Guidelines for International Breast Health and Cancer Control–Implementation

Supplement to ***Cancer***

Breast Radiation Therapy Guideline Implementation in Low- and Middle-Income Countries

Nuran Senel Bese, MD[1]
Anusheel Munshi, MD[2]
Ashwini Budrukkar, MBBS, DMRT, MD, DNB[2]
Ahmed Elzawawy, MD[3,4]
Carlos A. Perez, MD[5]
on behalf of the Breast Health Global Initiative Radiation Therapy Focus Group

[1] Istanbul University, Cerrahpasa Medical School Department of Radiation Oncology, Cerrahpasa, Istanbul, Turkey.

[2] Department of Radiation Oncology, Tata Memorial Hospital, Parel, Mumbai, India.

[3] Faculty of Medicine, Suez Canal University, Suez, Egypt.

[4] Al-Soliman Radiation Oncology Unit, Port Said Early Detection and Cancer Chemotherapy Unit, Port Said General Hospital, Insurance Hospitals, Port Said, Egypt.

[5] Department of Radiation Oncology, Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Missouri.

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Radiation therapy plays a critical role in the management of breast cancer and often is unavailable to patients in low- and middle-income countries (LMCs). There is a need to provide appropriate equipment and to improve the techniques of administration, quality assurance, and use of resources for radiation therapy in LMCs. Although the linear accelerator is the preferred equipment, telecobalt machines may be considered as an acceptable alternative in LMCs. Applying safe and effective treatment also requires well trained staff, support systems, geographic accessibility, and the initiation and completion of treatment without undue delay. In early-stage breast cancer, standard treatment includes the irradiation of the entire breast with an additional boost to the tumor site and should be delivered after treatment planning with at least 2-dimensional imaging. Although postmastectomy radiation therapy (PMRT) has demonstrated local control and overall survival advantages in all patients with axillary lymph node metastases, preference in limited resource settings could be reserved for patients who have $\geq$4 positive lymph nodes. The long-term risks of cardiac morbidity and mortality require special attention to the volume of heart and lungs exposed. Alternative treatment schedules like hypofractionated radiation and partial breast irradiation currently are investigational. Radiation therapy is an integral component for patients with locally advanced breast cancer after initial systemic treatment and surgery. For patients with distant metastases, radiation is an effective tool for palliation, especially for bone, brain, and soft tissue metastases. The implementation of quality-assurance programs applied to equipment, the planning process, and radiation treatment delivery must be instituted in all radiation therapy centers. ***Cancer*** **2008;113(8 suppl):2305–14.** © *2008 American Cancer Society.*

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Radiation therapy plays an essential role in the multimodal treatment of breast cancer, depending on the stage of the disease. It has a major impact on local tumor control for early and locally advanced disease, and effective and safe radiation therapy can improve overall survival rates as well.[1-3] Radiation therapy also is an

Address for reprints: Nuran Senel Bese, MD, Radiation Oncology, Istanbul University, Cerrahpasa Medical School Department of Radiation Oncology, Cerrahpasa, 34098 Istanbul, Turkey; Fax: (011) 90-212 414 31 01; E-mail: nuranbese@superonline.com

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effective tool for providing palliation for the symptoms of locally advanced and metastatic disease. Existing data suggest that there is a growing incidence of breast cancer in countries with limited resources,[4,5] where there often is no access or limited access to radiation therapy.[6-8] Expanding radiation therapy resources, education programs, and practical evidence-based recommendations will be crucial to assure the best possible outcome for women with breast cancer.

In a previous Breast Health Global Initiative (BHGI) article, we reviewed the requirements for implementing a radiation therapy program.[9] In the current article, we review the components needed for implementing a successful program, focusing on specific radiation therapy techniques and strategies for expanding the use of radiation therapy for breast cancer in countries with limited resources; we also discuss quality-assurance (QA) and cost issues. Our evidence-based recommendations include a discussion of new treatment modalities and alternate fractionation schedules.

Safe and Effective Radiation Therapy

The delivery of radiation therapy requires a healthcare system that can provide the basic equipment, the human resources, and patient access to scheduled care to ensure safe and effective radiation therapy.[10] The current supply of megavoltage radiation therapy machines—cobalt-60 or linear accelerator—is only 18% of the estimated need in some parts of the developing world.[11] Although the initial investment in establishing radiation therapy equipment is significant, the long life of radiation therapy equipment (20-30 years) means that the cost per patient treated can be surprisingly modest in an efficiently run facility; it has been demonstrated that radiotherapy is cost-effective for cure or palliation. Therefore, strategies for developing services are needed urgently.

The central equipment requirement for breast cancer radiotherapy is a megavoltage teletherapy unit, either a cobalt-60 device or a linear accelerator. Cobalt machines are cheaper and have lower QA, maintenance, and staffing needs.[12] Because treatment interruptions caused by machine breakdown or machine servicing adversely affect patient outcomes,[13] the ability to provide preventive maintenance is an important consideration. The colbalt-60 units have greater simplicity with regard to mechanical and electrical components and operations and, thus, are an attractive option for a low-resource setting. Linear accelerators have greater technical sophistication and, hence, greater maintenance requirements. Although cobalt-60 units have the advantages of a constancy of beam output and predictability of deterioration, compared with linear accelerators, they have a poorer field flatness, a lower percentage depth dose, greater penumbra, a lower dose rate, and a less favorable beam profile. Colbalt-60 is limited in its ability to deliver more complex treatments. Compared with a linear accelerator, cobalt-60 may result in an increased dose to the contralateral breast, a higher skin dose, or some dose in homogeneities in the treated breast, especially during breast-conservation irradiation. The advantages and disadvantages of cobalt-60 machines versus linear accelerators are outlined in Table 1. However, some of these disadvantages can be mitigated by proper treatment planning and the use of simple accessories, such as wedges.

QA tools are needed for a safe and effective radiotherapy program. At the planning stage, it is important to determine the amount of lung and heart volume in the radiation portal, because data suggest that radiotherapy can induce cardiac side effects with significant impact on overall survival.[1] This requires a conventional simulator; if one is not available, then the amount of lung and heart should be visualized with a portal verification film. In addition, the healthcare system must be able to support the delivery of radiotherapy over the entire planned therapy schedule, and it must have patient selection criteria developed for appropriate and priority treatment based on resource and capacity issues and education of professional and technical staff. Proposed requirements are listed in Table 2.

Treatment Recommendations

Breast cancer requires a multimodal treatment approach that includes surgery, systemic therapy (chemotherapy, hormone therapy, biologic therapies), and radiation therapy based on the stage of the disease. The integration of these therapies for an effective breast cancer treatment program, based on the level of resources available, is presented in the BHGI treatment guidelines in this supplement to *Cancer*.[14] That article focuses on the specifics of radiotherapy techniques, such as doses and schedules, and the different sequencing strategies for early, locally advanced, and metastatic stages of breast cancer.

Early-Stage Breast Cancer (Stages I and II)

Whole-breast radiation therapy

Breast-conserving surgery (BCS) is a widely accepted form of treatment for patients with early-stage dis-

TABLE 1
Advantages and Disadvantages of a Cobalt-60 Machine Versus Linear Accelerator for Countries With Limited Resources

Cobalt-60		Linear Accelerator	
Advantages	**Disadvantages**	**Advantages**	**Disadvantages**
Cheaper	Poor field flatness	Ability of delivering complex treatments	Preventive maintenance is essential, expensive and requires a maintenance technician
More simple mechanical, electrical components and operations	Lower % depth dose	Better dose distribution especially after BCS	More detailed QA program is needed
Easy to maintain	Greater penumbra	Decreased skin dose especially after BCS	
Relative constancy of beam output, predictability of decay	Lower dose rate	Decreased dose to the contralateral breast	
QA program is simple	Less favorable beam output Need of changing source every 5 y Inability to deliver complex treatments		

BCS indicates breast-conserving surgery; QA, quality assurance.

TABLE 2
Recommended Techniques, Equipment, Dosimetry, Accessories, and Quality Assurance by Allocation of Resources

Level of Resources	Simulator	Dosimetry	Teletherapy Equipment and Beam Energy	Accessories	APBI	Brachytherapy	QA
Basic	NA	NA	NA	NA	NA	NA	NA
Limited	Conventional	2D	Co60/4-6 MV x-rays	Wedges, blocks	No	No	Simple or intermediate
Enhanced	3D CT simulation	3D	Electrons	Compensators	No	Yes	Intermediate
Maximal	4D CT simulation	4D (Motion)	6-18 MV x-rays, particles	NA	Experimental	Yes	Complex

APBI indicates accelerated partial breast irradiation; QA, quality assurance; NA, not available; D, dimensional; Co60, cobalt 60; CT, computed tomography.

ease, and postoperative whole-breast irradiation is an essential component of BCS. Randomized trials of BCS, with or without adjuvant systemic therapy, have produced 4- to 5-fold reductions in the local recurrence rate among patients who received radiation therapy, although no difference was reported in overall survival rates.[15,16] Therefore, it is recommended that all women should receive postoperative radiotherapy after BCS. For patients without axillary involvement who have additional favorable prognostic factors (such as older age, small tumor size, or positive hormone receptor status), it has been demonstrated that radiotherapy increases local control even over the effects of hormone treatment.[17-20] However, because the risk of local recurrence generally is lower for women aged >70 years, the omission of radiotherapy for these older women who also have additional low-risk factors may be an option in limited resource settings in which resource and capacity issues are a concern.[21]

Although it has not been demonstrated that overall survival improves with postoperative radiotherapy for patients who undergo BCS, the prevention of local recurrence was demonstrated in a meta-analyses (1 avoided breast cancer death was reported for every fourth prevented local recurrence) regardless of other prognostic indicators.[1,22] Postoperative radiotherapy also reportedly resulted in a survival benefit, although increased mortality was reported, primarily in vascular mortality.[1] These results suggest that, to achieve significant survival benefit, cardiac safety should be a major QA concern for low- and middle-income countries.

Tangential field technique. The most widely accepted technique for whole-breast irradiation is the tangential field technique, in which the entire breast and chest wall, with a small portion of lung, is included in the irradiated volume. For simple, 2-dimensional planning, the best predictor of the percentage of ipsilateral lung volume treated by the tangential fields is central lung distance (CLD),[23] which is defined as the perpendicular distance from the posterior tangential edge to the posterior part of the anterior chest wall at the center of the field. A CLD of 1.5 cm predicts that approximately 6% of the lung is in the irradiation field; when CLD is increased to 3.5 cm, approximately 26% of the lung is included, which may augment the risk of developing radiation pneu-

monitis.[24] When the CLD is >3 cm, particularly in the left breast, a significant volume of the heart will be irradiated as well. Although controversy exists regarding the amount of the heart volume in the tangential field associated with the development of cardiovascular disease,[1,25] techniques like the addition of a medial port with the use of electrons should be considered, especially in patients with wide tangential fields and with an increased CLD because of large breasts.[26] A significant dose inhomogeneity is predictable, which could result in less satisfactory cosmetic outcomes. To minimize this problem, 10- to 15-megavolt, high-energy x-rays may be needed. Although these technical complexities require an enhanced-resource setting, BCS and postoperative breast irradiation may be the treatment of choice for a group of patients without major anatomic limitations and with a proper treatment plan in countries with limited resources.

Scheduled dose. The most common schedule for breast irradiation is to deliver 46 to 50 gray (Gy) to the whole breast over 5 to 6 weeks with daily doses of 1.8 to 2 Gy. Results of a 10-year randomized trial suggest that a boost dose of 16 Gy led to improved local control in all age groups, with the largest absolute risk reduction observed in patients aged ≤40 years.[27] No substantial difference in boost technique (photons, electrons, or brachytherapy) has been reported with regard to local control or cosmetic outcome.[28] Accurate localization will maximize the benefit of a boost, and surgical clips are the preferred method; diagnostic ultrasound may be used when surgical clips are not available.[29] The use of a concomitant boost on Saturday may help reduce the overall treatment time; however, this technique still investigational is and would require scheduled staff resources on weekends.[30]

Hypofractionation schedules in which doses per fraction >2 Gy are delivered, resulting in reduction of overall treatment time, are being investigated in randomized trials.[31-33] In a recent study with a median follow-up of >140 months, no statistically significant differences were observed in terms of local control or cosmetic outcomes.[31] Such schedules can have a huge impact on reducing resource expenditures but should be considered with caution, because it may take up to 15 years for cardiac side effects to manifest fully.

Radiotherapy should be initiated without a long delay after surgery if chemotherapy is not delivered. A delay longer than 3 months has been associated with decreased survival,[34] although the maximum interval between surgery and postoperative radiotherapy is controversial.[35] When chemotherapy is indicated, either chemotherapy or radiotherapy may be started after surgery, except in patients who have close surgical margins, in whom radiotherapy should be given first.[36] Overall, it has been demonstrated that concomitant chemoradiotherapy reduces treatment times; however, toxicity varies with chemotherapy agents. Concurrent administration of cyclophosphamide, methotrexate, and fluorouracil regimens reportedly had acceptable toxicity[37] and resulted in better local control among patients with axillary lymph node involvement compared with sequential administration. However, combined cyclophosphamide, mitoxantrone, and fluorouracil (CNF) regimens are have been with slightly more acute[38] and late toxicity[39] but with improved local control in patients with axillary lymph node metastases.[38,40] It is important to note that CNF no longer is considered standard adjuvant chemotherapy in breast cancer because of reports of secondary acute myeloid leukemias.[41] Concomitant administration of anthracyclines (eg, doxorubicin, epirubicin) should be avoided because of the serious increased risk of skin and cardiac toxicity.[39] Increased toxicity has been observed with the concomitant use of taxanes.[43] Hormone treatment (tamoxifen) given concurrently or sequentially with radiotherapy appears to be a reasonable option for patients who undergo BCS in terms of locoregional control and overall survival[44-46]; however, the results regarding skin and pulmonary toxicities are conflicting.[47,48]

Radiotherapy schedules should be completed as planned, because any interruption of more than a week during the postoperative irradiation of breast cancer has a negative impact both on local control and overall survival rates.[13] Treatment interruptions can be caused by early side effects, intercurrent diseases, machine breakdowns or servicing, public holidays, transportation problems, or patient noncompliance.

Accelerated partial breast irradiation

Accelerated partial breast irradiation (APBI) irradiates only the quadrant in which the primary tumor has been removed with a wide local excision. The rationale for APBI is backed by data reporting that the majority of recurrences after whole-breast irradiation in conservation therapy are in the quadrant of the original primary tumor. APBI often is combined with a sentinel lymph node biopsy and/or axillary lymph node dissection. APBI requires careful imaging, pathology analysis of specimens, and irradiation techniques, in addition to a rigorous QA program.

The techniques vary and include intracavitary (MammoSite) or interstitial high-dose brachytherapy

(multiple catheters) and external-beam (photon, electron, proton, or combination) irradiation. A few institutions have used single-dose intraoperative electrons, photons, or brachytherapy. The doses of irradiation reported include 34 Gy in 10 fractions twice daily for brachytherapy and 38 Gy in 10 fractions twice daily for external-beam, 3-dimensional, conformal or intensity-modulated irradiation. Intraoperative techniques have delivered 18 to 21 Gy in a single dose.

Criteria for patient selection for APBI have been outlined by both the American Brachytherapy Society and the American Society of Breast Surgeons.[49,50] APBI currently is used in patients aged >45 years with in situ or invasive ductal carcinoma that measures ≤3 cm in greatest dimension, positive hormone receptors, and <3 positive axillary lymph nodes (in some institutions).

Although APBI is being offered increasingly to selected patients in many institutions in the United States and Europe, it has not been accepted as proven alternative management for patients with early-stage breast cancer. Long-term follow-up, long-term cosmetic results, and morbidity analyses are needed. APBI is considered an experimental therapy for use only in approved clinical trials. Unanswered questions include patient eligibility, appropriate dose and fractionation of irradiation, optimal volume to be treated, imaging requirements, and other technical issues.[51] Cost analyses[52] have demonstrated that, although external-beam APBI has a lower cost than whole-breast irradiation, other brachytherapy- or proton-based techniques have a significantly higher cost. APBI is not recommended at this time for use in institutions in countries with limited resources because of the many associated technical and QA requirements and the need to involve various disciplines in the care of patients with early-stage breast cancer.

Postmastectomy radiation therapy

Mastectomy is still an appropriate treatment for many patients with primary breast cancer. In countries without radiotherapy units or with inadequate facilities for QA, it remains the standard surgical treatment, even for patients who are diagnosed at an early stage. PMRT generally includes radiation of the chest wall and regional lymphatics, and it has been demonstrated that PMRT drastically reduces locoregional recurrences and improves overall survival in patients with high-risk breast cancer.[2,3] The major risk factors for locoregional recurrence are axillary lymph node metastases and the number of involved lymph nodes, although there is no consensus on the number or percentage of involved lymph nodes needed to apply PMRT.[53] It is widely accepted that all patients with an adequate axillary dissection and ≥4 lymph nodes should receive postoperative chest wall and supraclavicular field radiation, because the majority of recurrences are observed in those locations.[54] Randomized trials and a meta-analyses have reported improved overall survival rates as well as improved local control for patients who have 1 to 3 positive lymph nodes.[1-3] These patients should be considered for chest wall and supraclavicular field irradiation, and priority should be given to patients who have ≥4 positive lymph nodes for limited-resource settings. Routine axillary irradiation is used only for patients who have not undergone adequate axillary dissection. Irradiation of the axilla, in general, is not recommended because of the low incidence of axillary recurrence and the increased risk of arm edema for patients who have <10 involved lymph nodes.[54,55]

Internal mammary lymphatics are relatively uncommon sites for recurrences; and, if cardiac toxicity is a concern, then irradiation of the internal mammary chain is not recommended. The results from randomized trials are needed.[56] Internal mammary chain irradiation is recommended for patients with clinically or pathologically positive internal mammary lymph nodes. Radiation therapy of internal mammary lymphatics should be considered if the primary tumor is located in the inner quadrant and if other adverse risk factors are present. Irradiation of the chest wall is recommended for patients with lymph node-negative breast cancer who have a primary tumor >5 cm in greatest dimension and/or positive surgical margins despite the contradictory results from retrospective series.[57-59] This applies especially to patients in limited-resource settings, who usually present with larger tumors, who may not receive sufficient systemic treatment, and whose local recurrences may be incurable. Chest wall irradiation also is considered for patients with negative axillary lymph nodes who have multiple adverse factors (ie, primary tumor >2 cm, close surgical margins, lymphovascular invasion, grade 3 disease, premenopausal status, or unavailability of systemic treatment).[60,61]

For chest wall and regional irradiation, a total dose of 46 to 50 Gy in fractions of 1.8 to 2 Gy is recommended. The target should be the chest wall, mastectomy scar, and drain sites, with special consideration given to the use of bolus material when photon fields are used to guarantee that the skin dose is adequate. Special attention also should be given to the intersection of the chest wall and regional lymphatics to prevent hot or cold spots and to limited lung and heart volume included in tangential

breast irradiation to reduce cardiac and pulmonary toxicity.

Locally Advanced Breast Cancer

Radiotherapy is an integral component of care for patients with locally advanced breast cancer (LABC). In low-resource countries, 30% to 60% of patients present with LABC[62] that is inoperable because of direct invasion to the ribs or intercostal muscles, skin edema (including peu d'orange), ulceration of the skin of the breast, satellite skin nodules confined to the same breast, inflammatory carcinoma, metastases to the ipsilateral internal mammary lymph nodes, or metastases to the ipsilateral supraclavicular lymph nodes. The initial treatment of LABC is systemic therapy. Although studies have not demonstrated that neoadjuvant chemotherapy yields a survival advantage, a significant number of inoperable tumors regress adequately after chemotherapy to become operable.[63] The conventional approach has been to administer chemotherapy to achieve a rapid response, with hormone treatment reserved for older patients who have strongly positive receptor status.[64] For patients who respond to neoadjuvant therapy, the generally accepted surgical approach is mastectomy. Selected patients with noninflammatory disease who have a complete or partial response to initial treatment can be considered for BCS followed by radiation treatment. Even for patients who achieve a complete response to neoadjuvant chemotherapy, the locoregional risk still is high, and the addition of postoperative radiotherapy can reduce the risk of recurrence.[65] Supraclavicular field irradiation is recommended in addition to chest wall or breast irradiation. Internal mammary chain irradiation is recommended if there is clinical or pathologic evidence of involved lymph nodes or if irradiation of this region is considered for central or inner quadrant tumors. Irradiation of axilla is omitted for patients without initial axillary presentation or with <10 involved lymph nodes after adequate axillary dissection.[55]

Patients who still are inoperable after noncross-resistant chemotherapies should be treated with radiotherapy. An operative evaluation is done after a total dose of 46 to 50 Gy to the breast and regional lymphatics. If the patient still is inoperable, then an additional radiotherapy dose of 20 to 25 Gy is applied either with external irradiation using shrinking fields or with a 192Ir implant to a total dose of 75 to 80 Gy. The boost dose is determined by the volume of the residual disease. Supraclavicular fields should not receive >60 Gy when brachial plexopathy risk is considered.

Metastatic Breast Cancer

For patients who have breast cancer with distant metastases, radiotherapy is a very effective tool for symptom palliation and for preventing loss of function, particularly in patients who have bone metastases with a risk of fracture or spinal cord compression. Patients with bone metastases are the largest group that requires palliative radiation therapy. Palliation is obtained in 60% to 80% of patients with a median response duration of 4 to 6 months.

Conventionally, local field radiotherapy has been used for bone metastases. Evidence suggests that significant pain relief is obtained with a cost-effective, single 8-Gy irradiation dose compared with the longer fractionation schedules.[66] Wide-field radiation treatment is recommended for patients who have multiple metastases, and it has been demonstrated that hemibody irradiation of 12 Gy in 4 fractions delivered in 2 days or in a single, 6- to 8-Gy regimen is safe and effective with intravenous corticosteroid support.[67,68]

Palliative whole-brain irradiation (WBI) with steroids is recommended to relieve symptoms of brain metastases. Patients with a limited number of brain metastases who have apposite localizations for surgery can undergo surgery if extracranial disease is under control. A massive lesion with necrosis also should be considered for surgery for immediate relief of the symptoms of intracranial pressure. It has been demonstrated that WBI after surgery improves intracranial control.[69] The most common fractionation schedule for WBI is 30 Gy in 10 fractions or 20 Gy in 5 fractions. A boost dose is recommended for single metastases. If it is available, then stereotactic radiosurgery is an alternative method of surgery for patients who have a poor performance status and for those who have lesions with unsuitable localizations for surgery.

Palliative radiotherapy also is used for soft tissue metastases if they cause bleeding, discharge, or pain. Patients with locoregional, recurrent disease after mastectomy should be treated with chest wall and regional lymphatic irradiation as well as systemic treatment. Surgical excision with negative margins is recommended before radiation therapy if possible. The probability of achieving tumor control is increased with a longer disease-free interval after initial treatment, the number of recurrences and sites, and the possibility of resection with tumor-free margins.

Quality Assurance

To ensure the correct administration of radiation therapy, a healthcare system must implement QA

programs that test the functionality of the equipment at specific time intervals and that test the precision of dose calibration, dose calculations, and radiation delivery used both in the treatment of the patient and in the treatment planning process. Other elements of QA include protocols and manuals that document the operating procedures in the radiation facility, appropriate clinical and physics records, detailed procedures for treatment planning and dose calculations, chart review sessions, audits of parameters of treatment, and dose verification, all with the participation of radiation oncologists, physicists, dosimetrists, therapists, and other personnel to ensure that the proposed treatment is being delivered accurately.

In patients who receive radiation to abutting fields, it is critical to verify the path of the radiation beams to ensure that there is no overlap that could result in higher doses delivered, leading to undesired fibrosis at the 'match lines'. When wedges or compensating filters are used, it is important to verify the alignment with the portal's isocenter (or central axis) to prevent distortion of the dose distributions in case of misalignment. If multileaf collimation is available, then a more detailed QA program is needed that includes the accurate performance of the multileaf collimator leaf (eg, submillimeter accuracy, speed) and of the radiation output with the accelerator gantry in motion.[70]

For any new radiation treatment technique, a specific patient-directed QA program should be required, including the irradiation of anatomic phantoms within the proposed treatment parameters using ionization chambers, film dosimetry (radiographic, radiochromic), and thermoluminescent dosimeters (when available), and comparing these data with the dose distributions generated by the treatment planning system. To determine the spatial accuracy of the treatment planning and delivery systems, the location in space of the measured and calculated doses must be verified precisely and independently.[70]

Movement issues must be considered when validating the target position, including the motion of the target volume in the breast (because of respiration) relative to the anatomy of adjacent organs (eg, heart, lung), the need to immobilize the patient during the simulation process, and the need for accurate repositioning of the patient for repeat treatments. Motion of the organs and the patient can lead to blurring of dose distribution and can cause an increased beam penumbra. Motion can lead to the displacement of 10% of the target volume out of the field 20% of the time, resulting in a complete treatment field only 80% of the time. These common inaccuracies can create hot spots and cold spots that are difficult to observe as part of the standard planning process.[71]

Calculating the margin can be a quality issue. There is a dramatic drop in the probability level of reaching an acceptable minimum dose if the clinical target volume margin in the breast or regional lymph nodes is reduced. If a very tight margin is defined (ie, zero margin or a few millimeters), then the probability of delivering the planned high dose to the clinical target volume approaches zero.

When treating patients with carcinoma of the breast, special care must be exercised in decreasing as much as possible the irradiation dose and volume of sensitive structures irradiated.[26] Numerous publications have reported a correlation of dose and volume with the incidence of cardiovascular effects, including myocardial infarction or perfusion and functional pulmonary sequelae.

In conclusion, it has been documented that adequate radiation therapy, with more precise coverage of the target volume and precise delivery of irradiation doses, increases locoregional tumor control and survival and improves quality of life. It is well known that the time and effort required for modern radiation therapy is impacted only partially by increased experience and proficiency of the staff. Depending on the method of financing of healthcare services in different countries, adequate equipment, facilities, and human resources involved must be provided to ensure the best possible management of patients with breast cancer who require radiation therapy. Furthermore, because this modality is used increasingly in conjunction with cytotoxic or molecular-targeted therapies that enhance the effects of irradiation, the overall management of the patient is more complex and time consuming, requiring careful attention to treatment techniques. The use of evidence-based doses and techniques is crucial for achieving the best possible clinical outcomes and for reducing complications. The cost of developing and maintaining a radiation therapy program should be balanced against the cost of managing the complications of treatment, because both contribute to the overall cost of managing the patient with breast cancer.

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