Lumpectomy

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Key Concepts

- Survival is equivalent to that in mastectomy in properly selected patients
- Radiation therapy is an integral part of lumpectomy
  - Decreases local recurrence rate
  - Increases time to recurrence
  - Three ways to deliver radiation therapy:
    - External beam irradiation
    - Accelerated partial breast irradiation
    - Intraoperative radiotherapy
- Indications
  - Stage I or II breast cancer
  - Patients with DCIS or an extensive intraductal component (EIC) may be candidates if adequate margins are attained
  - EIC is associated with an increased local recurrence rate
  - Patient must be willing to undergo radiation therapy
  - Tumor small enough relative to breast
  - Consider MRI for patients with dense breasts or tumors not seen well on mammography
  - Axillary metastases are not contraindications
  - Presence of implants not a contraindication
- Must attain negative margins
  - Orient the specimen accurately in the operating room
  - Must re-excise if necessary
  - Mastectomy if not able to get clean margins
- Consider neoadjuvant chemotherapy if tumor is large compared to the breast and the patient desires BCS

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Background

The goal of breast conserving therapy (BCT) for early breast cancer is to provide equivalent survival to more radical surgical treatments such as modified radical mastectomy while allowing patients to retain their own breast tissue. In 1985, Fisher et al. (1) published the first report of an American randomized controlled trial comparing mastectomy, lumpectomy followed by radiation, and lumpectomy alone for early breast cancer (stage I and II). In 2002, Fisher reported 20 years of follow-up of NSABP B-06 confirming that BCT offered equivalent survival to mastectomy, but the women who received BCT had a higher rate of in-breast local recurrence (2). One thousand eight hundred and fifty-one women with invasive breast cancers less than 4 cm were randomized to axillary dissection and either mastectomy, lumpectomy alone, or lumpectomy followed by radiation therapy. The tumors were excised with negative margins. The in-breast recurrence after lumpectomy alone was 39.2%. For patients who had lumpectomy followed by radiation therapy, in-breast recurrence was 14.3% ($P<0.001$). The risk of in-breast recurrence was lower for patients with tumor-free lymph nodes (negative nodes) than those with metastases to the nodes (positive nodes). Radiation therapy decreased the risk of in-breast recurrence in both groups (Table 32.1). Those patients who were treated with radiation therapy after lumpectomy had a nearly statistically significant survival advantage. The hazard ratio for survival was 0.87 (95% CI 0.75–1.01, $P=0.07$).

In 2002, Veronesi et al. (3) published 20 years of follow-up on 701 women randomized from 1973 to 1980 to either breast conservation or radical mastectomy. All of the women in this study had tumors less than 2 cm. After 1976, patients who had positive lymph nodes were treated with adjuvant chemotherapy which consisted of cyclophosphamide, methotrexate, and fluorouracil. No one in this study received tamoxifen. BCT included a quadrantectomy followed by radiation therapy including a boost to the scar. A quadrantectomy is removal of the tumor en bloc with a 2–3 cm cuff of normal tissue, the overlying skin, and the underlying pectoralis fascia. Quadrantectomy involves removal of a larger amount of breast tissue than the lumpectomy described in B-06. Among the women who received quadrantectomy followed by radiation therapy, 8.8% developed a local recurrence in the ipsilateral breast. The incidence of local recurrence after radical mastectomy was 2.3% ($P<0.001$). Even though the women who had BCT encountered local recurrence more frequently, there was no difference in the rate of death from breast cancer at 20 years

Table 32.1 Percent of patients with in-breast recurrence in B-06 at 20 years of follow-up (2)

	Lumpectomy alone (%)	Lumpectomy followed by radiation therapy (%)
Negative nodes	36.2	8.8
Positive nodes	44.2	17.0
<5 years	73.2	39.7
5–10 years	18.2	29.5
>10 years	8.6	30.8

All P values <0.001
Radiation therapy also delayed the time to in-breast recurrence

(BCT, 26.1%, and radical mastectomy, 24.3% ($P=0.8$)). There was also no difference in the rate of overall survival (BCT, 41.7%, and radical mastectomy, 41.2% ($P=1.0$)).

These two studies are cornerstones for the practice of breast conservation. The Veronesi study had a 8.8% local recurrence rate for patients treated with quadrantectomy followed by radiation therapy, vs. 14.3% for patients treated with lumpectomy followed by radiation therapy in the Fisher study. This may be accounted for by the earlier stage of the disease in the Veronesi study and there may be a contribution from the removal of more breast tissue. The Veronesi study was limited to tumors less than 2 cm and the incidence of negative nodes was only 74.2; 20.4% had 1–3 and 5.4% had four or more nodes. In the Fisher study, 62% had negative nodes, 26% had 1–3 and 12% had four or more nodes positive.

Current Technique of Breast Conserving Therapy with Lumpectomy

Local recurrence should be minimized through patient selection, sound surgical technique, careful margin analysis, and high-quality radiation therapy. Local recurrences are discouraging to patients and require additional operations (usually salvage mastectomy with or without immediate reconstruction). New data presented in the Oxford Overview in 2005 using metaanalysis statistical techniques suggests local recurrence may decrease survival (4). B-06 showed a trend toward improved survival after radiation therapy, but it was not statistically significant. In 1990, a National Cancer Institute Consensus Conference stated that BCT is the preferred primary treatment for most patients with Stage I or II breast cancer (5). The relative rates of BCT vs. mastectomy varied widely by geographic region both before and after the publication of results of randomized trials and consensus statements. Advocacy by women's groups has resulted in laws in some states requiring physicians to inform patients that early-stage breast cancer can be treated with mastectomy or BCT. After the implementation of these laws, BCT rates changed temporarily in the three cities studied, Detroit, Atlanta, and Hawaii, but reverted to prelegislation levels between 3 and 12 months after the laws went into effect (6). Many factors contribute to the decision of mastectomy vs. BCT and the goal to achieve successful treatment of breast cancer while maximizing cosmetic outcome and patient satisfaction and minimizing patient's fears, complications, local recurrence, and poor cosmetic outcomes.

How I do it
Preoperative wire localization for nonpalpable lesions
Incision over tumor
Point of maximum displacement of tip of wire
Need not excise tract or core biopsy site
Consideration for potential future mastectomy is less crucial
Remove tumor and surrounding tissue en bloc
Orient tumor and any additional margins
Specimen radiographs – compare with original mammograms
Separately submitted margins may facilitate assessment
Meticulous hemostasis
Close by mobilization of parenchyma and reapproximation

Patient selection for BCT is crucial to the success of the procedure. Most patients with Stage I and II invasive breast cancer are candidates for lumpectomy. Many patients with DCIS or EIC are also candidates for breast conservation as long as all of the disease can be removed with adequate margins. EIC is defined as 25% or more of the tumor with extension beyond the invasive component. EIC may present with nipple discharge or diffuse microcalcification, but there is often no indication of EIC preoperatively. Women with known EIC or diffuse suspicious microcalcifications have a higher risk of local recurrence (7). Voogd et al. showed that among 879 patients treated with breast conservation, 79 had local recurrence. Increased risk of local recurrence was associated with age less than 35 years and EIC. Women less than 35 years old had a hazard ratio of 9.24 (95% CI 3.74–22.81) compared to women over 60 years old. Women with EIC had a hazard ratio of 2.52 (95% CI 1.25–5.00) compared to women without EIC. Vascular invasion was associated with a higher risk of local recurrence in both BCT and mastectomy patients. As surgeons we can advise patients with an unacceptably high risk of local recurrence to consider mastectomy and we can diligently attend to obtaining negative margins. Among women with EIC, we can strive for margins greater than one centimeter (8). The patient should be the most important person in the decision-making process for breast conservation or mastectomy. Some women prefer the decreased chance of local recurrence offered by mastectomy to the smaller operation of lumpectomy.

To perform a successful lumpectomy, the tumor to breast size ratio must be small enough to allow the tumor to be removed with negative margins and the remaining breast to have an adequate cosmetic result. The tumor should be unifocal or additional foci confined to the same region of the breast. Local control is difficult to obtain when treating multiple primary tumors in one breast with more than one lumpectomy and is not routinely performed. Patients with biopsy-proven multicentric disease are probably better served with mastectomy. Evaluation for additional primary tumors should include bilateral mammograms, a careful physical exam, and ultrasound of any palpable masses. Preoperative MRI is expensive, but useful when additional suspicious lesions are identified and needle biopsied. Lehman et al. (9) identified unexpected contralateral breast cancers in 3.1% of patients (30/969) who underwent MRI upon diagnosis of breast cancer. Among these patients with unexpected disease, 20% had DCIS and 58% had infiltrating ductal carcinoma. MRI should be considered preoperatively on all patients who have dense breasts or who have tumors that were not apparent on mammogram and were detected by another means. Although preoperative MRI increases the biopsy rate, it is important to detect contralateral tumors or tumors that would change the operative plan from BCT to mastectomy. In another study by Berg et al. (10), 111 consecutive women with known or suspected breast cancer had clinical examination, mammography, ultrasonography, and MRI. Mammography sensitivity decreased from 100 to 45% in extremely dense breasts. Mammography detected 81% of infiltrating ductal carcinomas, but only 34% of invasive lobular carcinomas. MRI showed higher sensitivity than mammography for all invasive tumor types ($P < 0.01$). For 96 individual breasts of the women in the study, the surgical plan was altered for 30 when additional tumors were discovered by MRI. Of these patients, the extent of disease was overestimated in 21% by MRI. MRI findings of a moderately suspicious nature or a BIRADS 3 classification have the potential to frighten a patient and influence her to undergo mastectomy when she is an otherwise good candidate for BCT.

All suspicious imaging findings should be needle biopsied and proven to be benign or malignant. When searching for additional primary tumors with MRI prior to definitive resection, it is important to have the capacity to perform MRI-guided biopsy if the abnormalities are not apparent on other imaging modalities. The indications for preoperative MRI to determine the extent of the disease and to search for additional primaries are still evolving; at this time, not every patient requires a preoperative MRI because of the risk of overestimating the extent of the disease. However, in women with dense breasts or those in whom the tumor was not apparent on mammogram, MRI is a reasonable addition to preoperative diagnostic studies.

A patient considering BCT must also be able to undergo radiation therapy. Lumpectomy without radiation therapy has an unacceptably high incidence of local recurrence (39%) (2). Some of the most common contraindications for radiation therapy are pregnancy, connective tissue disorders with significant vasculitis (lupus, scleroderma, etc.), significant preexisting lung disease with compromised diffusion capacity, cardiomyopathy, pulmonary tuberculosis, previous radiation treatment of an area, and physical disabilities that prevent a patient from lying on her back and abducting the arm on the side of the tumor (11). Radiation therapy is expensive, often more expensive than mastectomy. Financial limitations may prevent some patients from obtaining radiation therapy. These patients should be treated with mastectomy. Not all areas of the country offer access to radiation therapy. Limitations of time off work and travel arrangements may also prevent some patients from receiving complete BCT. A patient's social and economic situation must be assessed when embarking on BCT.

Some patients who are not candidates for standard external beam radiation therapy may be able to undergo accelerated partial breast radiation therapy (APBI). There are at least three forms of APBI including: intraoperative radiation therapy (IORT) which is completed in 1 day, intracavitary balloon brachytherapy (MammoSite®) which is completed in 5 days and 3D Conformal/external beam radiation therapy which is also completed in 5 days. These techniques are emerging and show promise, but data beyond 5 years is not yet available.

The presence of axillary nodal metastases and/or breast implants are not contraindications to breast conservation. Inflammatory breast cancer is a contraindication to breast conservation. Pregnant patients in the first or second trimester of pregnancy cannot undergo radiation, but patients in the third trimester may. Successful BCT with removal of the nipple-areola complex for tumors that are immediately adjacent to these structures is possible (12).

The extent of DCIS is often more difficult to determine than the extent of invasive breast cancer. This is because of the branching pattern of growth along the breast ducts. DCIS is often represented by calcifications, but it is not uncommon for the disease to extend beyond the area of calcifications. MRI is not as effective in determining the extent of DCIS as it is for invasive cancers. This is because MRI abnormalities are demonstrated by increased vascularity of tumors. Because DCIS does not invade the basement membrane of the ducts, there is much less stromal response and neovascularity. DCIS usually grows in a radial pattern and extends toward the nipple. This growth pattern must be considered to achieve adequate margins.

Guidewires placed by a radiologist preoperatively allow surgeons to identify lesions that are not palpable. Guidewires may be placed using mammographic or ultrasound

localization. Once the guidewire is in place, the exact location of the tip can be determined using postwire placement mammograms as well as palpation of the breast skin for the "point of maximal displacement" of the guidewire. Although inexact, these techniques help to identify the direction of the wire under the skin which allows better incision placement. A titanium clip placed at the time of image-guided needle biopsy is often targeted with the guidewire. A rigid needle such as a Homer needle may make locating the tip easier. It is not necessary to excise the skin at the entry site or along the tract of the guidewire, or an old core biopsy site. A radiograph of the specimen should be obtained as soon as the tissue is removed. The image should be compared with the initial mammograms to verify removal of the tissue of interest and the entire guidewire. The radiologist reviews the films and places a needle into the tumor to guide the pathologist.

Incision selection considerations include: Might this patient need a mastectomy in the future? Will this incision be readily incorporated into a mastectomy incision? Historically, many surgical texts recommended that all lumpectomy incisions be placed into an elliptical zone surrounding the nipple-areola complex so that a mastectomy could be performed in the future. This is not absolutely necessary. Inframammary incisions are cosmetically appealing because the natural ptosis of the breast hides the incision. Periareolar incisions are also cosmetically satisfactory. Making an incision directly over tumor without tunneling allows easy access to a tumor and makes margins easier to re-excise if necessary. Curvilinear incisions along Langer's lines are recommended for cosmetically favorable scars. Skin should be removed when there is an unavoidable indentation due to lack of underlying breast parenchyma or when the tumor is so superficial that the skin is at risk for involvement or actually invaded by tumor.

Once the specimen has been removed, it should be *oriented* so that the margins can be accurately assessed and described by the pathologist. Inaccurately labeled specimens may result in misleading information that puts the patient at risk for residual positive margins. Attention to detail and clear communication with all members of the team handling the specimen and transcribing information are crucial. Careful hemostasis should be obtained at the end of the procedure; a large hematoma can make follow-up examination and imaging more difficult.

Accurate margins of a lumpectomy are easiest for a pathologist to assess when the specimen is removed in one piece. Fragmented lumpectomies can lead to margins that appear positive to the pathologist because the tumor has been transected. Additional specimens should be labeled so that the pathologist can understand the in vivo configuration of the tissue. Good communication between the surgeon and pathologist can spare the patient an unnecessary re-excision. Separately submitted marginal biopsies of the six cardinal points (medial, lateral, superior, inferior, anterior, and posterior) of the lumpectomy cavity may guide the pathologist's attention. Clips should be placed into the lumpectomy cavity to facilitate radiation therapy, boost site placement, and mammographic follow-up. Clips are not placed if accelerated partial breast irradiation (APBI) is to be performed with a balloon catheter delivery system such as the one available from MammoSite, because the clips may rupture the balloon. MammoSite is an APBI system with promising 5-year follow-up data. Longer follow-up is necessary before it can be incorporated into the standard of care for BCT.

Oncoplastic surgical planning and closure uses the techniques developed in plastic surgery to optimize cosmetic outcomes for BCT. Specifically, tissue flap mobilization may

be used to avoid skin indentation, nipple-areola complex depression, disruption of lower pole curvature, and persistent asymmetry. Parenchymal flaps are mobilized off the pectoralis and/or the skin and sutured together to provide durable substance to the breast.

Patients with *positive margins* should undergo re-excision until the margins are negative. If margins are persistently positive for residual tumor, a mastectomy should be performed. The optimal minimal margin width is unclear. Wider margins appear to have lower rates of local recurrence and this is especially true for DCIS. NSABP studies did not require specific margin widths other than "nontransected." Veronesi's margins obtained with quadrantectomy had 2–3 cm of normal tissue removed from around the primary. Veronesi et al. (3) reported a local recurrence rate of 8.8% at 20 years; this was lower than 14.3% reported by Fisher at 20 years (2). Determination of the exact location of the residual tumor depends on communication and understanding between surgeon and pathologist. Re-excised margins must be carefully labeled to convey the exact location from which they were taken.

Pitfalls and Complications
Failure to give postoperative radiation therapy is associated with increased risk of local recurrence
EIC is associated with an increased local recurrence rate (strive for margins >1 cm or consider mastectomy)
Biopsy-proven multicentric disease is probably best served by mastectomy

Neoadjuvant chemotherapy can be used to shrink locally advanced (stage IIB or above) tumors and increase the likelihood of successful BCT. Negative margins are still important for successful local control with BCT. Singletary et al. (13) performed the initial feasibility study on BCT after neoadjuvant chemotherapy. In this study 143 patients with stage IIB, IIIA, or IIIB breast cancer were treated with three cycles of preoperative vincristine, doxorubicin, cyclophosphamide, and prednisone. All patients underwent mastectomy and 33 (23%) were found to have tumors small enough to allow for breast conservation. Of these patients, the tumors decreased in size from a median of 5 cm to a median of 1 cm. Forty-two percent had no residual tumor and 45% had negative nodes. For patients with larger tumors, neoadjuvant chemotherapy may allow for BCT. A metal marker should be placed into the tumor before initiating chemotherapy to facilitate resection after clinical disappearance of the tumor. Axillary staging recommendations for these patients are still evolving, but SNB prior to beginning chemotherapy is probably optimal.

Conclusions

BCT has stood the test of time as an alternative to mastectomy. BCT should be offered to all eligible women. Small survival benefits from the prevention of local recurrence with mastectomy or radiation therapy remain unproven at this time and should not prevent surgeons from performing high-quality BCT.

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