FEP Medical Policy Manual

FEP 8.01.59 Intensity-Modulated Radiotherapy: Central Nervous System Tumors

Effective Policy Date: October 1, 2019

Original Policy Date: June 2012

Related Policies:
1.01.29 - Tumor Treating Fields Therapy
6.01.10 - Stereotactic Radiosurgery and Stereotactic Body Radiotherapy
8.01.08 - Intraoperative Radiotherapy
8.01.10 - Charged-Particle (Proton or Helium Ion) Radiotherapy for Neoplastic Conditions
8.01.48 - Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid

Intensity-Modulated Radiotherapy: Central Nervous System Tumors

Description

Radiotherapy (RT) is an integral component of treating many brain tumors, both benign and malignant. Intensity-modulated radiotherapy (IMRT) is a method that allows adequate radiation to the tumor while minimizing the dose to surrounding normal tissues and critical structures. IMRT also allows additional radiation to penetrate specific anatomic areas simultaneously, delivering radiation at a larger target volume.

IMRT, which uses computer software and CT and magnetic resonance images, offers better conformality than 3-dimensional conformal radiotherapy (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.

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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 under-dosing within the tumor and may decrease toxicity by avoiding overdosing.

Technologic developments have 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 deliver RT to the target volume more precisely.

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 computed tomography (CT) scan slices when radiation oncologists contour the tumor volume.

Investigators are exploring an active breathing control device combined with moderately deep inspiration breath-holding techniques to improve conformity and dose distributions during IMRT for breast cancer. Techniques presently being studied with other tumors (eg, lung cancer) either gate beam delivery to the patient’s respiratory movement or continuously monitor tumor (by in-room imaging) or marker (internal or surface) positions to aim radiation more accurately at the target. The impact of these techniques on the outcomes of 3D-CRT or IMRT for breast cancer is unknown. However, it appears likely that respiratory motion alters the dose distributions actually delivered while treating patients from those predicted by plans based on static CT scans or measured by dosimetry using stationary (non-breathing) targets.

OBJECTIVE

The objective of this evidence review is to determine whether treatment with intensity-modulated radiotherapy improves the net health outcome in individuals with brain tumors.

POLICY STATEMENT

Intensity-modulated radiotherapy may be considered medically necessary for the treatment of tumors of the central nervous system when the tumor is proximate to organs at risk (brain stem, spinal cord, cochlea and eye structures including optic nerve and chiasm, lens and retina) and 3-dimensional conformal radiotherapy planning is not able to meet dose-volume constraints for normal tissue tolerance (see Policy Guidelines section).

Intensity-modulated radiotherapy is considered investigational for the treatment of tumors of the central nervous system for all indications not meeting the criteria above.

POLICY GUIDELINES

Organs at risk are defined as normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed radiation dose. Organs at risk may be particularly vulnerable to clinically important complications from radiation toxicity. Table PG1 outlines radiation doses generally considered tolerance thresholds for these normal structures in the central nervous system. Dosimetry plans may be reviewed to demonstrate that radiation by 3-dimensional conformal radiotherapy would exceed tolerance doses to structures at risk.

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## Table PG1. Radiation Tolerance Doses for Normal Tissues

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5, Gray&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TD 50/5, Gray&lt;sup&gt;b&lt;/sup&gt;</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 2/3 3/3</td>
<td>1/3 2/3 3/3</td>
<td></td>
</tr>
<tr>
<td>Brain stem</td>
<td>60 53 50</td>
<td>NP</td>
<td>Necrosis, infarct</td>
</tr>
<tr>
<td>Spinal cord, cm</td>
<td>50 (5-10) NP 47 (20)</td>
<td>70 (5-10) NP</td>
<td>Myelitis, necrosis</td>
</tr>
<tr>
<td>Optic nerve and chiasm</td>
<td>50 50 50</td>
<td>65 65 65</td>
<td>Blindness</td>
</tr>
<tr>
<td>Retina</td>
<td>45 45 45</td>
<td>65 65 65</td>
<td>Blindness</td>
</tr>
<tr>
<td>Eye lens</td>
<td>10 10 10</td>
<td>18 18 18</td>
<td>Cataract requiring intervention</td>
</tr>
</tbody>
</table>


Radiation tolerance doses for the cochlea have been reported to be 50 gray.

NP: not provided; TD: tolerance dose.

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

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

### BENEFIT APPLICATION

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

### FDA REGULATORY STATUS

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

A number of intensity modulators have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Intensity modulators include the Innocure Intensity Modulating Radiation Therapy Compensators (Innocure) and decimal tissue compensator (Southeastern Radiation Products), 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.

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Radiotherapy treatment planning systems have also been cleared for marketing by the FDA through the 510(k) process. They include the Prowess Panther (Prowess) in 2003, TiGRT (LinaTech) in 2009, and the Ray Dose (RaySearch Laboratories). 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 the FDA through the 510(k) process is the Varian IMRT system (Varian Medical Systems). FDA product code: IYE.

**RATIONALE**

**Summary of Evidence**

For individuals who have malignant brain tumors who receive intensity-modulated radiotherapy (IMRT), the evidence includes dose-planning studies, nonrandomized comparison studies, and case series. The relevant outcomes are overall survival (OS), disease-specific survival, morbid events, functional outcomes, and treatment-related morbidity. Case series results have consistently shown low radiation toxicity but have not demonstrated better tumor control or improved survival with IMRT. Dose-planning studies have shown that IMRT delivers adequate radiation doses to tumors while simultaneously reducing radiation exposure to sensitive brain areas. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have benign brain tumors who receive IMRT, the evidence includes case series. The relevant outcomes are OS, disease-specific survival, functional outcomes, and treatment-related morbidity. Case series results have consistently shown low radiation toxicity but have not demonstrated better tumor control or improved survival with IMRT vs other radiotherapy techniques. It is expected that the dose-planning studies evaluating IMRT in patients with malignant tumors should generalize to patients with benign brain tumors because the benefit of minimizing radiation toxicity to sensitive brain areas is identical. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have brain tumor metastases who receive IMRT to avoid hippocampal exposure, the evidence includes nonrandomized comparison studies and case series. The relevant outcomes are OS, disease-specific survival, functional outcomes, and treatment-related morbidity. One prospective nonrandomized comparison study using IMRT to avoid hippocampal exposure showed a less cognitive decline with IMRT than with a prespecified historical control. Limitations of the historical control design and other aspects of the study make conclusions uncertain. The role of hippocampal radiation exposure as a cause of cognitive decline is less certain; thus, more definitive studies are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

**Practice Guidelines and Position Statements**

**National Comprehensive Cancer Network**

The National Comprehensive Cancer Network Clinical Practice Guidelines Central Nervous System (v.1.2019 update pending) support the use of radiotherapy (including IMRT) for low-grade and high-grade gliomas. 13, "When RT [radiotherapy] is given to patients with low-grade gliomas, it is administered with restricted margins...Every attempt should be made to decrease the RT dose outside the target volume. This can be achieved with 3-dimensional planning or intensity-modulated RT (IMRT)." 14, For high-grade gliomas, "[c]onformal techniques including 3-dimensional conformal RT and IMRT partial brain irradiation are recommended." 14.

The guidelines did not include recommendations for the use of IMRT to treat high-grade tumors as well as limited or extensive metastases to the central nervous system. 14.

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U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


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

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 2013</td>
<td>Replace policy</td>
<td>Policy updated with literature review. Policy statement added that IMRT is considered not medically necessary for the treatment of tumors of the central nervous system for indications not meeting the criteria for medically necessary.</td>
</tr>
<tr>
<td>June 2014</td>
<td>Replace policy</td>
<td>Policy updated with literature review. Reference added and reference 13 updated. Title changed from &quot;radiation therapy&quot; to &quot;radiotherapy&quot;.</td>
</tr>
<tr>
<td>June 2015</td>
<td>Replace policy</td>
<td>Policy updated with literature review. Policy statements unchanged except for other indications, policy statement changed from &quot;not medically necessary&quot; to &quot;investigational&quot;</td>
</tr>
<tr>
<td>September 2018</td>
<td>Replace policy</td>
<td>Policy updated with literature review through May 7, 2018; references 8 and 13 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>September 2019</td>
<td>Replace policy</td>
<td>Policy updated with literature review through May 6, 2019; references on NCCN updated. Policy statements unchanged.</td>
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