Protocol

Intensity-Modulated Radiotherapy: Abdomen and Pelvis

(80149)

Medical Benefit		**Effective Date**: 07/01/14	**Next Review Date**: 03/19
Preauthorization	No	**Review Dates**: 09/09, 09/10, 03/11, 03/12, 03/13, 03/14, 03/15, 03/16, 03/17, 03/18	

This protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

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 gastrointestinal tract cancers	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • Three-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Quality of life • Treatment-related morbidity
Individuals: • With gynecologic cancers	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • Three-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Quality of life • Treatment-related morbidity
Individuals: • With anorectal cancer	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • Three-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Quality of life • Treatment-related morbidity

Description

Radiotherapy may be an integral component of the treatment of cancers of the abdomen and pelvis. Intensity-modulated radiotherapy (IMRT) has been proposed as a method 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 gastrointestinal (GI) tract cancers who receive intensity-modulated radiotherapy (IMRT), the evidence includes nonrandomized comparative studies and retrospective series. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. IMRT has been compared with 3-dimensional conformal radiotherapy (3D-CRT) for the treatment of stomach, hepatobiliary, and pancreatic cancers, with some studies reporting longer overall survival and decreased toxicity with IMRT. The evidence on hepatobiliary cancer includes a series with historical controls; it found an increase in median

survival with no difference in toxicity. Two comparative studies (one prospective, one retrospective) were identified on IMRT for pancreatic cancer. The prospective comparative study found an increase in survival with a reduction in GI toxicity, while the retrospective study found a decrease in GI toxicity. The available comparative evidence, together with dosimetry studies of organs at risk, would suggest that IMRT improves survival and decreases toxicity compared to 3D-CRT in patients with GI cancers. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have gynecologic cancers who receive IMRT, the evidence includes two randomized controlled trials and several nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. There is limited comparative evidence on survival outcomes following IMRT or 3D-CRT. However, available results are generally consistent that IMRT reduces GI and genitourinary toxicity. Based on evidence with other cancers of the pelvis and abdomen that are proximate to organs at risk, it is expected that overall survival with IMRT would be at least as good as 3D-CRT, with a decrease in toxicity. A reduction in GI toxicity is likely to improve the quality of life in patients with gynecologic cancer. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have anorectal cancer who receive IMRT, the evidence includes a small randomized controlled trial (N=20), nonrandomized comparative studies, and case series. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. Survival outcomes have not differed significantly between IMRT and 3D-CRT. Recent studies have found IMRT with chemotherapy for the treatment of anal cancer reduces acute and late adverse events better than 3D-CRT plus chemotherapy. The comparative data on use of IMRT versus 3D-CRT in chemoradiotherapy for anal cancer have shown reductions primarily in GI toxicity. A reduction in GI toxicity is likely to improve the quality of life in patients with anorectal cancer. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Policy

Intensity-modulated radiotherapy (IMRT) may be considered **medically necessary** as an approach to delivering radiotherapy for patients with cancer of the anus and anal canal.

When dosimetric planning with standard 3-dimensional conformal radiotherapy predicts that the radiation dose to an adjacent organ would result in unacceptable normal tissue toxicity (see Policy Guidelines), IMRT may be considered **medically necessary** for the treatment of cancer of the abdomen and pelvis, including but not limited to:

- stomach (gastric);
- hepatobiliary tract;
- pancreas; or
- gynecologic tumors (including cervical, endometrial, and vulvar cancers).

IMRT would be considered **investigational** for all other uses in the abdomen and pelvis.

Note: Bladder cancer, esophageal cancer, and sarcoma, as well as colon and rectal cancers are not addressed in the above medical guideline.

Policy Guidelines

The table below outlines radiation doses that are generally considered tolerance thresholds for these normal

structures in the abdomen and pelvis. Dosimetry plans may be reviewed to demonstrate that radiation by 3-dimensional conformal radiotherapy (3D-CRT) would exceed tolerance doses to structures at risk.

Radiation Tolerance Doses for Normal Tissues of the Abdomen and Pelvis

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
Kidney	50	30	23	NP	40	28	Clinical nephritis
Liver	50	35	30	55	45	40	Liver failure
Stomach	60	55	50	70	67	65	Ulceration/perforation
Small intestine	50	NP	40	60	NP	55	Obstruction/perforation
Femoral head	NP	NP	52	NP	NP	65	Necrosis

The tolerance doses in the table are a 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. http://www.rooj.com/Radiation%20Tissue%20Tolerance.htm

NP: not provided; 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

For IMRT to provide outcomes that are superior to 3D-CRT, there must be a clinically meaningful decrease in the radiation exposure to normal structures with IMRT compared to 3D-CRT. There is not a standardized definition for a clinically meaningful decrease in radiation dose. In principle, a clinically meaningful decrease would signify a significant reduction in anticipated complications of radiation exposure. To document a clinically meaningful reduction in dose, dosimetry planning studies should demonstrate a significant decrease in the maximum dose of radiation delivered per unit of tissue, and/or a significant decrease in the volume of normal tissue exposed to potentially toxic radiation doses. While radiation tolerance dose levels for normal tissues are well-established, the decrease in the volume of tissue exposed that is needed to provide a clinically meaningful benefit has not been standardized. Therefore, precise parameters for a clinically meaningful decrease cannot be provided.

Note: This protocol does not address IMRT for treatment of cancers of the colon and rectum.

Background

Radiation Techniques

Conventional External-Beam Radiotherapy

Over the past several decades, methods to plan and deliver radiotherapy (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 termed 3D-CRT.

Intensity-Modulated Radiotherapy

IMRT, which uses computer software and CT and magnetic resonance imaging images, offers better conformality than 3D-CRT, because it is able to modulate the intensity of the overlapping radiation beams projected on the target and to use 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 development has 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 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.

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 one 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.

Note: The evidence for the following abdominal and pelvic cancers has not yet been reviewed and is beyond the scope of this document: bladder, kidney, ureter, and esophageal cancer and sarcoma.

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, Tempe, AZ), cleared in 2006, and the decimal tissue compensator (South-

eastern Radiation Products, Sanford, FL), 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 treatment planning systems have also been cleared for marketing by the FDA through the 510(k) process. These include the Prowess Panther™ (Prowess, Concord, CA) in 2003, TiGRT (LinaTech, Sunnyvale, CA) in 2009, and the RayDose (RaySearch Laboratories, Stockholm, Sweden) in 2008. FDA product code: MUJ.

Fully integrated IMRT systems also are available. These devices are customizable and support all stages of IMRT delivery, including planning, treatment delivery, and health record management. Varian Medical Systems (Palo Alto, CA), for example, has several 510(k) marketing clearances for high energy linear accelerator systems that can be used to deliver precision radiotherapy such as IMRT. FDA product code: IYE.

Related Protocols

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

Intensity-Modulated Radiotherapy: Central Nervous System Tumors

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Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment 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.**

References

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

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