Policy Statement

I. Intensity-modulated radiotherapy (IMRT) using a hypofractionated regimen (up to 16 treatments and up to 8 more if a boost is needed) may be considered **medically necessary** as a technique to deliver whole-breast irradiation in patients receiving treatment when **all** of the following conditions are met:
   A. Left-sided breast cancer
   B. Prior breast-conserving surgery
   C. Documentation of **all** of the following:
      1. Significant cardiac radiation exposure cannot be avoided using alternative radiotherapy
      2. IMRT dosimetry demonstrates significantly reduces cardiac target volume radiation exposure as documented by **both** of the following:
         a. With 3D-CRT, the target volume coverage results in cardiac radiation exposure that is expected to be greater than or equal to 25 gray (Gy) to 10 cm^3 or more of the heart (V25 ≥10 cm^3), despite the use of a complex positioning device (e.g., Vac-Lok™)
         b. With IMRT, there is a reduction in the absolute heart volume receiving 25 Gy or more by at least 20% (e.g., volume predicted to receive 25 Gy by 3D-CRT is 20 cm^3, and the volume predicted by IMRT is ≤16 cm^3

II. IMRT using conventional fractionation may be considered **medically necessary** if there are contraindications to hypofractionation and documentation of the contraindication to hypofractionation is provided.

III. IMRT may be considered **medically necessary** when **all** of the following conditions are met:
   A. Individual has large breasts (> 500 cc)
   B. 3-dimensional conformal radiotherapy dosimetry results in hot spots (focal regions with dose variation greater than10% of target)
   C. Hot spots can be avoided with IMRT

IV. IMRT of the breast is considered **investigational** as a technique of partial-breast irradiation after breast-conserving surgery.

V. IMRT may be considered **medically necessary** as a technique to deliver radiotherapy in patients with lung cancer when **all** of the following conditions are met:
   A. Radiotherapy is being given with curative intent
   B. Three-dimensional (3-D) conformal radiotherapy will expose greater than 35% of normal lung tissue to more than a 20-Gy dose-volume (V20)
   C. IMRT dosimetry demonstrates a reduction in the V20 to at least 10% below the V20 that is achieved with the 3-dimensional plan (e.g., from 40% down to 30% or lower)

VI. IMRT is considered **not medically necessary** as a technique to deliver radiotherapy in patients receiving palliative treatment for lung cancer.

VII. Intensity modulated radiation therapy to breast or lung cancers may be considered **medically necessary** when **one or more** of the following conditions are present:
   A. The target volume is in close proximity to critical structures that must be protected and **both** of the following: * (see source below)

1. Planned 3D-CRT exposure to critical adjacent structures is above normal tissue constraints
2. Planned IMRT exposure to these critical adjacent structures does not exceed normal tissue constraints

B. An immediately adjacent area has been previously irradiated and abutting portals must be established with high precision

VIII. IMRT is considered **not medically necessary** for the treatment of breast or lung cancer for all indications not meeting the criteria above, including palliative care when criteria for approval are not met.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Fractionation: Dose distribution may be delivered in standard doses (fractionated) or higher doses over a shorter period of time (hypofractionated). The advantages of hypofractionation include patient convenience and lower cost, although potential increased radiation toxicity remains a concern for some tumor types. For women with invasive breast cancer receiving whole breast irradiation (WBI) with or without inclusion of the low axilla, hypofractionated WBI to a dose of 4000-4250 cGy in 15-16 fractions is considered the treatment of choice. Boost treatments (4-8 fractions), generally using 3D conformal radiation therapy, is administered based on individual clinical circumstances, but is commonly used to treat axillary or other lymph nodes. Treatment regimens other than this may be considered medically necessary based on individual circumstances, which would require documentation to support.

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.

*The following Normal Tissue Constraint Guidelines are derived from the textbook: Radiation Oncology: A Question-Based Review published by Lippincott Williams & Wilkins, 2010 [author: Hristov et al., 2010]). According to the author, most dosages were derived from randomized studies or consensus guidelines however; pediatric dose constraints will vary greatly from protocol to protocol. Sources used in the development of the guidelines included the American Brachytherapy Society (ABS); Clinical practice guidelines from Johns Hopkins Hospital (JHH); the International Journal of Radiation Oncology *Biology* Physics (IJROBP); the National Comprehensive Cancer Network (NCCN), Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC); and the Radiation Therapy Oncology Group (RTOG) protocols at the time of publication.

The following guidelines are only intended to serve as a guide and may not be applicable to all clinical scenarios.

Organ	Constraints
Central Nervous System (1.8-2.0 Gray/fraction [Gy/fx])	
• Spinal Cord	max 50 Gy (full cord cross-section); tolerance increases by 25% 6 mos after 1st course (for re-irradiation)
• Brain	max 72 Gy (partial brain); avoid >2 Gy/fx or hyperfractionation
• Chiasm/Optic Nerves	max 55 Gy
• Brainstem	Entire brainstem <54 Gy, V59 Gy <1–10 cc
• Eyes (globe)	mean <35 Gy, max 54 Gy
• Lens	max 7 Gy
• Retina	max 50 Gy

Organ	Constraints
• Lacrimal Gland	max 40 Gy
• Inner ear/cochlea	mean </=45 Gy (consider constraining to </=35 Gy with concurrent cisplatin)
• Pituitary gland	max 45 Gy (for panhypopituitarism, lower for GH deficiency)
• Cauda equina	max 60 Gy
Central Nervous System (single fraction)	
• Spinal Cord	max 13 Gy (if 3 fxs, max 20 Gy)
• Brain	V12 Gy <5–10 cc
• Chiasm/Optic Nerves	max 10 Gy
• Brainstem	max 12.5 Gy
• Sacral plexus	V18 <0.035 cc, V14.4 <5 cc
• Cauda equina	V16 <0.035 cc, V14 <5 cc
Head and Neck (1.8–2.0 Gy/fx)	
• Parotid gland(s)	mean <25 Gy (both glands) or mean <20 Gy (1 gland)
• Submandibular gland(s)	mean <35 Gy
• Larynx	mean </=44 Gy, V50 </=27%, max 63–66 Gy (when risk of tumor involvement is limited)
• TMJ/mandible	max 70 Gy (if not possible, then V75 <1 cc)
• Oral cavity	Non-oral cavity cancer: mean <30 Gy, avoid hot spots >60 Gy Oral cavity cancer: mean <50 Gy, V55 <1 cc, max 65 Gy
• Esophagus (cervical)	V45 <33%
• Pharyngeal constrictors	mean <50 Gy
• Thyroid	V26 <20%
Thoracic (1.8–2.0 Gy/fx)	
• Brachial plexus	max 66 Gy, V60 <5%
• Lung (combined lung for lung cancer treatment)	mean <20–23 Gy, V20 <30%–35%
• Lung (ipsilateral lung for breast cancer treatment)	V25 <10%
• Single lung (after pneumonectomy)	V5 <60%, V20 <4–10%, MLD <8 Gy
• Bronchial tree	max 80 Gy
• Heart (lung cancer treatment)	Heart V45 <67%; V60 <33%
• Heart (breast cancer treatment)	V25 <10%
• Esophagus	V50 <32% ;V60 <33%
Thoracic (hypofractionation) Note: the max dose limits refer to volumes >0.035 cc (~3 mm^3).	
• Spinal cord	1 fraction: 14 Gy 3 fractions: 18 Gy (6 Gy/fx) 4 fractions: 26 Gy (6.5 Gy/fx) 5 fractions: 30 Gy (6 Gy/fx)
• Esophagus	1 fraction: 15.4 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 30 Gy (7.5 Gy/fx) 5 fractions: 32.5 Gy (6.5 Gy/fx)
• Brachial plexus	1 fraction: 17.5 Gy 3 fractions: 21 Gy (7 Gy/fx) 4 fractions: 27.2 Gy (6.8 Gy/fx) 5 fractions: 30 Gy (6 Gy/fx)
• Heart/Pericardium	1 fraction: 22 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 34 Gy (8.5 Gy/fx) 5 fractions: 35 Gy (7 Gy/fx)

Organ	Constraints
• Great vessels	1 fraction: 37 Gy 3 fractions: 39 Gy (13 Gy/fx) 4 fractions: 49 Gy (12.25 Gy/fx) 5 fractions: 55 Gy (11 Gy/fx)
• Trachea/Large Bronchus	1 fraction: 20.2 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 34.8 Gy (8.7 Gy/fx) 5 fractions: 40 Gy (8 Gy/fx)
• Rib	1 fraction: 30 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 32 Gy (7.8 Gy/fx) 5 fractions: 32.5 Gy (6.5 Gy/fx)
• Skin	1 fraction: 26 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 36 Gy (9 Gy/fx) 5 fractions: 40 Gy (8 Gy/fx)
• Stomach	1 fraction: 12.4 Gy 3 fractions: 27 Gy (9 Gy/fx) 4 fractions: 30 Gy (7.5 Gy/fx) 5 fractions: 35 Gy (7 Gy/fx)
Gastrointestinal (GI) (1.8–2.0 Gy/fx)	
• Stomach	TD 5/5 whole stomach: 45 Gy
• Small bowel	V45 <195 cc
• Liver (metastatic disease)	mean liver <32 Gy (liver = normal liver minus gross disease)
• Liver (primary liver cancer)	mean liver <28 Gy (liver = normal liver minus gross disease)
• Colon	45 Gy, max dose 55 Gy
• Kidney (bilateral)	mean <18 Gy, V28 <20%, V23 Gy <30%, V20 <32%, V12 <55%. If mean kidney dose to 1 kidney >18 Gy, then constrain remaining kidney to V6 <30%.
Gastrointestinal (GI) (single fraction)	
• Duodenum	V16 <0.035 cc, V11.2 <5 cc
• Kidney (Cortex)	V8.4 <200 cc
• Kidney (Hilum)	V10.6 <66%
• Colon	V14.3 <20 cc, V18.4 <0.035 cc
• Jejunum/Ileum	V15.4 <0.035 cc, V11.9 <5 cc
• Stomach	V16 <0.035 cc, V11.2 <10 cc
• Rectum	V18.4 <0.035 cc, V14.3 <20 cc
Genitourinary (GU) (1.8-2.0 Gy/fx)	
• Femoral heads	V50 <5%
• Rectum	V75 <15% , V70 <20%, V65 <25%, V60 <35%, V50 <50%
• Bladder	V80 <15%, V75 <25%, V70 <35%, V65 <50%
• Testis	V3 <50%
• Penile bulb	Mean dose to 95% of the volume <50 Gy. D70 </=70 Gy, D50 </=50 Gy
Genitourinary (GU) (LDR prostate brachytherapy)	
• Urethra	Volume of urethra receiving 150% of prescribed dose (Ur150) <30%
• Rectum	Volume of rectum receiving 100% of prescribed dose (RV100) <0.5 cc
Gynecological (GYN)	
• Bladder point (cervical brachytherapy)	Max 80 Gy (LDR equivalent dose)

Organ	Constraints
• Rectal point (cervical brachytherapy)	Max 75 Gy (LDR equivalent dose)
• Proximal vagina (mucosa) (cervical brachytherapy)	Max 120 Gy (LDR equivalent dose)
• Distal vagina (mucosa) (cervical brachytherapy)	Max 98 Gy (LDR equivalent dose

Coding

The following CPT codes are used for simple and complex IMRT delivery:
- **77385**: Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple
- **77386**: Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; complex

The Centers for Medicare & Medicaid Services did not implement these CPT codes and instead created HCPCS G codes with the language of the previous CPT codes. Therefore, the following codes may be used for IMRT:
- **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

Code 77301 remains valid:
- **77301**: Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications

The following CPT code may also be used and is to be reported only once per IMRT plan:
- **77338**: Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan

The following codes may be used for this application:
- **77261**: Therapeutic radiology treatment planning; simple
- **77262**: Therapeutic radiology treatment planning; intermediate
- **77263**: Therapeutic radiology treatment planning; complex
- **77293**: Respiratory motion management simulation (List separately in addition to code for primary procedure)
- **77300**: Basic radiation dosimetry calculation, central axis depth dose calculation, TDF, NSD, gap calculation, off axis factor, tissue inhomogeneity factors, calculation of non-ionizing radiation surface and depth dose, as required during course of treatment, only when prescribed by the treating physician
- **77306**: Teletherapy isodose plan; simple (1 or 2 unmodified ports directed to a single area of interest), includes basic dosimetry calculation(s)
- **77307**: Teletherapy isodose plan; complex (multiple treatment areas, tangential ports, the use of wedges, blocking, rotational beam, or special beam considerations), includes basic dosimetry calculation(s)
- **77331**: Special dosimetry (e.g., TLD, microdosimetry) (specify), only when prescribed by the treating physician
- **77332**: Treatment devices, design and construction; simple (simple block, simple bolus)
- **77334**: Treatment devices, design and construction; complex (irregular blocks, special shields, compensators, wedges, molds or casts)
- **77370**: Special medical radiation physics consultation
- **77470**: Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation)

- **77336**: Continuing medical physics consultation, including assessment of treatment parameters, quality assurance of dose delivery, and review of patient treatment documentation in support of the radiation oncologist, reported per week of therapy
- **77338**: Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan
- **77427**: Radiation treatment management, 5 treatments
- **77014**: Computed tomography guidance for placement of radiation therapy fields
- **77417**: Therapeutic radiology port image(s)
- **77387**: Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed
- **G6001**: Ultrasonic guidance for placement of radiation therapy fields
- **G6002**: Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy
- **G6017**: Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (e.g., 3D positional tracking, gating, 3D surface tracking), each fraction of treatment

Allowable Codes and Frequencies for IMRT/Proton

Description	Code	Maximum per course of treatment	Notes
Clinical Treatment Planning	77261, 77262 or 77263	1	
Simulation	77280, 77285, 77290	0	May not be billed with 77301. 1 unit of 77290 + 1 boost is allowed for proton therapy when using 77295 instead
Verification Simulation	77280	0	One per simulation allowed
Respiratory Motion Management	77293	0	1 for breast, lung, and upper abdominal or thoracic cancer areas
3D CRT Plan	77295	0	May not be billed with 77301. 1 unit may be allowed for proton therapy.
IMRT Plan	77301	1	If comparison 3D plan is generated, it is included in 77301
Basic Dosimetry	77300	4+ 1 boost, up to a max of 10 with documentation	0 if billed with 77306, 77307, 77321, 0394T or 0395T
Teletherapy Isodose Plan, Simple	77306	1 for mid-Tx change in volume/contour	Not on the same day as 77300; may not bill 77306 and 77307 together; documentation of medical necessity is required for more than 1
Teletherapy Isodose Plan, Complex	77307	1 for mid-Tx change in volume/contour	Not on the same day as 77300; may not bill 77306 and 77307 together; documentation of medical necessity is required for more than 1
Special Dosimetry Calculation	77331	0	Needs documentation for review
Treatment Devices, Designs, and Construction	77332, 77333, 77334	1, 5 or 10	-If billed w/ MLC (77338): 1 -If billed w/o MLC: 5 (any combination) -More may be allowed when documentation of medical necessity is provided (such as additional beams), maximum of 10
Multi-leaf Collimater (MLC)	77338	1	MLC may not be reported in conjunction with HCPCS G6016
Special Radiation Physics Consult	77370	0	May allow x 1; documentation of medical necessity required
Special MD Consultation (Special Tx Procedure)	77470	0	May allow x 1; documentation of medical necessity required

Description	Code	Maximum per course of treatment	Notes
Medical Physics Management	77336	8	Allowed once per 5 courses of therapy
Radiation Treatment Management	77427	8	Allowed once per 5 courses of therapy
Radiation (IMRT or Proton) Delivery, prostate and breast cancer	IMRT 77385 or G6015; Proton 77520, 77522, 77523	Using IMRT or Proton: 28 for prostate cancer Using IMRT only: -16 for breast cancer without boost -24 for breast cancer with boost (IMRT only)	Prostate cancer: Documentation of medical necessity needed for more than 28 treatments Breast cancer: documentation of medical necessity needed for treatments beyond 16 IMRT delivery sessions without boost and/or 24 IMRT delivery sessions with boost.
Radiation (IMRT or Proton) Delivery, all other cancers	IMRT 77385, 77386; or G6015-G6016: Proton 77520, 77522, 77523, 77525	No limit	All cancers other than hypofractionated prostate or breast

Description

Radiotherapy (RT) is an integral component of the treatment of breast and lung cancers. Intensity-modulated radiotherapy (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.

Related Policies

- Intensity-Modulated Radiotherapy of the Prostate
- Intensity-Modulated Radiotherapy: Abdomen and Pelvis
- Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid
- Intensity-Modulated Radiotherapy: Central Nervous System Tumors
- Radiation Oncology

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

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 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, and the Ray Dose (RaySearch Laboratories) in 2008. 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.

Rationale

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 (i.e., a beam of radiation is directed into the body) or internally (i.e., a radioactive source is placed inside the body, near a tumor).[3] External RT techniques include "conventional" or 2-dimensional (2D) RT, 3-dimensional (3D) conformal RT (3D-CRT), 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.[3] Bony landmarks 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 involves initially scanning the patient in the position that will be used for the radiation treatment.[3] 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

Intensity-modulated radiotherapy 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.[3] 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 arc 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.[4] Techniques presently being studied with other tumors (e.g., lung cancer)[5] 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 the 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.

Literature Review

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 (3D) conformal radiotherapy (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 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 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, absent 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 IMRT in patients who have breast cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of IMRT improve the net health outcome in patients with breast cancer?

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

Populations

The relevant population of interest is women 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 (2D) 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 (e.g., 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.[6] This is a concern because of the potential development of late cardiac complications (e.g., 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. Five-year to 10-year follow-up to monitor for recurrence have 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 long-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 in the treatment of breast cancer to quantify its potential benefits and to make recommendations for radiation treatment programs.[7] Based on a review of 6 studies (N = 2012 patients) 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 events 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.[2] In this RCT, IMRT was compared with 2D-RT. Computed tomography (CT) 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.[1] Enrolled patients had a "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 cm^3), 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, quality of life, 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 quality of life. 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 compared with 2D-RT using wedges.[2,8] Patients were assessed each week up to 6 weeks after RT and then at 8 to 10 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 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 quality of life. 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 quality of life (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 this 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 RT. 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)[4] assessed whether IMRT with deep inspiration breath hold (DIBH) reduces cardiac or pulmonary toxicity of breast RT compared to 3D-CRT. 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 1 year post-treatment compared to baseline, measured using attenuation corrected single-photon emission CT. 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 <.001). At 1 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, 6 patients had > 5% changes in left ventricular ejection fraction, 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 2 arms.

Choi et al (2021) compared disease control and safety of IMRT compared 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 groups in 3-year distant metastasis-free survival (98.8% 3D-CRT vs. 99.6% IMRT; p =.115), recurrence-free survival (97.4% vs. 98.2%; p =.418), or OS (99.6% vs. 100%; 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 V_5-V_{50} 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 2/3 radiation dermatitis (29.1% vs. 20.1% and 3.5% vs. 2.3%) occurred significantly more often in the IMRT arm (p =.02). Significantly more patients in the 3D-CRT arm experienced breast/chest wall pain at the initial follow-up visit (p =.02).

Nonrandomized Comparative Studies

Hardee et al (2012) compared the dosimetric and toxicity outcomes after treatment with IMRT or 3D-CRT 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.[14] Intensity-modulated radiotherapy significantly reduced the maximum radiation dose 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; p <.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. Intensity-modulated radiotherapy 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).[15] Of the patients, 212 underwent IMRT and 201 received 3D-CRT. 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 experienced by 59% of 3D-CRT patients and 62% of IMRT patients (p =.09). There was also no significant difference between 3D-CRT 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 1 week sooner than 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)[15]	Retrospective	U.S.	2011-2015	413	IMRT	3D-CRT	90 d

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

Table 2. Summary of Key Nonrandomized Trials Results

Study	Acute Radiation Dermatitis	Acute Fatigue	Acute Breast Pain
Guttmann et al (2018)[15]			
IMRT			
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
3D-CRT			
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 (e.g., 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.[16] 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.[17] 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. Intensity-modulated radiotherapy 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.[18.] 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.

Kivanc et al (2019)[19.] published a dosimetric comparison of 3D-CRT and IMRT for left-sided chest wall and lymphatic irradiation. The study compared 5 different techniques (i.e., 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 3D-CRT, 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).[20.] 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 RT is now delivered by 3D-CRT, these comparison data are of limited value.

Studies comparing IMRT with 3D-CRT include 1 RCT comparing IMRT with 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 assessments of whole-breast IMRT, and studies on treatment planning for chest wall

IMRT. These studies have suggested that IMRT might improve upon, or provide similar improvement in, clinical outcomes. The risk of secondary lung cancers needs further evaluation. Additionally, cardiac and pulmonary toxicity needs further evaluation. Despite this, evidence supports the use of IMRT for left-sided breast lesions in which alternative types of RT cannot avoid toxicity to the heart and lungs.

Lung Cancer

Clinical Context and Therapy Purpose

The purpose of IMRT in patients who have lung cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of IMRT improve the net health outcome in patients with lung cancer?

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 lung 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

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 long-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

Systematic Reviews

Bezjak et al (2012) conducted a systematic review that examined the evidence on the 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.[21] 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; the study by Liao et al (2010; reported below)[22] indicated that patients assessed 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, reviewers recommended that IMRT be considered for lung cancer patients when the tumor is proximate to an organ at risk, where the target volume includes a large volume of an organ at risk, or where dose escalation would be potentially beneficial while minimizing normal tissue toxicity.[21.]

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.[22.] 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 4-dimensional 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 endpoints were locoregional progression, distant metastasis, and OS. Disease covariates were gross tumor volume, nodal status, and histology. The toxicity endpoint 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 1 for all disease endpoints; the difference was significant only for OS. The median survival was 1.40 years for the IMRT group and 0.85 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 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 4-dimensional 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 a single center limit the ability to draw definitive treatment conclusions about IMRT.

Shirvani et al (2013) reported on a U.S. cancer center study that assessed the use of definitive IMRT in limited-stage small-cell lung cancer treated with definitive RT.[23.] 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 to 83 months) for IMRT and 27 months (range, 2 to 147 months) for 3D-CRT. In both multivariable and 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 NSCLC using a cohort of patients from the Surveillance, Epidemiology, and End Results-Medicare database treated between 2002 and 2009.[24.] 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 =.02) were associated with IMRT. However, IMRT was similar to 3D-CRT after controlling for confounders in OS (HR, 0.94, p =.23) and cancer-specific survival (HR, 0.94, p =.28). On multivariate analysis, toxicity risks with IMRT and 3D-CRT were also similar. Likewise, results were similar for the propensity score-matched models and the adjusted models.

Ling et al (2016) compared IMRT with 3D-CRT in patients who had stage III NSCLC treated with definitive RT.[25.] 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. The authors found no significant differences between the groups for any measure of acute toxicity (grade ≥ 2 esophagitis, grade ≥ 2 pneumonitis, percutaneous endoscopic gastrostomy, narcotics, hospitalization, or weight loss). There were no significant differences in oncologic and survival outcomes.

Chun et al (2017) reported on a secondary analysis of a trial that assessed the addition of cetuximab to a standard chemotherapy regimen and radiation dose escalation.[26.] 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 stage IIIB breast cancer patients (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% CI, 0.171 to 0.986; p =.046), with no significant differences between the groups in 2-year 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.[27.] Using the National Cancer Database, 7493 patients treated between 2004 and 2011 were assessed. Main outcomes were OS and the likelihood and effects of radiation treatment interruption, defined as a break in the treatment of 4 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. 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% vs. 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)[27.]	Cohort	U.S.	2004-2011	7493	IMRT	Non-IMRT	32 mo
Appel et al (2019)[28.]	Cohort	Israel	2012-2018	74	IMRT	3D-CRT	3.6 years (median)

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

Table 4. Summary of Key Observational Comparative Study Results

Study	OS	Major Pathologic Response Rate	Pathologic Complete Response Rate
Koshy et al (2017)[27.]	Months		
IMRT	20.0		
Non-IMRT	18.2		
p	<.001		
Appel et al (2019)[28.]	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; 3-dimensional conformal radiotherapy; CI: confidence interval; IMRT: intensity-modulated radiotherapy; OS: overall survival.

Section Summary: Lung Cancer

For the treatment of lung cancer, no RCTs were identified that compared IMRT with 3D-CRT. Dosimetry studies have reported that IMRT can reduce radiation exposure to critical surrounding structures, especially for large lung tumors. Based on nonrandomized 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 IMRT, the evidence includes systematic reviews, RCTs, and nonrandomized comparative studies. Relevant outcomes are 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 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 3D-CRT include 1 RCT comparing IMRT with 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 RT 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 nonrandomized, retrospective, comparative studies. Relevant outcomes are OS, disease-specific survival, locoregional control, quality of life, and treatment-related morbidity. 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, and reduce 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 from Blue Cross Blue Shield Association, input was received from 2 physician specialty societies and 3 academic medical centers (3 reviewers) in 201 2. There was a near-uniform consensus in responses that whole-breast and lung intensity-modulated radio-therapy (IMRT) is appropriate in select patients with breast and lung cancer. Respondents noted IMRT might 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 might reduce skin reactions and potentially improve cosmetic outcomes. Partial-breast IMRT was not supported by respondents, and the response was mixed on the value of chest wall IMRT postmastectomy.

2010 Input

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

National Comprehensive Cancer Network

Breast Cancer

Current National Comprehensive Cancer Network (NCCN) guidelines (v.4.2021) for breast cancer indicate the importance of individualizing radiotherapy (RT) planning and delivery. Computed tomography-based treatment planning is encouraged to delineate target volumes and adjacent organs at risk. Improved 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, such as the heart and lung.[29] The guideline states that "the panel recommends whole breast irradiation to include breast tissue in entirety. CT-based treatment planning is recommended to limit irradiation exposure of the heart and lungs, and to assure adequate coverage of the breast and lumpectomy site." The guidelines indicate chest wall and regional lymph node irradiation may be appropriate postmastectomy in select patients but IMRT is not mentioned as a technique for irradiation in these circumstances.

Lung Cancer

Current NCCN guidelines (v.4.2021) for non-small-cell lung cancer 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 versus older techniques demonstrate reduced toxicity and improved survival."[30]

Current NCCN guidelines (v.3.2021) for small-cell lung cancer indicate that "Use of more advanced technologies is appropriate when needed to deliver adequate tumor doses while respecting normal tissue dose constraints."[31] Intensity-modulated RT is included in the technologies listed. The guidelines also state that "IMRT is preferred over 3D conformal external-beam RT on the basis of reduced toxicity in the setting of concurrent chemotherapy/RT."

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]

Lung Cancer

In 2018, the American Society for Radiation Oncology also published evidence-based guidelines on RT for lung cancer. The guidelines recommended "moderately hypofractionated palliative thoracic radiation therapy" with chemotherapy as palliative care for stage III and IV incurable non-small-cell lung cancer.[33]

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 post mastectomy RT.[34] 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 T1-2 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."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Some local Medicare Part B carriers have indicated that IMRT for the lung is considered medically necessary. These documents do not detail the rationale for this conclusion.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and 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			
NCT02635009	Randomized Phase II/III Trial of Prophylactic Cranial Irradiation With or Without Hippocampal Avoidance for Small Cell Lung Cancer	392	Apr 2027
NCT01349322	A Phase III Trial of Accelerated Whole Breast Irradiation with Hypofractionation Plus Concurrent Boost Versus Standard Whole Breast Irradiation Plus Sequential Boost for Early-Stage Breast Cancer	2354	Aug 2022
NCT02003560	Accelerated Partial Breast Irradiation After Breast Conserving Surgery for Low-risk Invasive Breast Cancer: 3D Conformal Radiotherapy (3D-CRT) and Intensity Modulated Radiotherapy (IMRT) - Prospective Phase II Study	90	Mar 2024
NCT03786354	Prospective Evaluation of Shoulder Morbidity in Patients with Lymph-Node Positive Breast Cancer Receiving Regional Nodal Irradiation	60	Dec 2020
NCT01185132	A Phase III Randomized Study Comparing Intensity Modulated Planning vs 3-dimensional Planning for Accelerated Partial Breast Radiotherapy	660	Jul 2028
Unpublished			
NCT00520702	A Randomized Trial to Compare Time To Common Toxicity Criteria for Adverse Effect (CTC AEC) 3.0 Grade Treatment Related Pneumonitis (TRP) in Patients With Locally Advanced Non-Small Cell Carcinoma (NSCLC) Receiving Concurrent Chemoradiation Radiation Treated With 3-Dimensional Conformal Radiation Therapy (3D CRT, ARM 1) vs Intensity Modulated Radiation (IMRT, ARM 2) Using 4 Dimensional CT Planning and Image-Guided Adaptive Radiation Therapy (IGART)	168	Oct 2018
NCT01322854	Randomized Phase III Trial Comparing Intensity Modulated Radiotherapy With Integrated Boost to Conventional Radiotherapy With Consecutive Boost in Patients With Breast Cancer After Breast Conserving Surgery	502	Mar 2018 (unknown)

NCT: national clinical trial.

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Documentation for Clinical Review

Please provide the following documentation:

- (click here >>>) Fax Back Form for Radiation Oncology Services

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	77014	Computed tomography guidance for placement of radiation therapy fields
	77261	Therapeutic radiology treatment planning; simple
	77262	Therapeutic radiology treatment planning; intermediate
	77263	Therapeutic radiology treatment planning; complex
	77293	Respiratory motion management simulation (List separately in addition to code for primary procedure)
	77300	Basic radiation dosimetry calculation, central axis depth dose calculation, TDF, NSD, gap calculation, off axis factor, tissue inhomogeneity factors, calculation of non-ionizing radiation surface and depth dose, as required during course of treatment, only when prescribed by the treating physician
	77301	Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications
	77306	Teletherapy isodose plan; simple (1 or 2 unmodified ports directed to a single area of interest), includes basic dosimetry calculation(s)
	77307	Teletherapy isodose plan; complex (multiple treatment areas, tangential ports, the use of wedges, blocking, rotational beam, or special beam considerations), includes basic dosimetry calculation(s)
	77331	Special dosimetry (e.g., TLD, microdosimetry) (specify), only when prescribed by the treating physician
	77332	Treatment devices, design and construction; simple (simple block, simple bolus)
	77334	Treatment devices, design and construction; complex (irregular blocks, special shields, compensators, wedges, molds or casts)
	77336	Continuing medical physics consultation, including assessment of treatment parameters, quality assurance of dose delivery, and

Type	Code	Description
		review of patient treatment documentation in support of the radiation oncologist, reported per week of therapy
	77338	Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan
	77370	Special medical radiation physics consultation
	77385	Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple
	77386	Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; complex
	77387	Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed
	77417	Therapeutic radiology port image(s)
	77427	Radiation treatment management, 5 treatments
	77470	Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation)
HCPCS	G6001	Ultrasonic guidance for placement of radiation therapy fields
	G6002	Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy
	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
	G6017	Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (e.g., 3D positional tracking, gating, 3D surface tracking), each fraction of treatment

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
03/30/2015	Policy title change from Intensity Modulated Radiation Therapy (IMRT) BCBSA Medical Policy adoption Policy revision without position change
10/01/2016	Policy revision without position change
09/01/2017	Policy revision without position change
09/01/2018	Policy revision without position change
09/01/2019	Policy revision without position change
06/01/2020	Administrative update. Policy statement, guidelines and literature updated.
10/01/2020	Annual review. No change to policy statement. Literature review updated. Coding update.
11/20/2020	Policy statement and guidelines updated.
08/01/2021	Annual review. No change to policy statement. Policy guidelines updated.
12/01/2021	Administrative update. Policy statement, guidelines and literature updated.
08/01/2022	Annual review. No change to policy statement.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE Red font: Verbiage removed	**AFTER** Blue font: Verbiage Changes/Additions
Intensity-Modulated Radiotherapy of the Breast and Lung 8.01.46 **Policy Statement:** Intensity-modulated radiotherapy (IMRT) using a hypofractionated regimen (up to 16 treatments and up to 8 more if a boost is needed) may be considered **medically necessary** as a technique to deliver whole-breast irradiation in patients receiving treatment when **all** of the following conditions are met: I. Left-sided breast cancer II. Prior breast-conserving surgery III. Documentation of **all** of the following: A. Significant cardiac radiation exposure cannot be avoided using alternative radiotherapy B. IMRT dosimetry demonstrates significantly reduces cardiac target volume radiation exposure as documented by **both** of the following: 1. With 3D-CRT, the target volume coverage results in cardiac radiation exposure that is expected to be greater than or equal to 25 gray (Gy) to 10 cm^3 or more of the heart (V25 ≥10 cm^3), despite the use of a complex positioning device (e.g., Vac-Lok™) 2. With IMRT, there is a reduction in the absolute heart volume receiving 25 Gy or more by at least 20% (e.g., volume predicted to receive 25 Gy by 3D-CRT is 20 cm^3, and the volume predicted by IMRT is ≤16 cm^3 IMRT using conventional fractionation may be considered **medically necessary** if there are contraindications to hypofractionation and documentation of the contraindication to hypofractionation is provided. IMRT may be considered **medically necessary** when **all** of the following conditions are met: I. Individual has large breasts (> 500 cc)	**Intensity-Modulated Radiotherapy of the Breast and Lung 8.01.46** **Policy Statement:** I. Intensity-modulated radiotherapy (IMRT) using a hypofractionated regimen (up to 16 treatments and up to 8 more if a boost is needed) may be considered **medically necessary** as a technique to deliver whole-breast irradiation in patients receiving treatment when **all** of the following conditions are met: A. Left-sided breast cancer B. Prior breast-conserving surgery C. Documentation of **all** of the following: 1. Significant cardiac radiation exposure cannot be avoided using alternative radiotherapy 2. IMRT dosimetry demonstrates significantly reduces cardiac target volume radiation exposure as documented by **both** of the following: a. With 3D-CRT, the target volume coverage results in cardiac radiation exposure that is expected to be greater than or equal to 25 gray (Gy) to 10 cm^3 or more of the heart (V25 ≥10 cm^3), despite the use of a complex positioning device (e.g., Vac-Lok™) b. With IMRT, there is a reduction in the absolute heart volume receiving 25 Gy or more by at least 20% (e.g., volume predicted to receive 25 Gy by 3D-CRT is 20 cm^3, and the volume predicted by IMRT is ≤16 cm^3 II. IMRT using conventional fractionation may be considered **medically necessary** if there are contraindications to hypofractionation and documentation of the contraindication to hypofractionation is provided. III. IMRT may be considered **medically necessary** when **all** of the following conditions are met: A. Individual has large breasts (> 500 cc)

POLICY STATEMENT	
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II. 3-dimensional conformal radiotherapy dosimetry results in hot spots (focal regions with dose variation greater than10% of target) III. Hot spots can be avoided with IMRT	B. 3-dimensional conformal radiotherapy dosimetry results in hot spots (focal regions with dose variation greater than10% of target) C. Hot spots can be avoided with IMRT
IMRT of the breast is considered **investigational** as a technique of partial-breast irradiation after breast-conserving surgery.	IV. IMRT of the breast is considered **investigational** as a technique of partial-breast irradiation after breast-conserving surgery.
IMRT may be considered **medically necessary** as a technique to deliver radiotherapy in patients with lung cancer when **all** of the following conditions are met: I. Radiotherapy is being given with curative intent II. Three-dimensional (3-D) conformal radiotherapy will expose greater than 35% of normal lung tissue to more than a 20-Gy dose-volume (V20) III. IMRT dosimetry demonstrates a reduction in the V20 to at least 10% below the V20 that is achieved with the 3-dimensional plan (e.g., from 40% down to 30% or lower)	V. IMRT may be considered **medically necessary** as a technique to deliver radiotherapy in patients with lung cancer when **all** of the following conditions are met: A. Radiotherapy is being given with curative intent B. Three-dimensional (3-D) conformal radiotherapy will expose greater than 35% of normal lung tissue to more than a 20-Gy dose-volume (V20) C. IMRT dosimetry demonstrates a reduction in the V20 to at least 10% below the V20 that is achieved with the 3-dimensional plan (e.g., from 40% down to 30% or lower)
IMRT is considered **not medically necessary** as a technique to deliver radiotherapy in patients receiving palliative treatment for lung cancer.	VI. IMRT is considered **not medically necessary** as a technique to deliver radiotherapy in patients receiving palliative treatment for lung cancer.
Intensity modulated radiation therapy to breast or lung cancers may be considered **medically necessary** when one or more of the following conditions are present: I. The target volume is in close proximity to critical structures that must be protected and **both** of the following: * (see source below) A. Planned 3D-CRT exposure to critical adjacent structures is above normal tissue constraints B. Planned IMRT exposure to these critical adjacent structures does not exceed normal tissue constraints II. An immediately adjacent area has been previously irradiated and abutting portals must be established with high precision	VII. Intensity modulated radiation therapy to breast or lung cancers may be considered **medically necessary** when **one or more** of the following conditions are present: A. The target volume is in close proximity to critical structures that must be protected and **both** of the following: * (see source below) 1. Planned 3D-CRT exposure to critical adjacent structures is above normal tissue constraints 2. Planned IMRT exposure to these critical adjacent structures does not exceed normal tissue constraints B. An immediately adjacent area has been previously irradiated and abutting portals must be established with high precision

POLICY STATEMENT	
BEFORE **Red font: Verbiage removed**	**AFTER** **Blue font: Verbiage Changes/Additions**
IMRT is considered **not medically necessary** for the treatment of breast or lung cancer for all indications not meeting the criteria above, including palliative care when criteria for approval are not met.	VIII. IMRT is considered **not medically necessary** for the treatment of breast or lung cancer for all indications not meeting the criteria above, including palliative care when criteria for approval are not met.