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

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

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>• With gastrointestinal tract or gynecologic cancer</td>
<td>• Intensity-modulated radiotherapy</td>
<td>• 3-dimensional conformal radiotherapy</td>
<td>• Overall survival</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Disease-specific survival</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Change in disease status</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Quality of life</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Treatment-related morbidity</td>
</tr>
</tbody>
</table>

Description

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.

Summary of Evidence

For individuals who have gastrointestinal tract or gynecologic cancer who receive IMRT the evidence includes small randomized controlled trials (RCTs), nonrandomized comparative studies, and case series. Relevant outcomes are overall survival, disease-specific survival, change in disease status, quality of life, and treatment-related morbidity. IMRT has been investigated for the treatment of stomach and hepatobiliary cancers, with reports of longer overall survival with IMRT compared to 3-dimensional conformal radiation (3D-CRT). However, these studies have also used different chemotherapy regimens, confounding the results. Literature searches identified two comparative studies (one prospective, one retrospective), along with several retrospective series on IMRT for pancreatic cancer. Both comparative studies found a reduction in gastrointestinal (GI) toxicity with IMRT. One study found no difference in overall survival, while the other found a benefit in overall survival when patients selected the treatment. One randomized trial has compared results of whole-pelvis IMRT with whole-pelvis CRT to cervical cancer. Reports of case series, including concurrently treated control patients, are emerging. The available results have generally been viewed as hypothesis-generating for the design and execution of comparative trials of IMRT versus CRT that evaluate tumor control, survival outcomes, adverse events, and safety. For other tumors of the abdomen and pelvis, the evidence from treatment planning studies has shown that IMRT decreases radiation doses delivered to normal tissue adjacent to tumor. Through a chain of
indirect evidence, this potentially lowers the risk of adverse events (acute and late effects of radiation toxicity). The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Policy**

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

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

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

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

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

**Policy Guidelines**

The table below outlines radiation doses that are generally considered tolerance thresholds for these normal structures in the abdomen and pelvis.

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5 (Gy)*</th>
<th>TD 50/5 (Gy)**</th>
<th>Complication End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Portion of organ involved</td>
<td>Portion of organ involved</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>60 45 40</td>
<td>70 55 50</td>
<td>Pericarditis</td>
</tr>
<tr>
<td>Lung</td>
<td>45 30 17.5</td>
<td>65 40 24.5</td>
<td>Pneumonitis</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>50 50 47</td>
<td>70 70 NP</td>
<td>Myelitis/necrosis</td>
</tr>
<tr>
<td>Kidney</td>
<td>50 30 23</td>
<td>NP 40 28</td>
<td>Clinical nephritis</td>
</tr>
<tr>
<td>Liver</td>
<td>50 35 30</td>
<td>55 45 40</td>
<td>Liver failure</td>
</tr>
<tr>
<td>Stomach</td>
<td>60 55 50</td>
<td>70 67 65</td>
<td>Ulceration/perforation</td>
</tr>
<tr>
<td>Small intestine</td>
<td>50 NP 40</td>
<td>60 NP 55</td>
<td>Obstruction/perforation</td>
</tr>
<tr>
<td>Femoral head</td>
<td>NP NP 52</td>
<td>NP NP 65</td>
<td>Necrosis</td>
</tr>
</tbody>
</table>

The tolerance doses in the table are a compilation from the following two sources:

- 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](http://www.rooj.com/Radiation%20Tissue%20Tolerance.htm)

NP: not provided; TD: tolerance dose

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

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

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

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

**Background**

*Radiation Techniques*

**Conventional External-Beam Radiotherapy**

Over the past several decades, methods to plan and deliver radiotherapy (RT) have evolved in ways that permit more precise targeting of tumors with complex geometries. Most early trials used 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 two or three 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 3D-CRT.

**Intensity-Modulated Radiotherapy**

IMRT, which uses computer software and CT and magnetic resonance imaging (MRI) images, offers better conformality than 3D-CRT, because it is able to modulate the intensity of the overlapping radiation beams projected on the target and to use multiple shaped treatment fields. Treatment planning and delivery are more complex, time consuming, and labor intensive for IMRT than for 3D-CRT. The technique uses a multileaf collimator (MLC), which, when coupled with a computer algorithm, allows for “inverse” treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target’s prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and acceptable dose limits within the normal tissues. Based on these parameters and a digitally reconstructed radiographic image of the tumor, surrounding tissues, and organs at risk, computer software optimizes the location, shape, and intensities of the beam ports to achieve the treatment plan’s goals.

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

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

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

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

Regulatory Status

In general, IMRT systems include intensity modulators, which control, block, or filter the intensity of radiation; and radiotherapy (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 Inc., Tempe, AZ) and decimal tissue compensator (Southeastern Radiation Products, Sanford, FL), cleared in 2006. FDA product code: IXI. Intensity modulators may be added to standard linear accelerators to deliver IMRT when used with proper treatment planning systems.

RT treatment planning systems have also been cleared for marketing by FDA through the 510(k) process. These include the Prowess Panther (Prowess, Concord, CA) in 2003, TiGRT (LinaTech, Sunnyvale, CA) in 2009, and the Ray Dose (RaySearch Laboratories, Stockholm, Sweden). 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. One such device cleared for marketing by FDA through the 510(k) process is the Varian IMRT system (Varian Medical Systems, Palo Alto, CA). FDA product code: IYE.

Related Protocols

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

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.
It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

**References**

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


