Medical Policy Manual Medicine, Policy No. 166

Intensity Modulated Radiotherapy (IMRT) for Breast Cancer

Effective: January 1, 2025

Next Review: September 2025
Last Review: November 2024

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Intensity modulated radiotherapy (IMRT) is a form of radiation therapy that conforms closely to the targeted tumor shape and allows higher doses of radiation to be delivered while minimizing toxicity to surrounding healthy tissues.

MEDICAL POLICY CRITERIA

I. Intensity modulated radiotherapy (IMRT) may be considered **medically necessary** for breast cancer treatment (either definitive post lumpectomy or adjuvant post mastectomy) when any of the following criteria are met:

   A. When there is documented prior radiation treatment to the planned target volume; or

   B. For delivery of accelerated partial breast irradiation (APBI).

II. Intensity modulated radiotherapy (IMRT) may be considered **medically necessary** for breast cancer treatment (either definitive post lumpectomy or adjuvant post mastectomy) when both of the following criteria are met (A. and B.):

   A. The need for IMRT is demonstrated by one of the following:

1. Documentation (see Required Documentation) demonstrates need for IMRT to minimize focal hot spot(s) within the breast tissue from greater than 10% to less than 10% of the prescribed dose; or
2. When documentation (see Required Documentation) demonstrates that IMRT planning can achieve a 10% or greater reduction in mean dose to the heart, left ventricle, left main coronary, or left anterior descending artery; or
3. When comparative 3D versus IMRT dose/volume histograms are submitted in color AND the summary analysis (table preferred; with preauthorization request) is completed demonstrating that only through IMRT can published dose/volume constraints be met for organs at risk (see Required Documentation; quality assurance procedures are not required for preauthorization).

Example table (Click here for the template to use):

Summary Analysis of 3D Versus IMRT Planning					
Organ(s) At Risk	**Dose Constraint**	**Source of Constraint**	**3D**	**IMRT**	**Can constraint *only* be met with IMRT?**
Example: Brachial plexus	Max <66 Gy	RTOG	58 Gy	52 Gy	No (both meet constraint)
Example: Cauda equina	Max < 16 Gy	RTOG #6301	19 Gy	17 Gy	No (neither meets constraint)
Example: Brain stem	Max <54 Gy	Quantec	62 Gy	52 Gy	Yes (only iMRT meets constraint)

B. One of the following is met:
   1. There is documentation of mixed connective tissue disorder or collagen vascular disease; or
   2. Treatment is post-lumpectomy and one of the following is met:
      a. Treatment is directed to the whole breast plus the regional nodes (any number of fractions); or
      b. Treatment is directed to the whole breast when regional nodes are NOT to be treated and one of the following is met:
         i. ≤ 16 fractions are planned/delivered (ultra- or moderate-hypofractionation) +/- 4 to 8 boost treatments (preferred hypofractionated regimen); or
         ii. >16 fractions +/- 4 to 8 boost treatments are planned/delivered (conventional fractionation) AND documentation is submitted with detailed rationale for medical necessity of longer conventional regimen.

3. Treatment is post-mastectomy and one of the following is met:
    a. Treatment is directed to the chest wall plus the regional nodes (any number of fractions); or
    b. Treatment is directed to the chest wall when regional nodes are NOT to be treated and either of the following is met:
        i. ≤ 28 fractions are planned/delivered +/- 1 to 5 boost treatments (preferred hypofractionated regimen); or
        ii. > 28 treatment fractions +/- 1 to 5 boost treatments are planned/delivered (conventional fractionation) AND documentation is submitted with detailed rationale for medical necessity of longer conventional regimen.

III. Intensity-modulated radiotherapy (IMRT) is considered **not medically necessary** for the treatment of breast cancer not meeting the criteria above.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

ORGANS AT RISK

Organs at risk are defined as normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed radiation dose. These organs at risk may be particularly vulnerable to clinically important complications from radiation toxicity.

LIST OF INFORMATION NEEDED FOR REVIEW

REQUIRED DOCUMENTATION:

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome. Quality assurance for 3D and IMRT submitted plans are not required with a preauthorization request.

- Provider consultation and relevant follow-up notes
- Relevant pathology reports
- Relevant imaging reports documenting that the policy criteria are met for medical necessity
- If requesting IMRT for post-lumpectomy IMRT when >16 fractions are planned/delivered to partial or whole breast (+/- boost), or post-mastectomy when regional nodes are NOT to be treated and chest wall is to receive > 28 treatment fractions (+/- boost) additional documentation is required as below:
    - Detailed note explaining clinical rationale for choosing conventional, longer fractionation regimen rather than moderate- or ultra-hypofractionation.
- For requests to be reviewed via Criterion II.:
    - Comparative 3D versus IMRT dose/volume histograms in color and the completed analysis as described in the criteria above. The submitted information must demonstrate the need for IMRT to meet dose constraints as described in

the criteria not achievable through 3D planning. If possible please render both planning lines on the same graph to better permit review of contrasting lines.
- The best way to ensure criteria are met is to submit the provided summary analysis table. If using the table, please ensure all components are completed prior to submission. If any of these items are not provided it could impact our review and decision outcome.

CROSS REFERENCES

1. Charged-Particle (Proton) Radiotherapy, Medicine, Policy No. 49
2. Intensity Modulated Radiotherapy (IMRT) of the Central Nervous System (CNS), Head, Neck, and Thyroid, Medicine, Policy No. 164
3. Intensity Modulated Radiotherapy (IMRT) of the Thorax, Abdomen, Pelvis, and Extremities, Medicine, Policy No. 165
4. Intensity Modulated Radiotherapy (IMRT) for Tumors in Close Proximity to Organs at Risk, Medicine, Policy No. 167
5. Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy for Intracranial, Skull Base, and Orbital Sites, Surgery, Policy No. 213
6. Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy for Tumors Outside of Intracranial, Skull Base, or Orbital Sites, Surgery, Policy No. 214

BACKGROUND

RADIATION TECHNIQUES

Conventional External Beam Radiotherapy

Over the past several decades, methods to plan and deliver RT have evolved in ways that permit more precise targeting of tumors with complex geometries. Most early trials used two-dimensional radiation therapy (2D-RT) treatment planning, based on flat images and radiation beams with cross-sections of uniform intensity that were sequentially aimed at the tumor along two or three intersecting axes. Collectively, these methods are termed conventional external beam radiation therapy (EBRT).

Three-Dimensional Conformal Radiation

Treatment planning evolved by using three dimensional images, usually from computed tomography (CT) scans, to delineate the boundaries of the tumor and discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Computer algorithms were developed to estimate cumulative radiation dose delivered to each volume of interest by summing the contribution from each shaped beam. Methods also were developed to position the patient and the radiation portal reproducibly for each fraction and immobilize the patient, thus maintaining consistent beam axes across treatment sessions. Collectively, these methods are termed three-dimensional conformal radiation therapy (3D-CRT).

Intensity-Modulated Radiotherapy

IMRT, which uses computer software, CT images, and magnetic resonance imaging (MRI), offers better conformality than 3D-CRT, as it is able to modulate the intensity of the overlapping radiation beams projected on the target and to use multiple-shaped treatment fields. It uses a device (a multileaf collimator [MLC]) which, coupled to a computer algorithm, allows for “inverse” treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target’s prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and

acceptable dose limits within the adjoining organs at risk (OAR). Based on these parameters and a digitally reconstructed radiographic image of the tumor and surrounding tissues and organs at risk, computer software optimizes the location, shape, and intensities of the beams ports, to achieve the treatment plan's goals.

Increased conformality may permit escalated tumor doses without increasing normal tissue toxicity and thus may improve local tumor control, with decreased exposure to surrounding normal tissues, potentially reducing acute and late radiation toxicities. Better dose homogeneity within the target may also improve local tumor control by avoiding underdosing within the tumor and may decrease toxicity by avoiding overdosing. Alternatively, IMRT provides the opportunity to construct heterogenous dose deposition within the target volume thus tailoring differential dose in keeping with physician assessment of differential cancer cell density, etc. This may diminish local failure within the overall target volume.

Because most tumors move as patients breathe, dosimetry with stationary targets may not accurately reflect doses delivered within target volumes and adjacent tissues in patients. Furthermore, treatment planning and delivery are more complex, time-consuming, and labor-intensive for IMRT than for 3D-CRT. Thus, clinical studies must test whether IMRT improves tumor control or reduces acute and late toxicities when compared with 3D-CRT.

WHOLE AND PARTIAL BREAST IRRADIATION

Definitive or adjunctive irradiation to the breast may initially include the entire breast with or without subsequent "boost" to the lumpectomy cavity or be targeted solely to the lumpectomy cavity plus small safety margin (i.e. partial breast irradiation). Both formats of breast irradiation may be provided via a mixture of external irradiation techniques (i.e. teletherapy and/or insertion of needles or balloon like devices containing radioactive substances and implanted in the breast tissue), thus providing irradiation therapy from within the targeted tissues (i.e. brachytherapy). Whole breast irradiation is now recommended to be delivered in a hypofractionated dose of 40 to 42.5 Gy in 15 to 16 fractions while partial breast treatment is commonly delivered as 30 Gy in five fractions.

EVIDENCE SUMMARY

Multiple-dose planning studies generate three-dimensional conformal radiation (3D-CRT) and intensity-modulated radiotherapy (IMRT) treatment plans from the same scans, and then compare predicted dose distributions within the target area and adjacent organs. Results of such planning studies have shown that IMRT is better than 3D-CRT with respect to conformality to, and dose homogeneity within, the target. Results have also demonstrated that IMRT results in less radiation to nontarget areas. Dosimetry studies using stationary targets generally confirm these predictions. However, because patients move during treatment, dosimetry with stationary targets only approximate actual radiation doses received. Based on these dosimetry studies, radiation oncologists expect IMRT to improve treatment outcomes compared with those of 3D-CRT.

Comparative studies of radiation-induced adverse effects from IMRT versus alternative radiation delivery would constitute definitive evidence in establishing the benefit of IMRT. Single-arm series of IMRT can give some insights into the potential for benefit, particularly if an adverse effect that is expected to occur at high rates is shown to decrease by a large amount. Studies of treatment benefit are also important to establish that IMRT is at least as good as

other types of delivery, but, absent such comparative trials, it is likely that benefit from IMRT is at least as good as with other types of delivery.

In general, when the indication for IMRT is to avoid radiation to sensitive areas, dosimetry studies have been considered sufficient evidence to demonstrate that harm would be avoided by using IMRT.[1] For other IMRT indications, such as using IMRT to provide better tumor control, comparative studies of health outcomes are needed to demonstrate such a benefit.

BREAST CANCER

The grading of acute radiation dermatitis is relevant to studies of IMRT for treatment of breast cancer. Acute radiation dermatitis is graded on a scale of zero (no change) to five (death). Grade two is moderate erythema and patchy moist desquamation, mostly in skin folds; grade three is moist desquamation in other locations and bleeding with minor trauma. Publications have also reported on the potential for IMRT to reduce radiation to the heart (left ventricle) in patients with left-sided breast cancer and unfavorable cardiac anatomy.[2] This is a concern because of the potential development of late cardiac complications (e.g., coronary artery disease) following RT to the left breast.

Whole-Breast Irradiation

Systematic Reviews

The Agency for Healthcare Research and Quality (2023) published a systematic review comparing the effectiveness and harms of partial breast irradiation (PBI) to whole breast irradiation (WBI) for early stage breast cancer.[3] PBI included IMRT and five other treatment modalities. There were no significant differences in ipsilateral breast recurrence, overall survival, and cancer-free survival at five and ten years when all types of PBI were assessed in combination and when IMRT by itself was compared to WBI. PBI was associated with significantly fewer acute adverse events and less financial toxicity than WBI, but specific data on IMRT and other PBI subgroups were insufficient for subgroup assessment.

In 2012, Dayes published a systematic review that examined the evidence for IMRT for whole-breast irradiation in the treatment of breast cancer to quantify its potential benefits and to make recommendations for radiation treatment programs.[4] Based on a review of six published reports through March 2009 (one randomized controlled trial [RCT], three retrospective cohort studies, one historically controlled trial, one prospective cohort) including 2012 patients, the authors recommended IMRT over tangential RT after breast-conserving surgery to avoid acute adverse effects associated with radiation. There was insufficient data to recommend IMRT over standard tangential RT for reasons of oncologic outcomes or late toxicity. In the RCT included in this review, the Canadian multicenter trial by Pignol (2008) reported next, IMRT was compared with 2D-RT. CT scans were used in treatment planning for both arms of the study. The types of conventional RT regimens were not reported for the other studies.

Two of the six cohort studies reviewed by Dayes reported on breast cancer-related outcomes.[4] Neither of these studies reported statistically significant differences between treatment groups for contralateral breast cancer rates, clinical recurrence-free survival or disease-specific survival. Despite differences in reported outcomes, all six studies reported reductions in at least one measure of acute toxicity as a result of IMRT-based breast radiation. These toxicities typically related to skin reactions during the course of treatment, with reductions being in the order of one third. The RCT by Pignol (summarized below), for

example, found a reduction in moist desquamation specific to the inframammary fold by 39%. Only two retrospective cohort studies reported on late toxicity effects; one cohort study reported a significant difference between IMRT and tangential RT in favor of IMRT for breast edema (IMRT, 1% vs 25%, p<0.001), and the other study found a trend toward a reduction in lymphedema rates (p=0.06). No differences were observed across both studies in other late effects including fat necrosis or second malignancies.[4]

Randomized Controlled Trials

Choi (2021) compared disease control and safety of IMRT and 3D-CRT in a multicenter, phase III, open-label, randomized (1:1) trial that enrolled 693 women who had undergone breast-conserving surgery for breast cancer staging pT1-2N0M0 with a negative resection margin.[5] The 3D-CRT group received 50.4 Gy in 28 fractions on the ipsilateral breast with additional 9 Gy in five fractions on the tumor bed for 6.5 weeks. In the IMRT group, patients received 50.4 Gy in 28 fractions on the ipsilateral breast with a simultaneous integrated boost of 57.4 Gy in 28 fractions on the tumor bed for 5.5 weeks. The primary endpoint was three-year locoregional recurrence-free survival; secondary endpoints included recurrence-free survival, distant metastasis-free survival, OS, acute toxicity, irradiation dose to organs at risk, and fatigue inventory. Results revealed a three-year locoregional recurrence-free survival rate of 99.4% in the 3D-CRT arm versus 98.5% in the IMRT arm (p=0.523). Similarly, there was no statistically significant difference between the groups in three-year distant metastasis-free survival (98.8% 3D-CRT vs. 99.6% IMRT; p=0.115), recurrence-free survival (97.4% vs. 98.2%; p=0.418), or OS (99.6% vs. 100%; p=0.165). Regarding toxicity, grade 2 or higher radiation dermatitis occurred less frequently in the IMRT arm (37.1% vs. 27.8%; p=0.009). Fatigue was observed in 97.7% of patients in the 3D-CRT arm versus 98.5% of patients in the IMRT arm using a brief fatigue inventory survey. The mean lung dose and V5-V50 for the ipsilateral lung were significantly lower in the IMRT arm than the 3D-CRT arm (all p<0.05).

Horner-Rieber (2021) evaluated the effects of conventional fractionated IMRT with simultaneous integrated boost to 3D-CRT with sequential boost in the prospective, multicenter, randomized, noninferiority, phase III, IMRT-MC2 trial.[6] This trial enrolled 502 patients with breast cancer treated with breast-conserving surgery followed by adjuvant whole-breast irradiation with boost irradiation to the lumpectomy cavity. The IMRT group received a total dose of 50.4 Gy in 1.8 Gy daily fractions with a simultaneous integrated boost to the tumor bed, for a total dose of 64.4 Gy. The 3D-CRT group received a total dose of 50.4 Gy in 1.8 Gy daily fractions, followed by a sequential boost to a total dose of 66.4 Gy. Overall treatment times were 1 to 1.6 weeks shorter in the IMRT-simultaneous integrated boost arm as compared with the 3D-CRT-sequential boost arm. After a median follow-up of 5.1 years, results revealed noninferiority between the IMRT and 3D-CRT groups with regard to two-year local control rate: 99.6% in both arms (hazard ratio [HR], 0.602; 95% confidence interval [CI], 0.123 to 2.452; p =0.487). Additionally, noninferiority was seen for cosmesis (according to relative breast retraction assessment score) after IMRT and 3D-CRT at both six weeks and two years after RT (p=0.332). Overall survival rates were also not significantly different between the groups (99.6% for both arms; HR, 3.281; 95% CI, -0.748 to 22.585; p=0.148). The authors concluded that clinical outcomes between the groups were similar with a considerably shortened treatment time for the IMRT approach. In a separate published analysis of the IMRT-MC2 trial focused on acute toxicity.[7] There were no significant differences between the groups with regard to any grade radiation dermatitis at the end of treatment (p=0.26). However, radiation dermatitis Grade 2 (29.1% vs. 20.1%) and 3 (3.5% vs. 2.3%) occurred significantly more often in the IMRT arm (p=0.02). Significantly more patients in the 3D-CRT arm

experienced breast/chest wall pain at the initial follow-up visit (p=0.02). Another analysis of the IMRT-MC2 trial assessed quality of life outcomes six weeks to two years after RT.[8] The only significant difference in quality of life scores between the IMRT-simultaneous integrated boost arm as compared with the 3D-CRT-sequential boost arm was seen six weeks after RT for pain and for arm symptoms, both favoring IMRT. However, the between-group differences were diminished over time.

In their RCT, Jagsi (2018) assessed whether IMRT with deep inspiration breath hold (DIBH) reduces cardiac or pulmonary toxicity of breast RT compared to 3D-CRT, the current standard RT.[9] The study included 62 women with node-positive breast cancer in whom RT was indicated for treating the left breast or chest-wall and the internal mammary, infraclavicular and supraclavicular nodal regions. The primary outcome was the percentage decrease in heart perfusion at one-year post-treatment compared to baseline, measured using attenuation corrected single-photon emission computed tomography. A secondary outcome was a change in left ventricular ejection fraction. The 3D-CRT group received ≥5 Gy to 15.8% of the left ventricle; the IMRT-DIBH group received 5.6% to the left ventricle (p<0.001). At one year, no differences in perfusion of the heart were detected; however, significant differences were found in left ventricular ejection fraction. In the 3D-CRT arm, six patients had >5% changes in left ventricular ejection fraction, and the IMRT-DIBH arm had one patient with >5% change. The authors contend that their study is important because it demonstrates that the IMRT-DIBH technique's reduction in cardiac dose could be associated with better preservation of cardiac left ventricle function—a potentially clinically meaningful finding. One limitation of this study is its small size, and only one follow-up scan was conducted at one year due to resource constraints. A six-month scan might have shown greater differences between the two arms.

The 2008 multicenter, double-blind RCT by Pignol (2008) evaluated whether breast IMRT would reduce the rate of acute skin reaction (moist desquamation), decrease pain, and improve quality of life (QOL) compared with RT using wedges.[10, 11] Patients were assessed each week up to six weeks after RT and then at eight and ten years. A total of 358 patients were randomly assigned between July 2003 and March 2005 in two Canadian centers, and 331 were included in the analysis. The authors noted that breast IMRT significantly improved the dose distribution compared with 2D-RT. They also noted a lower proportion of patients with moist desquamation during or up to six weeks after radiation treatment (31% with IMRT vs 48% with standard treatment; p=0.002). A multivariate analysis found the use of breast IMRT and smaller breast size were significantly associated with a decreased risk of moist desquamation. The presence of moist desquamation significantly correlated with pain and a reduced QOL. At a median follow-up of 9.8 years, there was no significant difference in chronic pain between treatment arms. Young age (p=0.013) and pain during RT (p<0.001) were associated with chronic pain. Poorer self-assessed cosmetic outcome (p<0.001) and QOL (p<0.001) were also associated with pain during RT.

Donovan (2002) reported on an RCT comparing outcomes with conventional 2D-RT with wedged, tangential beams or IMRT in 300 breast cancer patients.[12] In an abstract, investigators reported interim cosmetic outcomes at two years postrandomization for 233 evaluable patients. In 2007, Donovan published a subsequent report on this trial.[13] Enrolled patients had "higher than average risk of late radiotherapy-adverse effects," which included patients having larger breasts. The authors stated that while breast size is not particularly good at identifying women with dose inhomogeneity falling outside current International Commission on Radiation Units and Measurements guidelines, their trial excluded women with small breasts (≤500 cm3), who generally have fairly good dosimetry with standard 2D compensators.

All patients were treated with six or 10 megavolt photons to a dose of 50 gray (Gy) in 25 fractions in five weeks followed by an electron boost to the tumor bed of 11.1 Gy in five fractions. The primary end point was change in breast appearance scored from serial photographs taken before RT and at one-, two-, and five-year follow-ups. Secondary end points included patient self-assessments of breast discomfort, breast hardness, QOL, and physician assessments of breast induration. Two hundred forty (79%) patients with five-year photographs were available for analysis. Change in breast appearance was identified in 71 (58%) of 122 allocated standard 2D treatment compared with 47 (40%) of 118 patients allocated IMRT. Significantly fewer patients in the IMRT group developed palpable induration assessed clinically in the center of the breast, pectoral fold, inframammary fold, and at the boost site. No significant differences between treatment groups were found in patient-reported breast discomfort, breast hardness, or quality of life. The authors concluded that minimization of unwanted radiation dose inhomogeneity in the breast reduced late adverse effects. While the change in breast appearance was statistically different, a beneficial effect on QOL was not demonstrated

In 2009, Barnett published baseline characteristics and dosimetry results of a single-center RCT of IMRT for early breast cancer after breast-conserving surgery.[14] Subsequently, in 2012, Barnett reported on the two-year interim results of the RCT.[15] In this trial, 1145 patients with early breast cancer were evaluated for external-beam radiotherapy. Twenty-nine percent had adequate dosimetry with standard RT. The other 815 patients were randomly assigned to receive either IMRT or 2D-RT. Inhomogeneity occurred most often when the dose-volume was greater than 107% (V107) of the prescribed dose to greater than 2 cm3 breast volume with conventional radiation techniques. When breast separation was 21 cm or more, 90% of patients had received greater than V107 of the prescribed dose to greater than 2 cm3 with standard radiation planning. The incidence of acute toxicity did not differ significantly between groups. Additionally, photographic assessment scores for breast shrinkage were not significantly different between groups. The authors noted overall cosmesis after 2D-RT and IMRT was dependent on surgical cosmesis, suggesting breast shrinkage and induration were due to surgery rather than radiation, thereby masking the potential cosmetic benefits of IMRT.

Nonrandomized Comparative Studies

Guttmann (2018) published a single-center retrospective analysis of 413 women who received tangential whole-breast irradiation between 2011 and 2015.[16] Of the patients, 212 underwent IMRT and 201 received 3D-CRT. The main end point was a comparison of acute radiation dermatitis (grade 2+), and secondary end points were acute fatigue and breast pain. Grade 2+ radiation dermatitis was experienced by 59% of 3D-CRT patients and 62% of IMRT (p=0.09). There was also no significant difference between 3D-CRT and IMRT for breast pain (grade 2+, 18% vs 18%, respectively; p=0.33) or fatigue (grade 2+, 18% vs 25.5%, respectively; p=0.24). A study limitation was that follow-up varied across patients because those treated with IMRT completed treatment one week sooner that those treated with 3D-CRT.

In 2012, Hardee compared the dosimetric and toxicity outcomes after treatment with IMRT or 3D-CRT for WBI in 97 consecutive patients with early-stage breast cancer, who were assigned to either approach after partial mastectomy based on insurance carrier approval for reimbursement for IMRT.[17] IMRT significantly reduced the maximum radiation dose to the breast (Dmax median, 110% for 3D-CRT vs 107% for IMRT; p<0.001) and improved median dose homogeneity (median, 1.15 for 3D-CRT vs 1.05 for IMRT; p<0.001) when compared with 3D-CRT. These dosimetric improvements were seen across all breast volume groups. Grade

two dermatitis occurred in 13% of patients in the 3D-CRT group and 2% in the IMRT group. IMRT moderately decreased rates of acute pruritus (p=0.03) and grade two and three subacute hyperpigmentation (p=0.01). With a minimum of six months of follow-up, the treatment was reported to be similarly well-tolerated by both groups, including among women with large breast volumes.[17]

Freedman studied the time spent with radiation-induced dermatitis during a course of RT for women with breast cancer treated with 2D-RT or IMRT.[18] For this 2009 study, the population consisted of 804 consecutive women with early-stage breast cancer treated with breast-conserving surgery and radiation from 2001 to 2006 at a single center. All patients were treated with whole-breast radiotherapy (WBRT) followed by a boost to the tumor bed. WBRT consisted of conventional wedged photon tangents (n=405) earlier in the study period, and mostly of photon IMRT (n=399) in later years. All patients had acute dermatitis graded weekly during treatment. The IMRT patients spent 82% of weeks during treatment with grade 0 or 1 dermatitis and 18% with grade two or three dermatitis, compared with 29% and 71% of patients, respectively, treated with 2D-RT (p<0.001). From this pre/post study, the authors concluded that breast IMRT is associated with a significant decrease both in the time spent during treatment with grade two or three dermatitis and in the maximum severity of dermatitis compared with that associated with conventional radiation. Interpretation of these results is limited by lack of a contemporaneous comparators.

Hardee (2012) compared the dosimetric and toxicity outcomes after treatment with IMRT or 3D-CRT for whole-breast irradiation in a consecutive series of 97 patients with early stage breast cancer, who were assigned to either approach after segmental mastectomy based on insurance carrier approval for reimbursement for IMRT.21 IMRT significantly reduced the maximum dose to the breast (Dmax median, 110% for 3D-CRT vs 107% for IMRT; Wilcoxon test, p<0.001) and improved median dose homogeneity (median, 1.15 for 3D-CRT vs 1.05 for IMRT; Wilcoxon test, p<0.001) when compared with 3D-CRT. These dosimetric improvements were seen across all breast volume groups. Grade two dermatitis occurred in 13% of patients in the 3D-CRT group and 2% in the IMRT group. IMRT moderately decreased rates of acute pruritus (p=0.03) and grade two to three subacute hyperpigmentation (Fisher exact test, p=0.01). With a minimum of six months of follow-up, the treatment was reported to be similarly well-tolerated in either group, including among women with large breast volumes.[17]

Partial Breast Irradiation

IMRT has also been investigated as a technique of partial breast irradiation, as an alternative to whole breast irradiation therapy after breast conserving surgery.

Randomized Controlled Trials

In 2010, Livi reported on preliminary results for 259 patients randomized in a phase three trial, which began in September 2008, that compared conventional fractionated WBI treatment (n=128) to accelerated partial-breast irradiation (APBI) with IMRT (n=131).[19] Radiation Therapy Oncology Group grade one and two skin toxicity were observed at rates of 22% and 19% in the whole-breast treatment group versus 5% and 0.8% in the partial-breast treatment group, respectively. The authors concluded partial-breast irradiation with IMRT is feasible but noted long-term results on health outcomes are needed. Additionally, 18 months after RT, one case of contralateral breast cancer was diagnosed in the partial-breast irradiation group, raising authors' concern that it may be related to the high dosage of IMRT.

Five-year survival analysis results of the Livi RCT were reported in 2015.[20] A total of 520 patients were accrued, with 260 per group. The WBI arm received conventional RT at total dose of 50 Gy in 25 fractions, followed by a boost to the tumor bed of 10 Gy in five fractions. The APBI arm received a total dose of 30 Gy to the tumor bed in five daily fractions. The primary end point was occurrence of Ipsilateral breast tumor recurrence, with main analysis by intention-to-treat. At median follow-up of five years for all patients (interquartile range, 3.4 to 7.0), the Ipsilateral breast tumor recurrence rate was 1.5% (three cases; 95% CI, 0.1 to 3.0) in the APBI group and 1.5% in the WBI group (three cases; 95% CI 0.0 to 2.8). Log-rank analysis showed no significant difference between the groups (p=0.86). The five-year OS rate was 99% for the APBI group and 97% for the WBI group (p=*NS*). The APBI group had significantly better acute (p≤0.000) and late (p=0.004) skin adverse events (grade ≤2) compared with the WBI group and better cosmetic outcome (p=0.045).

Ten-year results of the Livi RCT were reported by Meattini in 2020. Median follow-up was 10.7 years. Similar outcomes between groups were reported for 10-year cumulative incidence of ipsilateral breast tumor recurrence (WBI: 2.5%; APBI: 3.7%; p=0.40), 10-year OS (91.9% in both group; p=0.86), and 10-year breast cancer-specific survival (WBI: 96.7%; APBI: 97.8%; p=0.45). There were statistically significant differences reported for acute toxicity, late toxicity, and cosmetic outcome (all p=0.0001), with better outcomes reported in the APBI arm.

Chest Wall Irradiation

Few studies have examined the use of IMRT for chest wall irradiation in postmastectomy breast cancer patients. Available studies have mainly focused on treatment planning and techniques to improve dose distributions to targeted tissues while reducing radiation to normal tissue and critical surrounding structures, such as the heart and lungs.

Lee (2023) published a study comparing IMRT to conventional radiation therapy after mastectomy with a focus on breast reconstruction outcomes.[21] The study involved 202 patients and 206 breasts. Of these, 139 were treated with IMRT and 67 had conventional radiation therapy. Reconstruction failure was much lower in patients treated with IMRT; 3.0% vs. 16.4%; (p=0.002). Other major complications, including infection, capsular contracture, fat or soft tissue necrosis, and fibrosis were also significantly more common in patients treated with conventional radiation therapy (p<0.001). Survival outcomes and local recurrence were similar at two years (p=0.12; p=0.41).

Zhao (2021) retrospectively evaluated differences in survival rate, recurrence, and late adverse effects in 223 patients with clinical stage II to III breast cancer receiving IMRT or 3D-CRT.[22] Patients were included if they underwent a modified radical mastectomy, had positive axillary lymph nodes, and received either IMRT of the chest wall and regional nodes contoured as a whole planning target volume (n=129) or conventional segmented 3D-CRT (n=94). The mean follow-up of the study was 104.3 months. The eight-year disease-free survival rates were significantly improved in the IMRT group (86% vs. 73.4%; p=0.022); however, the OS rates were not significantly different between the groups (91.4% IMRT vs. 86.2% 3D-CRT; p=0.530). The number of patients that suffered from chronic skin toxicity was 96 in the IMRT arm and 73 in the 3D-CRT arm (p=0.577), with most patients experiencing grade 1 to 2 skin reactions. Similarly, there were no significant differences between the groups with regard to other late adverse effects including grade 1 to 2 ipsilateral lung injury (30.2% IMRT vs. 31.9% 3D-CRT; p=0.788) and grade 1 to 2 ipsilateral shoulder mobility (46.5% IMRT vs. 47.9% 3D-CRT; p=0.841). Additionally, the percentages of patients with left breast cancer who suffered from

grade 1 to 2 cardiac injury in the IMRT and 3D-CRT groups were 30.6% and 25.3%, respectively.

Ho (2019) published the long-term pulmonary outcomes of a feasibility study of inverse-planned, multibeam intensity modulated radiation therapy in node-positive breast cancer patients receiving regional nodal irradiation.[23] Authors determined that based on early treatment planning criteria, multibeam IMRT in this population was dosimetrically feasible. While the authors' primary endpoint was feasibility, they also observed the incidence of radiation pneumonitis grade 3 or greater and changes in pulmonary function. The later endpoints were measured with the Common Terminology Criteria for Adverse Events and pulmonary function tests and community-acquired pneumonia questions. Of 104 completed follow-up procedures, the overall rate of respiratory toxicity was 10.6%, with 1 grade 3 radiation pneumonitis event.

Rastogi (2018) published a retrospective study of 107 patients receiving radiotherapy post mastectomy to the left chest wall.[24] Patients were treated with 3D-CRT (n=64) or IMRT (n=43). The planning target volume, homogeneity index, and conformity index for both groups were compared. IMRT had a significantly improved conformity index score (1.127) compared with 3D-CRT (1.254; $p<0.001$), while results for both planning target volume (IMRT, 611.7 vs 3D-CRT, 612.2; $p=0.55$) and homogeneity index (IMRT, 0.094 vs 3D-CRT, 0.096; $p=0.83$) were comparable. Furthermore, secondary analyses showed that IMRT differed had significantly lower mean- and high-dose volumes to the heart and ipsilateral lung ($p<0.001$ and $p<0.001$, respectively), while 3D-CRT had superior low-dose volume ($p<0.001$). The study was limited by its small population size and short follow-up.

Wang (2017) reported a retrospective study of postmastectomy IMRT.[25] A total of 200 patients were evaluated for performance and complications. Follow-up was a minimum of one year and mean of 28.5 months. Toxicities reported were three patients with grade 3 acute radiation dermatitis, one patient with grade 2 acute radiation-induced lung injury, three patients with acute radiation esophagitis, and seven patients with edema. A subset of 125 patients were followed for two or more years. Two-year local-regional recurrent, distant metastasis, and disease-free survival were 1.6%, 6.4%, and 92.8%, respectively.

Rudat (2011) compared IMRT treatment planning for chest wall irradiation with 3D-CRT in 20 postmastectomy patients.[26] The authors reported that IMRT resulted in significantly decreased heart and lung high dose-volume with a significantly improved conformity index when compared with 3D-CRT. However, there was no significant difference reported in the homogeneity index. The authors noted that longer-term prospective studies are needed to further assess cardiac toxicity and secondary lung cancer risk with multifield IMRT, which while reducing high dose-volume, increases mean heart and lung dose.

Fractionation

Realization of the rough equality of the α/β ratio of cell survival of breast cancer cells compared to cells of neighboring organs at risk has prompted interest in exploring shorter “moderately hypofractionated” treatment schedules. In these schedules, fewer fractions of higher daily doses would be employed with total doses adjusted via biologic modeling to be biologically equally effective in local control, toxicity risk and cosmetic outcome.

The Royal Marsden Hospital and Gloucestershire Oncology Centre (RMH/GOC) conducted an initial exploratory trial attempting to find a more convenient three-week treatment schedule

which was iso-effective with conventional five-week approaches. A total of 1,410 women with breast cancer post-breast-conserving surgery were randomized to receive either conventional 50 Gy over five weeks or either 39 or 42.9 Gy over 13 fractions given in non-daily fashion over the same five weeks.[27, 28] The primary endpoint was late change in breast appearance based on blinded scoring of photographs. The 42.9 Gy group had the highest change from immediately post-surgery to a minimum of five-year follow-up at 45.7%, compared to 39.6 and 30.3% for the conventional fractionation and 39 Gy groups, respectively. Outcome analysis at 10 years (median follow-up of 9.7 years; interquartile range [IQR] 7.8 to 11.8) suggested higher local failure in the 39 Gy arm compared to the 42.9 Gy group (14.8% [11.2 to 18.3] in the 39 Gy group and 9.6% [6.7 to 12.6] in the 42.9 Gy group; chi^2 test, p=0.027; local recurrence was 12.1% with conventional fractionation).

Ten-year results of a randomized trial conducted by the Ontario Clinical Oncology Group (OCOG) was published by Whelan in 2010.[29] The study randomized women with invasive breast cancer who had undergone breast-conserving surgery to receive conventional fractionation (50.0 Gy in 25 fractions; n=612) or hypofractionation (42.5 Gy in 16 fractions; n=622). No statistically significant difference was found between groups for 10-year cumulative incidence of local recurrence (6.7% for conventional fractionation vs. 6.2% for hypofractionation; 95% CI -2.5 to 3.5; p<0.001).

The UK Standardisation of Breast Radiotherapy (START A and B) trials were conducted between 1999 and 2002 to evaluate 13 and 15 fraction regimens for the treatment of breast cancer post-surgery. These moderately hypofractionated regimens were compared to the historical standard regimen (50 Gy in 25 fractions). Initial results were published in 2008 and 10-year results were published by Haviland in 2013. The START A trial randomized 2,236 women to receive 50 Gy in 25 fractions of 2.0 Gy versus 41.6 Gy or 39 Gy in 13 fractions of 3.2 Gy or 3.0 Gy over five weeks. Median follow-up of surviving patients was 5.1 years (IQR 4.4 to 6.0). The estimated five-year local-regional relapse was 3.6%, 3.5%, and 5.2% in the 50 Gy, 41.6 Gy, and 39 Gy groups, respectively, with neither hypofractionated group varying significantly from the conventional fractionation group. No clinically significant differences were identified between either of the hypofractionated schedules compared with 50 Gy for rates of distant relapse, disease-free survival, and overall survival. Assessment of breast appearance based on photographs in 1,055 patients resulted in hazard ratios (HR) for any (mild or marked) change in breast appearance of 1.09 (95% CI 0.85 to 1.40, p=0.62) after 41.6 Gy and 0.69 (95% CI 0.52 to 0.91, p=0.01) after 39 Gy compared with the 50 Gy group.

The START B trial randomized 2,215 women to 40 Gy in 15 daily fractions over three weeks versus the conventional 50 Gy in 25 fractions over five weeks. The five-year rate of local-regional relapse was 2.2% (95% CI 1.3 to 3.1) in the 40 Gy group and 3.3% (95% CI 2.2 to 4.5) in the 50 Gy group (HR 0.79; 95% CI 0.48 to 1.29). Assessment of breast appearance based on photographs in 923 patients resulted in HR for change in breast appearance of 0.83 (95% CI 0.66 to 1.04; p=0.06).

There has also been interest in ultrahypofractionation, which was evaluated in the UK FAST trial.[30, 31] This trial included 915 women ≥ 50 years of age with low-risk invasive breast carcinoma (pT1-2 pN0). Participants were randomly assigned to receive 50 Gy in 25 fractions over five weeks or 30 or 28.5 Gy in five once-weekly fractions of 6.0 or 5.7 Gy, also over five weeks. The analysis of photographic breast appearance at two and five years (the primary end point) resulted in odds ratios (ORs) of 1.64 (95% CI 1.08 to 2.49; p=0.019) for 30 Gy and 1.10 (95% CI 0.70 to 1.71; p=0.686) for 28.5 Gy versus 50 Gy. Physician assessments of radiation-

induced breast changes (OR 2.12, p<0.001 for 30 Gy and OR 1.22, p=0.248 for 28.5 Gy, both versus 50 Gy) and ipsilateral disease in the breast (relapse or new primary; no significant differences reported) were secondary endpoints.

Summary

There is modest evidence from RCTs for a decrease in acute skin toxicity with IMRT compared with 2D-RT for WBI. One RCT reported improvements in moist desquamation of skin, but did not find differences in grade three or four skin toxicity, pain symptoms, or QOL. Another RCT found a change in breast appearance, but not QOL. A third RCT reported no differences in cosmetic outcomes at two years for IMRT compared with 2D-RT. Dosimetry studies have demonstrated that IMRT reduces inhomogeneity of radiation dose, thus potentially providing a mechanism for reduced skin toxicity. However, because WBRT is now delivered by 3D-CRT, these comparison data are of limited value. Studies on IMRT compared to 3D-CRT include one RCT on partial-breast IMRT and one nonrandomized comparative study on whole-breast IMRT. These studies have suggested that IMRT may improve short-term clinical outcomes. Ten-year follow-up is needed to evaluate the effect of partial-breast IMRT on recurrence and survival. Few studies have reported on health outcomes after IMRT for chest wall irradiation in postmastectomy breast cancer patients. The risk of secondary lung cancers and cardiac toxicity needs to be further evaluated.

Overview analysis of 10-year data from the above randomized trials on hypofractionation for WBI suggests that clinical outcomes including loco regional control, disease free survival, overall survival, late toxicity and cosmesis were comparable in the diverse hypofractionated and conventional treatment groups.

PRACTICE GUIDELINE SUMMARY

NATIONAL COMPREHENSIVE CANCER NETWORK

National Comprehensive Cancer Network (NCCN) guidelines for breast cancer (v.5.2024) indicate that for[32]:

- Whole-breast irradiation, the whole breast should receive a hypofractionated dose of 40-42.5 Gy in 15-16 fractions; in selected cases 45-50.4 Gy in 25-28 fractions.
- Post-mastectomy radiation, IMRT is included with other techniques as a treatment option.
- Regional node radiation, patients not undergoing breast reconstruction may [alternatively] receive 40 Gy at 2.67 Gy/fx or 42.5 Gy at 2.66 Gy/fx.

The guidelines state that “Dose-volume histograms (DVHs) should be used to evaluate, dose and constraints to normal tissues (i.e., heart, lung), and planning target volumes (PTVs). The guidelines recommend accelerated partial breast irradiation (APBI) for individuals who are BRCA negative and meet the 2016 ASTRO criteria. The preferred regimen for APBI is listed as 30 Gy/5 fractions QOD, which is delivered with IMRT. The preferred regimen for whole breast irradiation is 15 to 16 fractions +/- tumor bed boost post-lumpectomy and 25 to 28 fractions post-mastectomy to the chest wall +/- scar boost.

AMERICAN SOCIETY FOR RADIATION ONCOLOGY

In 2023, ASTRO published guidelines on partial breast irradiation (PBI) for patients with early-stage invasive breast cancer or ductal carcinoma in situ (DCIS).[33] IMRT was recommended for patients with early-stage invasive breast cancer or DCIS receiving PBI (strong recommendation, moderate quality of evidence). Other techniques including 3-D conformal radiation therapy are also recommended.

SUMMARY

The available research on intensity modulated radiotherapy (IMRT) for breast cancer suggests that IMRT may lead to clinical outcomes comparable with 3D-conformal radiation therapy (CRT). In addition, IMRT may reduce cardiac doses in left-sided breast cancer, avoid or minimize hotspots to the breast, and lead to a decrease in acute skin toxicity. Therefore, IMRT to deliver breast irradiation may be considered medically necessary in select patients when policy criteria are met.

For situations where policy criteria are not met, intensity-modulated radiotherapy (IMRT) has not been shown to improve net health outcomes compared to other treatment modalities. Therefore, except in the select group of patients identified in the policy criteria, IMRT is not medically necessary for the treatment of breast cancer.

Hypofractionation, the use of fewer treatment sessions with higher doses, is supported by the evidence and preferred by clinical practice guidelines for breast cancer in the clinical contexts outlined in the policy criteria. When a longer conventional fractionation regimen is planned, a note may be provided explaining clinical rationale for choosing that regimen rather than hypofractionation. Therefore, in the clinical contexts for which the policy criteria indicate that hypofractionation is preferred, if no clinical rationale for its use is provided, conventionally fractionated intensity modulated radiotherapy (IMRT) is considered not medically necessary.

REFERENCES

1. International Commission on Radiation Units and Measurements. *J icru.* 2014;14(1):Np. PMID: 27789602
2. Remouchamps VM, Vicini FA, Sharpe MB, et al. Significant reductions in heart and lung doses using deep inspiration breath hold with active breathing control and intensity-modulated radiation therapy for patients treated with locoregional breast irradiation. *Int J Radiat Oncol Biol Phys.* 2003;55(2):392-406. PMID: 12527053
3. Shumway DA CK, Farah MH, Viola KE, Nayfeh T, Saadi S, Shah V, Hasan B, Shah S, Mohammed K, Riaz IB, Prokop LJ, Wang Z, Murad, MH. Partial Breast Irradiation for Breast Cancer. *Comparative Effectiveness Review No 259.* 2023;AHRQ Publication No. 23-EHC001. PMID:
4. Dayes I, Rumble RB, Bowen J, et al. Intensity-modulated radiotherapy in the treatment of breast cancer. *Clin Oncol (R Coll Radiol).* 2012;24(7):488-98. PMID: 22748561
5. Choi KH, Ahn SJ, Jeong JU, et al. Postoperative radiotherapy with intensity-modulated radiation therapy versus 3-dimensional conformal radiotherapy in early breast cancer: A randomized clinical trial of KROG 15-03. *Radiotherapy and oncology : journal of the*

European Society for Therapeutic Radiology and Oncology. 2021;154:179-86. PMID: 32980384
6. Hörner-Rieber J, Forster T, Hommertgen A, et al. Intensity Modulated Radiation Therapy (IMRT) With Simultaneously Integrated Boost Shortens Treatment Time and Is Noninferior to Conventional Radiation Therapy Followed by Sequential Boost in Adjuvant Breast Cancer Treatment: Results of a Large Randomized Phase III Trial (IMRT-MC2 Trial). *Int J Radiat Oncol Biol Phys.* 2021;109(5):1311-24. PMID: 33321192
7. Krug D, Köder C, Häfner MF, et al. Acute toxicity of normofractionated intensity modulated radiotherapy with simultaneous integrated boost compared to three-dimensional conformal radiotherapy with sequential boost in the adjuvant treatment of breast cancer. *Radiat Oncol.* 2020;15(1):235. PMID: 33050920
8. Forster T, Hommertgen A, Häfner MF, et al. Quality of life after simultaneously integrated boost with intensity-modulated versus conventional radiotherapy with sequential boost for adjuvant treatment of breast cancer: 2-year results of the multicenter randomized IMRT-MC2 trial. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology.* 2021;163:165-76. PMID: 34480960
9. Jagsi R, Griffith KA, Moran JM, et al. A Randomized Comparison of Radiation Therapy Techniques in the Management of Node-Positive Breast Cancer: Primary Outcomes Analysis. *Int J Radiat Oncol Biol Phys.* 2018;101(5):1149-58. PMID: 30012527
10. Pignol JP, Olivotto I, Rakovitch E, et al. A multicenter randomized trial of breast intensity-modulated radiation therapy to reduce acute radiation dermatitis. *J Clin Oncol.* 2008;26(13):2085-92. PMID: 18285602
11. Pignol JP, Truong P, Rakovitch E, et al. Ten years results of the Canadian breast intensity modulated radiation therapy (IMRT) randomized controlled trial. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology.* 2016;121(3):414-19. PMID: 27637858
12. Donovan EM, Bleackley NJ, Evans PM, et al. Dose-position and dose-volume histogram analysis of standard wedged and intensity modulated treatments in breast radiotherapy. *Br J Radiol.* 2002;75(900):967-73. PMID: 12515705
13. Donovan E, Bleakley N, Denholm E, et al. Randomised trial of standard 2D radiotherapy (RT) versus intensity modulated radiotherapy (IMRT) in patients prescribed breast radiotherapy. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology.* 2007;82(3):254-64. PMID: 17224195
14. Barnett GC, Wilkinson J, Moody AM, et al. A randomised controlled trial of forward-planned radiotherapy (IMRT) for early breast cancer: baseline characteristics and dosimetry results. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology.* 2009;92(1):34-41. PMID: 19375808
15. Barnett GC, Wilkinson JS, Moody AM, et al. Randomized controlled trial of forward-planned intensity modulated radiotherapy for early breast cancer: interim results at 2 years. *Int J Radiat Oncol Biol Phys.* 2012;82(2):715-23. PMID: 21345620
16. Guttmann DM, Gabriel P, Kennedy C, et al. Comparison of acute toxicities between contemporary forward-planned 3D conformal radiotherapy and inverse-planned intensity-modulated radiotherapy for whole breast radiation. *The breast journal.* 2018;24(2):128-32. PMID: 28703444
17. Hardee ME, Raza S, Becker SJ, et al. Prone hypofractionated whole-breast radiotherapy without a boost to the tumor bed: comparable toxicity of IMRT versus a 3D conformal technique. *Int J Radiat Oncol Biol Phys.* 2012;82(3):e415-23. PMID: 22019349

18. Freedman GM, Li T, Nicolaou N, et al. Breast intensity-modulated radiation therapy reduces time spent with acute dermatitis for women of all breast sizes during radiation. *Int J Radiat Oncol Biol Phys.* 2009;74(3):689-94. PMID: 19362779
19. Livi L, Buonamici FB, Simontacchi G, et al. Accelerated partial breast irradiation with IMRT: new technical approach and interim analysis of acute toxicity in a phase III randomized clinical trial. *Int J Radiat Oncol Biol Phys.* 2010;77(2):509-15. PMID: 19700248
20. Livi L, Meattini I, Marrazzo L, et al. Accelerated partial breast irradiation using intensity-modulated radiotherapy versus whole breast irradiation: 5-year survival analysis of a phase 3 randomised controlled trial. *Eur J Cancer.* 2015;51(4):451-63. PMID: 25605582
21. Lee CT, Ruth K, Patel S, et al. Factors Associated with Reconstruction Failure and Major Complications After Postmastectomy Radiation to a Reconstructed Breast. *Pract Radiat Oncol.* 2023;13(2):122-31. PMID: 36332800
22. Zhao Y, Zhu J, Zhang X, et al. Integrated IMRT vs segmented 3D-CRT of the chest wall and supraclavicular region for Breast Cancer after modified Radical Mastectomy: An 8-year follow-up. *J Cancer.* 2021;12(5):1548-54. PMID: 33532000
23. Ho AY, Ballangrud A, Li G, et al. Long-Term Pulmonary Outcomes of a Feasibility Study of Inverse-Planned, Multibeam Intensity Modulated Radiation Therapy in Node-Positive Breast Cancer Patients Receiving Regional Nodal Irradiation. *Int J Radiat Oncol Biol Phys.* 2019;103(5):1100-08. PMID: 30508620
24. Rastogi K, Sharma S, Gupta S, et al. Dosimetric comparison of IMRT versus 3DCRT for post-mastectomy chest wall irradiation. *Radiat Oncol J.* 2018;36(1):71-78. PMID: 29621872
25. Wang Q, Jie W, Liang Z, et al. Postmastectomy intensity modulation radiated therapy of chest wall and regional nodes: Retrospective analysis of the performance and complications up for 5 years. *Medicine (Baltimore).* 2017;96(39):e7956. PMID: 28953618
26. Rudat V, Alaradi AA, Mohamed A, et al. Tangential beam IMRT versus tangential beam 3D-CRT of the chest wall in postmastectomy breast cancer patients: a dosimetric comparison. *Radiat Oncol.* 2011;6:26. PMID: 21418616
27. Owen JR, Ashton A, Bliss JM, et al. Effect of radiotherapy fraction size on tumour control in patients with early-stage breast cancer after local tumour excision: long-term results of a randomised trial. *Lancet Oncol.* 2006;7(6):467-71. PMID: 16750496
28. Yarnold J, Ashton A, Bliss J, et al. Fractionation sensitivity and dose response of late adverse effects in the breast after radiotherapy for early breast cancer: long-term results of a randomised trial. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology.* 2005;75(1):9-17. PMID: 15878095
29. Whelan TJ, Pignol JP, Levine MN, et al. Long-term results of hypofractionated radiation therapy for breast cancer. *N Engl J Med.* 2010;362(6):513-20. PMID: 20147717
30. Agrawal RK, Alhasso A, Barrett-Lee PJ, et al. First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015). *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology.* 2011;100(1):93-100. PMID: 21752481
31. Brunt AM, Haviland JS, Sydenham M, et al. Ten-Year Results of FAST: A Randomized Controlled Trial of 5-Fraction Whole-Breast Radiotherapy for Early Breast Cancer. *J Clin Oncol.* 2020;38(28):3261-72. PMID: 32663119
32. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Breast Cancer. v.5.2024. [cited 10/30/2024]. 'Available from:' https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.

33. Shaitelman SF, Anderson BM, Arthur DW, et al. Partial Breast Irradiation for Patients With Early-Stage Invasive Breast Cancer or Ductal Carcinoma In Situ: An ASTRO Clinical Practice Guideline. *Pract Radiat Oncol.* 2024;14(2):112-32. PMID: 37977261

CODES

NOTE: The correct code to use for image fusion performed to provide enhanced delineation of target and normal critical structures is CPT code 77399 (Unlisted procedure, medical radiation physics, dosimetry and treatment devices, and special services); however, it is considered part of the treatment planning.

Codes	Number	Description
CPT	77301	Intensity modulated radiotherapy plan, including dose volume histograms for target and critical structure partial tolerance specification
	77338	Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan
	77385	Intensity modulated radiation treatment deliver (IMRT), includes guidance and tracking, when performed; simple
	77386	;complex
HCPCS	G6015	Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
	G6016	Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session

Date of Origin: *July 2019*