Protocol

Intensity-Modulated Radiation Therapy (IMRT): Central Nervous System Tumors

(80159)

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

The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. ***Preauthorization is not required.*** *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

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

Background

Radiation therapy and brain tumors

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

For benign and low-grade brain tumors, gross total resection remains the primary goal. However, radiation therapy 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 radiotherapy even after gross total resection to reduce the risk of local recurrence. Therefore, radiation therapy, 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 radiation therapy. Over the past several decades, methods to plan and deliver radiation therapy 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 radiation therapy."

3-dimensional conformal radiation therapy (3D-CRT). 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 radiation therapy (3D-CRT).

Intensity-modulated radiation therapy (IMRT). 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.

Since 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.

Methodological 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 side 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

The U.S. Food and Drug Administration (FDA) has approved a number of devices for use in intensity-modulated radiation therapy (IMRT), including several linear accelerators and multileaf collimators. 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 Inc.), 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 Inc.).

Related Protocols

Intensity-Modulated Radiation Therapy (IMRT): Cancer of the Head and Neck or Thyroid

Intensity-Modulated Radiation Therapy (IMRT): Abdomen and Pelvis

Policy (Formerly Corporate Medical Guideline)

Intensity-modulated radiation therapy (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)

IMRT for central nervous system tumors not meeting these criteria would be considered **not medically necessary**.

Policy Guideline

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

	TD 5/5 (Gy)[a] Portion of organ involved			TD 50/5 (Gy)[b] Portion of organ involved			
Site	**1/3**	**2/3**	**3/3**	**1/3**	**2/3**	**3/3**	**Complication End Point**
Brain stem	60	53	50	NP	NP	65	Necrosis, infarct
Spinal cord	50 (5-10 cm)	NP	47 (20 cm)	70 (5-10 cm)	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

[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

NP: not provided

cm=centimeters

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

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

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.

1. Amelio D, Lorentini S, Schwarz M et al. Intensity-modulated radiation therapy in newly diagnosed glioblastoma: a systematic review on clinical and technical issues. Radiother Oncol 2010; 97(3):361-9.
2. Gupta T, Wadasadawala T, Master Z et al. Encouraging early clinical outcomes with helical tomotherapy-based image-guided intensity-modulated radiation therapy for residual, recurrent, and/or progressive benign/low-grade intracranial tumors: a comprehensive evaluation. Int J Radiat Oncol Biol Phys 2012; 82(2):756-64.
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7. Huang E, The BS, Strother DR et al. Intensity-modulated radiation therapy for pediatric medulloblastoma: early report on the reduction of ototoxicity. Int J Radiat Oncol Biol Phys 2002; 52(3):599-605.
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9. Mackley HB, Reddy CA, Lee SY et al. Intensity-modulated radiotherapy for pituitary adenomas: the preliminary report of the Cleveland Clinic experience. Int J Radiat Oncol Biol Phys 2007; 67(1):232-9.
10. Sajja R, Barnett GH, Lee SY et al. Intensity-modulated radiation therapy (IMRT) for newly diagnosed and recurrent intracranial meningiomas: preliminary results. Technol Cancer Res Treat 2005; 4(6):675-82.
11. Uy NW, Woo SY, Teh BS et al. Intensity-modulated radiation therapy (IMRT) for meningioma. Int J Radiat Oncol Biol Phys 2002; 53(5):1265-70.
12. National Comprehensive Cancer Network (NCCN) Guidelines. Central Nervous System Cancers (v1.2013). Available online at: http://www.nccn.org/professionals/physician_gls/PDF/cns.pdf. Last accessed March 2013.