Whole Breast Radiotherapy

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Key Concepts

- Postlumpectomy radiation therapy significantly decreases risk of recurrence and may improve long-term survival
- Contraindications:
  - Multicentric tumors (more than one quadrant of the breast)
  - Tumors associated with diffuse suspicious calcifications on mammography
  - Inability to attain clean margins after multiple resections
  - Pregnancy
  - Scleroderma
  - Previous history of high-dose irradiation of the breast area
- Radiation therapy is generally given after any needed chemotherapy is completed
- No consensus about sequencing with hormonal therapy
- Typical dose is 45–50 Gy delivered over 4.5–5 weeks
  - Boost of 10–16 Gy to tumor bed over 1–1.5 weeks
- Shorter dose schedules are sometimes used in elderly women to minimize need for travel
- Side effects:
  - Early – breast swelling and tenderness, mild redness of skin, dry or moist desquamation in skin folds
  - Late – thickening (fibrosis) of breast tissue, rib fracture, tenderness or swelling of breast, residual hyperpigmentation of skin

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Background

Since the 1970s, there have been six randomized trials comparing breast-conserving therapy (lumpectomy followed by whole breast radiotherapy) to mastectomy for early-stage invasive breast cancer. Each study demonstrated no significant differences in disease-free survival or overall survival between the two treatments (1–6). Although no randomized trial of breast-conserving therapy vs. mastectomy has been performed specifically in patients with ductal carcinoma in situ (DCIS), a small percentage of the patients enrolled in the National Surgical Adjuvant Breast and Bowel Project B-06 trial (5) were later found to have had DCIS, and in this subgroup, the overall survival rates were equivalent between the patients treated with breast-conserving therapy and those treated with total mastectomy (7). Several additional studies have demonstrated excellent survival rates with breast-conserving therapy in patients with DCIS, similar to rates previously reported in patients with DCIS treated with total mastectomy. Therefore, breast-conserving surgery followed by radiotherapy has become the treatment of choice for patients with stage 0, I, or II breast cancer (Tis, T1, T2).

Several trials have evaluated whether radiotherapy is necessary after breast-conserving surgery. In the National Surgical Adjuvant Breast and Bowel Project B-06 trial, the 20-year cumulative incidence of recurrence in the ipsilateral breast after lumpectomy alone was 39.2%, compared with 14.3% after lumpectomy followed by radiotherapy ($p < 0.001$) (6). The Early Breast Cancer Trialists' Collaborative Group's most recent meta-analysis included 7,311 women treated in randomized clinical studies comparing breast-conserving surgery with or without radiotherapy. Among the node-negative patients, the 10-year rate of ipsilateral breast cancer recurrence was 29% in patients treated with lumpectomy alone vs. 10% in those treated with lumpectomy followed by radiotherapy. Among the node-positive patients, the 10-year rate of ipsilateral breast cancer recurrence was 47% in patients treated with lumpectomy alone vs. 13% in those treated with lumpectomy followed by radiotherapy. Importantly, the decrease in breast cancer recurrence with radiotherapy resulted in a statistically significant decrease in the risk of death from breast cancer at 15 years. In the node-negative group, the breast cancer mortality rate was decreased from 31 to 26%, and in the node-positive group, the breast cancer mortality rate was decreased from 55 to 48% (8). These data not only show that radiotherapy significantly reduces the risk of recurrence after breast-conserving surgery, but also indicate that improved local control can lead to improved long-term survival in patients with breast cancer.

Candidates for Breast-Conserving Therapy

Historically, candidates for breast-conserving therapy have included patients with a primary tumor no larger than 4 cm and unicentric disease in whom a lumpectomy with negative margins will yield an acceptable cosmetic result. Previously, patients with retroareolar lesions that necessitated resection of the nipple-areolar complex to achieve negative margins were not offered breast-conserving therapy. However, the local control rates with

breast-conserving therapy in such patients are the same as those in patients with tumors in other locations of the breast, and therefore, retroareolar tumor location is no longer considered a contraindication to breast-conserving therapy. Patients with multifocal tumors (multiple foci within one quadrant of the breast) are also candidates for breast-conserving therapy if removal of the tumors will yield a lumpectomy cavity no larger than approximately 4 cm and an acceptable cosmetic result.

Contraindications to breast-conserving therapy can be either tumor-related or patient-related. Tumors that are multicentric (distinct lesions that involve more than one quadrant of the breast) or are associated with diffuse suspicious calcifications on mammography are considered contraindications to breast conservation. In addition, if a tumor cannot be removed with final negative margins after multiple surgical resections, mastectomy is necessary for optimal tumor control.

Patient-related contraindications to breast-conserving therapy include pregnancy, scleroderma, and previous history of high-dose irradiation of the breast area. Radiotherapy is contraindicated in pregnant patients because the out-of-field scattered radiation from the whole breast treatment can be teratogenic or lethal to the fetus or embryo, especially early in gestation (9). In patients with certain collagen vascular diseases, particularly scleroderma, there is a great deal of concern regarding severe late radiation-related side effects, such as breast fibrosis, pain, chest wall necrosis, and brachial plexopathy. Systemic scleroderma is an absolute contraindication to radiotherapy. Active systemic lupus erythematosus is considered a relative contraindication. However, treatment can be considered for patients with this disease who are very much motivated to preserve their breast; treatment is optimally delivered with the patient in the prone position if possible, to allow exclusion of the rib cage from the treated field while still ensuring coverage of the surgical bed and breast parenchyma. A history of rheumatoid arthritis is not a contraindication to radiotherapy, as no increase in the risk of adverse effects has been documented (10). Recently, it has been questioned whether any collagen vascular disease other than scleroderma increases the incidence of late radiation-related effects. In a double-matched, case-controlled analysis of 36 patients with documented collagen vascular disease, only scleroderma was found to be associated with an increased risk of severe complications after breast-conserving surgery and conventional radiotherapy to a total median dose of 64 Gy (11).

Age, race, family history of breast or ovarian cancer, *BRCA1* or *BRCA2* mutation status, histologic subtype, estrogen and progesterone receptor status, and Her-2/neu status do not influence the appropriateness of breast-conserving therapy. Although young age may increase the risk of local and distant metastatic recurrence after breast-conserving therapy, the same is true regarding the influence of young age on outcomes after mastectomy. Survival rates have been found to be similar for young patients (variably described as <35 or <40 years old) treated with breast-conserving therapy and young patients treated with mastectomy (12). Published data suggest that the rates of local recurrence in the breast after lumpectomy and radiotherapy do not differ by race. Retrospective studies concerning breast cancer patients with a positive family history of breast and/or ovarian cancer have shown that these patients have ipsilateral breast cancer recurrence rates after breast-conserving therapy similar to those of patients with no family history (13, 14).

In patients with a germline mutation of *BRCA1* or *BRCA2*, there have been conflicting results regarding the appropriateness of breast-conserving therapy. Pierce et al. (15) found,

in a comparison of 160 carriers of deleterious mutations vs. 445 matched controls, that there was no significant difference between the groups in ipsilateral breast cancer recurrence rates after breast-conserving therapy. A large number of the carriers had undergone bilateral oophorectomy. In the carriers who had not had their ovaries removed, the rate of breast cancer recurrence was higher than the rate in the controls (15). In another study, investigators from Yale (16) found that among patients 42 years of age or younger, the 12-year ipsilateral breast cancer recurrence rate after breast-conserving therapy was 49% in patients testing positive for a BRCA deleterious mutation vs. 21% in those testing negative for a mutation ($p=0.007$). As expected, contralateral breast cancer events were significantly more frequent in patients with BRCA mutations than in those without a mutation (42 vs. 9%, $p=0.001$) (16). Currently, breast-conserving therapy is considered an appropriate option for patients with known *BRCA1* or *BRCA2* mutations, particularly those patients who have undergone an oopherectomy.

Sequencing of Radiotherapy with Chemotherapy and Hormonal Therapy

In the past, it was often debated whether radiotherapy should precede or follow adjuvant chemotherapy after breast-conserving surgery. A randomized trial performed by the Joint Center for Radiation Therapy helped determine the now most common order of treatment: chemotherapy followed by radiotherapy. In the Joint Center for Radiation Therapy trial, 244 patients were randomly assigned, after surgery, to four cycles of doxorubicin-based chemotherapy followed by radiotherapy or radiotherapy followed by four cycles of the same doxorubicin-based chemotherapy. Initial results, published in 1996, demonstrated a lower rate of distant metastasis in the chemotherapy-first arm (17). However, with longer follow-up, there was no difference in distant metastasis rates between the two arms. Both the early results and results after longer-term follow-up showed that patients with close surgical margins, defined as ≤1 mm from tumor to inked edge, had an increased risk of local recurrence when chemotherapy was given first (18). Therefore, if chemotherapy is to be given first, reexcision is recommended in patients with a close margin.

The Cancer and Leukemia Group B conducted a trial that randomly assigned patients to four cycles of doxorubicin and cyclophosphamide followed by radiotherapy or four cycles of doxorubicin and cyclophosphamide and then four courses of paclitaxel followed by radiotherapy. The 5-year cumulative incidence of isolated local-regional recurrence was 3.7% in the patients who received eight cycles of chemotherapy vs. 9.7% in patients who received only four cycles of chemotherapy (19). These data support the safety of delivering an extended course of chemotherapy prior to radiotherapy.

Currently, there is no consensus regarding the sequencing of radiotherapy with hormonal therapy. More specifically, there are no randomized trials that have compared concurrent hormonal therapy and radiotherapy vs. radiotherapy followed by treatment with tamoxifen or an aromatase inhibitor. In theory, tamoxifen may arrest cells in the radioresistant phases of the cell cycle, which could result in decreased efficacy if tamoxifen were given concurrently with radiotherapy. In addition, the Southwest Oncology Group demonstrated an inferior outcome with concurrent tamoxifen plus chemotherapy vs. chemotherapy followed by tamoxifen (20). However, three retrospective studies have suggested no

difference in local or distant recurrence rates in patients who began taking tamoxifen during radiotherapy and those who began taking tamoxifen after the completion of radiotherapy (21–23).

Given the data available to date, if a patient with an estrogen-receptor-positive tumor is at relatively high risk for metastatic disease, it is reasonable to have her begin taking tamoxifen as soon as possible. For patients at lower risk, if they have not begun taking tamoxifen before starting radiotherapy, it is also reasonable to delay initiation of tamoxifen until radiotherapy is complete. Currently, there are no data available that address the sequencing of radiation with aromatase inhibitors.

Radiation Treatment

Simulation

The term "simulation" dates back prior to the use of computed tomography (CT)-based planning, to a time when the treatment fields for the patient were "simulated" or developed under fluoroscopic guidance. The ultimate goal of simulation is to develop a reproducible treatment plan encompassing the breast, surgical bed, surgical clips, and scar while minimizing the dose to normal structures, such as lung and heart.

Critical to successful radiotherapy, regardless of the site of disease, is reproducibility of the patient's treatment set-up from 1 day to the next. This is achieved by manufacturing a patient immobilization device known as a "cradle" that "cradles" the patient's upper body in the same treatment position each day (Fig. 67.1). The most commonly used position is a supine position with the patient's ipsilateral arm abducted and externally rotated above her head to avoid treatment of the arm by the tangential beams of radiation. If the patient has undergone axillary node dissection, it is important that she have regained the normal range of motion of her arm and shoulder. If she has not, arm exercises are recommended prior to simulation and treatment, and in some cases physical therapy is recommended to aid in the recovery. The custom cradle used to ensure the same patient positioning from day to day can be manufactured from any of several commercially available products. The patient lies back on the cradle, and a permanent impression is formed of the patient's head, shoulders, and abducted arm.

The cradle is placed on an "angle board" to allow the patient to be semireclined during treatment. The angle board is set at a specific level, such as 10°, to ensure reproducibility of the daily set-up and to minimize skin reactions. A semireclined position tends to be more comfortable for the patient, minimizing the chance of patient movement. The angle also helps compensate for the slope of the chest wall.

It is important to minimize breast and skin folds, such as in the inframammary region. Doing so reduces the risk of moist desquamation, since the presence of skin folds reduces the skin-sparing effect of the photon beam. Some patients are treated in the prone position, for this reason. The prone technique is described in more detail later in this chapter.

Once patient set-up has been optimized, CT images are acquired with the patient in the treatment position. With the prevalence of large-bore CT simulators, CT images can be obtained through the targeted breast with margin in the same treatment position.

Laser set-up marks are drawn on the patient at the time of simulation to aid in the patient set-up on the treatment machine. The CT images are then transferred to the three-dimensional planning computer, where the actual virtual simulation of the radiation treatment fields can begin. With computer-based virtual simulation, unlike with conventional fluoroscopic simulation, the patient does not need to be present during the design of the radiation fields. Treatment can be planned in a dosimetry workroom with the physician, dosimetrist, and physics team working together, with no need for the patient to lie still for prolonged periods with her arm abducted and rotated above her head in the treatment position, as was necessary with conventional fluoroscopic simulation. In addition, CT imaging allows three-dimensional planning of the whole breast irradiation (Fig. 67.1).

Treatment Planning

Using the three-dimensional planning computer, one can start with the traditional field borders outlined for whole breast radiotherapy and then modify these fields as needed to optimize coverage of the surgical resection bed and the rest of the breast while minimizing the dose to the cardiac and pulmonary structures. The proposed borders of the treatment fields start out at the midaxillary line laterally, the mid sternum medially, just below the clavicular head superiorly, and approximately 2 cm inferior to the inframammary fold

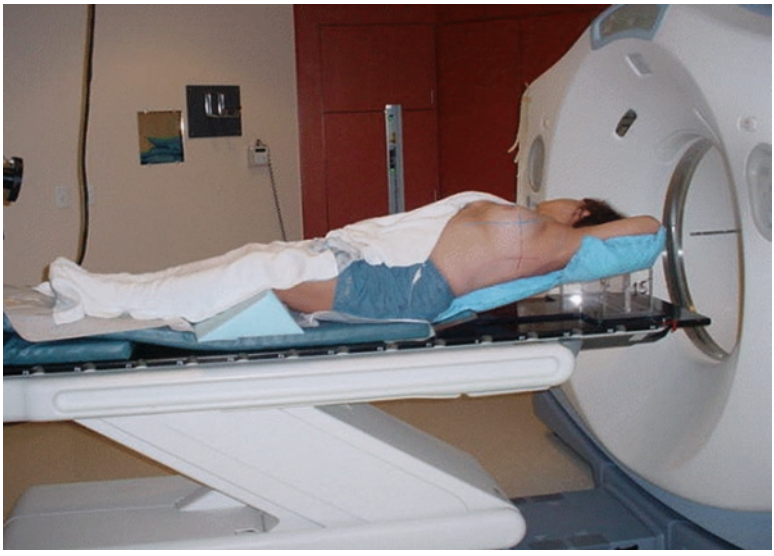

Fig. 67.1 Simulation. The patient is lying in the treatment position with her arm abducted and rotated above her head in a custom-designed cradle that will be used to reproduce the same treatment position each day. A 15-degree angle board was utilized to optimize both breast positioning and patient comfort. A computed tomography scan was obtained for treatment planning while the patient was in this position

inferiorly to cover the whole breast. To limit skin reactions in the axillary area, the superior border can be modified to insure coverage of the entire breast while minimizing the volume of superficial axillary tissue that is irradiated.

On the digitally reconstructed radiograph of the treatment fields, one can evaluate the volume of lung in the field as well as the distance from the surgical bed or surgical clips to the block edge. In general, there should be approximately 1.0–2.0 cm of lung tissue between the rib cage and the posterior field edge on the digitally reconstructed radiograph. Historically, Radiation Therapy Oncology Group protocols have allowed up to 3.0 cm in the field and have not resulted in undue pulmonary toxicity. In addition, one can confirm on the digitally reconstructed radiograph a minimum margin of at least 1.5 cm around the surgical bed or surgical clips marking the lumpectomy site. This margin allows for coverage of potential microscopic tumor spread, errors in outlining of the surgical bed, daily set-up error, and patient breathing motion during treatment while still ensuring coverage of the targeted areas. The surgical clips placed by the surgeon at the time of resection of the tumor to demarcate the boundaries of the surgical cavity greatly aid in identification of the target volume, especially at the time of boost planning (Fig. 67.2a, b). Boost planning is discussed in greater detail later in this section. The posterior field edge of each tangential beam is planned so that the posterior field edge has matched divergence to minimize exit dose into the lung parenchyma (Fig. 67.2c). If the fields were planned directly opposite (180° apart) to each other, a greater volume of lung would receive radiation dose. Matching the deep edge of each tangent ensures that the same volume of lung parenchyma is included in each field and no addition lung tissue is included.

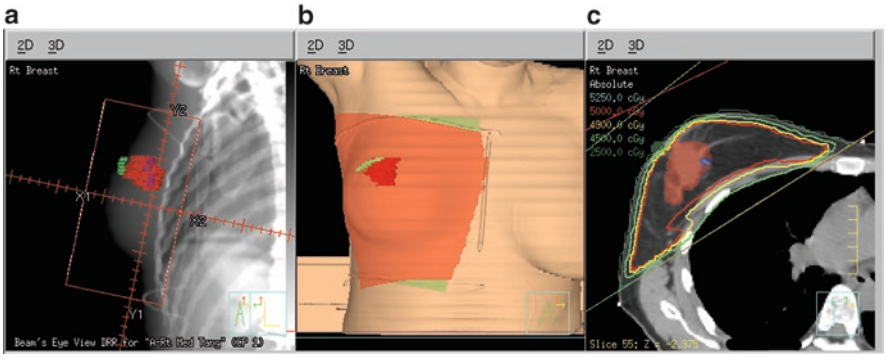

Fig. 67.2 Field boundaries for a 41-year-old woman with a pT1b, N0 (sn), M0 estrogen- and progesterone-receptor-positive invasive ductal carcinoma of the right breast who underwent lumpectomy and sentinel node biopsy and was receiving tamoxifen. Postoperative whole breast radiotherapy was planned to complete breast-conserving therapy. (**a**) Medial tangent digitally reconstructed radiograph with the tumor bed and surgical clips demarcated and at least a 1.5-cm margin around the tumor bed and surgical clips posteriorly with approximately 1.5–2.0 cm of lung in the field. (**b**) Skin rendering of the medial and lateral tangential beams demonstrating the standard field boundaries (the midaxillary line laterally, the mid sternum medially, just below the clavicular head superiorly, and approximately 2 cm below the inframammary fold inferiorly). (**c**) Axial view of the treatment plan demonstrates the coplanar posterior field edges used to minimize exit dose into the lung parenchyma

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With the advent of three-dimensional CT-based treatment planning, it is now possible to evaluate the dose deposited in every area of the breast, rather than in a single plane at the midlevel of the breast, as was the case in the era of two-dimensional treatment planning. In addition, dose calculations now take into account the heterogeneity of the various tissues included within the treatment field, such as breast parenchyma, bone, and lung.

At The University of Texas M. D. Anderson Cancer Center, the "field-in-field" technique is utilized for breast treatment planning. This technique provides greater dose homogeneity in all three dimensions of the breast, which in turn allows better coverage of the areas that need to be treated – the breast and lumpectomy cavity. It can help minimize acute and long-term side effects of radiotherapy, including moist desquamation of the skin, breast fibrosis, and rib fractures. The technique starts out with an open tangential beam arrangement. Then, sequentially, dose clouds of high-dose volumes (115, 110, 105%) are blocked with custom multileaf collimation, generating smaller segments within the main medial and lateral tangent open fields. These smaller field segments can be delivered as individual fields or as part of the original fields with a step-and-shoot technique (Fig. 67.3).

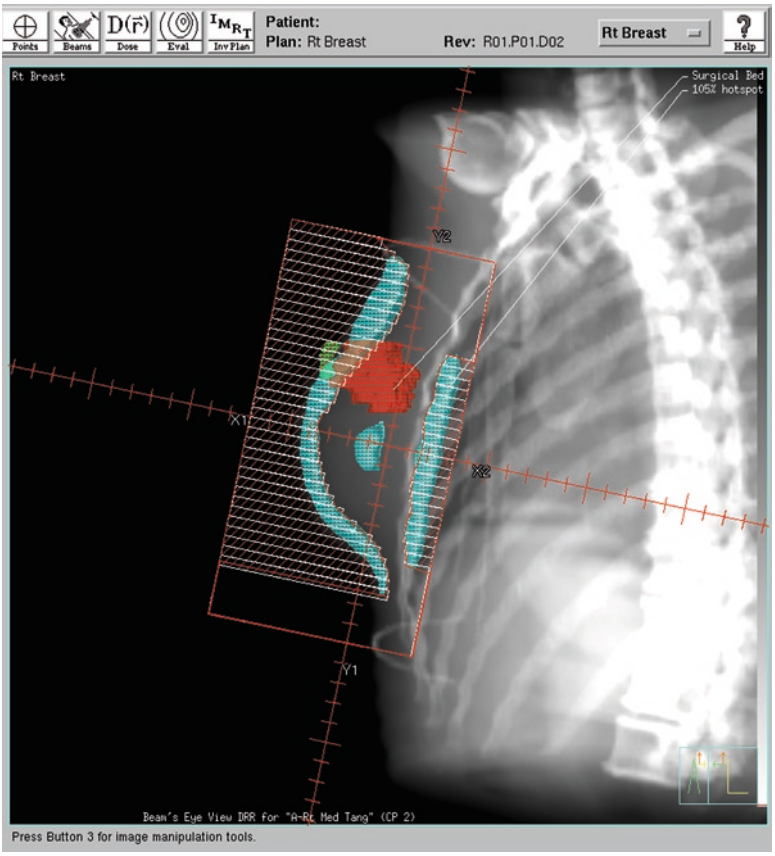

Fig. 67.3 Digitally reconstructed radiograph demonstrating blocking of the 105% dose cloud as part of the step-and-shoot treatment planning for the patient as shown in Fig. 67.2

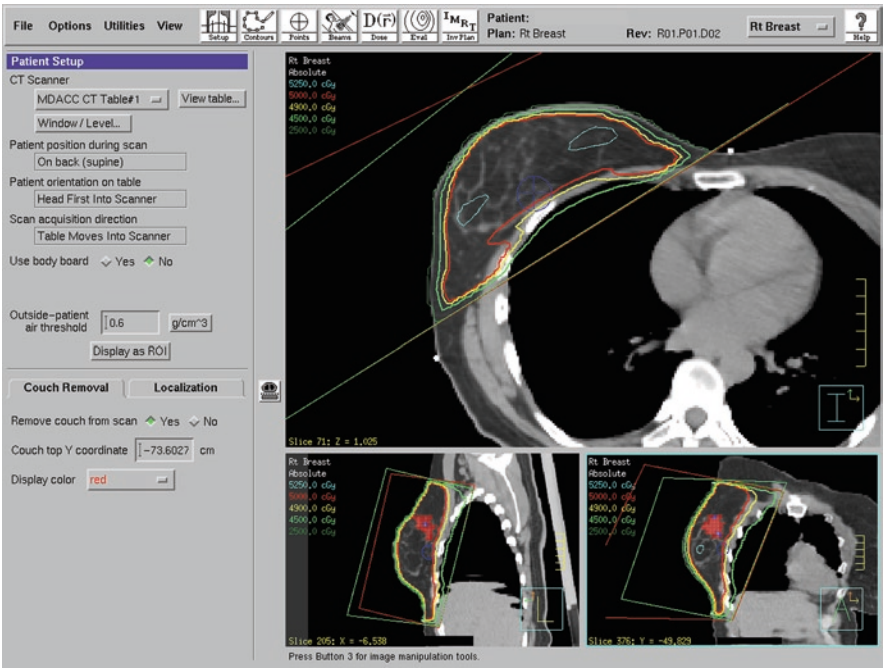

Fig. 67.4 Axial, sagittal, and coronal views of the treatment plan of the patient is shown in Fig. 67.2. Note the homogenous dose distribution throughout the breast, with excellent coverage of the tumor bed by the prescription line of 5,000 cGy

By delivering a percentage of the overall planned dose each day with these fields within the main open field, one can deliver a more homogeneous dose throughout the breast than was previously possible with two-dimensional wedge techniques (Fig. 67.4). Another advantage of this technique is that the dose delivered to the contralateral breast with the field-in-field technique is less than the dose delivered with a wedge technique (24). There are several similar methods used at different institutions around the United States. The forward-planned field-in-field breast intensity-modulated radiation therapy (IMRT) technique that is described above, a forward-planned step-and-shoot breast IMRT method, and an inversely planned breast IMRT technique all can improve dose homogeneity over a conventional wedge technique.

It is important that techniques also minimize the risk of long-term potential cardiac effects from radiation. In the case of left-sided tumors, the anterior lateral aspect of the heart, including the left anterior descending artery, closely approximate the posterior borders of traditional tangent radiotherapy fields. Changing the gantry angle, collimator angle, or medial or lateral treatment borders can often result in coverage of the segmental resection site and breast while excluding the heart from the treatment fields. In other cases, small cardiac blocks can be placed to avoid cardiac irradiation. All of this can be customized to the individual normal tissue anatomy of the patient, the location of the surgical bed, and the breast contour (Fig. 67.5). In addition, in cases where the tumor bed closely approximates the heart, the planning and delivery of treatment can be delivered during a

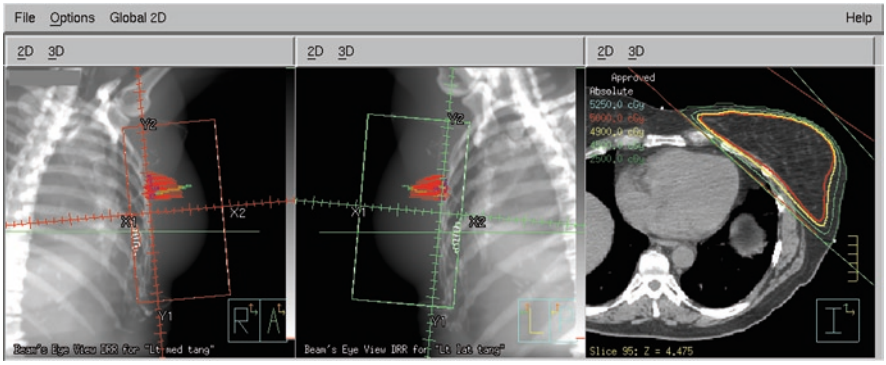

Fig. 67.5 Field boundaries for a 56-year-old woman with a pT1b, N0 (sn)(i-), M0 invasive ductal carcinoma of the left breast who underwent lumpectomy. A cardiac block was placed on both the medial and lateral tangent fields to block the heart out of the field while still allowing good coverage of the surgical bed and clips. The axial view is at the level of the cardiac block, as shown in the medial and lateral digitally reconstructed radiograph views

deep inspiratory phase of the respiratory cycle, which displaces the heart in an inferiomedial direction away from the treatment fields.

For patients with large breasts, the prone position may be used. This approach is especially important when the breast rests on the abdominal wall when the patient is in the traditional supine treatment position. A commercially available prone breast positioning board is used to elevate the entire body off the treatment table. This board has an aperture to allow the breast to be suspended above the linear accelerator treatment table. The contralateral breast rests on a custom-designed region of the prone breast board that maximizes patient comfort and avoids treatment of that breast. The prone treatment position eliminates skin folds in the breast, such as the inframammary fold.

The prone treatment position is also useful when the location of the heart in relation to the surgical bed in the supine position is such that if the heart is to be excluded from the field, a portion of the surgical bed will be too. Placing the patient in the prone position allows the surgical bed to fall farther away from the rib cage, increasing the distance from the cardiac structures to the lumpectomy site. This ensures coverage of surgical bed and the breast while preventing treatment of the heart (Fig. 67.6). It should be noted, however, that if surgery included removal of the pectoral fascia, the prone position is unlikely to increase the distance between the heart and the chest wall.

After completion of whole breast irradiation delivered over a course of approximately 5 weeks, a “boost” is generally delivered to the surgical bed and scar. The purpose of the boost is to deliver additional radiation to the area at highest risk of harboring microscopic residual disease – the surgical bed and immediately surrounding breast parenchyma. Multiple studies have demonstrated this area to be at highest risk for recurrence in the breast. The boost is generally given over a week to a week and a half. Electrons are typically utilized for the boost. The advantage of electrons is that they have a finite range. The higher the energy of electrons, the greater the distance in tissue they travel and the

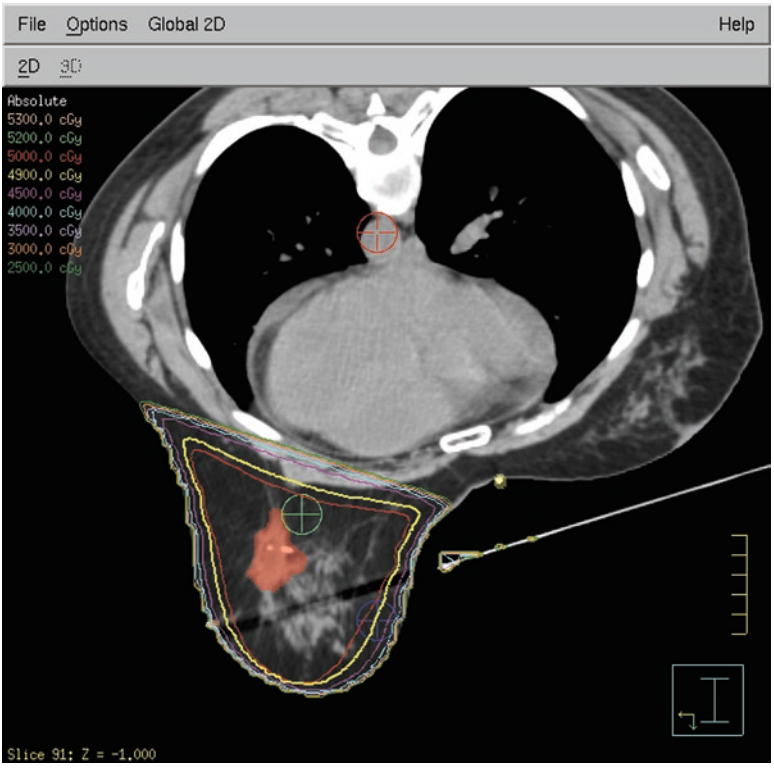

Fig. 67.6 Field boundaries for a 48-year-old woman with a pT1c, N0 (sn)(i-), M0 invasive ductal carcinoma of the left breast who underwent lumpectomy. The prone position allowed the surgical bed to fall a greater distance from the cardiac silhouette. There is good coverage of the isodose curves of the surgical bed, the surgical clips, and the rest of the breast without inclusion of the heart. Avoidance of the heart would have been more difficult to achieve in the supine position given the significant length of heart that abuts the rib cage underlying the breast. Given the patient's larger breast size, the prone position minimized skin folding. In addition, the prone position allowed a more homogeneous dose distribution throughout the breast by reducing the separation between the two tangential beams

higher the surface (skin) dose they deliver. Electrons travel a greater distance through lower-density tissue such as lung. Therefore, the goal is to choose an electron energy that results in deposition of at least 90% of the prescribed dose just distal to the surgical bed or clips. This minimizes the dose to normal breast tissue and lung tissue. In some cases, the surgical bed is too deep in the breast tissue to be reached by the highest-energy electrons. In some such cases, this problem can be solved if the treatment position is changed for the boost such that the distance from the surface of the breast to the deepest position of the surgical bed is reduced and the surface of the breast overlying the surgical bed is flattened (for example, see Fig. 67.7).

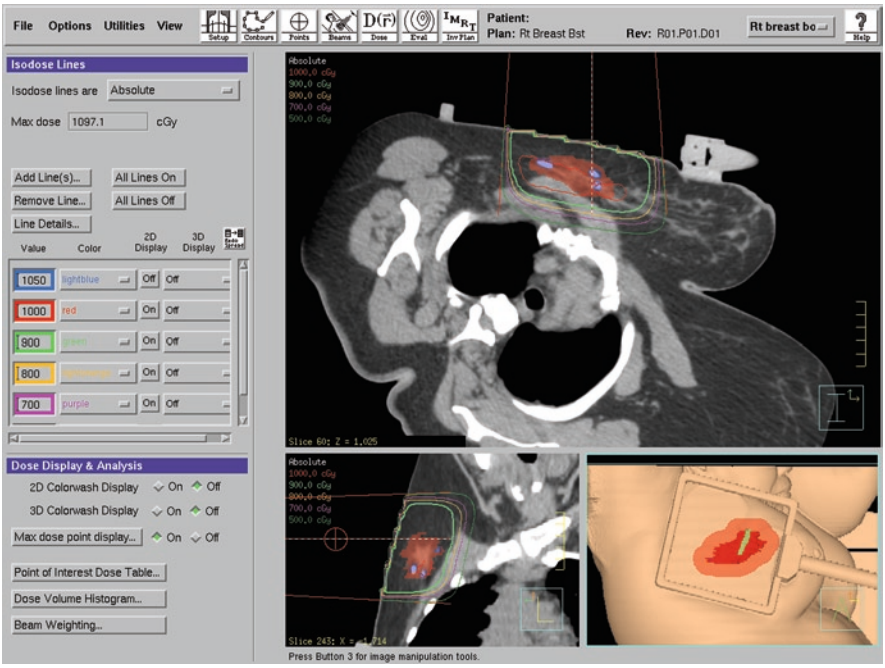

Fig. 67.7 Boost treatment plan for a patient whose surgical bed was located too deep in the breast to be reached by the highest-energy electrons in her original treatment position. Axial, sagittal, and three-dimensional rendering of the boost field after the patient had been treated with 50 Gy of whole breast radiotherapy delivered in 25 fractions. A boost of 10 Gy in 5 fractions was planned. The patient was placed in the left lateral decubitus position with her arm abducted over her head. A new custom-designed cradle was manufactured to reproduce this treatment position each day. This position facilitated flattening of the breast overlying the surgical bed. A breast compression device was then placed over the surgical bed and scar. A second CT simulation was necessary to design this set-up and obtain CT images of the breast in this position. The surgical bed, surgical clips, and scar were then outlined on the planning computer. A custom-designed electron-beam cutout was then manufactured that encompassed the surgical bed, surgical clips, and scar with a 2-cm margin utilizing 16-MeV electrons. This resulted in excellent coverage of the surgical bed while minimizing exit dose into the deeper tissues of the breast and lung. The lower electron energy also reduced the skin dose

Treatment

Standard whole breast radiotherapy consists of a total dose of 45–50 Gy delivered at 1.8–2 Gy per fraction over 4.5–5 weeks. It is followed by a boost dose to the surgical bed and scar of an additional 10–16 Gy delivered at 2 Gy per fraction over 1–1.5 weeks. Total treatment time is 6–6.5 weeks. Shorter fractionation schedules (so-called hypofractionated dose schedules) are sometimes used for elderly women felt to be at relatively lower risk for breast recurrence who live far from the radiotherapy facility or face other obstacles that

make it difficult to come to the facility for daily treatments for an extended period of time. However, there is a concern that with long-term follow-up, the larger doses per day used in hypofractionated dose schedules will lead to increased fibrosis in the breast and poorer cosmetic outcomes. Therefore, such schedules are generally not used in patients with longer life expectancies.

Each treatment lasts less than 15 min, including the time it takes the patient to change into the treatment gown, the treatment setup, the actual radiation treatment, and the time it takes the patient to change back into street clothing.

Side Effects

During the first 2 weeks of treatment, side effects typically include minor breast swelling or tenderness. Some patients complain of occasional sharp, shooting pains in the breast lasting only a few seconds. These are most likely due to breast swelling. Mild redness or hyperpigmentation of the treated breast skin generally begins in the third week of treatment. By the completion of treatment, there may be only mild to moderate erythema or hyperpigmentation of the skin with some itchiness due to dryness. In other patients, small areas of dry or moist desquamation in skin folds, such as the inframammary fold or folds in the low axilla may occur. On occasion, mild folliculitis develops in the upper inner quadrant of the breast in patients with years of previous sun exposure. Various prescription and nonprescription skin care products are available to treat radiation dermatitis and can be used to make these side effects more tolerable and reduce the risk of infection. However, treatment is usually well tolerated overall.

Late effects can include thickening of the breast tissue (fibrosis), rib fracture, tenderness of the breast or chest wall, breast swelling, and residual hyperpigmentation of the skin. All of these side effects are mild or of low risk. It is expected that with the more sophisticated, CT-based treatment planning current in use, the incidence and severity of both acute and late effects will be reduced.

Future Directions

Breast-conserving therapy has become preferred over mastectomy for early-stage breast cancer. With the immense progress that has been made in treatment planning software over the past 10 years, a great deal of research has addressed how to further improve the therapeutic ratio. Future advances will most likely include improvements in treatment positioning, four-dimensional simulation and treatment that accounts for respiratory and cardiac motion in relation to the targeted tissue, and on-board imaging (CT imaging on the treatment machine) during daily treatments. In addition, there is an ongoing phase III randomized trial comparing standard whole breast radiotherapy to partial breast irradiation for early-stage breast cancer. This trial will compare efficacy, side effects, and quality-of-life outcomes between the two treatment arms.

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References

1. Arriagada R, Le MG, Guinebretiere JM, Dunant A, Rochard F, Tursz T. Late local recurrences in a randomised trial comparing conservative treatment with total mastectomy in early breast cancer patients. Ann Oncol. 2003;14(11):1617–22.
2. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med. 2002;347(16):1227–32.
3. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2002;347(16):1233–41.
4. Poggi MM, Danforth DN, Sciuto LC, et al. Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy: the National Cancer Institute Randomized Trial. Cancer. 2003;98(4):697–702.
5. van Dongen JA, Voogd AC, Fentiman IS, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. J Natl Cancer Inst. 2000;92(14):1143–50.
6. Blichert-Toft M, Rose C, Andersen JA, et al. Danish randomized trial comparing breast conservation therapy with mastectomy: six years of life-table analysis. Danish Breast Cancer Cooperative Group. J Natl Cancer Inst Monogr. 1992;11:19–25.
7. Fisher ER, Leeming R, Anderson S, Redmond C, Fisher B. Conservative management of intraductal carcinoma (DCIS) of the breast. Collaborating NSABP investigators. J Surg Oncol Jul. 1991;47(3):139–47.
8. Clarke M, Collins R, Darby S, et al. Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet. 2005;366(9503):2087–106.
9. Stovall M, Blackwell CR, Cundiff J, et al. Fetal dose from radiotherapy with photon beams: report of AAPM Radiation Therapy Committee Task Group No. 36. Med Phys. 1995; 22(1):63–82.
10. Morris MM, Powell SN. Irradiation in the setting of collagen vascular disease: acute and late complications. J Clin Oncol. 1997;15(7):2728–35.
11. Chen AM, Obedian E, Haffty BG. Breast-conserving therapy in the setting of collagen vascular disease. Cancer J. 2001;7(6):480–91.
12. Zhou P, Recht A. Young age and outcome for women with early-stage invasive breast carcinoma. Cancer. 2004;101(6):1264–74.
13. Chabner E, Nixon A, Gelman R, et al. Family history and treatment outcome in young women after breast-conserving surgery and radiation therapy for early-stage breast cancer. J Clin Oncol. 1998;16(6):2045–51.
14. Haas JA, Schultz DJ, Peterson ME, Solin LJ. An analysis of age and family history on outcome after breast-conservation treatment: the University of Pennsylvania experience. Cancer J Sci. 1998;4(5):308–15.
15. Pierce LJ, Levin AM, Rebbeck TR, et al. Ten-year multi-institutional results of breast-conserving surgery and radiotherapy in BRCA1/2-associated stage I/II breast cancer. J Clin Oncol. 2006;24(16):2437–43.
16. Haffty BG, Harrold E, Khan AJ, et al. Outcome of conservatively managed early-onset breast cancer by BRCA1/2 status. Lancet. 2002;359(9316):1471–7.
17. Recht A, Come SE, Henderson IC, et al. The sequencing of chemotherapy and radiation therapy after conservative surgery for early-stage breast cancer. N Engl J Med. 1996; 334(21):1356–61.

18. Bellon JR, Come SE, Gelman RS, et al. Sequencing of chemotherapy and radiation therapy in early-stage breast cancer: updated results of a prospective randomized trial. J Clin Oncol. 2005;23(9):1934–40.
19. Sartor CI, Peterson BL, Woolf S, et al. Effect of addition of adjuvant paclitaxel on radiotherapy delivery and locoregional control of node-positive breast cancer: cancer and leukemia group B 9344. J Clin Oncol. 2005;23(1):30–40.
20. Albain K. Concurrent CAFT versus sequential CAF-T chemohormonal therapy (cyclophosphamide, doxorubicin, 5-fluorouracil, tamoxifen) versus T alone for postmenopausal , node-positive, estrogen (ER) and/or progesterone (PgR) receptor-positive breast cancer: mature outcomes and new biologic correlates on phase III intergroup trial 0100 (SWOG-8814). Breast Cancer Res Treat. 2005;89 Suppl 1:Abstract 37.
21. Pierce LJ, Hutchins LF, Green SR, et al. Sequencing of tamoxifen and radiotherapy after breast-conserving surgery in early-stage breast cancer. J Clin Oncol. 2005;23(1):24–9.
22. Ahn PH, Vu HT, Lannin D, et al. Sequence of radiotherapy with tamoxifen in conservatively managed breast cancer does not affect local relapse rates. J Clin Oncol. 2005;23(1):17–23.
23. Harris EE, Christensen VJ, Hwang WT, Fox K, Solin LJ. Impact of concurrent versus sequential tamoxifen with radiation therapy in early-stage breast cancer patients undergoing breast conservation treatment. J Clin Oncol. 2005;23(1):11–6.
24. Borghero YO, Salehpour M, McNeese MD, et al. Multileaf field-in-field forward-planned intensity-modulated dose compensation for whole-breast irradiation is associated with reduced contralateral breast dose: a phantom model comparison. Radiother Oncol. 2007;82(3):324–8.