BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 8.01.59 Intensity-Modulated Radiotherapy: Central Nervous System Tumors

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Related Policies:

1.01.29 - Tumor Treating Fields Therapy
6.01.10 - Stereotactic Radiosurgery and Stereotactic Body Radiotherapy
8.01.08 - Intraoperative Radiotherapy
8.01.48 - Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid
8.01.49 - Intensity-Modulated Radiotherapy: Abdomen, Pelvis and Chest

Intensity-Modulated Radiotherapy: Central Nervous System Tumors

Description

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Radiotherapy (RT) 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. Intensity-modulated radiotherapy also allows additional radiation to penetrate specific anatomic areas simultaneously, delivering radiation at a larger target volume.

Intensity-modulated radiotherapy 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.[1,] 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 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.

OBJECTIVE

The objective of this evidence review is to determine whether treatment with intensity-modulated radiotherapy improves the net health outcome in individuals with brain tumors.

POLICY STATEMENT

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 3-dimensional conformal radiotherapy planning is not able to meet dose-volume constraints for normal tissue tolerance (see Policy Guidelines section).

Hippocampal-avoiding intensity-modulated radiotherapy may be considered **medically necessary** for individuals with brain tumor metastases outside a 5-mm margin around either hippocampus and expected survival ≥4 months.

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. Table PG1 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 3-dimensional conformal radiotherapy would exceed tolerance doses to structures at risk.

Table PG1. 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

Compiled from 2 sources: (1) Morgan MA, Ten Taken RK, Lawrence TS. Essentials of radiation therapy. In DeVita, Hellman, and Rosenberg, *Cancer: Principles & Practice of Oncology*. Philadelphia: Lippincott Williams and Wilkins; 2019; and (2) 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. Accessed May 31, 2023.
Radiation tolerance doses for the cochlea have been reported to be 50 gray.
NP: not provided; TD: tolerance dose.
[a] TD 5/5 is the average dose that results in a 5% complication risk within 5 years.
[b] TD 50/5 is the average dose that results in a 50% complication risk within 5 years.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA 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.

RATIONALE

Summary of Evidence

For individuals who have malignant brain tumors who receive intensity-modulated radiotherapy (IMRT), the evidence includes dose-planning studies, nonrandomized comparison studies, and a systematic review. Relevant outcomes are overall survival (OS), disease specific survival (DSS), morbid events, functional outcomes, and treatment-related morbidity. Study 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 an improvement in the net health outcome.

For individuals who have benign brain tumors who receive IMRT, the evidence includes case series. Relevant outcomes are OS, DSS, 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 versus 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 an 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, DSS, functional outcomes, and treatment-related morbidity. One randomized trial and 1 prospective nonrandomized comparison study using IMRT to avoid hippocampal exposure showed less cognitive decline with IMRT than with either conventional whole brain radiotherapy (WBRT) or prespecified historical controls. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information" if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines on Central Nervous System Cancers (v.1.2024) support the use of highly conformal fractionated radiotherapy (RT) techniques (eg, IMRT) to "spare critical structures and uninvolved tissue."[16,] When RT is given to patients with low-grade gliomas, NCCN states that "every attempt should be made to decrease the RT dose outside the target volume. This can be achieved with 3-dimensional (3D) planning or IMRT, with improved target coverage and normal brain/critical structure sparing often shown with IMRT." The guideline also states that for high-grade gliomas: "conformal RT (CRT) techniques, which include 3D-CRT and IMRT are recommended for performing focal brain irradiation. IMRT often will provide superior dosimetric target coverage and better sparing of critical structures than 3D-CRT."

For patients with brain metastases and a prognosis of 4 months or longer, the guidelines recommend hippocampal-sparing WBRT and memantine during and after WBRT for a total of 6 months.[16,] The guidelines did not include recommendations for the use of IMRT to treat high-grade tumors as well as limited or extensive metastases to the central nervous system.

American Society for Radiation Oncology

In 2022, the American Society for Radiation Oncology (ASTRO) authored a white paper on safety considerations for IMRT.[17,] Many topics related to IMRT program quality are addressed, but there is no guidance about patient selection for IMRT.

Also in 2022, the ASTRO authored a guideline on managing grade 2 and grade 3 diffuse glioma with isocitrate dehydrogenase mutations.[18,] Intensity-modulated radiotherapy/volumetric modulated arc therapy (VMAT) was strongly recommended in this population to reduce toxicity, especially for tumors listed near organs at risk (low quality of evidence). If IMRT/VMAT is not available, 3-D CRT is strongly recommended (moderate quality of evidence).

A 2016 model policy from ASTRO on IMRT states that IMRT is considered reasonable and medically necessary when sparing the surrounding tissue is beneficial.[19,] Primary, metastatic, or benign tumors of the central nervous system (including brain, brain stem, and spinal cord) are listed as clinical indications that frequently support the use of IMRT, as well as medically necessary irradiation. The list of clinical scenarios that do not support the use of IMRT includes situations when IMRT does not offer an advantage over conventional or 3-D CRT, or in cases that are too urgent to allow for the planning that is required before administering IMRT.

American Association of Neurological Surgeons/Congress of Neurological Surgeons Joint Section on Tumors

In 2020, the American Association of Neurological Surgeons and Congress of Neurological Surgeons Joint Section on Tumors sponsored a systematic review and evidence-based clinical practice guideline update on the role of radiation therapy in the treatment of adults with newly diagnosed glioblastoma multiforme.[20,] Among the 14 clinical questions that were examined, 1 question was specific for the use of IMRT: "In adult patients with newly diagnosed supratentorial glioblastoma is image-modulated RT or similar techniques as effective as standard regional RT in providing tumor control and improved survival?" The authors reviewing the clinical data concluded that: "There is no evidence that IMRT is a better RT delivering modality when compared to conventional RT in improving survival in adult patients with newly diagnosed glioblastoma. Hence, IMRT should not be preferred over the conventional RT delivery modality."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
September 2012	New policy	
June 2013	Replace policy	Policy updated with literature review, Policy statement unchanged. References updated.
June 2014	Replace policy	Policy updated with literature review. Policy statement added that IMRT is considered not medically necessary for the treatment of tumors of the central nervous system for indications not meeting the criteria for medically necessary.
June 2015	Replace policy	Policy updated with literature review. Reference added and reference 13 updated. Title changed from "radiation therapy€š to "radiotherapy€š.
September 2018	Replace policy	Policy updated with literature review through May 7, 2018; references 8 and 13 added. Policy statements unchanged except for other indications, policy statement changed from "not medically necessary€š to "investigational€š
September 2019	Replace policy	Policy updated with literature review through May 6, 2019; references on NCCN updated. Policy statements unchanged.
September 2020	Replace policy	Policy updated with literature review through June 8, 2020; references added. Added policy statement that Hippocampal-avoiding IMRT may be considered medically necessary for individuals with brain tumor metastases outside a 5-mm margin around either hippocampus and expected survival 4 months or more.
September 2021	Replace policy	Policy updated with literature review through May 28, 2021; references added. Policy statements unchanged.
September 2022	Replace policy	Policy updated with literature review through June 8, 2022; no references added. Policy statements unchanged.
September 2023	Replace policy	Policy updated with literature review through May 22, 2023; references added. Policy statements unchanged.
September 2024	Replace policy	Policy updated with literature review through May 23, 2024; no references added; reference on NCCN updated. Policy statements unchanged.