



Kansas City

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# Intensity-Modulated Radiation Therapy (IMRT): Abdomen and Pelvis

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## **Policy**

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Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for IMRT of the abdomen and pelvis when it is determined to be medically necessary because the criteria shown below are met.

## **When Policy Topic is covered**

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Intensity modulated radiation therapy may be considered **medically necessary** as an approach to delivering radiation therapy for patients with cancer of the anus/anal canal.

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

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

## **When Policy Topic is not covered**

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Intensity-modulated radiation therapy (IMRT) would be considered **investigational** for all other uses in the abdomen and pelvis.

## **Considerations**

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

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

Site	TD 5/5 (Gray) <sup>a</sup>			TD 50/5 (Gray) <sup>b</sup>			Complication End Point
	Portion of Organ Involved			Portion of Organ Involved			
	1/3	2/3	3/3	1/3	2/3	3/3	
Heart	60	45	40	70	55	50	Pericarditis
Lung	45	30	17.5	65	40	24.5	Pneumonitis
Spinal cord	50	50	47	70	70	NP	Myelitis/necrosis
Kidney	50	30	23	NP	40	28	Clinical nephritis
Liver	50	35	30	55	45	40	Liver failure
Stomach	60	55	50	70	67	65	Ulceration/perforation
Small intestine	50	NP	40	60	NP	55	Obstruction/perforation
Femoral head	NP	NP	52	NP	NP	65	Necrosis

Compiled from 2 sources: (1) Morgan MA (2011). Radiation oncology. In DeVita, Lawrence, and Rosenberg, *Cancer* (p.308). Philadelphia: Lippincott Williams and Wilkins; and (2) Kehwar TS, Sharma SC. Use of normal tissue tolerance doses into linear quadratic equation to estimate normal tissue complication probability. <http://www.rooj.com/Radiation%20Tissue%20Tolerance.htm>  
 NP: not provided; TD: tolerance dose.

<sup>a</sup> TD 5/5, the average dose that results in a 5% complication risk within 5 years.

<sup>b</sup> TD 50/5, the average dose that results in a 50% complication risk within 5 years.

For intensity-modulated radiotherapy (IMRT) to provide outcomes superior to 3D-CRT, there must be a clinically meaningful decrease in the radiation exposure to normal structures with IMRT compared with 3D-CRT. There is no standardized definition for a clinically meaningful decrease in radiation dose. In principle, a clinically meaningful decrease would signify a significant reduction in anticipated complications of radiation exposure. To document a clinically meaningful reduction in dose, dosimetry planning studies should demonstrate a significant decrease in the maximum dose of radiation delivered per unit of tissue, and/or a significant decrease in the volume of normal tissue exposed to potentially toxic radiation doses. While radiation tolerance dose levels for normal tissues are well-established, the decrease in the volume of tissue exposed that is needed to provide a clinically meaningful benefit has not been standardized. Therefore, precise parameters for a clinically meaningful decrease cannot be provided.

### Description of Procedure or Service

Populations	Interventions	Comparators	Outcomes
Individuals: • With gastrointestinal tract cancers	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • 3-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Quality of life • Treatment-related morbidity
Individuals: • With gynecologic cancers	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • 3-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Quality of life • Treatment-related morbidity
Individuals: • With anorectal cancer	Interventions of interest are: • Intensity-	Comparators of interest are: • 3-dimensional	Relevant outcomes include: • Overall survival • Disease-specific survival

	modulated radiotherapy	conformal radiotherapy	<ul style="list-style-type: none"> <li>• Quality of life</li> <li>• Treatment-related morbidity</li> </ul>
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Radiotherapy may be an integral component in the treatment of cancers of the abdomen and pelvis. Intensity-modulated radiotherapy (IMRT) has been proposed as a method that allows adequate radiation to the tumor while minimizing the radiation dose to surrounding normal tissues and critical structures.

For individuals who have gastrointestinal (GI) tract cancers who receive IMRT, the evidence includes nonrandomized comparative studies and retrospective series. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. IMRT has been compared with 3-dimensional conformal radiotherapy (3D-CRT) for the treatment of stomach, hepatobiliary, and pancreatic cancers, with some studies reporting longer overall survival and decreased toxicity with IMRT. The evidence on hepatobiliary cancer includes a series with historical controls; it found an increase in median survival with no difference in toxicity. Two comparative studies (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. The available comparative evidence, together with dosimetry studies of organs at risk, would suggest that IMRT improves survival and decreases toxicity compared to 3D-CRT in patients with GI cancers. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have gynecologic cancers who receive IMRT, the evidence includes 2 randomized controlled trials and several nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. There is limited comparative evidence on survival outcomes following IMRT or 3D-CRT. However, available results are generally consistent that IMRT reduces GI and genitourinary toxicity. Based on evidence with other cancers of the pelvis and abdomen that are proximate to organs at risk, it is expected that overall survival with IMRT would be at least as good as 3D-CRT, with a decrease in toxicity. A reduction in GI toxicity is likely to improve the quality of life in patients with gynecologic cancer. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

quality of life in patients with anorectal cancer. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Input was obtained in 2010 and 2012. It supported the use of IMRT in tumors of the abdomen and pelvis when normal tissues would receive unacceptable doses of radiation. Through a chain of evidence, this reduced toxicity potentially lowers the risk of adverse events (acute and late effects of radiation toxicity). This input and a chain of evidence related to the potential to reduce harms led to the decision that IMRT may be considered medically necessary for the treatment of tumors of the abdomen and pelvis when dosimetric planning with standard 3D-CRT predicts that the radiation dose to an adjacent organ would result in unacceptable normal tissue toxicity.

## **Background**

### **Radiation techniques**

#### **Conventional External-Beam Radiotherapy**

Methods to plan and deliver radiotherapy (RT) have evolved in ways that permit more precise targeting of tumors with complex geometries. Most early trials used 2-dimensional treatment planning, based on flat images and radiation beams with cross-sections of uniform intensity that were sequentially aimed at the tumor along 2 or 3 intersecting axes. Collectively, these methods are termed *conventional external-beam radiotherapy*.

#### **Three-Dimensional Conformal Radiotherapy**

Treatment planning evolved by using 3-dimensional images, usually from computed tomography (CT) scans, to delineate the boundaries of the tumor and discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Computer algorithms were developed to estimate cumulative radiation dose delivered to each volume of interest by summing the contribution from each shaped beam. Methods also were developed to position the patient and the radiation portal reproducibly for each fraction and immobilize the patient, thus maintaining consistent beam axes across treatment sessions. Collectively, these methods are termed *3-dimensional conformal radiotherapy (3D-CRT)*.

#### **Intensity-Modulated Radiotherapy**

Intensity-modulated radiotherapy (IMRT) uses computer software and CT and magnetic resonance images, to offer better conformality than 3D-CRT, because it modulates the intensity of the overlapping radiation beams projected on the target and uses multiple shaped treatment fields. Treatment planning and delivery are more complex, time-consuming, and labor intensive for IMRT than for 3D-CRT. The technique uses a multileaf collimator [MLC]), which, when coupled with a computer algorithm, allows for "inverse" treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target's prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and acceptable dose

limits within the normal tissues. Based on these parameters and a digitally reconstructed radiographic image of the tumor, surrounding tissues, and organs at risk, computer software optimizes the location, shape, and intensities of the beam ports to achieve the treatment plan's goals.

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

Technologic development has produced advanced techniques that may further improve RT treatment by improving dose distribution. These techniques are considered variations of IMRT. Volumetric modulated arc therapy delivers radiation from a continuous rotation of the radiation source. The principal advantage of volumetric modulated arc therapy is greater efficiency in treatment delivery time, reducing radiation exposure and improving target radiation delivery due to less patient motion. Image-guided RT involves the incorporation of imaging before and/or during treatment to more precisely deliver RT to the target volume.

IMRT methods to plan and deliver RT are not uniform. IMRT may use beams that remain on as MLCs move around the patient (dynamic MLC) or that are off during movement and turn on once the MLC reaches prespecified positions ("step and shoot" technique). A third alternative uses a very narrow single beam that moves spirally around the patient (tomotherapy). Each method uses different computer algorithms to plan treatment and yields somewhat different dose distributions in and outside the target. Patient position can alter target shape and thus affect treatment plans. Treatment plans are usually based on a single imaging scan, a static 3D-CT image. Current methods seek to reduce positional uncertainty for tumors and adjacent normal tissues by various techniques. Patient immobilization cradles and skin or bony markers are used to minimize day-to-day variability in patient positioning. In addition, many tumors have irregular edges that preclude drawing tight margins on CT scan slices when radiation oncologists contour the tumor volume. It is unknown whether omitting some tumor cells or including some normal cells in the resulting target affects outcomes of IMRT.

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

### **Regulatory Status**

In general, IMRT systems include intensity modulators which control, block, or filter the intensity of radiation; and RT planning systems which plan the radiation dose to be delivered.

A number of intensity modulators have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Intensity

modulators include the Innocure Intensity Modulating Radiation Therapy Compensators (Innocure), 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 FDA through the 510(k) process. They include the FOCUS Radiation Treatment Planning System (Computerized Medical Systems) in 2002, Prowess Panther™ (Prowess) in 2003, TiGRT (LinaTech) in 2009, and the RayDose (RaySearch Laboratories) in 2008, and the Eclipse Treatment Planning System (Varian Medical Systems) 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**

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This evidence review was created in April 2009 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through May 7, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one 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. RCTs 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.

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

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 vs 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.

### **Clinical Context and Test Purpose**

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

The question addressed in this evidence review is: Does the use of IMRT for the treatment of patients with abdominal and pelvic cancers improve net health outcomes?

The following PICOTS were used to select literature to inform this review.

### ***Patients***

The relevant populations of interest are patients with gastrointestinal cancers (eg, stomach, hepatobiliary, and pancreatic cancers), gynecologic cancers (eg, cervical and endometrial cancers), and anorectal cancers who are recommended for radiotherapy (RT).

### ***Interventions***

The therapy being considered is IMRT. IMRT 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. 3D-CRT 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 (eg, toxicity). Toxicity can be assessed using 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).

### **Timing**

Toxicity and recurrence can be assessed acutely and long-term.

### **Setting**

IMRT is usually administered in a hospital or free-standing facility.

## **Gastrointestinal Tract Cancers**

### **Stomach**

Boda-Heggemann et al (2009) evaluated the efficacy and safety of 2 different adjuvant chemoradiotherapy regimens using 3D-CRT or IMRT in 2 consecutive cohorts who underwent primarily D2 resection for gastric cancer.<sup>1</sup> A subsequent report (2013) from this group included twenty-seven 3D-CRT patients and 38 IMRT patients.<sup>2</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 (see 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 vs 3-Dimensional Conformal Radiotherapy With 5-FU Plus FA for Stomach Cancer**

Outcomes	3-Dimensional Conformal Radiotherapy	Intensity-Modulated Radiotherapy	p
Sample	27	38	
Renal toxicity, n (%)	2 (8)	0	0.021

<b>Median disease-free survival, mo</b>	14	35	0.069
<b>Median overall survival, mo</b>	18	43	0.060
<b>Actuarial 2-y overall survival, %</b>	37	67	
<b>Actuarial 5-y overall survival, %</b>	22	44	

Adapted from Boda-Heggemann et al (2009, 2013).<sup>1,2</sup>

FA: folinic acid; 5-FU: 5-fluorouracil.

### **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>3</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 median OS of 17.6 months (range, 10.3-32.3 months), while the 3D-CRT cohort had a median OS of 9.0 months (range, 6.6-17.3 months). There were no significant differences between patient cohorts in acute gastrointestinal (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 treatment of borderline resectable pancreatic cancer.<sup>4</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 (see Table 2). OS 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>5</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, 1.26; 95% confidence interval, 1.08 to 1.45; p=0.001; see Table 2). Hematologic toxicity and median survival were similar in the 2 groups.

**Table 2. Outcomes for IMRT vs 3D-CRT for Pancreatic Cancer**

Comparison	3D-CRT	IMRT	p
Lee et al (2016) <sup>4</sup>	n=40	n=44	
Grade 1-2 gastroduodenal ulcers, n (%)	11 (42.3)	3 (9.1)	0.003
Overall survival, mo	15.8	22.6	0.006
Prasad et al (2016) <sup>5</sup>	n=71	n=134	
Grade 2+ gastrointestinal toxicity, n (%)	24 (33.8)	21 (15.7)	0.001
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. IMRT has been compared with 3D-CRT for the treatment of stomach, hepatobiliary, and pancreatic cancers, with some studies reporting longer OS and decreased toxicity with IMRT. For the treatment of stomach cancer, IMRT improved survival compared with 3D-CRT. However, this study also used different chemotherapy regimens, confounding the results. 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**

### **Randomized Controlled Trials**

A trial by Naik et al (2016) randomized 40 patients with cervical cancer to IMRT or to 3D-CRT.<sup>6</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 genitourinary (GU) toxicity were significantly higher in the 3D-CRT group (see Table 3).

Gandhi et al (2013) reported on a prospective randomized study that compared whole-pelvis IMRT with whole-pelvis 2-dimensional RT in 44 patients with locally advanced cervical cancer.<sup>7</sup> Each treatment arm had 22 patients. The OS rate at 27 months was 88% with IMRT and 76% with 2-dimensional RT (p=0.645). However, fewer grade 2, 3, or 4 GI toxicities were experienced in the IMRT group than in the conventional RT group (see Table 3).

**Table 3. Acute Toxicity of Grade 2, 3 or 4 With 3D-CRT vs IMRT for Cervical Cancer**

Toxicity	3D-CRT, n (%)	IMRT, n (%)	95% CI for the Difference	p
<b>Naik et al (2016)<sup>6</sup></b>				
Hematologic	8 (40)	7 (35)	-0.219 to 0.119	0.644
Leucopenia	3 (15)	2 (10)	-0.1479 to 0.479	0.424
Vomiting	7 (35)	3 (15)	0.338 to 0.061	0.007
Acute gastrointestinal toxicity	9 (45)	4 (20)	-0.408 to -0.091	0.003
Acute genitourinary toxicity	7 (35)	4 (20)	-0.295 to -0.004	0.058
<b>Gandhi et al (2013)<sup>7</sup></b>				
Gastrointestinal, grade $\geq 2$	14 (64)	7 (32)	0.002 to 0.604	0.034
Gastrointestinal, grade $\geq 3$	6 (27)	1 (5)	0.003 to 0.447	0.047
Genitourinary, grade $\geq 2$	7 (32)	5 (24)	-0.202 to 0.361	0.404
Genitourinary, grade $\geq 3$	3 (14)	0 (0)	-0.019 to 0.291	0.125

CI: confidence interval; IMRT: intensity-modulated radiotherapy; 3D-CRT: 3-dimensional conformal 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>8</sup> Groups were generally comparable, except more patients in the 3D-CRT group had open hysterectomy (81% vs 47%, p<0.001). 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=0.006). 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=0.022).

Chen et al (2014) reported on 101 patients with endometrial cancer treated with hysterectomy and adjuvant RT.<sup>9</sup> No significant differences between IMRT patients (n=65) and CRT patients (n=36) were found in 5-year OS (82.9% vs 93.5%; p=0.26), local failure-free survival (93.7% vs 89.3%; p=0.68), or disease-free survival (88.0% vs 82.8%; p=0.83). However, the IMRT patients experienced fewer acute and late toxicities.

Chen et al (2007) examined the use of posthysterectomy RT in 68 women with high-risk cervical cancer.<sup>10</sup> The initial 35 cases received 2-dimensional RT delivered to the whole pelvis; the next 33 patients underwent IMRT. All patients received RT at 50.4 Gy in 28 fractions and 6 Gy of high-dose rate vaginal cuff intracavitary brachytherapy in 3 insertions; chemotherapy (cisplatin) was administered concurrently to all patients. All patients completed the planned course of treatment. At a median follow-up of 34.6 months (range, 12-52 months) in 2-dimensional RT recipients and 14 months (range, 6-25 months) in IMRT recipients, the 1-year locoregional control rate was 94% for 2-dimensional RT and 93% for IMRT. Grade 1 or 2 acute GI toxicities were noted in 36% and 80% of IMRT and 2-dimensional RT recipients, respectively (p<0.001), while acute grade 1 or 2 GU toxicities occurred in 30% and 60%, respectively (p=0.022). There was no significant difference between IMRT and 2-dimensional RT in the incidence of

acute hematologic toxicities. Overall, the IMRT patients had lower rates of chronic GI toxicities ( $p=0.002$ ) than the 2-dimensional RT patients.

### **Section Summary: Gynecologic Cancers**

The evidence on IMRT for gynecologic cancers includes 2 small RCTs (<50 patients each) and several nonrandomized 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**

#### **Randomized Controlled Trials**

Rattan et al (2016) conducted a small (N=20) RCT assessing IMRT for the treatment of anal canal cancer.<sup>11</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 ( $p=0.010$ ). Hematologic grade 3 toxicity was not seen in any patients treated with IMRT but was noted in 20% of patients treated with 3D-CRT ( $p=0.228$ ). Other parameters indicating better tolerance to treatment with IMRT were reduced need for parenteral fluid (10% vs 60%,  $p=0.019$ ) and blood transfusion (0% vs 20%,  $p=0.060$ ).

#### **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>12</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,  $p<0.001$ ) and the occurrence of sphincter loss surgery was higher in the IMRT group (see 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 3D-CRT or IMRT for Rectal Cancer**

<b>Outcome</b>	<b>3D-CRT, %</b>	<b>IMRT, %</b>	<b>Adjusted Odds Ratio</b>	<b>95% CI</b>	<b>p</b>
<b>Pathologic downstaging</b>	57.0	55.0	0.89	0.79 to 1.01	0.051
<b>Sphincter loss</b>	28.3	34.7	1.32	1.14 to 1.52	<0.001

<b>surgery</b>					
<b>Positive resection margin</b>	5.6	8.0	1.57	1.21 to 2.03	<0.001
<b>Unplanned readmission</b>	7.9	6.4	0.79	0.61 to 1.02	0.07
<b>30-d mortality</b>	0.8	0.6	0.61	0.24 to 1.57	0.31
<b>Survival at 5 y</b>	64	64	1.06	0.89 to 1.28	0.47

Adapted from Sun et al (2017).<sup>12</sup>

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

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>13</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=0.039; see 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 (hazard ratio, 0.35; 95% confidence interval, 0.11 to 0.95; p=0.042).

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

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

Adapted from Huang et al (2017).<sup>13</sup>

IMRT: intensity-modulated radiotherapy; 3D-CRT: 3-dimensional conformal 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, locoregional control, and colostomy-free survival did not differ significantly between patients treated with IMRT or with 3D-CRT (p>0.1).<sup>14</sup> Adverse events with 3D-CRT were more frequent and severe, and required more treatment breaks than IMRT (11 days vs 4 days; p=0.006) even though the median duration of treatment breaks did not differ significantly (12.2 days vs 8.0 days; p=0.35). IMRT patients had fewer acute grade 3 or 4 nonhematologic toxicity (p<0.001), improved late grade 3 or 4 GI toxicity (p=0.012), and fewer acute grade 3 or 4 skin toxicity (p<0.001) than 3D-CRT patients.

Dasgupta et al (2013) retrospectively reviewed 223 patients (45 IMRT, 178 CRT) to compare outcomes for anal cancer.<sup>15</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 with 3D-CRT (n=27).<sup>16</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>17</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, 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 were 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 of toxicity and disease outcomes associated with IMRT in 47 patients with anal cancer.<sup>18</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 actuarial 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 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.

### **Summary of Evidence**

For individuals who have GI tract cancers who receive IMRT, the evidence includes nonrandomized comparative studies and retrospective series. Relevant outcomes

are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. IMRT has been compared with 3D-CRT for the treatment of stomach, hepatobiliary, and pancreatic cancers. Evidence has been inconsistent with the outcome of survival, with some studies reporting increased survival among patients receiving IMRT compared with patients receiving 3D-CRT, and other studies reporting no difference between groups. However, most studies found that patients receiving IMRT experienced significantly less GI toxicity compared with patients receiving 3D-CRT. The available comparative evidence, together with dosimetry studies of organs at risk, would suggest that IMRT decreases toxicity compared with 3D-CRT in patients who had GI cancers. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have gynecologic cancers who receive IMRT, the evidence includes 2 small randomized controlled trials and several nonrandomized comparative studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related morbidity. There is limited comparative evidence on survival outcomes following IMRT or 3D-CRT. However, results are generally consistent that IMRT reduces GI and genitourinary toxicity. Based on evidence with other cancers of the pelvis and abdomen that are proximate to organs at risk, it is expected that overall survival with IMRT would be at least as good as 3D-CRT, with a decrease in toxicity. A reduction in GI toxicity is likely to improve the quality of life in patients with gynecologic cancer. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

## **Supplemental Information**

### **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**

### **National Comprehensive Cancer Network Guidelines**

#### ***Gastrointestinal Tract Cancers***

The National Comprehensive Cancer Network (NCCN) guidelines for gastric cancer (v.2.2018) indicate that intensity-modulated radiotherapy (IMRT) “may be used in clinical settings where reduction in dose to organs at risk (eg, heart, lungs, liver, kidneys, small bowel) is required, which cannot be achieved by 3-D techniques.”<sup>19</sup> In addition, target volumes need to be carefully defined and encompassed while taking into account variations in stomach filling and respiratory motion.

NCCN guidelines for hepatobiliary cancers (v.1.2018) state that “All tumors irrespective of the location may be amenable to radiation therapy (3D conformal radiation therapy, intensity-modulated radiation therapy [IMRT], or stereotactic body radiation therapy [SBRT]).”<sup>20</sup>

IMRT is mentioned as an option in NCCN guidelines for pancreatic adenocarcinoma (v.1.2018), stating that 3-dimensional conformal radiotherapy or IMRT with breath-hold or gating techniques can improve coverage with decreased dose to organs at risk.<sup>21</sup> In addition, “studies have shown that the tolerability of radiation is largely dependent on PTV [planning target volume] size/ENI [elective nodal irradiation], types of concurrent systemic/targeted therapy, and whether conformal (3-D, IMRT, SBRT) vs. conventional radiation is used.”

#### ***Gynecologic Cancers***

For cervical cancer, NCCN guidelines (v.1.2018) indicate IMRT “may be 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” such as “when high doses are required to treat gross disease in regional lymph nodes.”<sup>22</sup> IMRT “should not be used as routine alternatives to brachytherapy for treatment of central disease in patients with an intact cervix.” The guidelines also mention 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.”

NCCN guidelines on uterine endometrial cancer (v.2.2018) state that radiotherapy for uterine neoplasms includes external-beam radiotherapy and/or brachytherapy, but that IMRT may be considered “for normal tissue sparing.” [23](#)

NCCN guidelines on ovarian cancer (v.2.2018) do not mention IMRT. [24](#)

### **Anorectal Cancers**

NCCN guidelines for anal carcinoma (v.1.2018) state 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’.” [25](#)

NCCN guidelines on rectal cancer (v.1.2018) indicate that “... IMRT ... should only be used in the setting of a clinical trial or in unique clinical situations such as reirradiation of previously treated patients with recurrent disease or unique anatomical situations.” [26](#)

### **American College of Radiology**

The American College of Radiology Appropriateness Criteria (2014) recommended that IMRT is usually appropriate to treat anal cancer if performed outside of a protocol setting but is still undergoing study. [27](#) The College also noted the most appropriate radiation dose for anal cancer has not been determined and quality control and technical problems are considered challenging with IMRT (eg, in target volume contouring).

### **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 unpublished trials that might influence this review are listed in Table 6.

**Table 6. Summary of Key Trials**

<b>NCT No.</b>	<b>Trial Name</b>	<b>Planned Enrollment</b>	<b>Completion Date</b>
<b>Ongoing</b>			
<b>NCT01672892</b>	Standard Versus Intensity-Modulated Pelvic Radiation Therapy in Treating Patients With	289	Dec 2018

	Endometrial or Cervical Cancer		
<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
<b>NCT02151019</b>	Randomised Phase II Study of Pre-operative 3-D Conformal Radiotherapy (3-DCRT) Versus Intensity Modulated Radiotherapy (IMRT) for Locally Advanced Rectal Cancer	268	Jul 2030
<b>NCT01164150</b>	Prospective Randomized Phase II Trial Evaluating Adjuvant Pelvic Radiotherapy Using Either IMRT or 3-Dimensional Planning for Endometrial Cancer	154	Dec 2033

NCT: national clinical trial.

## References

1. Boda-Heggemann J, Hofheinz RD, Weiss C, et al. Combined adjuvant radiochemotherapy with IMRT/XELOX improves outcome with low renal toxicity in gastric cancer. *Int J Radiat Oncol Biol Phys.* Nov 15 2009;75(4):1187-1195. PMID 19409725
2. Boda-Heggemann J, Weiss C, Schneider V, et al. Adjuvant IMRT/XELOX radiochemotherapy improves long-term overall- and disease-free survival in advanced gastric cancer. *Strahlenther Onkol.* May 2013;189(5):417-423. PMID 23558673
3. Fuller CD, Dang ND, Wang SJ, et al. Image-guided intensity-modulated radiotherapy (IG-IMRT) for biliary adenocarcinomas: Initial clinical results. *Radiother Oncol.* Aug 2009;92(2):249-254. PMID 19324442
4. Lee KJ, Yoon HI, Chung MJ, et al. A comparison of gastrointestinal toxicities between intensity-modulated radiotherapy and three-dimensional conformal radiotherapy for pancreatic cancer. *Gut Liver.* Mar 23 2016;10(2):303-309. PMID 26470767
5. Prasad S, Cambridge L, Huguet F, et al. Intensity modulated radiation therapy reduces gastrointestinal toxicity in locally advanced pancreas cancer. *Pract Radiat Oncol.* Mar-Apr 2016;6(2):78-85. PMID 26577010
6. Naik A, Gurjar OP, Gupta KL, et al. Comparison of dosimetric parameters and acute toxicity of intensity-modulated and three-dimensional radiotherapy in patients with cervix carcinoma: A randomized prospective study. *Cancer Radiother.* Jul 2016;20(5):370-376. PMID 27368915
7. Gandhi AK, Sharma DN, Rath GK, et al. Early clinical outcomes and toxicity of intensity modulated versus conventional pelvic radiation therapy for locally advanced cervix carcinoma: a prospective randomized study. *Int J Radiat Oncol Biol Phys.* Nov 1 2013;87(3):542-548. PMID 24074927
8. Shih KK, Hajj C, Kollmeier M, et al. Impact of postoperative intensity-modulated radiation therapy (IMRT) on the rate of bowel obstruction in gynecologic malignancy. *Gynecol Oncol.* Oct 2016;143(1):18-21. PMID 27486131
9. Chen CC, Wang L, Lu CH, et al. Comparison of clinical outcomes and toxicity in endometrial cancer patients treated with adjuvant intensity-modulated radiation therapy or conventional radiotherapy. *J Formos Med Assoc.* Dec 2014;113(12):949-955. PMID 24144528
10. Chen MF, Tseng CJ, Tseng CC, et al. Clinical outcome in posthysterectomy cervical cancer patients treated with concurrent Cisplatin and intensity-modulated pelvic radiotherapy: comparison with conventional radiotherapy. *Int J Radiat Oncol Biol Phys.* Apr 1 2007;67(5):1438-1444. PMID 17394944
11. Rattan R, Kapoor R, Bahl A, et al. Comparison of bone marrow sparing intensity modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3DCRT) in carcinoma of anal canal: a prospective study. *Ann Transl Med.* Feb 2016;4(4):70. PMID 27004217
12. Sun Z, Adam MA, Kim J, et al. Intensity-modulated radiation therapy is not associated with perioperative or survival benefit over 3D-conformal radiotherapy for rectal cancer. *J Gastrointest Surg.* Jan 2017;21(1):106-111. PMID 27510332
13. Huang CM, Huang MY, Tsai HL, et al. A retrospective comparison of outcome and toxicity of preoperative image-guided intensity-modulated radiotherapy versus conventional pelvic radiotherapy for locally advanced rectal carcinoma. *J Radiat Res.* Mar 01 2017;58(2):247-259. PMID 27738080

14. Chuong MD, Freilich JM, Hoffe SE, et al. Intensity-modulated radiation therapy vs. 3D conformal radiation therapy for squamous cell carcinoma of the anal canal. *Gastrointest Cancer Res.* Mar 2013;6(2):39-45. PMID 23745158
15. Dasgupta T, Rothenstein D, Chou JF, et al. Intensity-modulated radiotherapy vs. conventional radiotherapy in the treatment of anal squamous cell carcinoma: a propensity score analysis. *Radiother Oncol.* May 2013;107(2):189-194. PMID 23692961
16. Dewas CV, Maingon P, Dalban C, et al. Does gap-free intensity modulated chemoradiation therapy provide a greater clinical benefit than 3D conformal chemoradiation in patients with anal cancer? *Radiat Oncol.* Nov 2012;7:201. PMID 23190693
17. Devisetty K, Mell LK, Salama JK, et al. A multi-institutional acute gastrointestinal toxicity analysis of anal cancer patients treated with concurrent intensity-modulated radiation therapy (IMRT) and chemotherapy. *Radiother Oncol.* Nov 2009;93(2):298-301. PMID 19717198
18. Pepek JM, Willett CG, Wu QJ, et al. Intensity-modulated radiation therapy for anal malignancies: a preliminary toxicity and disease outcomes analysis. *Int J Radiat Oncol Biol Phys.* Dec 1 2010;78(5):1413-1419. PMID 20231064
19. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Gastric Cancer. Version 2.2018.  
[https://www.nccn.org/professionals/physician\\_gls/pdf/gastric.pdf](https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf). Accessed May 31, 2018.
20. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Hepatobiliary Cancers. Version 1.2018.  
[https://www.nccn.org/professionals/physician\\_gls/PDF/hepatobiliary.pdf](https://www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf). Accessed May 31, 2018.
21. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Pancreatic Adenocarcinoma. Version 1.2018.  
[https://www.nccn.org/professionals/physician\\_gls/pdf/pancreatic.pdf](https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf). Accessed May 31, 2018.
22. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Cervical Cancer. Version 1.2018.  
[https://www.nccn.org/professionals/physician\\_gls/PDF/cervical.pdf](https://www.nccn.org/professionals/physician_gls/PDF/cervical.pdf). Accessed May 31, 2018.
23. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Uterine Neoplasms. Version 2.2018.  
[https://www.nccn.org/professionals/physician\\_gls/PDF/uterine.pdf](https://www.nccn.org/professionals/physician_gls/PDF/uterine.pdf). Accessed May 31, 2018.
24. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Ovarian Cancer. Version 2.2018.  
[https://www.nccn.org/professionals/physician\\_gls/pdf/ovarian.pdf](https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf). Accessed May 31, 2018.
25. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Anal Carcinoma. Version 1.2018.  
[https://www.nccn.org/professionals/physician\\_gls/pdf/anal.pdf](https://www.nccn.org/professionals/physician_gls/pdf/anal.pdf). Accessed May 31, 2018.
26. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: Rectal Cancer. Version 1.2018.  
[https://www.nccn.org/professionals/physician\\_gls/pdf/rectal.pdf](https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf). Accessed May 31, 2018.
27. Expert Panel on Radiation Oncology-Rectal/Anal Cancer, Hong TS, Pretz JL, et al. ACR Appropriateness Criteria(R)-Anal Cancer. *Gastrointest Cancer Res.* Jan 2014;7(1):4-14. PMID 24558509

## **Billing Coding/Physician Documentation Information**

- 77301** Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications
- 77338** Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan
- 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 delivery, includes intrafraction tracking, when performed

- G6001** Ultrasonic guidance for placement of radiation therapy fields
- G6002** Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy
- G6015** Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
- G6016** Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session

**ICD-10 Codes:**

- C16.0-** Malignant neoplasm of stomach, code range
- C16.9**
- C17.0-** Malignant neoplasm of small intestine code range
- C17.9**
- C18.0-** Malignant neoplasm of colon code range
- C18.9**
- C19** Malignant neoplasm of rectosigmoid junction
- C20** Malignant neoplasm of rectum
- C21.0-** Malignant neoplasm of anus, code range
- C21.8**
- C22.0-** Malignant neoplasm of liver and intrahepatic bile ducts code range
- C22.9**
- C23** Malignant neoplasm of gallbladder
- C24.0-** Malignant neoplasm of other and unspecified parts of biliary tract code
- C24.9** range
- C25.0-** Malignant neoplasm of pancreas code range
- C25.9**
- C26.0-** Malignant neoplasm of other and ill-defined sites within the digestive
- C26.9** organs and peritoneum code range
- C51.0-** Malignant neoplasm of vulva code range
- C51.9**
- C52** Malignant neoplasm of vagina
- C53.0-** Malignant neoplasm of cervix uteri code range
- C53.9**
- C54.0-** Malignant neoplasm of corpus uteri code range
- C54.9**

Effective in 2015, code 77418 was deleted and new codes for simple and complex IMRT delivery were created:

- 77385: Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple
- 77386: complex.

The Centers for Medicare and Medicaid Services (CMS) decided not to implement this change for 2015 and instead created HCPCS G codes for the radiotherapy codes being deleted 12/31/14. So the following codes may be used for IMRT:

G6015: Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC [multileaf collimator], per treatment session  
G6016: Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session.

Code 77301 remains valid:

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

0073T: (code deleted 12/31/14)

77418: (code deleted 12/31/14)

### **Additional Policy Key Words**

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N/A

### **Policy Implementation/Update Information**

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11/1/09	New policy; considered investigational. This policy is effective 12/15/2009.
1/1/10	Updated coding.
5/13/10	Policy statement revised to indicate use in anal cancers may be considered medically necessary.
11/1/10	No policy statement changes.
1/1/11	Coding updated.
11/1/11	No policy statement changes.
11/1/12	No policy statement changes.
12/13/12	Policy statement changed to state that IMRT may be considered medically necessary for all anal cancers (not limited to squamous cell carcinoma). Policy statement changed to state that IMRT may be considered medically necessary for the treatment of tumors of the abdomen and pelvis when dosimetric planning predicts the volume of small intestine receiving doses >45 Gy with standard 3-D conformal radiation would result in unacceptable risk of small intestine injury. Added a policy statement that IMRT would be considered investigational for all other uses in the abdomen and pelvis. Paragraph added to policy guidelines regarding toxic radiation dose to tissues and definition of a clinically significant decrease in radiation dose.
2/1/14	No policy statement changes.
2/1/15	Updated CPT and HCPCS codes. No policy statement changes.
2/1/16	No policy statement changes.

4/1/16 No policy statement changes.  
2/1/17 No policy statement changes.  
2/1/18 No policy statement changes.  
2/1/19 No policy statement changes.

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