Protocol

Intensity-Modulated Radiotherapy: Abdomen and Pelvis

(80149)

<table>
<thead>
<tr>
<th>Medical Benefit</th>
<th>Effective Date: 06/01/20</th>
<th>Next Review Date: 03/23</th>
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<td>Preauthorization</td>
<td>No</td>
<td>Review Dates: 09/09, 09/10, 03/11, 03/12, 03/13, 03/14, 03/15, 03/16, 03/17, 03/18, 03/19, 03/20, 03/21, 11/21, 03/22</td>
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Preauthorization is not required.

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.

RELATED PROTOCOLS

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

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<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
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<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
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<td>With gastrointestinal</td>
<td>• Intensity-modulated radiotherapy</td>
<td>• Three-dimensional conformal radiotherapy</td>
<td>• Overall survival</td>
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<td>• Treatment-related morbidity</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Treatment-related morbidity</td>
</tr>
</tbody>
</table>
### Populations
- With esophageal cancer

### Interventions
- Interventions of interest are:
  - Intensity-modulated radiotherapy

### Comparators
- Comparators of interest are:
  - Three-dimensional conformal radiotherapy

### Outcomes
- Relevant outcomes include:
  - Overall survival
  - Disease-specific survival
  - Recurrence
  - Quality of life
  - Treatment-related morbidity

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### DESCRIPTION

Radiotherapy may be an integral component of the treatment of cancers of the abdomen and pelvis. Intensity-modulated radiotherapy (IMRT) has been proposed as a method that allows adequate radiation to the tumor while minimizing the radiation dose to surrounding normal tissues and critical structures.

### SUMMARY OF EVIDENCE

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

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

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

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

POLICY

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

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

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

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

POLICY GUIDELINES

The table below 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 three-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

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5 (Gray)³</th>
<th>TD 50/5 (Gray)³</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></td>
<td>1/3</td>
<td>2/3</td>
<td>3/3</td>
</tr>
<tr>
<td>Heart</td>
<td>60</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>Lung</td>
<td>45</td>
<td>30</td>
<td>17.5</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>50</td>
<td>50</td>
<td>47</td>
</tr>
<tr>
<td>Kidney</td>
<td>50</td>
<td>30</td>
<td>23</td>
</tr>
<tr>
<td>Liver</td>
<td>50</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>Stomach</td>
<td>60</td>
<td>55</td>
<td>50</td>
</tr>
<tr>
<td>Small intestine</td>
<td>50</td>
<td>NP</td>
<td>40</td>
</tr>
<tr>
<td>Femoral head</td>
<td>NP</td>
<td>NP</td>
<td>52</td>
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</table>

Compilation from 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

³TD 5/5, the average dose that results in a 5% complication risk within five years.
For 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.

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). 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. 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. 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 (MLCs) 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

Intensity-modulated radiotherapy 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. 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, com-
puter 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.

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) in 2002, Prowess Panther™ (Prowess) in 2003, TiGRT (LinaTech) in 2009, 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.

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


