Intensity-Modulated Radiotherapy (IMRT): Central Nervous System Tumors

Policy Number: 8.01.59  Last Review: 09/2020
Origination: 06/2013  Next Review: 06/2021

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for IMRT for central nervous system tumors when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Intensity-modulated radiotherapy (IMRT) may be considered medically necessary for individuals with malignant or benign brain tumors 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 Considerations)

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.

When Policy Topic is not covered
Intensity modulated radiotherapy (IMRT) is considered investigational for the treatment of tumors of the CNS for all indications not meeting the criteria above.

Considerations
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

<table>
<thead>
<tr>
<th>Site</th>
<th>TD 5/5, Gray(^a)</th>
<th>TD 50/5, Gray(^b)</th>
<th>Complication End Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portion of Organ Involved</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</td>
<td>NP</td>
<td>Necrosis, infarct</td>
</tr>
<tr>
<td>Spinal cord, cm</td>
<td>50 (5-10)</td>
<td>NP</td>
<td>Myelitis, necrosis</td>
</tr>
<tr>
<td>Optic nerve and chiasm</td>
<td>50</td>
<td>47 (20)</td>
<td>70 (5-10)</td>
</tr>
<tr>
<td>Retina</td>
<td>45</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Eye lens</td>
<td>10</td>
<td>65</td>
<td>65</td>
</tr>
</tbody>
</table>


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.

### Coding

The following CPT codes are used for simple and complex intensity-modulated radiotherapy (IMRT) delivery:

77385 Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple

77386 complex.

The Centers for Medicare & Medicaid Services did not implement these CPT codes and instead created HCPCS G codes with the language of the previous CPT codes. Therefore, the following codes may be used for IMRT:

G6015 Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session

G6016 Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session.

Code 77301 remains valid:

77301 Intensity-modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications.

The following CPT code may also be used:
77338 Multi-leaf collimator (MLC) device(s) for intensity-modulated radiation therapy (IMRT), design and construction per IMRT plan.

Code 77338 is to be reported only once per IMRT plan.

### Description of Procedure or Service

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals: ▪ With malignant brain tumors</td>
<td>Interventions of interest are: ▪ Intensity-modulated radiotherapy</td>
<td>Comparators of interest are: ▪ 3-dimensional conformal radiotherapy</td>
<td>Relevant outcomes include: ▪ Overall survival ▪ Disease-specific survival ▪ Morbid events ▪ Functional outcomes ▪ Treatment-related morbidity</td>
</tr>
<tr>
<td>Individuals: ▪ With benign brain tumors</td>
<td>Interventions of interest are: ▪ Intensity-modulated radiotherapy</td>
<td>Comparators of interest are: ▪ 3-dimensional conformal radiotherapy</td>
<td>Relevant outcomes include: ▪ Overall survival ▪ Disease-specific survival ▪ Functional outcomes ▪ Treatment-related morbidity</td>
</tr>
<tr>
<td>Individuals: ▪ With brain metastases</td>
<td>Interventions of interest are: ▪ Intensity-modulated radiotherapy to avoid hippocampal exposure</td>
<td>Comparators of interest are: ▪ Whole-brain radiotherapy</td>
<td>Relevant outcomes include: ▪ Overall survival ▪ Disease-specific survival ▪ Functional outcomes ▪ Treatment-related morbidity</td>
</tr>
</tbody>
</table>

Radiotherapy is an integral component in 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 specific anatomic areas at the same time as delivering radiation to a larger target volume.

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 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 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 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 a randomized trial, nonrandomized studies and case series. Relevant outcomes are OS, disease-specific survival, functional outcomes, and treatment-related morbidity. One randomized trial and one prospective nonrandomized comparison study using IMRT to avoid hippocampal exposure showed less cognitive decline with IMRT than with either conventional WBRT or prespecified historical controls. The evidence is sufficient to determine the effects of the technology on health outcomes.

**Additional Information**
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 3-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.

**Background**

**Radiotherapy Techniques**
Radiation therapy may be administered externally (ie, a beam of radiation is directed into the body) or internally (ie, a radioactive source is placed inside the body, near a tumor). External radiotherapy (RT) techniques include "conventional" or 2-dimensional (2D) RT, 3-dimensional (3D) conformal RT, and intensity-modulated radiation therapy (IMRT).

**Conventional External-Beam Radiotherapy**
Methods to plan and deliver RT have evolved that permit more precise targeting of tumors with complex geometries. Conventional 2D treatment planning utilizes X-ray films to guide and position radiation beams. Bony landmarks bones visualized on X-ray are used to locate a tumor and direct the radiation beams. The radiation is typically of uniform intensity.

**Three-Dimensional Conformal Radiotherapy**
Radiation treatment planning has evolved to use 3D images, usually from computed tomography (CT) scans, to more precisely delineate the boundaries of the tumor and to discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Three-dimensional conformal RT (3D-CRT) involves initially scanning the patient in the position that will be used for the radiation treatment. The tumor target and surrounding normal organs are then outlined in 3D on the scan. Computer software assists in determining the
orientation of radiation beams and the amount of radiation the tumor and normal tissues receive to ensure coverage of the entire tumor in order to minimize radiation exposure for at risk normal tissue and nearby organs. Other imaging techniques and devices such as multileaf collimators (MLCs) may be used to "shape" the radiation beams. Methods have also been developed to position the patient and the radiation portal reproducibly for each fraction and to immobilize the patient, thus maintaining consistent beam axes across treatment sessions.

**Intensity-Modulated Radiotherapy**

IMRT 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. 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 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 more precisely deliver RT to the target volume.

**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

Literature Review

This evidence review was created in April 2012 and has been updated regularly with searches of the PubMed database. The most recent literature update was performed through June 8, 2020.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Multiple dose-planning studies generate 3-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy (IMRT) treatment plans from the
same scans and then compare predicted dose distributions within the target area and adjacent organs. Results of such planning studies have shown that IMRT is better than 3D-CRT with respect to conformality to, and dose homogeneity within, the target. Results have also demonstrated that IMRT spreads less radiation to nontarget areas. Dosimetry studies using stationary targets generally confirm these predictions. However, because patients move during treatment, dosimetry with stationary targets only approximate actual radiation doses received. Based on these dosimetry studies, radiation oncologists expect IMRT to improve treatment outcomes compared with those of 3D-CRT.

Comparative studies of radiation-induced adverse events from IMRT vs alternative radiation delivery would constitute definitive evidence of establishing the benefit of IMRT. Single-arm series of IMRT can give some insights into the potential for benefit, particularly if an adverse event 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, absent such comparative trials, it is likely that benefit from IMRT is at least as good as with other types of delivery.

In general, when the indication for IMRT is to avoid radiation to sensitive areas, dosimetry studies have been considered sufficient evidence to demonstrate that harm would be avoided by using IMRT. For other IMRT indications, such as using IMRT to provide better tumor control, comparative studies of health outcomes are needed to demonstrate such a benefit.

Malignant Brain Tumors

Clinical Context and Therapy Purpose
The purpose of IMRT in patients who have malignant brain tumors is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does treatment with IMRT improve health outcomes in individuals with malignant brain tumors?

The following PICO was used to select literature to inform this review.

Patients
The relevant population of interest is individuals with malignant brain tumors.

Interventions
The therapy being considered is IMRT.

Radiotherapy (RT) is an integral component of treating many brain tumors, both benign and malignant. 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.
IMRT is performed by radiation oncologists in an outpatient clinical setting.

Comparators
The following therapy is currently being used: 3D-CRT.

Treatment planning evolved by using 3D 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.

3D-CRT is performed by radiation oncologists in an outpatient clinical setting.

Outcomes
The general outcomes of interest are overall survival (OS), recurrence-free survival (locoregional control), reductions in symptoms, and treatment-related adverse events. A proposed benefit of IMRT is to reduce toxicity to adjacent structures, allowing dose escalation to the target area and fewer breaks in treatment courses due to a reduction in side effects. However, this may come with a loss of locoregional control and OS due to the factors discussed above. The time frame for outcome measures varies from short-term management of toxicity and symptoms to long-term procedure-related complications, cancer progression or recurrence, and OS.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews
Amelio et al (2010) conducted a systematic review of the clinical and technical issues of using IMRT in newly diagnosed glioblastoma multiforme. Articles were selected through December 2009 and included 17 studies (9 on dosimetric data and technical considerations, 7 on clinical results, 1 on both dosimetric and clinical results) for a total of 204 treated patients and 148 patient datasets used in
planning studies. No RCTs were identified, and a meta-analysis was not performed.

For the 6 articles related to planning studies that compared 3D-CRT with IMRT, the report by Fuller et al (2007) showed a noticeable difference between 3D-CRT and IMRT for the planning target volume (PTV; 13% benefit in V95 [volume that received 95% of the prescribed dose] from IMRT, p<0.001)³; the remaining studies suggested that IMRT and 3D-CRT provided similar PTV coverage, with differences between 0% and 1%. Target dose conformity was improved with IMRT. The organs at risk in the studies typically were the brainstem, optic chiasm, optic nerves, lens, and retina. In general, IMRT provided better sparing of the organs at risk than 3D-CRT but with considerable variation from study to study.

Of the 8 studies that included clinical results, 3 were retrospective; 1 was a prospective phase 1 study, and 4 were prospective phase 2 single-institution studies. Of these 8 studies, 2 used conventional total dose and dose per fraction, 2 used a hypofractionated regimen, and the others used a hypofractionated scheme with a simultaneous integrated boost. The median follow-up ranged from 8.8 to 24 months. Almost all patients (96%) completed treatment without interruption or discontinuation due to toxicity. Acute toxicity was reported as negligible, with grade 3 adverse events observed in only 2 studies at rates of 7% and 12%. Grade 4 toxicity was recorded in only 1 series, with an absolute rate of 3%. Data for late toxicities were available in 6 of 8 studies, with 1 recording grade 4 adverse events with an incidence of 20%. One- and 2-year OS rates varied between 30% and 81.9% and between 0% and 55.6%, respectively. When OS was reported as a median time and ranged from 7 to 24 months. Progression-free survival (PFS) rates ranged from 0% to 71.4% at 1 year from 0% to 53.6% at 2 years. The median PFS ranged from 2.5 to 12 months.

Reviewers also conducted a comprehensive qualitative comparison using data reported in the literature on similar non-IMRT clinical studies, offering the following conclusions. The planning comparisons revealed that 3D-CRT and IMRT provided similar results in terms of target coverage. IMRT was somewhat better than 3D-CRT in reducing the maximum dose delivered to the organs at risk—although the extent varied by case. IMRT was better than 3D-CRT when it came to dose conformity and sparing of the healthy brain tissue at medium to low doses; there were no aspects where IMRT performed worse than 3D-CRT.

The systematic review evidence was limited by a number of factors: there was an absence of comparative studies with clinical outcomes; all studies were small in size, from a single institution; most patients (53%) were retrospectively analyzed; chemotherapy administration varied across studies.

**Dose-Planning Studies**

A representative sample of dose-planning, case series, and comparative studies are discussed next. For example, MacDonald et al (2007) compared the dosimetry of IMRT with 3D-CRT in 20 patients treated for high-grade glioma. Prescription dose and normal tissue constraints were identical for the 3D-CRT and IMRT
treatment plans. The IMRT plan yielded superior target coverage compared with the 3D-CRT plan. The IMRT plan reduced the percent volume of brainstem receiving a dose greater than 45 gray (Gy) by 31% (p=0.004) and the percent volume of brain receiving a dose greater than 18 Gy, 24 Gy, and 45 Gy by 10% (p=0.059), 14% (p=0.015), and 40% (p<0.001), respectively. With IMRT, the percent volume of optic chiasm receiving more than 45 Gy was reduced by 30.4% (p=0.047). Compared with 3D-CRT, IMRT significantly increased the tumor control probability (p<0.001) and lowered the normal tissue complication probability for brain and brainstem (p<0.033).

Narayana et al (2006) compared IMRT treatment plans with 3D plans performed in 20 patients of a case series of 58 patients. Regardless of tumor location, IMRT did not improve PTV compared with 3D planning. However, IMRT decreased the maximum dose to the spinal cord, optic nerves, and eye by 16%, 7%, and 15%, respectively.

Nonrandomized Comparison Studies
Paulsson et al (2014) compared treatment failure rates in glioblastoma patients with differing target margins (the size of the region between the tumor and edge of the PTV). In 161 patients, treatment margins were not associated with treatment failure. There was no difference in treatment failure rates between IMRT and 3D-CRT.

A large cohort study conducted by Xiang et al that included >450,000 patients with cancer (of which 12,143 had brain or central nervous system cancer) compared the risk of secondary tumors following treatment with IMRT and 3D-CRT across cancer types. After a mean 5 years follow-up, multivariate, matched analysis showed no difference in risk of secondary cancers between IMRT and 3D-CRT (OR 1.00, 95% CI 0.98 to 1.03). These results were consistent when limited to patients who had not received chemotherapy (OR 1.01, 95% CI 0.96 to 1.06).

Section Summary: Malignant Brain Tumors
Dosimetry studies have demonstrated lower radiation exposure to organs at risk with IMRT treatment plans than with 3D-CRT treatment plans. Limited comparative evidence has shown lower rates of hearing loss with IMRT than with conventional RT. The evidence appears to be consistent in supporting lower neurotoxicity associated with IMRT. No conclusions can be made about the efficacy of IMRT compared with conventional RT.

Benign Brain Tumors

Clinical Context and Therapy Purpose
The purpose of IMRT in patients who have benign brain tumors is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

The question addressed in this evidence review is: Does treatment with IMRT improve health outcomes in individuals with benign brain tumors?

The following PICO was used to select literature to inform this review.

**Patients**
The relevant population of interest is individuals with benign brain tumors.

**Interventions**
The therapy being considered is IMRT.

Radiotherapy is an integral component of treating many brain tumors, both benign and malignant. 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. IMRT is usually administered by radiation oncologists in an outpatient setting.

**Comparators**
The following therapy is currently being used: 3D-CRT.

Treatment planning evolved by using 3D images, typically from 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.

The comparator being used in this evidence review is 3D-CRT, which is performed by radiation oncologists.

**Outcomes**
The general outcomes of interest are OS, recurrence-free survival (locoregional control), reductions in symptoms, and treatment-related adverse events. A proposed benefit of IMRT is to reduce toxicity to adjacent structures, allowing dose escalation to the target area and fewer breaks in treatment courses due to a reduction in side effects. However, this may come with a loss of locoregional control and OS due to the factors discussed above. The time frame for outcome measures varies from short-term management of toxicity and symptoms to long-term procedure-related complications, cancer progression or recurrence, and OS.
Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Case Series
The evidence for the use of IMRT in patients with benign brain tumors consists mostly of case series. Previously discussed dosimetry studies, which evaluated patients with malignant brain tumors, should be generalizable to patients with benign tumors.

Milker-Zabel et al (2007) reported on results of treatment of complex-shaped meningiomas at the skull base with IMRT. Ninety-four patients received RT as primary treatment (n=26), for residual disease after surgery (n=14), or after local recurrence (n=54). Tumor histology, classified using the World Health Organization, was grade 1 in 54.3%, grade 2 in 9.6%, and grade 3 in 4.2%. Median follow-up was 4.4 years. The overall local tumor control rate was 93.6%. After IMRT, 69 patients had stable disease (by CT or magnetic resonance imaging [MRI]), and 19 had a tumor volume reduction. Six patients had local tumor progression on MRI at a median of 22.3 months after IMRT. In 39.8% of patients, preexisting neurologic deficits improved. Treatment-induced loss of vision was seen in 1 of 53 re-irradiated patients with a grade 3 meningioma 9 months after retreatment with IMRT.

Mackley et al (2007) reported on outcomes of treating pituitary adenomas with IMRT. A retrospective chart review was conducted on 34 patients treated between 1998 and 2003. Median follow-up was 42.5 months. Radiographic local control was 89% and, among patients with secretory tumors, 100% had a biochemical response. One patient required salvage surgery for disease progression, resulting in a clinical PFS of 97%. One patient who received more than 46 Gy experienced optic neuropathy 8 months after radiation.

Sajja et al (2005) reported on outcomes for 35 patients with 37 meningiomas treated with IMRT. Tumor histology was benign in 35 tumors and atypical in 2 tumors. The median CT with MRI follow-up was 19.1 months (range, 6.4-62.4 months). Fifty-four percent of the meningiomas had received surgery or radiosurgery before IMRT, and 46% were treated with IMRT, primarily after diagnosis was established by CT or MRI. Three patients had local failure after
treatment. No long-term complications from IMRT were documented among the 35 patients.

A more recent case series (Rogers et al, 2020) included 57 patients with new or recurrent meningioma (WHO Grade 2 or 3) treated with 60 Gy high dose and 54 Gy low dose IMRT following resection. Three year PFS was 58.8% and overall survival at a mean followup of 4 years was 78.6%. Serious adverse events were rare (1.9%).

Section Summary: Benign Brain Tumors
The evidence on IMRT for treating benign brain tumors includes case series. Case series results have consistently shown with low radiation toxicity but have not demonstrated better tumor control or improved survival with IMRT vs other RT 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.

Brain Metastases
IMRT can deliver additional radiation boosts to specific metastases concurrent with whole-brain radiotherapy (WBRT). Clinicians have treated patients using this RT technique rather than treating them separately with WBRT and stereotactic radiosurgery (SRS), the latter having been shown to be more effective than WBRT alone in an RCT.

Clinical Context and Therapy Purpose
The purpose of IMRT to avoid hippocampal exposure in patients who have brain metastases is to provide a treatment option that is an alternative to or an improvement on existing therapies.

Brain metastases occur in up to 40% of adults with cancer and can shorten survival and detract from the quality of life. Many patients who develop brain metastases will die of progressive intracranial disease. Among patients with good performance status, controlled extracranial disease, favorable prognostic features, and solitary brain metastasis, randomized studies have shown that surgical excision followed by WBRT prolongs survival. SRS can replace surgery in certain circumstances, delivering high single doses to discrete metastases. For bulky cerebral metastases, level 1 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 2" or SRS) and its additional labor and expense. Another indication for the use of IMRT in WBRT is to avoid radiation exposure to the hippocampus. It is thought that avoiding the hippocampus may minimize cognitive decline associated with WBRT.

The question addressed in this evidence review is: Does treatment with IMRT improve health outcomes in individuals with brain metastases when it is necessary to avoid hippocampal exposure?
The following PICO was used to select literature to inform this review.

**Patients**
The relevant population of interest is individuals with brain metastases.

**Interventions**
The therapy being considered is IMRT to avoid hippocampal exposure. IMRT is provided by radiation oncologists in an outpatient setting.

**Comparators**
The following therapy is currently being used: WBRT. WBRT is performed by radiation oncologists in an outpatient clinical setting.

**Outcomes**
The general outcomes of interest are OS, recurrence-free survival, reductions in symptoms and other functional outcomes, and treatment-related adverse events. A proposed benefit of IMRT is to reduce toxicity to adjacent structures, allowing dose escalation to the target area and fewer breaks in treatment courses due to a reduction in side effects. However, this may come with a loss of locoregional control and OS due to the factors discussed above. The time frame for outcome measures varies from short-term management of toxicity and symptoms to long-term procedure-related complications, cancer progression or recurrence, and OS.

**Review of Evidence**

**Randomized Controlled Studies**
Dosimetry studies have previously established techniques that avoided radiation exposure to this region but still provided coverage and conformality to the remaining brain. Dosimetry studies alone have not been sufficient to establish IMRT as a standard treatment because the toxic effects of radiation on the hippocampus are less well established.

Brown et al (2020) reported results from a phase III trial of 518 patients with brain metastases that assessed the comparative effectiveness of hippocampal-avoiding WBRT (HA-WBRT) using IMRT with conventional WBRT; both groups received memantine. Study inclusion criteria required that patients have no brain metastases outside a 5-mm margin around either hippocampus (Table 1). The primary outcome was time to loss of cognitive function, though OS and toxicity were also reported. After a mean 8-months follow-up, HA-WBRT was associated with a reduced loss of cognitive function (adjusted HR 0.74, 95% CI 0.58 to 0.95) without any difference between groups in overall survival (HR, 1.13, 95% CI 0.90 to 1.41) (Table 2). Specifically, at 4-month follow-up, the HA-WBRT showed less loss of executive function (23.3% v 40.4%; P = .01), while at 6 months, there was less decline in learning (11.5% v 24.7%, P = 0.049) and memory (16.4% vs. 33.3%, P=0.02) in the HA-WBRT group. At 6 months, patients in the HA-WBRT plus memantine arm reported less difficulty with remembering things (mean, 0.16 v 1.29; P = .01) and less difficulty speaking...
(mean, 20.20 v 0.45; P = .049) compared with the WBRT plus memantine arm. There was no difference between groups in quality of life at any time point, nor was there a difference between groups in grade 3 or higher toxicity. The study authors noted that the treatment was likely to be most effective in patients with >4 months expected survival, due to cognitive deterioration likely to occur in those with shorter expected survival. This trial indicates evidence of benefit of HA-WBRT versus WBRT on cognitive outcomes (absolute risk difference 10%) and there were no differences in toxicity, intracranial PFS, or OS.

The study has some limitations. At 4-month follow up, only about half of the enrolled participants in both groups provided data for the individual cognitive assessments, because a large proportion of the participants had died. This was also the time point at which a clear difference emerged between groups showing a lower risk of cognitive failure in the HA-WBRT group. In addition, a significantly higher proportion of those allocated to HA-WBRT did not receive treatment 10.7% (28/261) compared to 3.1% (8/257) in the WBRT group (p=0.0016).

Table 1. Summary of RCT Characteristics

<table>
<thead>
<tr>
<th>Study; Trial</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown et al (2020); NRG Oncology CC001 (Phase 3)¹³</td>
<td>US, Canada</td>
<td>220</td>
<td>2015-2018</td>
<td>Adults with brain metastases outside a 5-mm margin around either hippocampus; Karnofsky performance score ≥70; pathologically proven diagnosis of solid tumor malignancy. Prior resection or radiosurgery was allowed.</td>
<td>N=261</td>
</tr>
<tr>
<td>N=257</td>
<td>WBRT (30 Gy in 10 fractions) + memantine (5-7 mg/day titrated to 20-28 mg/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HA-WBRT: hippocampal-avoiding whole body radiation

Table 2. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study; Trial</th>
<th>Cognitive failure, cumulative incidence, 12 months</th>
<th>Overall survival</th>
<th>Quality of Life</th>
<th>Grade ≥3 adverse event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown et al (2020); NRG Oncology CC001 (Phase 3)¹³</td>
<td>N=518</td>
<td>N=518</td>
<td>N=135</td>
<td>N=433</td>
</tr>
<tr>
<td>HA-WBRT + memantine</td>
<td>117/261 (44.8%)</td>
<td>144/261 (55.2%)</td>
<td>5.34 (SD 21.80)</td>
<td>124/211 (58.8%)</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------------</td>
<td>-----------------</td>
<td>----------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>WBRT + memantine</td>
<td>142/257 (55.2%)</td>
<td>150/257 (58.4%)</td>
<td>3.18 (SD 24.98)</td>
<td>137/222 (61.7%)</td>
</tr>
<tr>
<td>HR/Diff/OR/RR (95% CI)</td>
<td>unadjusted HR 0.76 (95% CI 0.60 to 0.98)¹</td>
<td>adjusted HR 0.74 (95% CI 0.58 to 0.95)</td>
<td>ARD -0.10 (95% CI -0.19 to -0.02)</td>
<td>HR, 1.13 (95% CI 0.90 to 1.41)</td>
</tr>
</tbody>
</table>

ARD: absolute risk difference; CI: confidence interval; HR: hazard ratio; MD: mean difference; RR: relative risk.
1 Calculated estimate based on available data

### Table 3. Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation</th>
<th>Blinding</th>
<th>Selective Reporting</th>
<th>Data Completeness</th>
<th>Power</th>
<th>Statistical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown et al (2020); NRG Oncology CC001 (Phase 3)</td>
<td>--</td>
<td>1</td>
<td>--</td>
<td>1</td>
<td>--</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Due to the nature of the treatment, blinding was deemed not possible. However, assessors were blinded for the cognitive outcome.</td>
<td>The proportion of patients withdrawing from the study in the first 6 months ranged from 14% to 27%; the study protocol adjusted for missing data using imputation</td>
<td>Risk estimates were not reported for individual timepoints for the primary outcome &quot;time to cognitive failure&quot;</td>
<td>Risk estimates not reported for quality of life outcome or harms</td>
<td></td>
</tr>
</tbody>
</table>

² Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician. 3. Blinding unclear
⁴ Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
⁵ Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
⁶ Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.
Nonrandomized Comparative Studies
Gondi et al (2014) evaluated IMRT as a method to avoid radiation exposure to the hippocampus and prevent adverse cognitive events in patients receiving WBRT. The Gondi et al (2014) study was a prospective trial with a prespecified comparison to a historical control group derived from a previously conducted clinical trial. The outcomes were standardized cognitive assessments, and health-related quality of life evaluated at baseline and 2 month intervals (out to 6 months).

Of 100 eligible patients, 42 patients were evaluable at 4 months; 17 patients were alive but did not have cognitive testing, and 41 had died. The mean decline in the primary cognitive endpoint was 7.0%, which was significantly less than the 30% decline in the historical control group ($p<0.001$). Median survival in the experimental group was 6.8 months and 4.9 months in the historical control group. Although the trial results suggested that hippocampal-sparing WBRT using IMRT is associated with less cognitive decline, the historical control design adds uncertainty to the conclusion. Because the experimental group had survived longer, even though the radiation dose was intended to be equivalent to the historical control, possible unmeasured patient factors associated with better survival may have also caused less cognitive decline. The trial did not provide conclusive evidence that hippocampal-sparing IMRT causes less cognitive decline.

Case Series
A retrospective study by Zhou et al (2014) evaluated the feasibility of WBRT plus simultaneous integrated boost with IMRT for inoperable brain metastases of non-small-cell lung cancer. Twenty-nine non-small-cell lung cancer patients with 87 inoperable brain metastases were included. All patients received WBRT at a dose of 40 Gy and simultaneous integrated boost with IMRT at a dose of 20 Gy concurrent with WBRT in week 4. Prior to each fraction of image-guided IMRT boost, online positioning verification and correction were used to ensure that the set-up errors were within 2 mm by cone beam CT in all patients. The 1-year intracranial control rate, local brain failure rate (BFR), and distant BFR were 63%, 14%, and 19%, respectively. The 2-year intracranial control rate, local BFR, and distant BFR were 42%, 31%, and 36%, respectively. Both the median intracranial PFS and the median OS were 10 months; 6-month, 1-year, and 2-year OS rates were 66%, 41%, and 14%, respectively. Patients had better survival rates when their Score Index for Radiosurgery in Brain Metastases was greater than 5, when they had fewer than 3 intracranial lesions, and when they had a history of epidermal growth factor receptor tyrosine kinase inhibitor treatment. Radiation necrosis was observed in 3 (3.5%) lesions after RT. Grades 2 and 3 cognitive impairment with grade 2 radiation leukoencephalopathy were observed in 4 (14%) patients. No dosimetric parameters were found to be associated with these late toxicities. Patients who received epidermal growth factor receptor tyrosine kinase inhibitor treatment had higher incidences of grades 2 and 3 cognitive impairment with grade 2 leukoencephalopathy. This evidence would suggest WBRT plus simultaneous integrated boost with IMRT is a tolerable treatment for non-small-cell lung cancer patients with inoperable brain metastases. However, the evidence does not permit conclusions about efficacy.
Section Summary: Brain Metastases
For the treatment of brain metastases, IMRT has been investigated as a technique to avoid hippocampal radiation exposure when delivering WBRT and to deliver additional radiation to specific areas of the brain as a substitute for SRS. Evidence from randomized and nonrandomized studies found IMRT associated with better cognitive outcomes versus WBRT and historical controls. Evidence regarding improvements in other health outcomes is not definitive.

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 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. 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 a randomized trial, nonrandomized studies and case series. Relevant outcomes are OS, disease-specific survival, functional outcomes, and treatment-related morbidity. One randomized trial and one prospective nonrandomized comparison study using IMRT to avoid hippocampal exposure showed less cognitive decline with IMRT than with either conventional WBRT or prespecified historical controls. The evidence is sufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Clinical Input From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an
endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 3 specialty medical societies (8 reviewers) and 3 academic medical centers (3 reviewers) while this policy was under review in 2012. There was a near-uniform consensus that intensity-modulated radiotherapy (IMRT) to treat central nervous system tumors should be considered medically necessary, particularly for tumors in close proximity to critical structures. Reviewers considered the evidence sufficient that IMRT is regarded equally effective as 3-dimensional conformal radiotherapy; further, given the possible adverse events that could result if nearby critical structures receive toxic radiation doses (eg, blindness), IMRT dosimetric improvements should be accepted as meaningful evidence for its benefit.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network
The National Comprehensive Cancer Network Clinical Practice Guidelines Central Nervous System (v. 2.2020) support the use of radiotherapy (including IMRT) for low-grade and high-grade gliomas. "When RT [radiotherapy] is given to patients with low-grade gliomas, it is administered with restricted margins...Every attempt should be made to decrease the RT dose outside the target volume. This can be achieved with 3-dimensional planning or intensity-modulated RT (IMRT)." For high-grade gliomas, “[c]onformal techniques including 3D-CRT and IMRT for performing focal brain irradiation are recommended.”

For patients with brain metastases and a prognosis of 4 months or greater, the guidelines recommend considering hippocampal-sparing WBRT and memantine during and after WBRT for a total of 6 months.

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.

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.

Ongoing and Unpublished Clinical Trials
Some currently unpublished or uncompleted trials that might influence this review are listed in Table 4.
### Table 4. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02393131</td>
<td>Neurocognitive Outcome of Conformal Whole Brain Radiotherapy With or Without Hippocampal Avoidance for Brain Metastases: A Phase II Single Blind Randomized Trial</td>
<td>60</td>
<td>Aug 2019</td>
</tr>
<tr>
<td>NCT02147028</td>
<td>Hippocampal Sparing Whole Brain Radiotherapy vs Conventional Whole Brain Radiotherapy in Patients With Brain Metastases (HIPPO)</td>
<td>84</td>
<td>Jan 2020</td>
</tr>
<tr>
<td>NCT04397679</td>
<td>Partial Brain Radiation Therapy, Temozolomide, Chloroquine, and Tumor Treating Fields Therapy for the Treatment of Newly Diagnosed Glioblastoma</td>
<td>10</td>
<td>March 2022</td>
</tr>
<tr>
<td>NCT02635009</td>
<td>Randomized Phase II/III Trial of Prophylactic Cranial Irradiation With or Without Hippocampal Avoidance for Small Cell Lung Cancer</td>
<td>304</td>
<td>Apr 2027</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

### REFERENCES


**Billing Coding/Physician Documentation Information**

77301 Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications

77338 Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan

77385 Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple

77386 Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; complex

77387 Guidance for localization of target volume for delivery of radiation treatment delivery, includes intrafraction tracking, when performed

G6001 Ultrasonic guidance for placement of radiation therapy fields

G6002 Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy

G6015 Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session

G6016 Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session

**ICD-10 Codes**

C71.0- Malignant neoplasm of brain, code range

C71.9

C72.0- Malignant neoplasm of spinal cord, cranial nerves and other parts of central nervous system, code range

C72.9

C79.31- Secondary malignant neoplasm of brain and cerebral meninges, code

C79.32 Range

C79.40- Secondary malignant neoplasm of other and unspecified parts of nervous
In 2015 Codes 0073T and 77418 were deleted.

The following CPT codes are used for simple and complex intensity-modulated radiotherapy (IMRT) delivery:

77385: Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple
77386: complex.

The Centers for Medicare and Medicaid Services decided not to implement these CPT codes and instead created HCPCS G codes with the language of the previous CPT codes. So the following codes may be used for IMRT:

G6015: Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
G6016: Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session.

Code 77301 remains valid:

77301: Intensity-modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications.

The following CPT code may also be used:

77338: Multi-leaf collimator (MLC) device(s) for intensity-modulated radiation therapy (IMRT), design and construction per IMRT plan.

Code 77338 is to be reported only once per IMRT plan.

**Additional Policy Key Words**

N/A

**Policy Implementation/Update Information**

<table>
<thead>
<tr>
<th>Date</th>
<th>Update Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/1/13</td>
<td>New policy; may be considered medically necessary.</td>
</tr>
<tr>
<td>6/1/14</td>
<td>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.</td>
</tr>
<tr>
<td>1/1/2015</td>
<td>New HCPCS codes. No policy statement changes.</td>
</tr>
<tr>
<td>6/1/15</td>
<td>Title changed from “radiation therapy” to “radiotherapy” to be consistent with other MPRM policies. Policy statements unchanged.</td>
</tr>
</tbody>
</table>
6/1/16 No policy statement changes.
10/1/16 For other indications, policy statement changed to investigational.
6/1/17 No policy statement changes.
6/1/18 No policy statement changes.
6/1/19 No policy statement changes.
6/1/20 No policy statement changes.
9/1/20 Added policy statement that Hippocampal-avoiding iIMRT may be considered medically necessary for individuals with brain tumor metastases outside a 5-mm margin around either hippocampus and expected survival ≥4 months.

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.