

Protocol

Intensity-Modulated Radiotherapy: Central Nervous System Tumors

(80159)

Medical Benefit		Effective Date: 06/01/20	Next Review Date: 03/21
Preauthorization	No	Review Dates: 07/12, 07/13, 03/14, 03/15, 03/16, 03/17, 05/17, 03/18, 03/19, 03/20	

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: <ul style="list-style-type: none">• With malignant brain tumors	Interventions of interest are: <ul style="list-style-type: none">• Intensity-modulated radiotherapy	Comparators of interest are: <ul style="list-style-type: none">• Three-dimensional conformal radiotherapy	Relevant outcomes include: <ul style="list-style-type: none">• Overall survival• Disease-specific survival• Morbid events• Functional outcomes• Treatment-related morbidity
Individuals: <ul style="list-style-type: none">• With benign brain tumors	Interventions of interest are: <ul style="list-style-type: none">• Intensity-modulated radiotherapy	Comparators of interest are: <ul style="list-style-type: none">• Three-dimensional conformal radiotherapy	Relevant outcomes include: <ul style="list-style-type: none">• Overall survival• Disease-specific survival• Functional outcomes• Treatment-related morbidity
Individuals: <ul style="list-style-type: none">• With brain tumors	Interventions of interest are: <ul style="list-style-type: none">• Intensity-modulated radiotherapy to avoid hippocampal exposure	Comparators of interest are: <ul style="list-style-type: none">• Whole-brain radiotherapy	Relevant outcomes include: <ul style="list-style-type: none">• Overall survival• Disease-specific survival• Functional outcomes• Treatment-related morbidity

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. The relevant outcomes are overall survival, disease-specific survival, morbid 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. The 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 nonrandomized comparison studies and case series. The relevant outcomes are overall survival, disease-specific survival, functional outcomes, and treatment-related morbidity. One prospective nonrandomized comparison study using IMRT to avoid hippocampal exposure showed a less cognitive decline with IMRT than with a prespecified historical control. Limitations of the historical control design and other aspects of the study make conclusions uncertain. The role of hippocampal radiation exposure as a cause of cognitive decline is less certain; thus, more definitive studies are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 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 three-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. 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.

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 (5-10)	NP	47 (20)	70 (5-10)	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

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>

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

Conventional External-Beam Radiotherapy

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, typically 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 3D-CRT.

Intensity-Modulated Radiotherapy

IMRT, which uses computer software and CT and magnetic resonance images, offers better conformality than 3D-CRT because it modulates the intensity of the overlapping radiation beams projected on the target and uses 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 prespecified 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.

Investigators are exploring an active breathing control device combined with moderately deep inspiration breath-holding techniques to improve conformality and dose distributions during IMRT for breast cancer.¹ Techniques presently being studied with other tumors (e.g., lung cancer)² either gate beam delivery to the patient's respiratory movement or continuously monitor tumor (by in-room imaging) or marker (internal or surface) positions to aim radiation more accurately at the target. The impact of these techniques on the outcomes of 3D-CRT or IMRT for breast cancer is unknown. However, it appears likely that respiratory motion alters the dose distributions actually delivered while treating patients from those predicted by plans based on static CT scans or measured by dosimetry using stationary (nonbreathing) targets.

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.

RELATED PROTOCOLS

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 or Metastasis to the Brain

Stereotactic Radiosurgery and Stereotactic Body Radiotherapy

Tumor Treating Fields Therapy

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.

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