Medical Policy

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Title: Intensity Modulated Radiation Therapy (IMRT) of the Breast and Lung

Description/Background

For certain stages of many cancers, including breast and lung, randomized controlled trials (RCTs) have shown that postoperative radiotherapy (RT) improves outcomes for operable patients. Adding radiation to chemotherapy also improves outcomes for those with inoperable lung tumors that have not metastasized beyond regional lymph nodes.

RADIOTHERAPY TECHNIQUES

Radiation therapy may be administered externally (ie, a beam of radiation is directed into the body) or internally (ie, a radioactive source is placed inside the body, near a tumor).[1] External radiotherapy (RT) techniques include "conventional" or 2-dimensional (2D) RT, 3-dimensional (3D) conformal RT, and intensity-modulated radiation therapy (IMRT).

Conventional External-Beam Radiotherapy

Methods to plan and deliver RT have evolved that permit more precise targeting of tumors with complex geometries. Conventional 2D treatment planning utilizes X-ray films to guide and position radiation beams.[1] Bony landmarks bones visualized on X-ray are used to locate a tumor and direct the radiation beams. The radiation is typically of uniform intensity.

Three-Dimensional Conformal Radiotherapy

Radiation treatment planning has evolved to use 3D images, usually from computed tomography (CT) scans, to more precisely delineate the boundaries of the tumor and to discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Three-dimensional conformal RT (3D-CRT) involves initially scanning the patient in the position that will be used for the radiation treatment.[1] The tumor target and surrounding normal organs are then outlined in 3D on the scan. Computer software assists in determining the orientation of radiation beams and the amount of radiation the tumor and normal tissues receive to ensure coverage of the entire tumor in order to minimize radiation exposure for at risk normal tissue and nearby organs. Other imaging techniques and devices such as multileaf

collimators (MLCs) may be used to "shape" the radiation beams. Methods have also been developed to position the patient and the radiation portal reproducibly for each fraction and to immobilize the patient, thus maintaining consistent beam axes across treatment sessions.

Intensity-Modulated Radiotherapy
IMRT is the more recent development in external radiation. Treatment planning and delivery are more complex, time-consuming, and labor-intensive for IMRT than for 3D-CRT. Similar to 3D-CRT, the tumor and surrounding normal organs are outlined in 3D by a scan and multiple radiation beams are positioned around the patient for radiation delivery.[1] In IMRT, radiation beams are divided into a grid-like pattern, separating a single beam into many smaller "beamlets". Specialized computer software 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 normal tissues. Based on these parameters and a digitally reconstructed radiographic image of the tumor, surrounding tissues, and organs at risk, computer software optimizes the location, shape, and intensities of the beam ports to achieve the treatment plan’s goals.

Increased conformality may permit escalated tumor doses without increasing normal tissue toxicity and is proposed to 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.

Other advanced techniques may further improve RT treatment by improving dose distribution. These techniques are considered variations of IMRT. Volumetric modulated arc therapy delivers radiation from a continuous rotation of the radiation source. The principal advantage of volumetric modulated therapy is greater efficiency in treatment delivery time, reducing radiation exposure and improving target radiation delivery due to less patient motion. Image-guided RT involves the incorporation of imaging before and/or during treatment to more precisely deliver RT to the target volume.

Investigators are exploring an active breathing control device combined with moderately deep inspiration breath-holding techniques to improve conformality and dose distributions during IMRT for breast cancer.[2] Techniques presently being studied with other tumors (eg, lung cancer)[3] either gate beam delivery to the patient’s respiratory movement or continuously monitor tumor (by in-room imaging) or marker (internal or surface) positions to aim radiation more accurately at the target. The impact of these techniques on outcomes of 3D-CRT or IMRT for breast cancer is unknown. However, it appears likely that respiratory motion alters the dose distributions actually delivered while treating patients from those predicted by plans based on static CT scans or measured by dosimetry using stationary (nonbreathing) targets.

Regulatory Status

In general, IMRT systems include intensity modulators, which control, block, or filter the intensity of radiation; and RT planning systems, which plan the radiation dose to be delivered.

A number of intensity modulators have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Intensity modulators include the Innocure Intensity Modulating Radiation Therapy Compensators (Innocure) cleared in 2006, and the Decimal Tissue Compensator (Southeastern Radiation Products), cleared in 2004. FDA product code: IXI. Intensity modulators may be added to standard linear accelerators to deliver IMRT when used with proper treatment planning systems.

Radiotherapy planning systems have also been cleared for marketing by the FDA through the 510(k) process. They include the Prowess Panther (Prowess) in 2003, TiGRT (LinaTech) in 2009, Ray Dose (RaySearch Laboratories) in 2008, and the Accuray Precision Treatment Planning System (Accuray Incorporated) in 2021. FDA product code: MUJ.

Fully integrated IMRT systems are also available. These devices are customizable and support all stages of IMRT delivery, including planning, treatment delivery, and health record management. One such device cleared for marketing by the FDA through the 510(k) process is the Varian® IMRT system (Varian Medical Systems). FDA product code: IYE.

Medical Policy Statement

Breast Cancer:
Intensity-modulated radiotherapy (IMRT) may be considered established for the treatment of breast cancer based on analysis of dosimetric data including comparative models if necessary.

Lung Cancer:
IMRT may be considered established for the treatment of lung cancer based on analysis of dosimetric data including comparative models if necessary.

Inclusionary and Exclusionary Guidelines

Refer to medical policy statements.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

77301 77338 77385 77386 77387 G6015
G6016

Other codes (investigational, not medically necessary, etc.):

N/A

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Multiple dose-planning studies generate 3-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 delivers 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 approximates 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 events from IMRT versus alternative radiation delivery would constitute definitive evidence of establishing the benefit of IMRT. Single-arm series of IMRT can give insights into the potential for benefit, particularly if an adverse event 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, in the absence of such comparative trials, it is likely that the 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. For other indications, such as using IMRT to provide better tumor control, comparative studies of health outcomes are needed to demonstrate such a benefit.

BREAST CANCER

Clinical Context and Therapy Purpose

The purpose of the use of IRMT in individuals who have breast cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with breast cancer.

Interventions

The therapy being considered is IMRT. Radiotherapy (RT) is an integral component of the treatment of breast cancer. IMRT has been proposed as a method of RT that allows adequate radiation to the tumor while minimizing the radiation dose to surrounding normal tissues and critical structures.

Comparators

The following therapy is currently being used to make decisions about breast cancer: 2-dimensional and 3D-CRT.

Outcomes

The general outcomes of interest are overall survival (OS), disease-specific survival, locoregional control, quality of life, and treatment-related adverse events (eg, radiation dermatitis).

The grading of acute radiation dermatitis is relevant to studies of IMRT for the treatment of breast cancer. Acute radiation dermatitis is graded on a scale of 0 (no change) to 5 (death). Grade 2 is moderate erythema and patchy moist desquamation, mostly in skin folds; grade 3 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.[4] This is a concern because of the potential development of late cardiac complications (eg, coronary artery disease) following fractionated radiotherapy (FRT) to the left breast.

In addition, IMRT may reduce toxicity to structures adjacent to tumors, allowing dose escalation to the target area and fewer breaks in treatment courses due to a reduction in side effects. However, this may come with a loss of locoregional control and OS.

Follow-up after IMRT varies by the staging of breast cancer and patient age at diagnosis. A 5- to 10-year follow-up to monitor for recurrence has been recommended.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

WHOLE-BREAST IRRADIATION WITH INTENSITY-MODULATED RADIOTHERAPY VERSUS 2-DIMENSIONAL RADIOTHERAPY

Systematic reviews

Dayes et al (2012) conducted a systematic review of the evidence for IMRT for whole-breast irradiation (WBI) in the treatment of breast cancer to quantify its potential benefits and to make recommendations for radiation treatment programs.[5] Based on a review of 6 studies (N=2012) published through March 2009 (1 RCT, 3 retrospective cohort studies, 1 historically controlled trial, 1 prospective cohort), reviewers recommended IMRT over conventional RT after breast-conserving surgery to avoid acute adverse effects associated with radiation. There were insufficient data to recommend IMRT over conventional RT based on oncologic outcomes or late toxicity. The RCT included in this review was the Canadian multicenter trial by Pignol et al (2008), details of which are reported in the next section.[6] In this RCT, IMRT was compared with 2D-RT. Computed tomography scans were used in treatment planning for both arms of the study. The types of conventional RT regimens used in the other studies were not reported.

Randomized Controlled Trials

Donovan et al (2007) evaluated IMRT as compared to 2D-RT (using standard wedge compensators) regarding late adverse effects after whole breast RT.[7] Enrolled patients had "higher than average risk of late radiotherapy-adverse effects," which included patients with larger breasts. Trialists stated that while breast size was 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 6 or 10 megavolt photons to a dose of 50 gray (Gy) in 25 fractions in 5 weeks followed by an electron boost to the tumor bed of 11.1 Gy in 5 fractions. The primary endpoint (change in breast appearance) was scored from serial photographs taken before RT and at 1-, 2-, and 5-year follow-ups. Secondary endpoints included patient self-assessments of breast discomfort, breast hardness, QOL, and physician assessments of breast induration. Two hundred forty (79%) patients with 5-year photographs were available for analysis. Change in breast appearance was identified in 71 (58%) of 122 patients 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 QOL. The authors concluded that minimization of unwanted radiation dose inhomogeneity in the breast reduced late adverse events. While the change in breast appearance differed statistically, a beneficial effect on quality of life was not demonstrated.

The multicenter, double-blind RCT by Pignol et al (2008, 2016) 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.[6,8] Patients were assessed each week up to six weeks after RT and then at eight to ten years. A total of 358 patients were

randomized between 2003 and 2005 at 2 Canadian centers, and 331 were analyzed. Of these, 241 patients were available for long-term follow-up. The trialists 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 6 weeks after RT (31% with IMRT vs 48% with standard treatment; p=.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=.013) and pain during RT (p<.001) were associated with chronic pain. Poorer self-assessed cosmetic outcome (p<.001) and QOL (p<.001) were also associated with pain during RT.

Barnett et al (2009) published baseline characteristics and dosimetry results of a single-center RCT assessing IMRT for early breast cancer after breast-conserving surgery.[9] Subsequently, Barnett et al (2012) reported on the 2-year interim results of their RCT.[10] In this trial, 1145 patients with early breast cancer were evaluated for external-beam RT. Twenty-nine percent had adequate dosimetry with standard RT. The other 815 patients were randomized to IMRT or 2D-RT. Inhomogeneity occurred most often when the dose-volume was greater than 107% (V107) of the prescribed dose to a breast volume greater than 2 cm^3 with conventional radiotherapy. When breast separation was 21 cm or more, 90% of patients had received greater than V107 of the prescribed dose to greater than 2 cm^3 with standard radiation planning. The incidence of acute toxicity did not differ significantly between groups. Additionally, photographic assessment scores for breast shrinkage did not differ significantly 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.

WHOLE-BREAST IRRADIATION WITH INTENSITY-MODULATED RADIOTHERAPY VERSUS 3-DIMENSIONAL CONFORMAL RADIOTHERAPY

Randomized Controlled Trials

In their RCT, Jagsi et al (2018) assess whether IMRT with deep inspiration breath hold (DIBH) reduces cardiac or pulmonary toxicity of breast radiotherapy compared to 3-dimensional conformal radiotherapy (3D-CRT), the current standard radiotherapy.[2] The study included 62 women with node-positive breast cancer in whom radiotherapy was indicated for treating the left breast or chest-wall and the internal mammary, infraclavicular, and supraclavicular nodal regions. The primary outcome was percentage decrease in heart perfusion at 1 year post-treatment compared to baseline, measured using attenuation corrected single-photon emission computed tomography (SPECT/CT). A secondary outcome was change in left ventricular ejection fraction (LVEF). 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 1 year, no differences in perfusion of the heart were detected; however, significant differences were found in LVEF. In the 3D-CRT arm, 6 patients had > 5% changes in LVEF, and the IMRT-DIBH arm had 1 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 1 follow-up scan was conducted at 1 year due to resource constraints. A 6-month scan might have shown greater differences between the two arms.

Choi et al (2021) compared disease control and safety of IMRT to 3D-CRT in a multicenter, phase III, open-label, randomized (1:1) trial enrolling 693 women who had undergone breast-conserving surgery for breast cancer staging pT1-2N0M0 with a negative resection margin in Korea.[11] The 3D-CRT group received 50.4 Gy in 28 fractions on the ipsilateral breast with additional 9 Gy in 5 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 3-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 3-year locoregional recurrence-free survival rate of 99.4% in the 3D-CRT arm versus 98.5% in the IMRT arm (p =.523). Similarly, there was no statistically significant difference between the 3D-CRT and IMRT groups in 3-year distant metastasis-free survival (98.8% vs. 99.6% , respectively; p =.115), recurrence-free survival (97.4% vs. 98.2%, respectively; p =.418), or OS (99.6% vs. 100%, respectively; p =.165). Regarding toxicity, grade 2 or higher radiation dermatitis occurred less frequently in the IMRT arm (37.1% vs. 27.8%; p =.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 to V50 for the ipsilateral lung were significantly lower in the IMRT arm than the 3D-CRT arm (all p <.05).

Horner-Rieber et al (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.[12] 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 2-year local control rate: 99.6% in both arms (hazard ratio [HR], 0.602; 95% confidence interval [CI], 0.123 to 2.452; p =.487). Additionally, noninferiority was seen for cosmesis (according to relative breast retraction assessment score) after IMRT and 3D-CRT at both 6 weeks and 2 years after RT (p =.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 =.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,[13] there were no significant differences between the groups with regard to any grade radiation dermatitis at the end of treatment (p =.26). However, Grade 2 and 3 radiation dermatitis occurred significantly more often in the IMRT arm (29.1% vs. 20.1% and 3.5% vs. 2.3%) (p =.02). Significantly more patients in the 3D-CRT arm experienced breast/chest wall pain at the initial follow-up visit (p =.02). Another analysis of the IMRT-MC2 trial assessed quality of life outcomes 6 weeks to 2 years after RT.[14] The only significant difference in quality of life scores between the IMRT-simultaneous integrated boost arm as compared with the 3D-CRT-sequential boostarm was seen 6 weeks after RT for pain and for arm symptoms, both favoring IMRT. However, the between-group differences were diminished over time.

Nonrandomized Comparative Studies

Hardee et al (2012) compared the dosimetric and toxicity outcomes after treatment with IMRT or 3DCRT for whole-breast irradiation 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.[15] Intensity-modulated radiotherapy significantly reduced the maximum radiation dose (Dmax) to the breast (Dmax median, 110% for 3D-CRT vs 107% for IMRT; p<.001) and improved median dose homogeneity (median, 1.15 for 3D-CRT vs 1.05 for IMRT; p0.001) compared with 3D-CRT. These dosimetric improvements were seen across all breast volume groups. Grade 2 dermatitis occurred in 13% of patients in the 3D-CRT group and in 2% in the IMRT group. IMRT moderately decreased rates of acute pruritus (p=.03) and grade 2 and 3 subacute hyperpigmentation (p=.01). With a minimum of 6 months of follow-up, the treatment was reported to be similarly well-tolerated by both groups, including among women with large breast volumes.

Guttmann et al (2018) published a single-center retrospective analysis of 413 women who received tangential whole-breast irradiation between 2011 and 2015 (Table 1).[16] Of the patients, 212 underwent IMRT and 201 received field-in-field 3D-CRT (FiF3D). The main endpoint was a comparison of acute radiation dermatitis (grade 2+), and secondary endpoints were acute fatigue and breast pain. Grade 2+ radiation dermatitis was experience by 59% of FiF3D patients and 62% of IMRT patients (p=.09). There was also no significant difference between FiF3D and IMRT for breast pain (grade 2+,18% vs 18%, respectively; p=.33) or fatigue (grade 2+,18% vs 25.5%, respectively; p=.24) (Table 2). 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.

Table 1. Summary of Key Nonrandomized Trials Characteristics

Study	Study Type	Country	Dates	Participants	Treatment	Comparator	FU
Guttmann et al (2018)[16]	Retrospective	U.S.	2011-2015	413	IMRT	3D-CRT	90 d

FU: follow-up; 3D-CRT: 3-dimensional conformal radiotherapy.

Table 2. Summary of Key Nonrandomized Trial Results

Study	Acute Radiation Dermatitis	Acute Fatigue	Acute Breast Pain
Guttmann et al (2018)[16]			
Intensity-modulated radiotherapy			
N	212	212	212
Grade	• Grade 0=1 • Grade 1=78 • Grade 2=129 • Grade 3=3	• Grade 0=46 • Grade 1=127 • Grade 2=39 • Grade 3=0	• Grade 0=26 • Grade 1=127 • Grade 2=39 • Grade 3=0
3-dimensional conformal radiotherapy			
N	201	201	201

Grade	• Grade 0=0 • Grade 1=83 • Grade 2=109 • Grade 3=9	• Grade 0=44 • Grade 1=121 • Grade 2=33 • Grade 3=3	• Grade 0=44 • Grade 1=121 • Grade 2=33 • Grade 3=3
p	.09	.24	.33

3D-CRT: 3-dimensional conformal radiotherapy; IMRT: intensity-modulated radiotherapy

Chest Wall Irradiation

Studies have examined the use of IMRT for chest wall irradiation in postmastectomy breast cancer patients. Available studies have focused on treatment planning and techniques to improve dose distributions to targeted tissues while reducing radiation to normal tissue and critical surrounding structures (eg, heart, lung). In a study by Rudat et al (2011), treatment planning for chest wall irradiation with IMRT was compared with 3D-CRT in 20 postmastectomy patients.[17] The authors reported IMRT significantly decreased heart and lung high dose volume with a significantly improved conformity index compared with 3D-CRT. However, there were no significant differences in the homogeneity index. The authors noted 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. As noted, health outcomes were not reported in this study.

Rastogi et al (2018) published a retrospective study of 107 patients receiving RT postmastectomy to the left chest wall.[18] 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<.001), while results for both planning target volume (IMRT, 611.7 vs 3D-CRT, 612.2; p=.55) and homogeneity index (IMRT, 0.094 vs 3D-CRT, 0.096; p=.83) were comparable. Furthermore, secondary analyses showed that IMRT had significantly lower mean- and high-dose volumes to the heart and ipsilateral lung (p<.001 and p<.001, respectively), while 3D-CRT had superior low-dose volume (p<.001). The study was limited by its small population size and short follow-up.

Ho et al (2019) published the long-term pulmonary outcomes of a feasibility study of inverse-planned, multibeam IMRT in node-positive breast cancer patients receiving regional nodal irradiation.[19] While the authors' primary endpoint was feasibility, they also observed the incidence of radiation pneumonitis grade 3 or greater and changes and in pulmonary function. The later endpoints were measured with the Common Terminology Criteria for Adverse Events and pulmonary function tests and community-acquired pneumonia questionnaires. Of 104 completed follow-up procedures, the overall rate of respiratory toxicity was 10.6%, with 1 grade 3 radiation pneumonitis event.

Kivanc et al (2019)[20] published a dosimetric comparison of 3D-CRT and IMRT for left-sided chest wall and lymphatic irradiation. The study compared 5 different techniques (ie, 3D-CRT, forward-planned IMRT, inverse-planned IMRT [7- or 9-field], and hybrid inverse-planned/ forward-planned IMRT) in 10 patients. Results revealed no differences among the techniques for doses received by 95% of the volume (D95%) of lymphatics. Forward-planned IMRT was associated with a significantly lower D95% dose to the chest wall-planning target volume as compared to the other techniques (p=.002). Of the evaluated techniques, the 9-field inverse-

planned IMRT achieved the lowest volumes receiving higher doses. Overall, the dose homogeneity in chest wall-clinical target volume was improved with IMRT techniques versus 3DCRT, especially 9-field inverse-planned IMRT. The hybrid IMRT plans had the advantages of both forward-planned and inverse-planned IMRT techniques.

Zhao et al (2021) retrospectively evaluated differences in survival rate, recurrence, and late adverse effects in 223 patients with clinical stage II to III breast cancer who 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).[21] The mean follow-up of the study was 104.3 months. The 8-year disease-free survival rates were significantly improved in the IMRT group (86% vs. 73.4%; p =.022); however, the OS rates were not significantly different between the groups (91.4% IMRT vs. 86.2% 3D-CRT; p =.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 =.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 =.788) and grade 1 to 2 ipsilateral shoulder mobility (46.5% IMRT vs. 47.9% 3D-CRT; p =.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.

Section Summary: Breast Cancer
There is evidence from RCTs that IMRT decreases acute skin toxicity more than 2D-RT for whole-breast irradiation. One RCT reported improvements in moist desquamation of skin but did not find differences in grade 3 or 4 skin toxicity, pain symptoms, or quality of life. Another RCT found a change in breast appearance, but not quality of life. A third RCT reported no differences in cosmetic outcomes at 2 years for IMRT or 2D-RT. Dosimetry studies have demonstrated that IMRT reduces inhomogeneity of radiation dose, thus potentially providing a mechanism for reduced skin toxicity. However, because whole-breast radiotherapy is now delivered by 3D-CRT, these comparison data are of limited value.

Studies comparing IMRT with 3D-CRT CRT include 1 RCT comparing IMRT with deep inspiration breath hold to 3D-CRT, 2 additional RCTs comparing IMRT to 3D-CRT in women who had undergone breast-conserving surgery (with 1 RCT evaluating simultaneous vs. sequential boost therapy), 2 nonrandomized comparative assessments of whole-breast IMRT, and studies on treatment planning for chest wall IMRT. These studies have suggested that IMRT might improve upon, or provider similar improvement in, clinical outcomes. The risk of secondary lung cancers needs further evaluation. Additionally, cardiac and pulmonary toxicity need further evaluation. Despite this, evidence supports the use of IMRT for left-sided breast lesions in which alternative types of radiotherapy cannot avoid toxicity to the heart and lungs.

LUNG CANCER

Clinical Context and Therapy Purpose
The purpose of IMRT in individuals who have lung cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with lung cancer.

Interventions
The therapy being considered is IMRT. Radiotherapy is an integral component of the treatment of breast cancer. IMRT has been proposed as a method of RT that allows adequate radiation to the tumor while minimizing the radiation dose to surrounding normal tissues and critical structures.

Comparators
The following therapy is currently being used to make decisions about lung cancer: 3D-CRT.

Outcomes
The general outcomes of interest are OS, disease-specific survival, locoregional control, quality of life, and treatment-related adverse events.

Study Selection Criteria
See the information under the first indication.

REVIEW OF EVIDENCE

Systematic reviews
Bezjak et al (2012) conducted a systematic review that examined the evidence on use of IMRT for the treatment of lung cancer to quantify its potential benefits and make recommendations for RT programs considering adopting this technique in Ontario, Canada.[22] This review consisted of 2 retrospective cohort studies (through March 2010) reporting on cancer outcomes, which was considered insufficient evidence on which to make evidence-based recommendations. These 2 cohort studies reported on data from the same institution (M.D. Anderson Cancer Center); the study by Liao et al (2010, reported below)[23] acknowledged that patients included in their cohort (n=409) were previously reported in another cohort involving 290 subjects, but it is not clear exactly how many patients were added in the second report. However, due to the known dosimetric properties of IMRT and extrapolating from clinical outcomes from other disease sites, the reviewers recommended that IMRT should be considered for lung cancer patients where the tumor is in close proximity to an organ at risk, where the target volume includes a large volume of an organ at risk, or in scenarios where dose escalation would be potentially beneficial while minimizing normal tissue toxicity.[22]

Randomized Controlled Trials
Louie et al (2022) published an RCT that evaluated whether esophageal-sparing IMRT (n=41) achieves a clinically relevant reduction in esophageal adverse events compared with standard RT (n=39) in patients with stage III/IV incurable non-small-cell lung cancer (NSCLC).[24] Results

demonstrated that the occurrence of the primary outcome, which measured esophageal quality of life 2 weeks following RT using the esophageal cancer subscale of the Functional Assessment of Cancer Therapy: Esophagus questionnaire, did not significantly differ between treatment groups. However, symptomatic RT-associated esophagitis occurred in 11 patients who received standard RT compared to 1 patient who received esophageal-sparing IMRT (p = .002). Overall survival was similar with esophageal-sparing IMRT (median, 8.7 months; 95% CI, 5.1 to 10.2 months) and standard RT (median, 8.6 months; 95% CI, 5.7 to 15.6; p = .62).

Nonrandomized Comparative Studies

Liao et al (2010) compared patients who received RT, along with chemotherapy, for inoperable non-small-cell lung cancer (NSCLC) at a single institution.[23] This study retrospectively compared 318 patients who received CT plus 3D-CRT and chemotherapy from 1999 to 2004 (mean follow-up, 2.1 years) with 91 patients who received 4D-CT plus IMRT and chemotherapy from 2004 to 2006 (mean follow-up, 1.3 years). Both groups received a median dose of 63 Gy. Disease end points were locoregional progression, distant metastasis, and OS. Disease covariates were gross tumor volume, nodal status, and histology. The toxicity end point was grade 3, 4, or 5 radiation pneumonitis; toxicity covariates were gross tumor volume, smoking status, and dosimetric factors. Using Cox proportional hazards models, the hazard ratios (HRs) for IMRT were less than one for all disease end points; the difference was significant only for OS. The median (SD) survival was 1.40 (1.36) years for the IMRT group and 0.85 (0.53) years for the 3D-CRT group. The toxicity rate was significantly lower in the IMRT group than in the 3D-CRT group. The volume of the lung receiving 20 Gy (V20) was higher in the 3D-CRT group and was a factor in determining toxicity. Freedom from distant metastasis was nearly identical in both groups. The authors concluded that treatment with 4D-CT plus IMRT was at least as good as that with 3D-CRT in terms of the rates of freedom from locoregional progression and metastasis. This retrospective study found significant reductions in toxicity and improvement in survival. The nonrandomized, retrospective aspects of this study from 1 center limit the ability to draw definitive treatment conclusions about IMRT.

Shirvani et al (2013) reported on a U.S. cancer study that assessed the use of definitive IMRT in limited-stage small cell lung cancer treated with definitive RT.[25] In this study of 223 patients treated from 2000 to 2009, 104 received IMRT and 119 received 3D-CRT. Median follow-up times were 22 months (range, 4-83 months) for IMRT and 3D-CRT and 27 months (range, 2-147 months) for IMRT. In either multivariable or propensity score-matched analyses, OS and disease-free survival did not differ between IMRT and 3D-CRT. However, rates of esophagitis-related percutaneous feeding tube placements were lower with IMRT (5%) than with 3D-CRT (17%; p=.005).

Harris et al (2014) compared the effectiveness of IMRT, 3D-CRT, or 2D-RT in treating stage III non-small-cell lung cancer (NSCLC) using a cohort of patients from the Surveillance, Epidemiology, and End Results–Medicare database treated between 2002 and 2009.[26] Overall survival was better with IMRT and 3D-CRT than with 2D-CRT. In univariate analysis, improvements in OS (HR=0.90, p=.02) and cancer-specific survival (HR=0.89, p=0.02) were associated with IMRT. However, IMRT was similar to 3D-CRT after controlling for confounders in OS and cancer-specific survival (HR=0.94, p=0.23; HR=0.94, p=.28, respectively). On multivariate analysis, toxicity risks with IMRT and 3D-CRT were also similar. Results were similar for the propensity score matched models and the adjusted models.

Ling et al (2016) compared IMRT and 3D-CRT in patients who had stage III NSCLC treated with definitive RT.[27] In this study of 145 consecutive patients treated between 1994 and 2014, the choice of treatment was at the treating physician's discretion, but all IMRT treatments were performed in the last 5 years. Ling found no significant differences between the groups for any measure of acute toxicity (grade ≥2 esophagitis, grade ≥2 pneumonitis, percutaneous endoscopic gastrostomy, narcotic use, hospitalization, or weight loss). There were no significant differences in oncologic and survival outcomes.

Chun et al (2017) reported a secondary analysis of trial that assessed the addition of cetuximab to a standard chemotherapy regimen and radiation dose escalation.[28] Use of IMRT or 3D-CRT was a stratification factor in the 2 x 2 design. Of 482 patients in the trial, 53% were treated with 3D-CRT and 47% were treated with IMRT, though treatment allocation was not randomized. Compared with the 3D-CRT group, the IMRT group had larger planning treatment volumes (486 mL vs 427 mL, p=.005), larger planning treatment volume/volume of lung ratio (median, 0.15 vs 0.13; p=.13), and more patients with stage IIIB disease (38.6% vs 30.3%, p=.056). Even though there was an increase in treatment volume, IMRT was associated with less grade 3 or greater pneumonitis (3.5% vs 7.9%, p=.039) and a reduced risk (odds ratio [OR], 0.41; 95% confidence interval [CI], 0.171 to 0.986; p=.046), with no significant differences between the groups in 2-year overall survival (OS), progression-free survival, local failure, or distant metastasis-free survival.

Koshy et al (2017) published a retrospective cohort analysis of patients with stage III NSCLC, comparing those treated with IMRT and with non-IMRT.[29] Using the National Cancer Database, 7493 patients treated between 2004 and 2011 were assessed (see Table 3). Main outcomes were OS and the likelihood and effects of radiation treatment interruption, defined as a break in the treatment of four or more days. Overall survival for non-IMRT and IMRT patients, respectively, were 18.2 months and 20 months (p<.001) (Table 4). Median survival with and without a radiation treatment interruption was 16.1 and 19.8 months, respectively (p<.001), and IMRT significantly reduced the likelihood of a radiation treatment interruption (OR, 0.84; p=.04). The study was limited by unavailable information regarding RT planning and potential mechanisms affecting survival, and by a possible prescription, bias causing patients with better performance status to be given IMRT.

Appel et al (2019) conducted another retrospective, single institution, cohort evaluating the impact of radiation technique on pathological and clinical outcomes in 74 patients with locally advanced NSCLC managed with a trimodality strategy.[30] Key study characteristics and results are presented in Tables 3 and 4. The 2-year overall local control rate was 81.6% (95% CI, 69% to 89.4%), disease-free survival was 58.3% (95% CI, 45.5% to 69%), and 3-year OS was 70% (95% CI, 57% to 80%). When comparing radiation techniques for these outcomes, there were no significant differences in local control (p=.94), disease-free survival (p=.33), or OS (p=.72). Grade 2 esophageal toxicity was non significantly reduced with IMRT as compared to 3D-CRT (32% versus 37%; p=.66). As with other studies, the retrospective design and single-center nature of this cohort make generalizability of the results to other cancer centers limited.

Table 3. Summary of Key Observational Comparative Study Characteristics

Study	Study Type	Country	Dates	Participants	Treatment	Comparator	FU
Koshy et al (2017)[29]	Cohort	U.S.	2004-2011	7493	IMRT	Non-IMRT	32 mo

Appel et al (2019)[30]	Cohort	Israel	2012-2018	74	IMRT	3D-CRT	3.6 years (median)

Table 4. Summary of Key Observational Study Results

Study	OS	Major Pathologic Response Rate	Pathologic Complete Response Rate
Koshy et al (2017)[29]	Months		
IMRT	20.0		
Non-IMRT	18.2		
p	<.001		
Appel et al (2019)[30]	2-year		
IMRT % (95% CI)	85% (60 to 95)	65.2%	34.8%
3D-CRT % (95% CI)	82% (68 to 90)	62.7%	33.3%
p	.72	.83	.9

3D-CRT; three-dimensional conformal radiotherapy; IMRT: intensity-modulated radiotherapy; OS: overall survival.

Section Summary: Lung Cancer

For the treatment of lung cancer, 1 RCT was identified that compared IMRT with 3D-CRT, but the focus was on the development of esophageal adverse events only. Dosimetry studies have reported that IMRT can reduce radiation exposure to critical surrounding structures, especially in large lung cancers. Based on available comparative studies, IMRT appears to produce survival outcomes comparable with those of 3D-CRT, with a reduction in adverse events.

SUMMARY OF EVIDENCE

For individuals who have breast cancer who receive intensity-modulated radiotherapy (IMRT) , the evidence includes systematic reviews, randomized controlled trials (RCTs), and nonrandomized comparative studies. Relevant outcomes are overall survival (OS), disease-specific survival, locoregional control, quality of life, and treatment-related morbidity. There is modest evidence from RCTs for a decrease in acute skin toxicity with IMRT compared with 2-dimensional radiotherapy (2D-RT) for whole-breast irradiation, and dosimetry studies have demonstrated that IMRT reduces inhomogeneity of radiation dose, thus potentially providing a mechanism for reduced skin toxicity. However, because whole-breast RT is now delivered by 3D-CRT, these comparative data are of limited value. Studies comparing IMRT with 3-dimensional conformal radiotherapy (3D-CRT) include 1 RCT comparing IMRT with deep inspiration breath hold (DIBH) to 3D-CRT, 2 additional RCTs comparing IMRT to 3D-CRT in women who had undergone breast-conserving surgery (with 1 RCT evaluating simultaneous vs. sequential boost therapy), 2 nonrandomized comparative studies on whole-breast IMRT, and a few studies on chest wall IMRT. These studies suggest that IMRT requires less radiation exposure to nontarget areas and may improve upon, or provide similar improvement in, clinical outcomes. The available studies on chest wall IMRT for postmastectomy breast cancer patients have focused on treatment planning and techniques. However, when dose-planning studies have indicated that radiotherapy will lead to unacceptably high radiation doses, the studies suggest IMRT will lead to improved outcomes. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have lung cancer who receive IMRT, the evidence includes 1 RCT that focused on esophageal adverse events and multiple nonrandomized, retrospective, comparative studies. Relevant outcomes are overall survival, disease-specific survival, locoregional control, quality of life, and treatment-related morbidity (eg, adverse events).

Dosimetry studies have shown that IMRT can reduce radiation exposure to critical surrounding structures, especially in large lung tumors. Based on nonrandomized comparative studies, IMRT appears to produce survival outcomes comparable to those of 3D-CRT, while reducing toxicity. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2012 Input

In response to requests by the Blue Cross Blue Shield Association, input was received from 2 physician specialty societies and 3 academic medical centers (3 reviewers) while their policy was under review in 2012. There was near-uniform consensus in responses that suggested whole-breast and lung IMRT are appropriate in select patients with breast and lung cancer. Respondents noted IMRT may reduce the risk of cardiac, pulmonary, or spinal cord exposure to radiation in some cancers such as those involving the left breast or large cancers of the lung. Respondents also indicated whole-breast IMRT may reduce skin reactions and potentially improve cosmetic outcomes. Partial-breast IMRT was not supported by the respondents, and the response was mixed on the value of chest wall IMRT postmastectomy.

2010 Input

In response to requests by the Blue Cross Blue Shield Association, input was received from 1 physician specialty society and 2 academic medical centers (3 reviewers) while their policy was under review in 2010. Input suggested that IMRT is used in select patients with breast cancer (eg, some cancers involving the left breast) and lung cancer (eg, some large cancers).

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information’ if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Society of Clinical Oncology/American Society for Radiation Oncology/Society of Surgical Oncology

Breast Cancer

In 2016, the American Society of Clinical Oncology (ASCO), American Society for Radiation Oncology, and the Society of Surgical Oncology developed a focused update of a prior ASCO

guideline related to the use of postmastectomy radiotherapy (RT).[31,] The Expert Panel unanimously agreed that "available evidence shows that post mastectomy RT reduces the risk of locoregional failure, any recurrence, and breast cancer mortality for patients with T1 to T2 breast cancer with 1 to 3 positive axillary nodes. However, some subsets of these patients are likely to have such a low risk of locoregional failure that the absolute benefit of post mastectomy RT is outweighed by its potential toxicities." Additionally, the guideline noted that "the decision to recommend post mastectomy RT requires a great deal of clinical judgment."

American Society for Radiation Oncology

Breast Cancer

In 2018, the American Society for Radiation Oncology published evidence-based guidelines on whole-breast irradiation with or without low axilla inclusion. The guidance recommended a "preferred" radiation dosage of "4000 cGy [centigray] in 15 fractions or 4250 cGy in 16 fractions."[32,]

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.

Lung Cancer

In 2018, the American Society for Radiation Oncology also published evidence-based guidelines on palliative RT for non-small-cell lung cancer (NSCLC). The guidelines recommended "moderately hypofractionated palliative thoracic radiation therapy" with chemotherapy as palliative care for stage III and IV incurable NSCLC. [34]

In 2020, the American Society for Radiation Oncology also published evidence-based guidelines RT for small-cell lung cancer (SCLC).[35] The guidelines listed IMRT as one of several treatment strategies for patients with pathologically confirmed limited stage-SCLC with no evidence of M1 disease. The guideline also notes that the use of "modulated techniques (eg, IMRT or volumetric modulated arc therapy) over 3-dimensional conformal treatment is recommended in an attempt to decrease normal tissue toxicities...however...there are limited data on advanced RT techniques in SCLC treatment."

National Comprehensive Cancer Network

Breast Cancer

NCCN guidelines (v.4.2024)) for breast cancer indicate the importance of individualizing RT planning and delivery.[36] Specifically, the guidelines note that "treatment planning should be optimized to maximally improve homogeneity across the target volume while minimizing dose to organs at risk." A related discussion section in this guideline states the following: “Computed tomography (CT)-based treatment planning is encouraged to delineate target volumes and adjacent organs at risk. Greater target dose homogeneity and sparing of normal tissues can be accomplished utilizing various "compensators such as wedges, forward planning using segments, and IMRT." Respiratory control techniques including deep inspiration breath-hold and prone positioning may be used to try to further reduce dose in adjacent normal tissues, in particular heart and lung.” In the post-mastectomy setting the guidelines state, "Based on anatomic considerations and presence of reconstruction, various 3-D-, IMRT, or

VMAT [volumetric modulated arc therapy] techniques using photons and/or electrons are appropriate.

Lung Cancer
Current NCCN guidelines (v.7.2024) for non-small cell lung cancer (NSCLC) indicate that "More advanced technologies are appropriate when needed to deliver curative RT safely. These technologies include (but are not limited to) IMRT/VMAT [volumetric modulated arc therapy]…Nonrandomized comparisons of using advanced technologies demonstrate reduced toxicity and improved survival versus older techniques."[37]

Current NCCN guidelines (v.3.2024) for small cell lung cancer (SCLC) indicate that "Use of more advanced technologies is appropriate when needed to deliver adequate tumor doses while respecting normal tissue dose constraints."[38] Among the technologies listed is IMRT. The guidelines also states that "IMRT is preferred over 3D [3-dimensional] conformal external-beam RT on the basis of reduced toxicity in the setting of concurrent chemotherapy/RT."

U.S. Preventive Services Task Force Recommendations
Not applicable.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03786354	Prospective Evaluation of Shoulder Morbidity in Patients with Lymph-Node Positive Breast Cancer Receiving Regional Nodal Irradiation	61	Dec 2024
Unpublished			

NCT: national clinical trial.

Government Regulations

National:
There is no national coverage determination on this topic.

Local:
Wisconsin Physicians Service Insurance Corporation – LCD Radiation Oncology Including Intensity Modulated Radiation Therapy (IMRT) (L34652)
Original Effective Date 10/01/2015
Retirement Date 04/01/2016

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated

and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Intensity Modulated Radiation Therapy (IMRT): Central Nervous System Tumors
Intensity-Modulated Radiation Therapy (IMRT): Head and Neck Cancers
Intensity Modulated Radiation Therapy (IMRT) of the Abdomen,Pelvis and chest
Intensity-Modulated Radiation Therapy (IMRT) of the Prostate

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 8/6/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
11/1/13	8/20/13	9/10/13	Joint policy established
1/1/15	10/21/14	11/3/14	Routine maintenance
7/1/16	4/19/16	4/19/16	Routine maintenance G codes added to policy
7/1/17	4/18/17	4/18/17	Routine maintenance
11/1/17	8/15/17	8/15/17	Routine maintenance References and rationale updated
11/1/18	8/21/18	8/21/18	Routine maintenance Removed qualifier of large breasts for hot spots; removed E/I statements; removed specific dose volume constraints listed under inclusions for lung
1/1/19	10/16/18	10/16/18	Routine maintenance: revised MPS to be more general, no exclusions; diverge from BCBSA with broader scope.
1/1/20	10/15/19		Routine maintenance
1/1/21	10/20/20		Routine maintenance New references 17,25,30
1/1/22	10/19/21		Routine maintenance Ref 11,12,12,20 added
1/1/23	10/18/22		Routine maintenance (ls) Ref 9,10 added
1/1/24	10/17/23		Routine maintenance (jf) Vendor Managed: eviCore Added ref 31,32,33 & 34
1/1/25	10/15/24		Routine maintenance (jf) Vendor Managed: eviCore Added Ref: 33

Next Review Date: 4th Qtr, 2025

POLICY: INTENSITY MODULATED RADIATION THERAPY (IMRT) OF THE BREAST AND LUNG

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria applies
BCNA (Medicare Advantage)	See Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.

Attachment A
ICD10 Codes for IMRT for Breast and Lung

ICD10 Codes	Code Descriptions
C33	Malignant neoplasm of trachea
C34.0	Malignant neoplasm of unspecified main bronchus
C34.1	Malignant neoplasm of right main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of left main bronchus
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.12	Malignant neoplasm of nipple and areola, left female breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.19	Malignant neoplasm of nipple and areola, unspecified female breast
C50.21	Malignant neoplasm of nipple and areola, right male breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.22	Malignant neoplasm of nipple and areola, left male breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.29	Malignant neoplasm of nipple and areola, unspecified male breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast

Attachment A
ICD10 Codes for IMRT for Breast and Lung

ICD10 Codes	Code Descriptions
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast