Intensity-Modulated Radiotherapy: Central Nervous System Tumors

Medical Benefit
Effective Date: 03/01/14
Next Review Date: 03/17
Preauthorization: No
Review Dates: 07/12, 07/13, 03/14, 03/15, 03/16

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.

Description
Radiotherapy (RT) is an integral component in the treatment of many brain tumors, both benign and malignant. Intensity-modulated radiotherapy (IMRT) has been proposed as a method of RT that allows adequate RT to the tumor while minimizing the radiation dose to surrounding normal tissues and critical structures.

Summary of Evidence
The body of evidence available to evaluate intensity-modulated radiotherapy (IMRT) in the treatment of central nervous system (CNS) tumors consists of dose planning studies and case series. The case series are limited by small numbers, heterogeneous patient populations, and different types of tumors. No randomized trials have been reported that compare results using IMRT with other conformal radiotherapy (CRT) modalities, nor do any of the reported case series using IMRT include concurrently treated control groups.

In general, the limited evidence suggests that IMRT provides tumor control and survival outcomes comparable with existing radiotherapy techniques. The evidence from treatment planning studies has shown that the use of IMRT decreases radiation doses delivered to critical CNS structures (e.g., optic chiasm, brainstem) and normal tissue adjacent to the tumor. This potentially lowers the risk of adverse events (acute and late effects of radiation toxicity), although the clinical benefit of reducing the radiation dose to critical structures and surrounding normal tissue using IMRT is theoretical. Determination of whether adverse event rates are reduced with IMRT is further complicated by a lack of high-quality literature defining the adverse effects using 3-dimensional CRT (3D-CRT) therapy for the CNS, the main comparator with IMRT. The single-arm case series are of limited usefulness in determining the benefits of IMRT over other conformal radiation modalities.

Due to the limitations in this evidence, this Protocol underwent clinical vetting in 2012. There was near-uniform consensus that the use of IMRT in the CNS is at least as effective as 3D-CRT and that given the possible adverse events that could result if nearby critical structures receive toxic radiation doses that IMRT dosimetric improvements should be accepted as meaningful evidence for its benefit. The results of the vetting, together with a strong indirect chain of evidence and the potential to reduce harms, led to the decision that IMRT may be considered medically necessary for the treatment of tumors of the CNS that are in close proximity to organs at risk.
Policy

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

Intensity-modulated radiotherapy (IMRT) is considered not medically necessary for the treatment of tumors of the CNS 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. These organs at risk may be particularly vulnerable to clinically important complications from radiation toxicity. The following table outlines radiation doses that are generally considered tolerance thresholds for these normal structures in the CNS.

Radiation Tolerance Doses for Normal Tissues

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5 Gy&lt;sup&gt;a&lt;/sup&gt;</th>
<th>TD 50/5 Gy&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        NP        65</td>
<td>Necrosis, infarct</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>50 (5-10 cm) NP NP 47 (20 cm)</td>
<td>70 (5-10 cm) NP 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 Gy. 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

*cm=centimeters

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

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

Note: This Protocol does not address radiation treatment for metastasis to the brain or spine.

Background

RT and Brain Tumors

The standard approach to the treatment of brain tumors depends on the type and location of tumor. For glioblastoma multiforme, a malignant high-grade tumor, treatment is multimodal, with surgical resection followed by adjuvant RT and chemotherapy.<sup>1</sup>

For benign and low-grade brain tumors, gross total resection remains the primary goal. However, RT may be used in selected cases. Some examples are when total resection is not possible, when a more conservative surgical approach may be necessary to achieve long-term treatment goals, and with atypical tumors that may
need RT even after gross total resection to reduce the risk of local recurrence. Therefore, RT, either definitive or in the postoperative adjuvant setting, remains an integral component in the management of residual, recurrent, and/or progressive benign and low-grade brain tumors for maximizing local control.²

Brain metastases occur in up to 40% of adults with cancer and can shorten survival and detract from quality of life. Many patients who develop brain metastases will eventually die of progressive intracranial disease. Among patients with good performance status, controlled extracranial disease, favorable prognostic features, and a solitary brain metastasis, randomized studies have shown that surgical excision followed by whole-brain radiotherapy (WBRT) prolongs survival.³ Stereotactic radiosurgery (SRS) may be able to replace surgery in certain circumstances, delivering obliteratively high single doses to discrete metastases.³ For bulky cerebral metastases, level one evidence has also shown that delivering a higher radiation dose with an SRS boost is beneficial in addition to standard WBRT. The use of a concomitant boost with IMRT during WBRT has been attempted to improve overall local tumor control without the use of SRS to avoid additional planned radiation after WBRT (“phase II” or SRS) and its additional labor and expense.³

Radiation Techniques

Conventional External Beam Radiotherapy

Over the past several decades, methods to plan and deliver RT have evolved in ways that permit more precise targeting of tumors with complex geometries. Most early trials used two-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 RT.”

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 3-dimensional conformal radiotherapy (3D-CRT).

Intensity-Modulated Radiotherapy

IMRT, which uses computer software and CT and magnetic resonance imaging (MRI) images, offers better conformality than 3D-CRT, as it is able to modulate the intensity of the overlapping radiation beams projected on the target and to use multiple shaped treatment fields. It uses a device (a multileaf collimator [MLC]) which, coupled to 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 and surrounding tissues and organs at risk, computer software optimizes the location, shape and intensities of the beams 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.
Because most tumors move as patients breathe, dosimetry with stationary targets may not accurately reflect doses delivered within target volumes and adjacent tissues in patients. Furthermore, treatment planning and delivery are more complex, time consuming, and labor intensive for IMRT than for 3D-CRT. Thus, clinical studies must test whether IMRT improves tumor control or reduces acute and late toxicities when compared with 3D-CRT.

Methodologic Issues With IMRT Studies

Multiple-dose planning studies have generated 3D-CRT and IMRT treatment plans from the same scans, then compared predicted dose distributions within the target and in adjacent organs at risk. Results of such planning studies show that IMRT improves on 3D-CRT with respect to conformality to, and dose homogeneity within, the target. Dosimetry using stationary targets generally confirms these predictions. Thus, radiation oncologists hypothesized that IMRT may improve treatment outcomes compared with those of 3D-CRT. However, these types of studies offer indirect evidence on treatment benefit from IMRT, and it is difficult to relate results of dosing studies to actual effects on health outcomes.

Comparative studies of radiation-induced adverse effects from IMRT versus alternative radiation delivery are probably the most important type of evidence in establishing the benefit of IMRT. Such studies would answer the question of whether the theoretical benefit of IMRT in sparing normal tissue translates into real health outcomes. Single-arm series of IMRT can give some insights into the potential for benefit, particularly if an adverse effect that is expected to occur at high rates is shown to decrease by a large amount. Studies of treatment benefit are also important to establish that IMRT is at least as good as other types of delivery, but in the absence of such comparative trials, it is likely that benefit from IMRT is at least as good as with other types of delivery.

Regulatory Status

FDA has approved a number of devices for use in IMRT, including several linear accelerators and MLCs. Examples of approved devices and systems are the NOMOS Slit Collimator (BEAK™) (NOMOS Corp.), the Peacock™ System (NOMOS Corp.), the Varian Multileaf Collimator with dynamic arc therapy feature (Varian Oncology Systems), the Saturne Multileaf Collimator (GE Medical Systems), the Mitsubishi 120 Leaf Multileaf Collimator (Mitsubishi Electronics America), the Stryker Leibinger Motorized Micro Multileaf Collimator (Stryker Leibinger), the Mini Multileaf Collimator, model KMI (MRC Systems GMBH), and the Preference® IMRT Treatment Planning Module (Northwest Medical Physics Equipment).

Related Protocols

Charged-Particle (Proton or Helium Ion) Radiation Therapy
Hematopoietic Stem-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 or Metastasis to the Brain
Stereotactic Radiosurgery and Stereotactic Body Radiotherapy
Tumor-Treatment Fields Therapy for Glioblastoma
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.


