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**
- Charged-Particle (Proton or Helium Ion) Radiotherapy for Neoplastic Conditions
- Hematopoietic Cell Transplantation for Central Nervous System Embryonal Tumors and Ependymoma
- Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid
- Intracavitary Balloon Catheter Brain Brachytherapy for Malignant Gliomas
- Stereotactic Radiosurgery and Stereotactic Body Radiotherapy
- Tumor Treating Fields Therapy

### Populations, Interventions, Comparators, and Outcomes

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<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
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<tr>
<td>• With malignant</td>
<td>• Intensity-modulated radiotherapy</td>
<td>• Three-dimensional conformal radiotherapy</td>
<td>• Overall survival</td>
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<td>brain tumors</td>
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<td>• Disease-specific survival</td>
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<td>• Morbid events</td>
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<td>• Functional outcomes</td>
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<td>• Treatment-related morbidity</td>
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<td>Individuals:</td>
<td>Interventions of interest are:</td>
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<tr>
<td>• With benign brain</td>
<td>• Intensity-modulated radiotherapy</td>
<td>• Three-dimensional conformal radiotherapy</td>
<td>• Overall survival</td>
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<td>tumors</td>
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<td>• Disease-specific survival</td>
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<td>Relevant outcomes include:</td>
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<tr>
<td>• With brain</td>
<td>• Intensity-modulated radiotherapy to avoid</td>
<td>• Whole-brain radiotherapy</td>
<td>• Overall survival</td>
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<tr>
<td>metastases</td>
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<td>• Disease-specific survival</td>
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<td></td>
<td></td>
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<td>• Treatment-related morbidity</td>
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DESCRIPTION

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.

SUMMARY OF EVIDENCE

For individuals who have malignant brain tumors who receive IMRT, the evidence includes dose-planning studies, nonrandomized comparison studies, and case series. Relevant outcomes are overall survival, disease-specific survival, morbidity 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. 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.

ADDITIONAL INFORMATION

Clinical input was obtained in 2012 on the use of IMRT, including its use close to critical structures. There was a near-uniform consensus that use of IMRT in the central nervous system is at least as effective as three-dimensional conformal radiotherapy and that, given the adverse events that could result if nearby critical structures receive toxic radiation doses, IMRT dosimetric improvements should be accepted as meaningful evidence for its benefit. Input, a strong chain of evidence, and the potential to reduce harms supported a decision that IMRT may be considered medically necessary for the treatment of tumors of the central nervous system that are proximate to organs at risk.

POLICY

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 three-dimensional conformal radiotherapy planning is not able to meet dose volume constraints for normal tissue tolerance (see Policy Guidelines).
Hippocampal-avoiding intensity-modulated radiotherapy may be considered medically necessary for individuals with brain tumor metastases outside a 5-mm margin around either hippocampus or expected survival four months or more.

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. The following table 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 three-dimensional conformal radiotherapy would exceed tolerance doses to structures at risk.

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5 Graya</th>
<th>TD 50/5 Grayb</th>
<th>Complication End Point</th>
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</thead>
<tbody>
<tr>
<td>Brain stem</td>
<td>60</td>
<td>53</td>
<td>50</td>
</tr>
<tr>
<td>Spinal cord, cm</td>
<td>50 (5-10)</td>
<td>NP</td>
<td>47 (20)</td>
</tr>
<tr>
<td>Optic nerve and chiasm</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Retina</td>
<td>45</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Eye lens</td>
<td>10</td>
<td>10</td>
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</tr>
</tbody>
</table>

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. Available online: http://www.rooj.com/Radiation%20Tissue%20Tolerance.htm

Radiation tolerance doses for the cochlea have been reported to be 50 gray
NP: not provided, cm: centimeters, TD: tolerance dose
aTD 5/5, the average dose that results in a 5% complication risk within five years
bTD 50/5, the average dose that results in a 50% complication risk within five years

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 two-dimensional (2D) RT, three-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 bones 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

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.

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)
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.

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.