Protocol

Intensity-Modulated Radiotherapy of the Breast and Lung

(80146)

Medical Benefit		**Effective Date**: 06/01/20	**Next Review Date**: 03/21
Preauthorization	No	**Review Dates**: 03/20	

Preauthorization is not required but is recommended if, despite this protocol position, you feel this service is medically necessary; supporting documentation must be submitted to Utilization Management.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With breast cancer	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • Three-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Morbid events • Functional outcomes • Treatment-related morbidity
Individuals: • With lung cancer	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • Three-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Functional outcomes • Treatment-related morbidity

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.

SUMMARY OF EVIDENCE

For individuals who have breast cancer who receive IMRT, the evidence includes randomized controlled trials and nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. There is modest evidence from randomized controlled trials for a decrease in acute skin toxicity with IMRT compared with two-dimensional 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 three-dimensional conformal radiotherapy (3D-CRT), these comparative data are of limited value. Studies comparing IMRT with 3D-CRT include one randomized controlled trial comparing IMRT with deep inspiration breath hold to 3D-CRT, two nonrandomized comparative studies on whole-breast IMRT, and a few studies on chest wall IMRT.

These studies suggest that IMRT require less radiation exposure to nontarget areas and may improve short-term clinical outcomes. The available studies on the chest wall IMRT for postmastectomy breast cancer patients have only 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 a meaningful improvement in the net health outcome.

Strong evidence supports the use of IMRT for left-sided breast lesions in which alternative types of RT cannot avoid toxicity to the heart. Based on available evidence, input from clinical vetting, a strong chain of evidence, and the potential to reduce harms, IMRT may be considered medically necessary for whole-breast irradiation when (1) alternative forms of RT cannot avoid cardiac toxicity, and (2) IMRT dose-planning demonstrates a substantial reduction in cardiac toxicity. IMRT for the palliative treatment of lung cancer is considered not medically necessary because conventional radiation techniques are adequate for palliation.

Clinical vetting also provided strong support for IMRT when alternative RT dosimetry exceeds a threshold of 20-gray dose-volume (V20) to at least 35% of normal lung tissue. Based on available evidence, clinical vetting, a strong chain of evidence, and the potential to reduce harms, IMRT may be considered medically necessary for lung cancer when: (1) RT is given with curative intent, (2) alternative RT dosimetry demonstrates radiation dose exceeding V20 for at least 35% of normal lung tissue, and (3) IMRT reduces the V20 of radiation to the lung at least 10% below the V20 of 3D-CRT (e.g., 40% reduced to 30%).

POLICY

Intensity-modulated radiotherapy (IMRT) may be considered **medically necessary** as a technique to deliver whole-breast irradiation in patients receiving treatment for left-sided breast cancer after breast-conserving surgery when all the following conditions have been met:

- Significant cardiac radiation exposure cannot be avoided using alternative radiotherapy, and
- IMRT dosimetry demonstrates significantly reduced cardiac target volume radiation exposure (see Policy Guidelines section).

IMRT may be considered **medically necessary** in individuals with large breasts when treatment planning with three-dimensional conformal radiotherapy results in hot spots (focal regions with dose variation >10% of target) and the hot spots can be avoided with IMRT (see Policy Guidelines section).

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

IMRT of the chest wall is considered **investigational** as a technique of postmastectomy irradiation.

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:

- Radiotherapy is being given with curative intent,
- Three-dimensional conformal radiotherapy will expose >35% of normal lung tissue to more than a 20-Gy dose-volume (V20), and
- IMRT dosimetry demonstrates a reduction in the V20 to at least 10% below the V20 that is achieved with the three-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.

IMRT is **not medically necessary** for the treatment of breast or lung cancer for all indications not meeting the criteria above.

POLICY GUIDELINES

Table PG1 outlines radiation doses generally considered tolerance thresholds for these normal structures for the chest and abdomen. Dosimetry plans may be used to demonstrate that radiation by three-dimensional conformal radiotherapy (3D-CRT) would exceed tolerance doses to structures at risk.

Table PG1. Radiation Tolerance Doses for Normal Tissues of the Chest and Abdomen

Site	TD 5/5, Gray[a]			TD 50/5, Gray[b]			Complication End Point
	Portion of Organ Involved			Portion of Organ Involved			
	1/3	2/3	3/3	1/3	2/3	3/3	
Heart	60	45	40	70	55	50	Pericarditis
Lung	45	30	17.5	65	40	24.5	Pneumonitis
Spinal cord	50	50	47	70	70	NP	Myelitis, necrosis

Compilation from the following two sources:

Morgan MA (2011). Radiation Oncology. In DeVita, Lawrence and Rosenberg, Cancer (p.308). Philadelphia: Lippincott Williams and Wilkins.

Kehwar TS, Sharma SC. Use of normal tissue tolerance doses into linear quadratic equation to estimate normal tissue complication probability. Available online: http://www.rooj.com/Radiation%20Tissue%20Tolerance.htm

Radiation tolerance doses for the cochlea have been reported to be 50 gray

NP: not provided, cm: centimeters, TD: tolerance dose

[a]TD 5/5, the average dose that results in a 5% complication risk within five years

[b]TD 50/5, the average dose that results in a 50% complication risk within five years

The following is an example of clinical guidelines that may be used with intensity-modulated radiotherapy (IMRT) in left-sided breast lesions:

- 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) with 3D-CRT, despite the use of a complex positioning device (e.g., Vac-Lok), and
- With the use of 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).

The following are examples of criteria to define large breast size when using IMRT to avoid hot spots, as derived from randomized studies:

- Donovan et al (2007) enrolled patients with "higher than average risk of late radiotherapy-adverse effects," which included patients having larger breasts. The authors stated that while breast size is not particularly good at identifying women with dose inhomogeneity falling outside current International Commission on Radiation Units and Measurements guidelines, they excluded women with small breasts (≤500 cm^3), who generally have fairly good dosimetry with standard two-dimensional compensators.
- In the trial by Pignol et al (2008), which reported that the use of IMRT significantly reduced the proportion of patients experiencing moist desquamation, breast size was categorized as small, medium, or large by cup size. Multivariate analysis found that smaller breast size was significantly associated with a decreased risk of moist desquamation ($p<0.001$).

BACKGROUND

For certain stages of many cancers, including breast and lung, randomized controlled trials 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

Conventional External-Beam Radiotherapy

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

Three-Dimensional Conformal Radiotherapy

Treatment planning evolved by using three-dimensional images, usually from computed tomography (CT) scans, to delineate the boundaries of the tumor and discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Computer algorithms were developed to estimate cumulative radiation dose delivered to each volume of interest by summing the contribution from each shaped beam. Methods also were developed to position the patient and the radiation portal reproducibly for each fraction and immobilize the patient, thus maintaining consistent beam axes across treatment sessions. Collectively, these methods are termed3D-CRT.

Intensity-Modulated Radiotherapy

IMRT, which uses computer software along with CT and magnetic resonance images, offers better conformality than 3D-CRT because it modulates the intensity of the overlapping radiation beams projected on the target and uses multiple shaped treatment fields. Treatment planning and delivery are more complex, time-consuming, and labor-intensive for IMRT than for 3D-CRT. The technique uses a multileaf collimator (MLC), which, when coupled with a computer algorithm, allows for “inverse” treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target’s prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and acceptable dose limits within the 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 thus may improve local tumor control, with decreased exposure to surrounding, normal tissues, potentially reducing acute and late radiation toxicities. Better dose homogeneity within the target may also improve local tumor control by avoiding underdosing within the tumor and may decrease toxicity by avoiding overdosing.

Technologic developments have produced advanced techniques that 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 its 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 deliver RT to the target volume more precisely.

IMRT methods to plan and deliver RT are not uniform. IMRT may use beams that remain on as MLCs move around the patient (dynamic MLC) or that are off during movement and turn on once the MLC reaches prespecified positions (“step and shoot” technique). A third alternative uses a very narrow, single beam that moves spirally around the patient (tomotherapy). Each method uses different computer algorithms to plan treatment and

yields somewhat different dose distributions in and outside the target. Patient position can alter target shape and thus affect treatment plans. Treatment plans are usually based on a single imaging scan, a static 3D-CT image. Current methods seek to reduce positional uncertainty for tumors and adjacent normal tissues by various techniques. Patient immobilization cradles and skin or bony markers are used to minimize day-to-day variability in patient positioning. In addition, many tumors have irregular edges that preclude drawing tight margins on CT scan slices when radiation oncologists contour the tumor volume. It is unknown whether omitting some tumor cells or including some normal cells in the resulting target affects outcomes of IMRT.

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.[1] Techniques presently being studied with other tumors (e.g., lung cancer)[2] 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.

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.

RT 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.

RELATED PROTOCOLS

Intensity-Modulated Radiotherapy: Abdomen and Pelvis

Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid

Intensity-Modulated Radiotherapy: Central Nervous System Tumors

Intensity-Modulated Radiotherapy of the Prostate

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary

Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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