine tool when evaluating patients for breast-conserving therapy.

Tillman et al. [73] reported the results of a similar study of the impact of breast MRI on the management of 207 women with intraductal carcinoma or stage I and II disease. The MRI findings affected clinical management in 20% of cases. In 11%, the effect of MRI was judged to be beneficial due to the identification of cancer that was confirmed histologically. In 2% of cases, the benefit of MRI was uncertain, and in 6%, MRI had an unfavorable effect due to false-positive findings that resulted in unnecessary mastectomy or additional breast biopsies. The benefit of MRI was greatest when it was done prior to any surgical excision and in patients with larger tumors. However, it is noteworthy that in this study, only a marginal benefit of MRI was seen.

The work of Holland et al. [33] clearly indicates that microscopic foci of invasive and noninvasive cancer are present at a distance from apparently localized primary tumors in a significant number of patients. Only 39% of specimens showed no evidence of cancer beyond the reference tumor. In 20%, additional cancer was found, but it was confined to a distance of not more than 2 cm from the reference tumor. 41% of patients

had residual cancer more than 2 cm from the reference tumor; of those, two thirds had pure intraductal carcinoma, and one third had mixed intraductal and invasive carcinoma. The percentage of patients with residual cancer more than 2 cm from the reference tumor corresponds well to the rate of local failure reported in patients treated with excision of the primary tumor alone. In these series, local recurrence in the breast occurs at or near the site of the primary tumor in most cases, emphasizing that multifocal breast cancer commonly remains after an excision of the tumor and that this multifocal involvement is biologically important. This is true even if the margins of surgical resection are assessed to be negative. However, radiotherapy is effective in controlling the majority of these occult foci of carcinoma. The importance of these microscopic foci of tumor in the patient treated with excision and radiotherapy has again become an issue of clinical significance with the development of imaging modalities, such as magnetic resonance and ultrasound, which allow preoperative detection of very small foci of cancer.

Clinical experience has demonstrated that the majority of this disease is controlled with radiotherapy. The ability of MRI and ultrasound imaging to identify these microscopic tumor foci raises the possibility that significant numbers of women who could be treated with lumpectomy/segmentectomy and radiotherapy will be subject to mastectomy. Prospective trials demonstrating a decrease in the rate of recurrence in patients

selected for breast-conserving therapy with ultrasound or MRI are needed before these examinations are routinely used for patient selection.

Histologic subtype other than invasive ductal carcinoma does not appear to be associated with an increased risk of recurrence. In particular, patients with invasive lobular carcinoma are candidates for breast-conserving surgery and radiation if the tumor is not diffuse in the breast and can be completely excised with negative margins. Because of the increased incidence of multicentricity and bilaterality, invasive lobular can-

cer associated with increased mammographic density (ACR 3 and 4) is an accepted indication for preoperative MRI before breast-conserving therapy.

The translation of breast imaging, interventional procedures, and wire-guided surgical excision into a concept of oncoplastic breast-conserving surgery (termed 'translational oncoplastics' by W. Audretsch) is mandatory and an interdisciplinary task for the breast radiologist and the breast surgeon to achieve the best oncological and aesthetic outcomes for patients with breast cancer.

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