BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 8.01.49 Intensity-Modulated Radiotherapy: Abdomen, Pelvis and Chest

Effective Policy Date: October 1, 2023

Original Policy Date: September 2012

Related Policies:

8.01.48 - Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid
8.01.59 - Intensity-Modulated Radiotherapy: Central Nervous System Tumors

Intensity-Modulated Radiotherapy: Abdomen, Pelvis and Chest

Description

Radiotherapy may be an integral component of the treatment of cancers of the abdomen, pelvis, and chest. Intensity-modulated radiotherapy 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.

IMRT is the more recent development in external radiation. Treatment planning and delivery are more complex, time-consuming, and labor-intensive for IMRT than for 3D-CRT. Similar to 3D-CRT, the tumor and surrounding normal organs are outlined in 3D by a scan and multiple radiation beams are positioned around the patient for radiation delivery.[1,] In IMRT, radiation beams are divided into a grid-like pattern, separating a single beam into many smaller "beamlets". Specialized computer software allows for “inverse” treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target's prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and acceptable dose limits within the normal tissues. Based on these parameters and a digitally reconstructed radiographic image of the tumor, surrounding tissues, and organs at risk, computer software optimizes the location, shape, and intensities of the beam ports to achieve the treatment plan's goals.

Increased conformality may permit escalated tumor doses without increasing normal tissue toxicity and is proposed to improve local tumor control, with decreased exposure to surrounding, normal tissues, potentially reducing acute and late radiation toxicities. Better dose homogeneity within the target may also improve local tumor control by avoiding underdosing within the tumor and may decrease toxicity by avoiding overdosing.

Other advanced techniques may further improve RT treatment by improving dose distribution. These techniques are considered variations of IMRT. Volumetric modulated arc therapy delivers radiation from a continuous rotation of the radiation source. The principal advantage of volumetric modulated 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.

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OBJECTIVE

The objective of this evidence review is to evaluate whether intensity-modulated radiotherapy improves the net health outcome when used to treat cancers of the abdomen, pelvis, and chest.

POLICY STATEMENT

Intensity-modulated radiotherapy may be considered **medically necessary** as an approach to delivering radiotherapy for individuals 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 section), intensity-modulated radiotherapy 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;
- esophageal cancer;
- rectal locations; or
- gynecologic tumors (to include cervical, endometrial, and vulvar cancers).

Intensity-modulated radiotherapy would be considered **investigational** for all other uses in the abdomen and pelvis.

POLICY GUIDELINES

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

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

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 (5 cm)	50 (10 cm)	47 (20 cm)	70 (5 cm)	70 (10 cm)	NP	Myelitis/necrosis
Kidney	50	30	23	NP	40	28	Clinical nephritis

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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

Compiled from 2 sources: (1) Morgan MA, Ten Taken RK, Lawrence TS. Essentials of radiation therapy. In DeVita, Hellman, and Rosenberg, *Cancer: Principles & Practice of Oncology*. Philadelphia: Lippincott Williams and Wilkins; 2019; and (2) 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. Accessed May 18, 2023.
NP: not provided; TD: tolerance dose.
[a] TD 5/5, the average dose that results in a 5% complication risk within 5 years.
[b] TD 50/5, the average dose that results in a 50% complication risk within 5 years.

For intensity-modulated radiotherapy (IMRT) to provide outcomes superior to 3D-CRT, there must be a clinically meaningful decrease in the radiation exposure to normal structures with IMRT compared with 3D-CRT. There is no 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.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA 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 FOCUS Radiation Treatment Planning System (Computerized Medical Systems) cleared in 2002, Prowess Panther™ (Prowess) cleared in 2003, TiGRT (LinaTech) cleared in 2009, the RayDose (RaySearch Laboratories) cleared in 2008, and the Eclipse Treatment Planning System (Varian Medical Systems) cleared in 2017. 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 has several 510(k) marketing clearances for high-energy linear accelerator systems that can be used to deliver precision RT such as IMRT. FDA product code: IYE.

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RATIONALE

Summary of Evidence

For individuals who have gastrointestinal (GI) tract cancers who receive intensity-modulated radiotherapy (IMRT) , the evidence includes nonrandomized comparative studies, retrospective series, and a systematic review. Relevant outcomes are overall survival (OS) , disease-specific survival, recurrence, 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. Evidence has been inconsistent with the outcome of survival, with some studies reporting increased survival among patients receiving IMRT compared with patients receiving 3D-CRT, and other studies reporting no difference between groups. However, most studies found that patients receiving IMRT experienced significantly less GI toxicity compared with patients receiving 3D-CRT. The available comparative evidence, together with dosimetry studies of organs at risk, would suggest that IMRT decreases toxicity compared with 3D-CRT in patients who had GI cancers. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have gynecologic cancers who receive IMRT, the evidence includes a systematic review, 6 randomized controlled trials (RCTs) , and nonrandomized comparative studies. Relevant outcomes are OS, disease-specific survival, recurrence, quality of life, and treatment-related morbidity. There is limited comparative evidence on survival outcomes following IMRT or 3D-CRT. However, results are generally consistent in 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 OS 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 an improvement in the net health outcome.

For individuals who have anorectal cancer who receive IMRT, the evidence includes a small RCT (N=20), nonrandomized comparative studies, and case series. Relevant outcomes are OS, disease-specific survival, recurrence, quality of life, and treatment-related morbidity. Survival outcomes have not differed significantly between patients receiving IMRT and 3D-CRT. However, studies have found that patients receiving IMRT plus chemotherapy for the treatment of anal cancer experience fewer acute and late adverse events than patients receiving 3D-CRT plus chemotherapy, 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 an improvement in the net health outcome.

For individuals who have esophageal cancer who receive IMRT, the evidence includes a systematic review and nonrandomized comparative studies. Relevant outcomes are OS, disease-specific survival, recurrence, quality of life, and treatment-related morbidity. Survival outcomes have been mixed with some studies concluding that IMRT is associated with a significant improvement in OS, progression-free survival , or distant-metastases-free survival versus 3D-CRT and others reporting no difference between the radiotherapy techniques. IMRT appears to be associated with a reduced dose for organs at risk and may result in less radiation-induced toxicity. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

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 Guidelines

Gastrointestinal Tract Cancers

The National Comprehensive Cancer Network (NCCN) guideline (v.1.2023) for gastric cancer indicates that "CT [computed tomography] simulation and conformity treatment planning should be used with either 3D conformal radiation [3D-CRT] or intensity-modulated radiation therapy (IMRT)."[29,] In addition, target volumes need to be carefully defined and encompassed while taking into account variations in stomach filling and respiratory motion.

The NCCN guideline (v.1.2023) for hepatocellular carcinoma states that "All tumors irrespective of the location may be amenable to RT [radiation therapy] (3D conformal radiation therapy, intensity-modulated radiation therapy [IMRT], or stereotactic body radiation therapy [SBRT])."[30,]The NCCN guideline (v.2.2023) on biliary tract cancers also states that "all tumors irrespective of the location may be amenable to RT (3D-CRT, IMRT, or SBRT)."[31,]

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IMRT is mentioned as an option in the NCCN guideline (v.1.2023) for pancreatic adenocarcinoma, stating that IMRT "is increasingly being applied for the therapy of locally advanced pancreatic adenocarcinoma and in the adjuvant setting with the aim of increasing radiation dose to the gross tumor while minimizing toxicity to surrounding tissues."[32] In addition, the guideline states that "there is no clear consensus on the appropriate maximum dose of radiation when IMRT technique is used."

Gynecologic Cancers

For cervical cancer, the NCCN guideline (v.1.2023) indicates IMRT "is helpful in minimizing the dose to the bowel and other critical structures in the post-hysterectomy setting and in treating the para-aortic nodes when necessary." This technique can also be useful "when high doses are required to treat gross disease in regional lymph nodes."[33] IMRT "should not be used as routine alternatives to brachytherapy for treatment of central disease in patients with an intact cervix." The guideline also mentions that "very careful attention to detail and reproducibility (including consideration of target and normal tissue definitions, patient and internal organ motion, soft tissue deformation, and rigorous dosimetric and physics quality assurance) is required for proper delivery of IMRT and related highly conformal technologies."

The NCCN guideline (v.2.2023) on uterine neoplasms states that radiotherapy for uterine neoplasms includes external-beam radiotherapy and/or brachytherapy but that IMRT may be considered "for normal tissue sparing."[34]

The NCCN guideline (v.1.2023) on ovarian cancer does not mention IMRT.[35]

Anorectal Cancers

The NCCN guideline (v.2.2023) for anal carcinoma states that IMRT "is preferred over 3D conformal RT [radiotherapy] in the treatment of anal carcinoma"; and that its use "requires expertise and careful target design to avoid reduction in local control by so-called 'marginal-miss'."[36]

The NCCN guideline (v.2.2023) on rectal cancer indicates that "IMRT is preferred for reirradiation of previously treated patients with recurrent disease, patients treated postoperatively due to increased acute or later toxicity, or in unique anatomical situations."[37]

Esophageal Cancer

The NCCN guideline (v.2.2023) for esophageal and esophagogastric junction cancers states that "CT stimulation and conformal treatment planning should be used with either 3D conformal radiation or intensity-modulated radiation therapy (IMRT)."[38]

American Society for Radiation Oncology

In 2020, the American Society for Radiation Oncology published a clinical practice guideline on RT for cervical cancer.[39] One key question within the guideline asked when it was appropriate to deliver IMRT for women administered definitive or postoperative RT for cervical cancer. Recommendations regarding this clinical scenario included:

- "In women with cervical cancer treated with postoperative RT with or without chemotherapy, IMRT is recommended to decrease acute and chronic toxicity." This was a strong recommendation based on moderate quality evidence for acute toxicity and low quality evidence for chronic toxicity.
- "In women with cervical cancer treated with definitive RT with or without chemotherapy, IMRT is conditionally recommended to decrease acute and chronic toxicity." This was a conditional recommendation based on moderate quality evidence for acute and chronic toxicity.

The guideline also notes that there are "no data that IMRT improves disease-specific survival or OS [overall survival] over 2D/3D [2-dimensional/3-dimensional] techniques."

In 2021, the American Society for Radiation Oncology published a clinical practice guideline on RT for rectal cancer.[40] Within this guideline, IMRT-specific recommendations include:

- "For patients with rectal cancer treated with RT, an IMRT/volumetric modulated arc therapy (VMAT) technique is conditionally recommended (low quality of evidence). IMRT/VMAT may be beneficial when the external iliac nodes and/or the inguinal nodes require treatment or when 3-D conformal techniques may confer a higher risk for toxicity."

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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.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
September 2012	New policy	
March 2013	Replace policy	Policy updated with literature review, no new references added, reordered. Policy statement changed to IMRT may be considered medically necessary for all anal cancers (not limited to squamous cell carcinoma); IMRT may be medically necessary for treatment of tumors of abdomen and pelvis when dosimetric planning predicts the volume of small intestine receiving doses > 45 Gy with standard 3-D conformal radiation would result in unacceptable risk of small intestine injury. Added statement that IMRT is considered investigational for all other uses in the abdomen and pelvis. Paragraph added to guidelines regarding toxic radiation dose to tissues and definition of a clinically significant decrease in radiation dose.
March 2014	Replace policy	Policy updated with literature search. References 8, 13, 24-30 and 36-37 added. Policy statements unchanged.
March 2015	Replace policy	Policy updated with literature review. References 38-46 added. Policy statements unchanged.
September 2018	Replace policy	Policy updated with literature review through May 7, 2018 ; references 6-8, 12-13 and 23 added; references 19-26 and 33-40 updated; Policy statements unchanged.
September 2019	Replace policy	Policy updated with literature review through May 6, 2019; references on NCCN updated. Policy statements unchanged.
September 2020	Replace policy	Policy updated with literature review through June 7, 2020; references added. Policy statements unchanged
September 2021	Replace policy	Policy updated with literature review through June 3, 2021; references added and esophageal cancer indication added. Policy statements updated to include medically necessary statement for use of IMRT for esophageal cancer.
September 2022	Replace policy	Policy updated with literature review through June 1, 2022; references added. Minor editorial refinements to policy statements; Title of policy changed to include the chest. Intent unchanged.
September 2023	Replace policy	Policy updated with literature review through May 19, 2023; references added. Policy statements unchanged.

The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.