

<b>8.01.49</b>	<b>Intensity-Modulated Radiotherapy: Abdomen, Pelvis and Chest</b>		
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<b>Section:</b>	8.0 Therapy	<b>Page:</b>	Page 1 of 31

### Policy Statement

- I. Intensity-modulated radiotherapy (IMRT) may be considered **medically necessary** as an approach to delivering radiotherapy for individuals with cancer of the anus and anal canal.
- II. IMRT may be considered **medically necessary** for the treatment of the abdomen, pelvis, and chest 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, as documented by **BOTH** of the following:
  - A. IMRT is used to treat cancer of **one or more** of the following:
    1. Stomach (gastric)
    2. Hepatobiliary tract
    3. Pancreas
    4. Esophageal cancer
    5. Rectal locations
    6. Gynecologic tumors (to include cervical, endometrial, and vulvar cancers)
    7. Other pelvic, abdominal, or chest tumor not listed
  - B. Documentation of **one or more** of the following:
    1. 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
    2. The same or immediately adjacent area has been previously irradiated and abutting portals must be established with high precision
- III. Intensity-modulated radiotherapy is considered **investigational** for all other uses in the abdomen, pelvis, and chest not addressed above.

### Image Guided Radiation Therapy (IGRT)

- IV. IGRT may be considered **medically necessary** as an approach to delivering radiotherapy when combined with **any** of the following treatments (see [Policy Guidelines](#)):
  - A. Intensity-modulated radiotherapy (IMRT)
  - B. Stereotactic body radiation therapy (SBRT)
  - C. Proton delivery
- V. IGRT is considered **investigational** as an approach to delivering radiotherapy when combined with **any** of the following treatments:
  - A. Conventional three-dimensional conformal radiation therapy (3D CRT) (see Policy Guidelines for [considerations](#))
  - B. Stereotactic radiosurgery (SRS)
  - C. Electronic brachytherapy

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

## Policy Guidelines

**Note:** Breast and lung cancers are addressed in Blue Shield of California Medical Policy: Intensity-Modulated Radiotherapy of the Breast and Lung

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.

Requests for the above exceptions and all other indications not discussed in this policy will be reviewed on a case-by-case basis.

\*The 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
<b>Central Nervous System (1.8-2.0 Gray/fraction [Gy/fx])</b>	
• 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
• 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
<b>Central Nervous System (single fraction)</b>	
• 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

Organ	Constraints
• Sacral plexus	V18 <0.035 cc, V14.4 <5 cc
• Cauda equina	V16 <0.035 cc, V14 <5 cc
<b>Head and Neck (1.8–2.0 Gy/fx)</b>	
• 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%
<b>Thoracic (1.8–2.0 Gy/fx)</b>	
• 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%
<b>Thoracic (hypofractionation)</b>	
Note: the max dose limits refer to volumes >0.035 cc (~3 mm <sup>3</sup> ).	
• 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)
• 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)

Organ	Constraints
	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)
<b>Gastrointestinal (GI) (1.8–2.0 Gy/fx)</b>	
• 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%.
<b>Gastrointestinal (GI) (single fraction)</b>	
• 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
<b>Genitourinary (GU) (1.8–2.0 Gy/fx)</b>	
• 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
<b>Genitourinary (GU) (LDR prostate brachytherapy)</b>	
• Urethra	Volume of urethra receiving 150% of prescribed dose (Ur150) <30%
• Rectum	Volume of rectum receiving 100% of prescribed dose (RV100) <0.5 cc
<b>Gynecological (GYN)</b>	
• Bladder point (cervical brachytherapy)	Max 80 Gy (LDR equivalent dose)
• 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

### Image Guided Radiation Therapy (IGRT) Considerations:

The following codes are for hospital outpatient IMRT/SBRT delivery use which includes image guidance in the delivery code for the facility (technical, or -TC modifier) component. However, the professional component (-26 modifier) is still allowed for payment.

- **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
- **77373:** Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance, entire course not to exceed 5 fractions

**Note:** Proton delivery codes do not include image guidance, so IGRT codes for both TC and professional components can be billed separately when indicated. IGRT may be indicated for some conventional 3D CRT cases such as a morbidly obese patient with an abdominal target in which standard approaches for guidance are inadequate. Cases can be considered for approval on an individual basis

The Centers for Medicare & Medicaid Services (CMS) did not implement the above mentioned CPT codes (77385 & 77386) and instead created HCPCS G codes for freestanding outpatient centers. The following delivery codes may also be used for IMRT depending on the setting. They do not include image guidance, so both the technical and professional components are allowed when criteria are met.

- **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 three or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session

The following codes are typical for IGRT. Up to one unit per session can be allowed (although balanced by additional radiation for the imaging, so IGRT may not take place with every treatment session).

- **77014:** Computed tomography guidance for placement of radiation therapy fields
- **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

The following codes do not have a technical (facility) component but can be used for professional services only. Since there is no specific code for MRI guidance, 77387 can be considered for approval for professional services for MRI guidance when appropriate documentation is submitted, but can also be used for other types of guidance.

- **77387:** Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed
- **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

Note: G6017 does not have a technical (facility) component (usually done by a technician covered by the facility delivery fee), and intra-fraction tracking is unusual to involve physician guidance, so documentation of that service should be provided if billed for professional services.

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 CPT and HCPCS codes may also be used:

- **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
- **77427**: Radiation treatment management, 5 treatments
- **77417**: Therapeutic radiology port image(s)

Additional documentation will be required to confirm medical necessity when a given code is billed at a frequency greater than that allowed in the code set.

#### Allowable codes and frequencies for IMRT/Proton

Description	Code	Maximum per course of treatment	Notes
For IMRT: IGRT (Image Guided Radiation Therapy)	77014 (CT) 77387 (any) G6001 (stereotactic) G6002 (US) G6017	Professional portion allowed for up to 1 unit for each delivery session when provided	Facility fee (TC) included with delivery codes 77385/ 77386/ 77373 for IMRT/ SBRT. 77387 and G6017 are for pro fee only. Others need -26 modifier for approval
For Proton: IGRT (Image Guided Radiation Therapy)	77014, 77387, G6001, G6002, G6017	Up to 1 unit per delivery session when provided	Facility fee (TC) not included with delivery codes for proton so they can be billed. 77387 and G6017 are for pro fee only. Others need -26 or TC modifiers.
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.

Description	Code	Maximum per course of treatment	Notes
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 Collimator (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
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;	Using IMRT or Proton: 28 for prostate cancer	Prostate cancer: Documentation of medical necessity needed for more than 28 treatments
	Proton 77520, 77522, 77523	Using IMRT only: -16 for breast cancer without boost -24 for breast cancer with boost (IMRT only)	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 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.

## Related Policies

- Intensity-Modulated Radiotherapy of the Prostate

- 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 (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.

## Rationale

### Background

#### 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).<sup>1</sup> External radiotherapy (RT) techniques include "conventional" or 2-dimensional (2D) RT, 3-dimensional (3D) conformal RT, and intensity-modulated radiation therapy (IMRT).

#### Conventional External-Beam Radiotherapy

Methods to plan and deliver RT have evolved that permit more precise targeting of tumors with complex geometries. Conventional 2D treatment planning utilizes X-ray films to guide and position



radiation beams.<sup>1</sup> 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 (3D-CRT) involves initially scanning the patient in the position that will be used for the radiation treatment.<sup>1</sup> 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 may be used to "shape" the radiation beams. Methods have also been developed to position the patient and the radiation portal reproducibly for each fraction and to immobilize the patient, thus maintaining consistent beam axes across treatment sessions.

### Intensity-Modulated Radiotherapy

IMRT is the more recent development in external radiation. Treatment planning and delivery are more complex, time-consuming, and labor-intensive for IMRT than for 3D-CRT. Similar to 3D-CRT, the tumor and surrounding normal organs are outlined in 3D by a scan and multiple radiation beams are positioned around the patient for radiation delivery.<sup>1</sup> 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.

### Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of 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 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 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.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Note that the evidence for the following abdominal and pelvic cancers has not yet been assessed and is beyond the scope of this review: bladder, kidney, and ureter cancer and sarcoma.

### **Intensity-Modulated Radiotherapy for Cancers of the Abdomen, Pelvis, and Chest**

Multiple-dose planning studies generate 3-dimensional 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 the target 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 expected to occur at high rates is shown to decrease significantly. 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 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 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.

### **Gastrointestinal Tract Cancers**

#### **Clinical Context and Therapy Purpose**

The purpose of IMRT in individuals who have gastrointestinal (GI) tract cancers is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

### **Populations**

The relevant population of interest is individuals with GI cancers (e.g., stomach, hepatobiliary, and pancreatic cancers) who are recommended for radiotherapy (RT).

### **Interventions**

The therapy being considered is IMRT. This therapy uses computer software and magnetic resonance imaging for increased conformality, permitting the delivery of higher doses of radiation to the tumor while limiting the exposure of surrounding normal tissues.

### **Comparators**

The following therapy is currently being used: 3D-CRT. This therapy uses 3-dimensional images typically from computed tomography to discriminate tumor tissue from adjacent normal tissue and nearby organs. Computer algorithms are used to estimate radiation doses being delivered to each treatment segment.

### **Outcomes**

The general outcomes of interest are overall survival (OS), recurrence (locoregional control), quality of life, and treatment-related adverse events (e.g., toxicity). Toxicity can be assessed using the U.S. Department of Health and Human Services grading criteria for adverse events (1=mild, 2=moderate, 3=severe or medically significant, 4=life-threatening, and 5=death).

### **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**

#### **Stomach**

#### **Systematic Review**

Ren et al (2019) completed a systematic review and meta-analysis evaluating the efficacy and safety of IMRT versus 3D-CRT that included 9 controlled clinical trials enrolling 516 patients with gastric cancer.<sup>2</sup> Results revealed a slightly improved 3-year OS rate (risk ratio [RR], 1.16; 95% confidence interval [CI], 0.98 to 1.36) and a significantly better 2-year OS rate with IMRT (RR, 2.49; 95% CI, 1.18 to 5.25;  $p=.02$ ) as compared to 3D-CRT. Additionally, the 3-year rate of locoregional recurrence was improved with IMRT versus 3D-CRT (RR, 0.62; 95% CI, 0.39 to 0.98;  $p<.05$ ). Similar 3-year disease-free survival rates were noted between the techniques (RR, 1.16; 95% CI, 0.95 to 1.43;  $p>.05$ ). No significant differences in liver, GI, and kidney toxicity were observed among patients receiving IMRT compared with 3D-CRT. Limitations of this analysis included the small number of enrolled subjects (i.e., the majority of studies had <100 subjects), retrospective nature of included studies, which increased the risk of selective reporting bias, and the heterogeneity of IMRT or 3D-CRT techniques in studies. Additionally, the detail and radiation fields of RT varied considerably among the studies, impacting the efficacy and toxicity seen by investigators.

#### **Nonrandomized Comparative Studies**

Boda-Heggemann et al (2009) evaluated the efficacy and safety of 2 different adjuvant chemo-radiotherapy regimens using 3D-CRT or IMRT in 2 consecutive cohorts who underwent primarily D2 resection for gastric cancer.<sup>3</sup> A subsequent report (2013) from this group included 27 3D-CRT patients and 38 IMRT patients.<sup>4</sup> The cohorts were generally well-matched, with American Joint Committee on Cancer advanced stage (II-IV) disease. Most (96%) who received 3D-CRT were treated with 5-

fluorouracil plus folinic acid. Patients in the IMRT cohort received capecitabine plus oxaliplatin (70%) or 5-fluorouracil plus folinic acid (30%). Radiation was delivered to a total prescribed dose of 45 gray (Gy) at 1.8 Gy per fraction. In the 3D-CRT cohort, 5 patients received less than 45 Gy because of treatment intolerance. Two patients in the IMRT cohort did not tolerate the full course, and 1 patient received 47 Gy. Overall, the IMRT plus chemotherapy regimen decreased renal toxicity with a trend toward improved survival (Table 1). However, interpretation of the safety and efficacy of IMRT in this study is limited by differences in the chemotherapy regimens.

**Table 1. Outcomes for Intensity-Modulated Radiotherapy With Capecitabine Plus Oxaliplatin versus 3-Dimensional Conformal Radiotherapy With 5-Fluorouracil Plus Folinic Acid for Stomach Cancer**

Outcomes	3D-CRT	Intensity-Modulated Radiotherapy	p
Sample	27	38	
Renal toxicity, n (%)	2 (8)	0	.021
Median disease-free survival, mo	14	35	.069
Median overall survival, mo	18	43	.060
Actutimes 2-y overall survival, %	37	67	
Actutimes 5-y overall survival, %	22	44	

Adapted from Boda-Heggemann et al (2009, 2013).<sup>3,4</sup>

3D-CRT: 3-dimensional conformal radiotherapy.

### *Hepatobiliary*

Fuller et al (2009) compared a retrospective series with a historical control cohort. Clinical results using image-guided IMRT (n=24) were compared with results using 3D-CRT (n=24) in patients with primary adenocarcinoma of the biliary tract.<sup>5</sup> Most patients underwent postsurgical chemoradiotherapy with concurrent fluoropyrimidine-based regimens. Treatment plans prescribed 46 to 56 Gy to the planning target volume that included the tumor and involved lymph nodes, in daily fractions of 1.8 to 2 Gy. Both groups received boost doses of 4 to 18 Gy as needed. The IMRT cohort had a median OS of 17.6 months (range, 10.3 to 32.3), while the 3D-CRT cohort had a median OS of 9.0 months (range, 6.6 to 17.3). There were no significant differences between patient cohorts in acute GI toxicity. Generalization of results is limited by the small numbers of patients, use of retrospective chart review data, nonrepresentative case spectrum (mostly advanced/metastatic disease), and comparison to a nonconcurrent control RT cohort.

### *Pancreatic*

Literature searches have identified a few comparative studies and case series on IMRT for pancreatic cancer. For example, Lee et al (2016) reported on a prospective comparative study of GI toxicity in patients treated with concurrent chemoradiotherapy plus IMRT or 3D-CRT for the treatment of borderline resectable pancreatic cancer.<sup>6</sup> Treatment selection was by patient choice after consultation with a radiation oncologist. Symptoms of dyspepsia, nausea or vomiting, and diarrhea did not differ between groups. Upper endoscopy revealed more patients with gastroduodenal ulcers in the 3D-CRT group than in the IMRT group (Table 2). Overall survival was longer in the IMRT group than in the 3D-CRT group but the interpretation of survival results was limited by the risk of bias in this nonrandomized study.

Prasad et al (2016) retrospectively reviewed charts of patients with locally advanced pancreatic cancer who were treated with IMRT (n=134) or 3D-CRT (n=71).<sup>7</sup> Propensity score analysis was performed to account for potential confounding variables, including age, sex, radiation dose, RT field size, and concurrent RT. Grade 2 GI toxicity occurred in significantly more patients treated with 3D-CRT than with IMRT (propensity score odds ratio [OR], 1.26; 95% CI, 1.08 to 1.45; p=.001; Table 2). Hematologic toxicity and median survival were similar in the 2 groups.

**Table 2. Outcomes for Intensity-Modulated Radiotherapy versus 3-Dimensional Conformal Radiotherapy for Pancreatic Cancer**

Comparison	3D-CRT	IMRT	p
Lee et al (2016) <sup>6</sup>	n=40	n=44	
Grade 1-2 gastroduodenal ulcers, n (%)	11 (42.3)	3 (9.1)	.003
Overall survival, mo	15.8	22.6	.006
Prasad et al (2016) <sup>7</sup>	n=71	n=134	
Grade 2+ gastrointestinal toxicity, n (%)	24 (33.8)	21 (15.7)	.001
Overall survival whole population, mo	NR	NR	NS

3D-CRT: 3-dimensional conformal radiotherapy; IMRT: intensity-modulated radiotherapy; NR: not reported; NS: not significant.

### Section Summary: Gastrointestinal Tract Cancers

The evidence on IMRT for GI tract cancers includes nonrandomized comparative studies, retrospective series, and a systematic review. IMRT has been compared to 3D-CRT for the treatment of stomach, hepatobiliary, and pancreatic cancers, with some data reporting longer OS and decreased toxicity with IMRT. For the treatment of stomach cancer, IMRT improved survival compared with 3D-CRT, with a comparable or improved safety profile. The evidence on hepatobiliary cancer includes a series of historical controls that found an increase in median survival with no difference in toxicity. Two comparative studies (1 prospective, 1 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. Although most studies were limited by their retrospective designs and changes in practice patterns over time, the available evidence would suggest that IMRT improves survival and decreases toxicity better than 3D-CRT in patients with GI cancers.

### Gynecologic Cancers

#### Clinical Context and Therapy Purpose

The purpose of IMRT in individuals who have gynecologic cancers is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

#### *Populations*

The relevant population of interest is individuals with gynecologic cancers (i.e., cervical and endometrial cancers) who are recommended for RT.

#### *Interventions*

The therapy being considered is IMRT. This therapy uses computer software and magnetic resonance imaging for increased conformality, permitting the delivery of higher doses of radiation to the tumor while limiting the exposure of surrounding normal tissues.

#### *Comparators*

The following therapy is currently being used: 3D-CRT. This therapy uses 3-dimensional images typically from computed tomography to discriminate tumor tissue from adjacent normal tissue and nearby organs. Computer algorithms are used to estimate radiation doses being delivered to each treatment segment.

#### *Outcomes*

The general outcomes of interest are OS, recurrence (locoregional control), quality of life, and treatment-related adverse events (e.g., toxicity). Toxicity can be assessed using the U.S. Department of Health and Human Services grading criteria for adverse events (1=mild, 2=moderate, 3=severe or medically significant, 4=life-threatening, and 5=death).

### 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 Review

Lin et al (2018) completed a meta-analysis of 6 studies enrolling 1008 subjects in order to compare the efficacy and safety of IMRT with 3D-CRT or 2D (2-dimensional)-RT for definitive treatment of cervical cancer.<sup>8</sup> Results revealed a nonsignificant difference in 3-year OS (OR, 2.41; 95% CI, 0.62 to 9.39;  $p=.21$ ) and disease-free survival rates (OR, 1.44; 95% CI, 0.69 to 3.01;  $p=.33$ ) between IMRT and 3D-CRT or 2D-RT. However, IMRT was associated with a significantly reduced rate of acute GI and genitourinary (GU) toxicity: grade 2 GI: OR, 0.5; 95% CI, 0.28 to 0.89;  $p=.02$ ; grade 3 or higher GI: OR, 0.55; 95% CI, 0.32 to 0.95;  $p=.03$ ; grade 2 GU: OR, 0.41; 95% CI, 0.2 to 0.84;  $p=.01$ ; and grade 3 or higher GU: OR, 0.31; 95% CI, 0.14 to 0.67;  $p=.003$ . Some chronic GU toxicity also occurred less frequently with IMRT (grade 3: OR, 0.09; 95% CI, 0.01 to 0.67;  $p=.02$ ). This analysis had several limitations including the fact that most included studies had relatively small sample sizes and were retrospective and nonrandomized in nature. Additionally, some of the included studies did not compare clinical outcomes between the RT techniques.

#### Randomized Controlled Trials

Kapoor et al (2023) conducted a prospective, randomized, single-center, phase 3 trial that compared hematologic and GI toxicities in patients with cervical cancer (Stage IB to IVA) treated with IMRT and 3D-CRT.<sup>9</sup> A total of 80 patients were randomized 1:1 to receive either IMRT ( $n=40$ ) or 3D-CRT ( $n=40$ ). The median patient age was 56.5 years (range, 36 to 67) and 59.5 years (range, 37 to 68) in the IMRT and 3D-CRT groups, respectively. The median dose of external radiation was 50 Gy in 25 fractions, and of brachytherapy was 24 Gy in 3 fractions in both groups. All patients received concurrent chemotherapy with cisplatin; the median number of cycles was 5 (range, 3 to 5) in both groups. All 5 cycles of concurrent chemotherapy could be completed in 25 (62.5%) patients and 24 (60%) patients in the IMRT and 3D-CRT groups, respectively. The median overall treatment time was 57 days (range, 56 to 85) and 57.5 days (range, 49 to 88) in patients receiving IMRT and 3D-CRT, respectively. The incidence of neutropenia (grade 2 or higher) was 15% and 42.5% in the IMRT and 3D-CRT groups, respectively ( $p<.001$ ). Diarrhea (grade 2 or higher) was observed in 42.5% of patients in the IMRT group compared to 90% of patients in the 3D-CRT group. The study found that IMRT also had a better dosimetry profile compared to 3D-CRT.

Chopra et al (2021) conducted the open-label, parallel-group, randomized, phase 3, Postoperative Adjuvant Radiation in Cervical Cancer (PARCER) trial in order to evaluate whether postoperative image-guided IMRT was associated with an improvement in late GI toxicity compared to 3D-CRT.<sup>10</sup> In PARCER, 300 patients with cervical cancer and an indication for adjuvant postoperative RT were randomly assigned to image-guided IMRT ( $n=151$ ) or 3D-CRT ( $n=149$ ), with a median follow-up of 46 months (interquartile range, 20 to 72). Results revealed significantly fewer primary endpoint events (i.e., late GI toxicity of grade 2 or higher) in the image-guided IMRT arm versus the 3D-CRT arm (29 vs. 54). The 3-year cumulative incidence of late GI toxicity of grade 2 or higher was significantly reduced in the IMRT arm (21.1% vs. 42.4%; hazard ratio [HR], 0.46; 95% CI, 0.29 to 0.73;  $p<.001$ ) as was the cumulative incidence of 3-year late GI toxicity of grade 3 or higher (2.9% vs. 15.5%; HR, 0.22; 95% CI, 0.08 to 0.59;  $p<.003$ ). The cumulative incidence of any late toxicity of grade 2 or higher was also significantly reduced with IMRT (28.1% vs. 48.9%; HR, 0.50; 95% CI, 0.33 to 0.76;  $p<.001$ ). Patients administered IMRT reported less diarrhea ( $p=.04$ ), improvement in appetite

( $p=.008$ ), and fewer bowel symptoms ( $p=.002$ ) compared to those administered 3D-CRT. No differences in disease outcomes were noted between the RT techniques including 3-year pelvic relapse-free survival ( $p=.55$ ) and disease-free survival ( $p=.89$ ).

In the international, randomized, Adjuvant Chemoradiotherapy Versus Radiotherapy Alone in Women With High-Risk Endometrial Cancer (PORTEC-3) trial, Wortman et al (2021) evaluated whether IMRT compared to 3D-CRT resulted in fewer adverse events and patient-reported symptoms among 658 patients with high-risk endometrial cancer.<sup>11</sup> Of these patients, 559 received 3D-CRT and 99 received IMRT; median follow-up at the time of analysis was 74.6 months. Results revealed no significant differences in frequency and grades of adverse events between the RT techniques. There was an increase in adverse events of grade 3 or higher (mainly GI and hematologic) with 3D-CRT (37.7% vs. 26.3%;  $p=.03$ ). During follow-up, significantly more diarrhea of grade 2 or higher (15.4% vs. 4%;  $p<.01$ ) and hematologic adverse events of grade 2 or higher (26.1% vs. 13.1%;  $p<.01$ ) were observed in patients administered 3D-CRT as compared to IMRT. More patients reported diarrhea (37.5% vs. 28.6%;  $p=0.125$ ), bowel urgency (22.1% vs. 10%;  $p=.0039$ ), and abdominal cramps (18.2% vs. 8.6%;  $p=.058$ ) following 3D-CRT as compared to IMRT.

Klopp et al (2018) designed a randomized trial that measured the impact of pelvic IMRT versus standard 4-field RT on patient-reported toxicity and quality of life in 278 women with cervical and endometrial cancer.<sup>12</sup> Results revealed that the mean Expanded Prostate Cancer Index Composite (EPIC) bowel score decreased significantly less in the IMRT as compared to the standard RT group from baseline to end of RT (18.6 vs. 23.6 points;  $p=.048$ ). Additionally, both the mean EPIC urinary score (5.6 vs. 10.4 points;  $p=.03$ ) and Trial Outcome Index score (8.8 vs. 12.8 points;  $p=.06$ ) declined significantly less with IMRT compared to standard RT. Frequent or almost constant diarrhea was also reported more frequently among women receiving standard RT versus IMRT at the end of RT (51.9% vs. 33.7%;  $p=.01$ ) and significantly more women administered standard RT were taking antidiarrheal medications 4 or more times daily (20.4% vs. 7.8%;  $p=.04$ ).

A trial by Naik et al (2016) randomized 40 patients with cervical cancer to IMRT or 3D-CRT.<sup>13</sup> Both arms received concurrent chemotherapy (cisplatin) plus RT at 50 Gy in 25 fractions. Dosimetric planning showed higher conformality and lower doses to organs at risk with IMRT. With follow-up through 90 days posttreatment, vomiting and acute GI and GU toxicity were significantly higher in the 3D-CRT group (Table 3).

Gandhi et al (2013) reported on a prospective randomized study that compared whole-pelvis IMRT with whole-pelvis 2D-RT in 44 patients with locally advanced cervical cancer.<sup>14</sup> Each treatment arm had 22 patients. The OS rate at 27 months was 88% with IMRT and 76% with 2D-RT ( $p=.645$ ). However, fewer grade 2, 3, or 4 GI toxicities were experienced in the IMRT group than in the conventional RT group (Table 3).

**Table 3. Acute Toxicity of Grade 2, 3 or 4 With 3-Dimensional Conformal Radiotherapy versus Intensity-Modulated Radiotherapy for Cervical Cancer**

Toxicity	3D-CRT, n (%)	IMRT, n (%)	95% CI for the Difference	p
<b>Naik et al (2016)<sup>13</sup></b>				
Hematologic	8 (40)	7 (35)	-0.219 to 0.119	.644
Leukopenia	3 (15)	2 (10)	-0.1479 to 0.479	.424
Vomiting	7 (35)	3 (15)	0.338 to 0.061	.007
Acute gastrointestinal toxicity	9 (45)	4 (20)	-0.408 to -0.091	.003
Acute genitourinary toxicity	7 (35)	4 (20)	-0.295 to -0.004	.058
<b>Gandhi et al (2013)<sup>14</sup></b>				
Gastrointestinal, grade $\geq 2$	14 (64)	7 (32)	0.002 to 0.604	.034
Gastrointestinal, grade $\geq 3$	6 (27)	1 (5)	0.003 to 0.447	.047
Genitourinary, grade $\geq 2$	7 (32)	5 (24)	-0.202 to 0.361	.404
Genitourinary, grade $\geq 3$	3 (14)	0 (0)	-0.019 to 0.291	.125

3D-CRT: 3-dimensional conformal radiotherapy; CI: confidence interval; IMRT: intensity-modulated radiotherapy.

### Nonrandomized Comparative Studies

Shih et al (2016) conducted a retrospective comparison of bowel obstruction following IMRT (n=120) or 3D-CRT (n=104) after hysterectomy for endometrial or cervical cancer.<sup>15</sup> Groups were generally comparable, except more patients in the 3D-CRT group had open hysterectomy (81% vs. 47% ;  $p<.001$ ). Patients received regular examinations throughout a median follow-up of 67 months, and the 5-year rate of bowel obstruction was 0.9% in the IMRT group compared with 9.3% in the 3D-CRT group ( $p=.006$ ). A body mass index of 30 kg/m<sup>2</sup> or more was also associated with less bowel obstruction. However, on multivariate analysis, the only significant predictor of less bowel obstruction was IMRT ( $p=.022$ ).

Chen et al (2014) reported on 101 patients with endometrial cancer treated with hysterectomy and adjuvant RT.<sup>16</sup> No significant differences between IMRT (n=65) and CRT (n=36) were found in 5-year OS (82.9% vs. 93.5%;  $p=.26$ ), local failure-free survival (93.7% vs. 89.3%;  $p=.68$ ), or disease-free survival (88.0% vs. 82.8%;  $p=.83$ ). However, IMRT patients experienced fewer acute and late toxicities.

### Section Summary: Gynecologic Cancers

The evidence on IMRT for gynecologic cancers includes a systematic review, 6 RCTs, and non-randomized comparative studies. There is limited comparative evidence on survival outcomes following IMRT or 3D-CRT. However, available results have generally been consistent that IMRT reduces GI and GU toxicity. Based on evidence with other cancers of the pelvis and abdomen in close proximity 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.

### Anorectal Cancer

#### Clinical Context and Therapy Purpose

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

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

#### *Populations*

The relevant population of interest is individuals with anorectal cancer who are recommended for RT.

#### *Interventions*

The therapy being considered is IMRT. This therapy uses computer software and magnetic resonance imaging for increased conformality, permitting the delivery of higher doses of radiation to the tumor while limiting the exposure of surrounding normal tissues.

#### *Comparators*

The following therapy is currently being used: 3D-CRT. This therapy uses 3-dimensional images typically from computed tomography to discriminate tumor tissue from adjacent normal tissue and nearby organs. Computer algorithms are used to estimate radiation doses being delivered to each treatment segment.

#### *Outcomes*

The general outcomes of interest are OS, recurrence (locoregional control), quality of life, and treatment-related adverse events (e.g., toxicity). Toxicity can be assessed using the U.S. Department of Health and Human Services grading criteria for adverse events (1=mild, 2=moderate, 3=severe or medically significant, 4=life-threatening, and 5=death).



### 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

#### Randomized Controlled Trials

Rattan et al (2016) conducted a small (N=20 ) RCT assessing IMRT for the treatment of anal canal cancer.<sup>17</sup> Grade 3 GI toxicity during treatment was not observed in any patients in the IMRT group but was seen in 60% of patients treated with 3D-CRT (p=.010). Hematologic grade 3 toxicity was not seen in any patients treated with IMRT but was noted in 20% of patients treated with 3D-CRT (p=.228). Other parameters indicating better tolerance to treatment with IMRT were reduced need for parenteral fluid (10% vs. 60%; p=.019) and blood transfusion (0% vs. 20%; p=.060).

#### Nonrandomized Comparative Studies

Sun et al (2017) reported on a comparative analysis of the National Cancer Database of IMRT with 3D-CRT for the treatment of rectal adenocarcinoma.<sup>18</sup> A total of 7386 patients with locally advanced rectal carcinoma were treated with neoadjuvant chemoradiotherapy (45 to 54 Gy) from 2006 to 2013; 3330 (45%) received IMRT and 4065 (55%) received 3D-CRT. Use of IMRT increased from 24% in 2006 to 50% in 2013. Patient age, race, insurance status, Charlson-Deyo comorbidity score, hospital type, income and education status, and clinical disease stage were not predictive of which RT was used. The mean radiation dose was higher with IMRT (4735 centigray vs. 4608 centigray; p<.001) and the occurrence of sphincter loss surgery was higher in the IMRT group (Table 4). However, patients treated with IMRT had a higher risk of positive margins. Multivariate analysis found no significant differences between the treatments for pathologic downstaging, unplanned readmission, 30-day mortality, or long-term survival. This study used unplanned readmission as a surrogate measure of adverse events but could not assess acute or late toxicity.

**Table 4. Outcomes Following Radiochemotherapy With 3-Dimensional Conformal Radiotherapy or Intensity-Modulated Radiotherapy for Rectal Cancer**

Outcome	3D-CRT, %	IMRT, %	Adjusted OR	95% CI	p
Pathologic downstaging	57.0	55.0	0.89	0.79 to 1.01	.051
Sphincter loss surgery	28.3	34.7	1.32	1.14 to 1.52	<.001
Positive resection margin	5.6	8.0	1.57	1.21 to 2.03	<.001
Unplanned readmission	7.9	6.4	0.79	0.61 to 1.02	.07
30-d mortality	0.8	0.6	0.61	0.24 to 1.57	.31
Survival at 5 y	64	64	1.06	0.89 to 1.28	.47

Adapted from Sun et al (2017).<sup>18</sup>

3D-CRT: 3-dimensional conformal radiotherapy; CI: confidence interval; IMRT: intensity-modulated radiotherapy; OR: odds ratio.

Huang et al (2017) reported on a retrospective comparison of outcomes and toxicity for preoperative image-guided IMRT and 3D-CRT in locally advanced rectal cancer.<sup>19</sup> A total of 144 consecutive patients treated between 2006 and 2015 were analyzed. The 3D-CRT group was treated with 45 Gy in 25 fractions while the IMRT group was treated with 45 Gy in 25 fractions with a simultaneous integrated boost of 0.2 Gy per day for the primary tumor up to a total dose of 50 Gy. Statistical analysis was performed for grade 0, 1, 2, 3, or 4 toxicity and was significant only for acute GI toxicity (p=.039; Table 5). Four-year OS and disease-free survival did not differ between the 2 groups.

Multivariate analysis found IMRT to be an independent predictor of local failure-free survival (HR, 0.35; 95% CI, 0.11 to 0.95;  $p=0.042$ ).

**Table 5. Grade 3 or Greater Toxicity Following Chemoradiotherapy for Rectal Cancer**

Comparison	3D-CRT (n=99), n (%)	IMRT (n=45), n (%)
Skin	3 (3)	1 (2.2)
Acute gastrointestinal	14 (14.1)	3 (6.7)
Acute genitourinary	3 (3)	0 (0)
Hematologic	2 (2.0)	0 (0)
Late gastrointestinal	10 (10.1)	2 (4.4)
Late genitourinary	3 (3.1)	0 (0)

Adapted from Huang et al (2017).<sup>19</sup>

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

In a retrospective review of 89 consecutive patients (52 IMRT, 37 3D-CRT), Chuong et al (2013) found that 3-year OS, progression-free survival (PFS), locoregional control, and colostomy-free survival did not differ significantly between patients treated with IMRT or with 3D-CRT ( $p>.1$ ).<sup>20</sup> Adverse events with 3D-CRT were more frequent and severe and required more treatment breaks than IMRT (11 days vs. 4 days;  $p=.006$ ) even though the median duration of treatment breaks did not differ significantly (12.2 days vs. 8.0 days;  $p=.35$ ). Intensity-modulated radiotherapy patients had fewer acute grade 3 or 4 nonhematologic toxicity ( $p<.001$ ), improved late grade 3 or 4 GI toxicity ( $p=.012$ ), and fewer acute grade 3 or 4 skin toxicity ( $p<.001$ ) than 3D-CRT patients.

Dasgupta et al (2013) retrospectively reviewed 223 patients (45 IMRT, 178 CRT) to compare outcomes for anal cancer.<sup>21</sup> They reported that 2-year OS, distant metastases-free survival, and locoregional recurrence-free survival did not differ significantly between patients in the IMRT and CRT groups. Dewas et al (2012) retrospectively reviewed 51 patients with anal cancer treated with IMRT (n=24) or 3D-CRT (n=27).<sup>22</sup> Outcomes also did not differ significantly between patients in the IMRT and 3D-CRT groups in 2-year OS, locoregional relapse-free survival, and colostomy-free survival. Grade 3 acute toxicity occurred in 11 IMRT patients and in 10 3D-CRT patients.

### Case Series

A GI toxicity study by Devisetty et al (2009) reported on 45 patients who received concurrent chemotherapy plus IMRT for anal cancer.<sup>23</sup> IMRT was administered to a dose of 45 Gy in 1.8 Gy fractions, with areas of gross disease subsequently boosted with 9 to 14.4 Gy. Acute GU toxicity was grade 0 in 25 (56%) cases, grade 1 in 10 (22%) patients, and grade 2 in 5 (11%) patients, with no grade 3 or 4 toxicities reported; 5 (11%) patients reported no GU tract toxicities. Grades 3 and 4 leukopenia was reported in 26 (56%) cases, neutropenia in 14 (31%), and anemia in 4 (9%). Acute GI toxicity included grade 0 in 2 (4%) patients, grade 1 in 11 (24%), grade 2A in 25 (56%), grade 2B in 4 (9%), grade 3 in 3 (7%), and no grade 4 toxicities. Univariate analysis of data from these patients suggested a statistical correlation between the volume of bowel that received 30 Gy or more of radiation and the risk for clinically significant (grade  $\geq 2$ ) GI toxicities.

Peppek et al (2010) retrospectively analyzed toxicity and disease outcomes associated with IMRT in 47 patients with anal cancer.<sup>24</sup> Thirty-one patients had squamous cell carcinoma. IMRT was prescribed to a dose of at least 54 Gy to areas of gross disease at 1.8 Gy per fraction. Forty (89%) patients received concurrent chemotherapy with various agents and combinations. The 2-year OS for all patients was 85%. Eight (18%) patients required treatment breaks. Toxicities included grade 4 leukopenia (7%) and thrombocytopenia (2%); grade 3 leukopenia (18%) and anemia (4%); and grade 2 skin toxicity (93%). These rates were lower than those reported in previous trials of chemoradiation, where grade 3 or 4 skin toxicity was noted in about 50% of patients, and grade 3 or 4 GI toxicity was noted in about 35%. In addition, the rate of treatment breaks was lower than in many studies; and some studies of chemoradiation included a break from RT.

**Section Summary: Anorectal Cancer**

The evidence on IMRT for anorectal cancer includes a small RCT with 20 patients, nonrandomized comparative studies, and case series. Survival outcomes have not differed significantly between IMRT and 3D-CRT. 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.

**Esophageal Cancer****Clinical Context and Therapy Purpose**

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

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

***Populations***

The relevant population of interest is individuals with esophageal cancer who are recommended for RT.

***Interventions***

The therapy being considered is IMRT. This therapy uses computer software and magnetic resonance imaging for increased conformality, permitting the delivery of higher doses of radiation to the tumor while limiting the exposure of surrounding normal tissues.

***Comparators***

The following therapy is currently being used: 3D-CRT. This therapy uses 3-dimensional images typically from computed tomography to discriminate tumor tissue from adjacent normal tissue and nearby organs. Computer algorithms are used to estimate radiation doses being delivered to each treatment segment.

***Outcomes***

The general outcomes of interest are OS, recurrence (locoregional control), quality of life, and treatment-related adverse events (e.g., toxicity). Toxicity can be assessed using the U.S. Department of Health and Human Services grading criteria for adverse events (1=mild, 2=moderate, 3=severe or medically significant, 4=life-threatening, and 5=death).

**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**

Xu et al (2017) performed a systematic review and meta-analysis to compare IMRT and 3D-CRT in the treatment of esophageal cancer with regard to dosimetry and clinical outcomes (n=7 studies).<sup>25</sup> For the dosimetric comparison of organs at risk, 5 studies were included. Results revealed that the mean dose of 3D-CRT was significantly higher as compared to IMRT for the lung (mean difference dose, 2.18; 95% CI, 0.83 to 3.53; p=.002), with patients treated with 20 Gy or more having significantly higher irradiated volumes for 3D-CRT than for IMRT. For the heart, the mean dose was not significantly different between 3D-CRT and IMRT (mean difference dose, 0.17; 95% CI, -3.73 to 4.07;

$p=.93$ ); however, the heart in patients treated with 50 Gy had significantly higher irradiated volumes for 3D-CRT. The maximum dose in the spinal cord revealed no difference between the 2 RT techniques ( $p=.33$ ). Evaluated clinical outcomes included OS ( $n=3$  studies; 871 patients) and toxicity ( $n=2$  studies; 205 patients). The 3-year OS was significantly improved with IMRT as compared to 3D-CRT (OR, 0.68; 95% CI, 0.52 to 0.90;  $p=.007$ ). No difference between the 2 RT techniques was seen with regard to the incidence of radiation pneumonitis or radiation esophagitis, regardless of grade. Limitations of the review were the small number of studies available for OS and toxicity outcome analyses and the retrospective nature of clinical outcomes studies.

### Nonrandomized Comparative Studies

Lan et al (2020) retrospectively compared survival outcomes and symptomatic radiation pneumonitis in patients with esophageal cancer who received either IMRT ( $n=297$ ) or 3D-CRT ( $n=91$ ) from 2010 through 2017.<sup>26</sup> The median age of patients was 60 years and the median radiation dose for the entire cohort was 60 Gy. Results revealed significantly improved OS ( $p=.001$ ), PFS ( $p=.008$ ), and distant-metastases-free survival ( $p=.011$ ) with IMRT versus 3D-CRT; locoregional failure-free survival was not significantly different between the groups ( $p=.721$ ). Intensity-modulated radiotherapy was also associated with significantly less radiation pneumonitis of grade 2 or higher as compared to 3D-CRT (5.4% vs. 23.1%;  $p<.001$ ).

Ito et al (2017) retrospectively compared failure patterns and toxicities between IMRT ( $n=32$ ) and 3D-CRT ( $n=48$ ) in patients with esophageal cancer.<sup>27</sup> All patients were administered systemic chemotherapy consisting of either induction chemotherapy or concurrent chemoradiotherapy, with or without adjuvant chemotherapy. The median follow-up of the entire cohort was 24.6 months and the median follow-up time for survivors was 35.9 months. Results revealed a 3-year OS of 81.6%, 57.2% ( $p=.037$  vs. IMRT), and 66.6% for the IMRT, 3D-CRT, and total groups, respectively. However, there was no significant difference between IMRT and 3D-CRT in complete response rate (75% vs. 68.9%;  $p=.62$ ). Rates of locoregional control or PFS were not different between the groups as well. Overall, 47 patients developed recurrence of any type; there was no apparent difference in the failure pattern between the 2 RT techniques. The incidence of late toxicities was also not significantly different between IMRT and 3D-CRT. Ten patients in the IMRT groups were salvaged, and 60% survived without recurrence compared to 20% of the 3D-CRT group.

Haefner et al (2017) reported a retrospective analysis of 93 patients with esophageal cancer and compared outcomes and acute toxicity among patients receiving definitive CRT with either 3D-CRT ( $n=49$ ) or IMRT ( $n=44$ ).<sup>28</sup> The median follow-up for all patients was 20.1 months. The 1- and 3-year local relapse rates were 20.4% and 28.6% in the 3D-CRT group and 15.9% and 22.7% in the IMRT group, respectively ( $p=.62$  for the 3-year rate). Median PFS and OS were not significantly different between the groups; 13.8 months 3D-CRT versus 16.6 months IMRT ( $p=.448$ ) and 18.4 months 3D-CRT versus 42 months IMRT ( $p=.198$ ), respectively. The incidence of acute toxicities (dysphasia, radio-dermatitis, nausea/vomiting, mucositis, bleeding, pneumonitis) was also not significantly different between the 2 RT techniques.

### Section Summary: Esophageal Cancer

The evidence on IMRT for esophageal cancer includes a systematic review and nonrandomized comparative studies. Survival outcomes from studies have been mixed with some concluding improved survival with IMRT and others demonstrating no difference from 3D-CRT. Similarly, some studies have concluded that IMRT is associated with a reduced dose for organs at risk and potentially less radiation-related toxicity as compared to 3D-CRT.

### 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, input was received from 1 physician specialty society (4 reviewers) and 3 academic medical centers while this policy was under review in 2012. Input was mixed but there was support for use of intensity-modulated radiotherapy (IMRT) in a number of cancers discussed herein. In general, this support was based on normal tissue constraints for radiation doses and whether these dose constraints could not be met without IMRT.

#### **2010 Input**

In response to requests, input was received from 1 physician specialty society (2 reviewers) and 3 academic medical centers while this policy was under review in 2010. There was support for use of IMRT in a number of cancers discussed herein. In general, this support was based on normal tissue constraints for radiation doses and whether these dose constraints could not be met without IMRT.

### **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)."<sup>29</sup> 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])."<sup>30</sup> 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)."<sup>31</sup>

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."<sup>32</sup> 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."<sup>33</sup> 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."<sup>34</sup>

The NCCN guideline (v.1.2023) on ovarian cancer does not mention IMRT.<sup>35</sup>

### **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'."<sup>36</sup>

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."<sup>37</sup>

### **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)."<sup>38</sup>

### **American Society for Radiation Oncology**

In 2020, the American Society for Radiation Oncology published a clinical practice guideline on RT for cervical cancer.<sup>39</sup> 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.<sup>40</sup> 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."

### **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.

**Ongoing and Unpublished Clinical Trials**

Some currently ongoing and unpublished trials that might influence this review are listed in Table 6.

**Table 6. Summary of Key Trials**

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
<b>NCT03239626</b>	Postoperative Hypofractionated Intensity-Modulated Radiation Therapy in Cervical Cancer: A Prospective Exploratory Trial (POHIM_RT Trial)	120	Apr 2025
<b>NCT03239613</b>	Postoperative Hypofractionated Intensity-Modulated Radiation Therapy with Concurrent Chemotherapy in Cervical Cancer: A Prospective Exploratory Trial (POHIM_CCRT Trial)	84	Apr 2024
<i>Unpublished</i>			
<b>NCT02964468</b>	Multicenter Dose-escalation Trial of Radiotherapy in Patients with Locally Advanced Rectal Cancer	525	May 2020

NCT: national clinical trial.

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## Documentation for Clinical Review

### Please provide the following documentation:

- (click here >>>) [Radiation Oncology – Prior Authorization fax form](#)
- (click here >>>) [Radiation Oncology – Post Service fax form](#)

## 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 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)	

Type	Code	Description
	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 three 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
04/05/2007	BCBSA Medical Policy adoption
05/16/2008	Policy Title Revision, criteria revised Added medically necessary indication for prostate cancer
12/05/2008	Policy Revision Added medically necessary indications for head and neck cancer, CNS lesions, and prostate fiducial markers
04/02/2010	Policy revision with position change Coding update
08/02/2010	Administrative Review
04/01/2011	Policy revision with position change
10/12/2012	Policy revision with position change
03/29/2013	Policy revision with position change
01/30/2015	Coding Update
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
10/01/2019	Policy revision without position change
06/01/2020	Administrative update. Policy statement and guidelines updated.
11/20/2020	Annual review. No change to policy statement. Policy guidelines and literature updated. Coding update.
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.
09/01/2022	Administrative update. Policy statement, guidelines and literature updated. Policy title changed from Intensity-Modulated Radiotherapy: Abdomen and Pelvis to current one.

Effective Date	Action
02/01/2023	Annual review. Policy statement and guidelines updated.
06/01/2023	Administrative update.
09/01/2023	Administrative update. No change to policy statement. Literature review updated.
03/01/2024	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 and Feedback (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](http://www.blueshieldca.com/provider).

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: [MedPolicy@blueshieldca.com](mailto:MedPolicy@blueshieldca.com)

*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*

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

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*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 <u>Red font: Verbiage removed</u>	AFTER <u>Blue font: Verbiage Changes/Additions</u>
<p><b>Intensity-Modulated Radiotherapy: Abdomen, Pelvis and Chest 8.01.49</b></p> <p><b>Policy Statement:</b></p> <ol style="list-style-type: none"> <li>I. Intensity-modulated radiotherapy (IMRT) may be considered <b>medically necessary</b> as an approach to delivering radiotherapy for individuals with cancer of the anus and anal canal.</li>   <li>II. IMRT may be considered <b>medically necessary</b> for the treatment of the abdomen, pelvis, and chest 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, as documented by <b>all</b> of the following:                     <ol style="list-style-type: none"> <li>A. IMRT is used to treat cancer of <b>one or more</b> of the following:                             <ol style="list-style-type: none"> <li>1. Stomach (gastric)</li> <li>2. Hepatobiliary tract</li> <li>3. Pancreas</li> <li>4. Esophageal cancer</li> <li>5. Rectal locations</li> <li>6. Gynecologic tumors (to include cervical, endometrial, and vulvar cancers)</li> <li>7. Other pelvic, abdominal, or chest tumor not listed</li> </ol> </li> <li>B. Documentation of <b>one or more</b> of the following:                             <ol style="list-style-type: none"> <li>1. The target volume is in close proximity to critical structures that must be protected and <b>both</b> of the following: * (see source below)                                     <ol style="list-style-type: none"> <li>a. Planned 3D-CRT exposure to critical adjacent structures is above normal tissue constraints</li> <li>b. Planned IMRT exposure to these critical adjacent structures does not exceed normal tissue constraints</li> </ol> </li> <li>2. The same or immediately adjacent area has been previously irradiated and abutting portals must be established with high precision</li> </ol> </li> </ol> </li> </ol>	<p><b>Intensity-Modulated Radiotherapy: Abdomen, Pelvis and Chest 8.01.49</b></p> <p><b>Policy Statement:</b></p> <ol style="list-style-type: none"> <li>I. Intensity-modulated radiotherapy (IMRT) may be considered <b>medically necessary</b> as an approach to delivering radiotherapy for individuals with cancer of the anus and anal canal.</li>   <li>II. IMRT may be considered <b>medically necessary</b> for the treatment of the abdomen, pelvis, and chest 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, as documented by <b>BOTH</b> of the following:                     <ol style="list-style-type: none"> <li>A. IMRT is used to treat cancer of <b>one or more</b> of the following:                             <ol style="list-style-type: none"> <li>1. Stomach (gastric)</li> <li>2. Hepatobiliary tract</li> <li>3. Pancreas</li> <li>4. Esophageal cancer</li> <li>5. Rectal locations</li> <li>6. Gynecologic tumors (to include cervical, endometrial, and vulvar cancers)</li> <li>7. Other pelvic, abdominal, or chest tumor not listed</li> </ol> </li> <li>B. Documentation of <b>one or more</b> of the following:                             <ol style="list-style-type: none"> <li>1. The target volume is in close proximity to critical structures that must be protected and <b>both</b> of the following: * (see source below)                                     <ol style="list-style-type: none"> <li>a. Planned 3D-CRT exposure to critical adjacent structures is above normal tissue constraints</li> <li>b. Planned IMRT exposure to these critical adjacent structures does not exceed normal tissue constraints</li> </ol> </li> <li>2. The same or immediately adjacent area has been previously irradiated and abutting portals must be established with high precision</li> </ol> </li> </ol> </li> </ol>

## POLICY STATEMENT

BEFORE <b>Red font: Verbiage removed</b>	AFTER <b>Blue font: Verbiage Changes/Additions</b>
<p>III. Intensity-modulated radiotherapy is considered <b>investigational</b> for all other uses in the abdomen, pelvis, and chest not addressed above.</p> <p><b>Image Guided Radiation Therapy (IGRT)</b></p> <p>IV. IGRT may be considered <b>medically necessary</b> as an approach to delivering radiotherapy when combined with <b>any</b> of the following treatments (see <a href="#">Policy Guidelines</a>):</p> <ul style="list-style-type: none"> <li>A. Intensity-modulated radiotherapy (IMRT)</li> <li>B. Stereotactic body radiation therapy (SBRT)</li> <li>C. Proton delivery</li> </ul> <p>V. IGRT is considered <b>investigational</b> as an approach to delivering radiotherapy when combined with <b>any</b> of the following treatments:</p> <ul style="list-style-type: none"> <li>A. Conventional three-dimensional conformal radiation therapy (3D CRT) (see Policy Guidelines for <a href="#">considerations</a>)</li> <li>B. Stereotactic radiosurgery (SRS)</li> <li>C. Electronic brachytherapy</li> </ul>	<p>III. Intensity-modulated radiotherapy is considered <b>investigational</b> for all other uses in the abdomen, pelvis, and chest not addressed above.</p> <p><b>Image Guided Radiation Therapy (IGRT)</b></p> <p>IV. IGRT may be considered <b>medically necessary</b> as an approach to delivering radiotherapy when combined with <b>any</b> of the following treatments (see <a href="#">Policy Guidelines</a>):</p> <ul style="list-style-type: none"> <li>A. Intensity-modulated radiotherapy (IMRT)</li> <li>B. Stereotactic body radiation therapy (SBRT)</li> <li>C. Proton delivery</li> </ul> <p>V. IGRT is considered <b>investigational</b> as an approach to delivering radiotherapy when combined with <b>any</b> of the following treatments:</p> <ul style="list-style-type: none"> <li>A. Conventional three-dimensional conformal radiation therapy (3D CRT) (see Policy Guidelines for <a href="#">considerations</a>)</li> <li>B. Stereotactic radiosurgery (SRS)</li> <li>C. Electronic brachytherapy</li> </ul>