Radiotherapy 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.

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). IMRT is the more recent development in external radiation. Treatment planning and delivery are more complex, time-consuming, and labor-intensive for IMRT than for 3D-CRT. Similar to 3D-CRT, the tumor and surrounding normal organs are outlined in 3D by a scan and multiple radiation beams are positioned around the patient for radiation delivery. In IMRT, radiation beams are divided into a grid-like pattern, separating a single beam into many smaller "beamlets". Specialized computer software allows for "inverse" treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target's prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and acceptable dose limits within the normal tissues. Based on these parameters and a digitally reconstructed radiographic image of the tumor, surrounding tissues, and organs at risk, computer software optimizes the location, shape, and intensities of the beam ports to achieve the treatment plan's goals.
Increased conformality may permit escalated tumor doses without increasing normal tissue toxicity and is proposed to improve local tumor control, with decreased exposure to surrounding, normal tissues, potentially reducing acute and late radiation toxicities. Better dose homogeneity within the target may also improve local tumor control by avoiding underdosing within the tumor and may decrease toxicity by avoiding overdosing.

Other advanced techniques 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.

**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 individuals with malignant or benign brain tumors 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).

Hippocampal-avoiding intensity-modulated radiotherapy may be considered medically necessary for individuals with brain tumor metastases outside a 5-mm margin around either hippocampus and expected survival ≥4 months.

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.

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5, Gray a</th>
<th>TD 50/5, Gray b</th>
<th>Complication End Point</th>
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<tbody>
<tr>
<td></td>
<td>Portion of Organ Involved</td>
<td>Portion of Organ Involved</td>
<td></td>
</tr>
<tr>
<td>Brain stem</td>
<td>1/3 2/3 3/3</td>
<td>1/3 2/3 3/3</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 65</td>
<td>Myelitis, necrosis</td>
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### Optic nerve and chiasm

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<td>Eye lens</td>
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Radiation tolerance doses for the cochlea have been reported to be 50 gray.

NP: not provided; TD: tolerance dose.

- **a** TD 5/5 is the average dose that results in a 5% complication risk within 5 years.
- **b** 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.

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. Relevant outcomes are overall survival (OS), disease-specific survival, morbidity events, functional outcomes, and treatment-related morbidity. Case series results have consistently shown with 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. Relevant outcomes are overall survival, 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 a randomized trial, nonrandomized studies and case series. Relevant outcomes are OS, disease-specific survival, functional outcomes, and treatment-related morbidity. One randomized trial and one prospective nonrandomized comparison study using IMRT to avoid hippocampal exposure showed less cognitive decline with IMRT than with either conventional WBRT or prespecified historical controls. The evidence is sufficient 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. 2.2020) support the use of radiotherapy (including IMRT) for low-grade and high-grade gliomas. "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)." For high-grade gliomas, "[c]onformal techniques including 3D-CRT and IMRT for performing focal brain irradiation are recommended." For patients with brain metastases and a prognosis of 4 months or greater, the guidelines recommend considering hippocampal-sparing WBRT and memantine during and after WBRT for a total of 6 months.

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.

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:

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<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>
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<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>
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<tr>
<td>June 2015</td>
<td>Replace policy</td>
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<tr>
<td>September 2019</td>
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<td>Policy updated with literature review through May 6, 2019; references on NCCN updated. Policy statements unchanged.</td>
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<td>Policy updated with literature review through June 8, 2020; references added. Added policy statement that Hippocampal-avoiding IMRT may be considered medically necessary for individuals with brain tumor metastases outside a 5-mm margin around either hippocampus and expected survival 4 months or more.</td>
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