Protocol

Intensity-Modulated Radiotherapy: Central Nervous System Tumors

(80159)

Medical Benefit		**Effective Date**: 07/01/17	**Next Review Date**: 03/19
Preauthorization	No	**Review Dates**: 07/12, 07/13, 03/14, 03/15, 03/16, 03/17, 05/17, 03/18	

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.

Populations	Interventions	Comparators	Outcomes
Individuals: • With malignant brain tumors	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • Three-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Morbid events • Functional outcomes • Treatment-related morbidity
Individuals: • With benign brain tumors	Interventions of interest are: • Intensity-modulated radiotherapy	Comparators of interest are: • Three-dimensional conformal radiotherapy	Relevant outcomes include: • Overall survival • Disease-specific survival • Functional outcomes • Treatment-related morbidity

Description

Radiotherapy is an integral component of the treatment of 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, morbid events, functional outcomes, and treatment-related morbidity. Case series results are consistent 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 are consistent with low radiation toxicity but have not demonstrated better tumor control or

improved survival with IMRT vs. other radiotherapy techniques. 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.

Policy

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).

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. 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. Dosimetry plans may be reviewed to demonstrate that radiation by three-dimensional conformal radiotherapy would exceed tolerance doses to structures at risk.

Radiation Tolerance Doses for Normal Tissues

Site	TD 5/5 Gray[a]			TD 50/5 Gray[b]			Complication End Point
	Portion of organ involved			Portion of organ involved			
	1/3	2/3	3/3	1/3	2/3	3/3	
Brain stem	60	53	50	NP	NP	65	Necrosis, infarct
Spinal cord, cm	50 (five-10)	NP	47 (20)	70 (five-10)	NP	NP	Myelitis, necrosis
Optic nerve and chiasm	50	50	50	65	65	65	Blindness
Retina	45	45	45	65	65	65	Blindness
Eye lens	10	10	10	18	18	18	Cataract requiring intervention

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:

Morgan MA (2011). Radiation Oncology. In DeVita, Lawrence and Rosenberg, Cancer (p.308). Philadelphia: Lippincott Williams and Wilkins.

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

NP: not provided, cm: centimeters, TD: tolerance dose

[a] TD 5/5, the average dose that results in a 5% complication risk within five years

[b] 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

Radiotherapy and Brain Tumors

The standard approach to treat brain tumors depends on the type and location of the tumor. For glioblastoma multiforme, a high-grade malignant tumor, treatment is multimodal, with surgical resection followed by adjuvant radiotherapy (RT) and chemotherapy.[1]

For benign and low-grade brain tumors, gross total resection remains the primary goal. However, RT may be used in select 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 when atypical tumors 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]

Radiotherapy 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 radiotherapy*.

Three-Dimensional Conformal Radiotherapy

Treatment planning evolved by using three-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 *three-dimensional conformal radiotherapy* (3D-CRT).

Intensity-Modulated Radiotherapy

IMRT, which uses computer software and CT and magnetic resonance imaging images, offers better conformality than 3D-CRT, because it is able to modulate the intensity of the overlapping radiation beams projected on the target and to use 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.

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.

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 pre-specified 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 CT scan slices when radiation oncologists contour the tumor volume. It is unknown whether omitting some tumor cells or including some normal cells in the resulting target affects outcomes of IMRT.

Regulatory Status

A number of devices for use in IMRT, including several linear accelerators and MLCs, have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Examples of approved devices and systems are the NOMOS Slit Collimator (BEAK™; NOMOS), the Peacock™ System (NOMOS), 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) 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 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.

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