

Intensity Modulated Radiotherapy (IMRT) for Central Nervous System (CNS) Tumors

Effective: October 1, 2018

Next Review: August 2019

Last Review: September 2018

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

IMRT is a form of radiation therapy that conforms closely to the targeted tumor shape and allows higher doses of radiation to be delivered while minimizing toxicity to surrounding healthy tissues.

MEDICAL POLICY CRITERIA

- I. Intensity modulated radiotherapy (IMRT) may be considered **medically necessary** for primary and metastatic tumors of the central nervous system for tumors in close proximity to organs at risk, when comparative 3D versus IMRT dose/volume histograms are submitted AND the summary analysis (table preferred; with preauthorization request) is completed demonstrating that only through IMRT can published dose/volume constraints be met for organs at risk (quality assurance procedures are not required for preauthorization).

Example table ([Click here for a template to use](#)):

Summary Analysis of 3D vs IMRT Planning				
Organ(s) At Risk	Quantec Constraint	3D	IMRT	Can constraint

				only be met with IMRT?
Example: Brain stem	Max < 54 Gy	62 Gy	52 Gy	Yes
Example: Brain stem	Max < 54 Gy	62 Gy	58 Gy	No
Example: Brain stem	Max < 54 Gy	53 Gy	51 Gy	No

- II. Intensity modulated radiotherapy (IMRT) may be considered **medically necessary** for central nervous system tumors when there is documented prior radiation treatment to the planned target volume.
- III. Intensity-modulated radiotherapy (IMRT) is considered **not medically necessary** for the treatment of central nervous system tumors not meeting the criteria above.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome. Quality assurance for 3D and IMRT submitted plans are not required with a preauthorization request.

- Clinical history, physical/chart notes, and relevant imaging reports documenting that the policy criteria are met for medical necessity.
- For tumors close to organ(s) at risk, the provider must submit comparative dose/volume histograms and completed analysis as detailed in Criterion I. above. The submitted information must demonstrate the need for IMRT to meet dose constraints not achievable through 3D planning. The best way to ensure criteria are met is to submit the provided summary analysis table. If using the table, please ensure all components are completed prior to submission. If any of these items are not provided it could impact our review and decision outcome.

ORGANS AT RISK

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. At-risk organs may include temporal lobe, hippocampus, brain stem, spinal cord, cochlea and eye structures including optic nerve and chiasm, lens, retina and lacrimal gland.

CROSS REFERENCES

1. [Charged-Particle \(Proton\) Radiotherapy](#), Medicine, Policy No. 49
2. [Intensity Modulated Radiotherapy \(IMRT\) of the Thorax](#), Medicine, Policy No. 136
3. [Intensity Modulated Radiotherapy \(IMRT\) of the Prostate](#), Medicine, Policy No. 137
4. [Intensity Modulated Radiotherapy \(IMRT\) of the Head and Neck](#), Medicine, Policy No. 138
5. [Intensity-Modulated Radiotherapy \(IMRT\) of the Abdomen and Pelvis](#), Medicine, Policy No. 139
6. [Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy](#), Surgery, Policy No. 16

RADIOTHERAPY AND BRAIN TUMORS

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

For benign and low-grade brain tumors, gross total resection remains the primary goal. However, RT may be used in 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 RT even after gross total resection to reduce the risk of local recurrence. Therefore, RT, either definitive or in the postoperative adjuvant setting, remains an integral component in the management of residual, recurrent, and/or progressive benign and low-grade brain tumors for maximizing local control.^[2]

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) or stereotactic radiotherapy to the post resection cavity prolongs survival.^[3] Stereotactic radiosurgery (SRS) may be able to replace surgery in certain circumstances, delivering obliteratively high single doses to discrete metastases. 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 Radiotherapy

Over the past several decades, methods to plan and deliver RT have evolved in ways that permit more precise targeting of tumors with complex geometries. Most early trials used two-dimensional treatment planning based on flat images and radiation beams with cross-sections of uniform intensity that were sequentially aimed at the tumor along two or three intersecting axes. Collectively, these methods are termed “conventional external beam RT.”

Three-Dimensional Conformal Radiotherapy

Treatment planning evolved by using three-dimensional images, usually from computed tomography (CT) scans, to delineate the boundaries of the tumor and discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Computer algorithms were developed to estimate cumulative radiation dose delivered to each volume of interest by summing the contribution from each shaped beam. Methods also were developed to position the patient and the radiation portal reproducibly for each fraction and immobilize the patient, thus maintaining consistent beam axes across treatment sessions. Collectively, these methods are termed three-dimensional conformal radiotherapy (3D-CRT).

Intensity-Modulated Radiotherapy

IMRT, which uses computer software and CT and magnetic resonance imaging (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.

Because 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.

EVIDENCE SUMMARY

BACKGROUND

Multiple-dose planning studies have generated 3D-CRT and intensity-modulated radiotherapy (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.

Evidence from randomized controlled trials comparing IMRT with other radiation techniques is needed in order to establish safety (e.g., toxicity) and efficacy (i.e., impact on clinical outcomes such as survival) of IMRT in the treatment of tumors of the central nervous system (CNS).

The available evidence on IMRT for treatment of tumors of CNS comes from observational studies (retrospective comparisons, single arm studies) with methodological limitations such as

small sample sizes and heterogeneous study populations. A significant number of the available studies are dose planning reports. Only a limited number of studies address clinical outcomes (e.g., overall survival, tumor control). These studies report inconsistent findings. However, the available studies consistently report better sparing of healthy tissues and reduced toxicity in IMRT-treated patients.

HIGH-GRADE MALIGNANT TUMORS

Systematic Reviews

Amelio (2010) conducted a systematic review on the clinical and technical issues of using IMRT in newly diagnosed glioblastoma multiforme (GBM).^[4] The articles included in the review were through December 2009 and included 17 studies (nine related to dosimetric data and technical considerations, seven to clinical results, and one to both dosimetric and clinical results) for a total of 204 treated patients and 148 patient datasets used in planning studies. No randomized controlled studies (RCTs) were identified, and a meta-analysis was not performed.

For the six papers related to planning studies that compared either 3D-CRT versus IMRT, one study 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, $p < 0.001$)^[5]; the remaining studies suggested that IMRT and 3D-CRT provide similar PTV coverage, with differences between 0 and 1%. Target dose conformity was found to be improved with IMRT.

The organs at risk (OAR) typically under consideration in the studies were the brainstem, optic chiasm, optic nerves, lens and retina. In general, IMRT allowed better sparing of the OAR than 3D-CRT but with considerable variation from study to study.

The eight studies that included clinical results included three retrospective, one prospective Phase I and IV prospective Phase II single institution studies. Of these eight studies, two used conventional total dose and dose per fraction, two used a hypofractionated regimen, and in the remaining, a hypofractionated scheme using a simultaneous integrated boost. Chemotherapy was administered in six of eight series, concomitantly with radiation and in the adjuvant phase. Median follow-up ranged from 8.8 and 24 months. Almost all patients (96%) were able to complete the treatment without interruption/discontinuation due to toxicity. Acute toxicity was reported as negligible with grade-3 side effects observed in only two studies at rates of 7% and 12%. Grade-4 toxicity was recorded in only one series with an absolute rate of 3%. Data for late toxicities were available in 6/8 studies, with one study recording grade 4 side effects with an incidence of 20%. One-year and two-year overall survival (OS) varied between 30% and 81.9% and between 0% and 55.6%, respectively. When OS was reported as a median time, its value ranged from 7 to 24 months. Progression-free survival (PFS) ranged from 0% and 71.4% at one year and 0% and 53.6% at two years. Median PFS was reported as ranging from 2.5 to 12 months.

The authors also carried out a comprehensive qualitative comparison with data reported in the literature on similar non-IMRT clinical studies and offered the following conclusions. The results of the planning comparisons showed 3D-CRT and IMRT techniques provide similar results in terms of target coverage, IMRT is somewhat better than 3D-CRT in reducing the maximum dose to the OAR, although the extent varied from case to case, IMRT is clearly better than 3D-CRT in terms of dose conformity and sparing of the healthy brain at medium to

low doses and that (in general) there were no aspects where IMRT seemed worse than 3D-CRT.

This evidence is limited by a number of factors. There is an absence of comparative studies with clinical outcomes, all of the studies were small in size, from a single institution, a majority of patients (53%) were retrospectively analyzed, and the administration of chemotherapy was variable across studies.

Nonrandomized Studies

A representative sample of the comparative studies on dose planning and the single-arm studies with clinical outcomes are discussed below.

Paulsson (2014) compared treatment failure rates in GBM patients treated with IMRT or 3D conformal RT with differing target margins (the size of the region between tumor and edge of the planning target volume).^[6] This comparison indirectly evaluated IMRT and older techniques, because the use of IMRT has been accompanied by changes in treatment planning. In 161 patients, treatment margins were not associated with treatment failure. There was no difference in treatment failure between IMRT and 3D-CRT.

Chen (2013) assessed whether IMRT improved clinical outcomes compared with 3D-CRT in patients with GBM in a retrospective study of 54 patients.^[7] The median follow-up was 13 months. Of the 54 patients, 50 (92.6%) completed the combined modality treatment (patients underwent postoperative IMRT or 3D-CRT with concurrent and adjuvant temozolomide). The one-year overall survival rate (OS) was 79.6%. The pattern of failure was predominantly local. A comparative analysis revealed that no statistical difference was observed between the IMRT group (n = 21) and the 3D-CRT group (n = 33) for one-year OS (89.6% vs. 75.8%, P = 0.795), or one-year progression-free survival (PFS) (61.0% vs. 45.5%, P = 0.867). In dosimetric comparison, IMRT seemed to allow better sparing of organs at risk than 3D-CRT (P = 0.050, P = 0.055). However, there was no significant difference for toxicities of irradiation between the IMRT group and the 3D-CRT group. The authors concluded that preliminary results suggest that delivering standard radiation doses by IMRT is unlikely to improve local control or overall survival for GBM compared with 3D-CRT.

MacDonald (2007) compared the dosimetry of IMRT and 3D-CRT in 20 patients treated for high-grade glioma.^[8] Prescription dose and normal-tissue constraints were identical for the 3D-CRT and IMRT treatment plans. The IMRT plan yielded superior target coverage as compared with the 3D-CRT plan. The IMRT plan reduced the percent volume of brainstem receiving a dose greater than 45 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< or=0.0001), respectively. With IMRT, the percent volume of optic chiasm receiving more than 45 Gy was reduced by 30.4% (p=0.047). As compared with 3D-CRT, IMRT significantly increased the tumor control probability (p< or=0.0005) and lowered the normal-tissue complication probability for brain and brain stem (p<0.033).

Narayana (2006) reported the outcomes of 58 consecutive patients with high-grade gliomas treated with IMRT.^[9] GBM accounted for 70% of cases and anaplastic gliomas for the remainder. Surgery consisted of biopsy alone in 26% of patients and of those that underwent resection, 63% had total or near total resection and 37% had partial resection. Eighty percent of patients received adjuvant chemotherapy. Median follow-up was 24 months. Acute neurotoxicities were grade 1 or 2 in 36% of patients, grade 3 in 7%, and grade 4 in 3%. Late

toxicities were grade 1 or two in 10%, grade 3 in 7%, and no grade four or five. Freedom from late neurotoxicity at 24 months was 85%. Median OS for the anaplastic astrocytomas was 36 months and nine months for the GBM group. From these data, the authors concluded that the use of IMRT in high-grade gliomas does not appear to improve survival

Narayana (2006)^[9] also performed a comparison of the IMRT treatment plans with 3D plans performed in 20 patients out of 58 total in that case series. Regardless of tumor location, IMRT did not improve PTV target coverage compared to 3D planning. IMRT decreased the maximum dose to the spinal cord, optic nerves, and eye by 16%, 7%, and 15%, respectively. These data indicate that IMRT may result in decreased late toxicities.

Huang (2002) compared ototoxicity with use of conventional (2D) radiotherapy (n=11) versus IMRT (n=15) in 26 pediatric patients with medulloblastoma.^[10] All of the patients also received chemotherapy. When compared to conventional radiotherapy, IMRT delivered 68% of the radiation dose to the auditory apparatus, but full doses to the desired target volume. Median follow-up for audiometric evaluation was 51 months (9-107 months) for the conventional radiotherapy group and 18 months (8-37 months) for the group that received IMRT. Thirteen percent of the IMRT group had grade 3 or 4 hearing loss, compared to 64% of the conventional radiotherapy group (p<0.014).

Section Summary

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

BENIGN TUMORS

Reddy (2012) published a prospective phase II trial (n=24) of patients with newly diagnosed glioblastoma multiforme treated with hypofractionated IMRT with concurrent adjuvant temozolomide.^[11] After a median follow-up of 14 months, there were no grade 3 or higher nonhematologic toxicities and the median overall survival was 16.6 months. There were six patients with suspected recurrence. The authors concluded that treatment was comparable to current standards of care.

Milker-Zabel (2007) reported the results of the treatment of complex-shaped meningiomas of the skull base with IMRT in 94 patients.^[12] Patients received radiotherapy as primary treatment (n=26) postoperatively for residual disease (n=14) or after local recurrence (n=54). Tumor histology was World Health Organization grade 1 in 54.3%, grade two in 9.6%, and grade 3 in 4.2%. Median follow-up was 4.4%. Overall local tumor control was 93.6%. Sixty-nine patients had stable disease (by computed tomography [CT]/magnetic resonance imaging [MRI]), and 19 had a tumor volume reduction after IMRT. Six patients had local tumor progression on MRI 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 one of 53 re-irradiated patients with a grade 3 meningioma nine months after retreatment with IMRT.

Mackley (2007) reported outcomes of treating pituitary adenomas with IMRT.^[13] A retrospective chart review was conducted on 34 patients treated between 1998 and 2003 at the Cleveland Clinic. 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 progressive disease, resulting in a clinical PFS of 97%. One patient who received more than 46 Gy experienced optic neuropathy eight months after radiation.

Sajja (2002) reported the outcomes of 35 patients with 37 meningiomas treated with IMRT.^[14] Tumor histology was benign in 35 and atypical in two tumors. The median CT/MRI follow-up was 19.1 months (range 6.4-62.4 months). Fifty-four percent of the meningiomas had been previously treated with surgery/radiosurgery prior to IMRT, and 46% were treated with IMRT, primarily after a diagnosis was established by CT/MRI. Three patients had local failure after treatment. No long-term complications from IMRT were documented among the 35 patients.

Uy (2002) assessed the safety and efficacy of IMRT in the treatment of intracranial meningioma in 40 patients treated between 1994 and 1999.^[15] Twenty-five patients received IMRT after surgery either as adjuvant therapy for incomplete resection or for recurrence, and 15 patients received definitive IMRT after a presumptive diagnosis of meningioma on imaging. Thirty-two patients had skull base lesions and eight had nonskull base lesions. Follow-up ranged from 6 to 71 months (median 30 months). Defined normal structures generally received a significantly lower dose than the target. The most common acute CNS toxicity was mild headache, usually relieved with steroids. One patient experienced Radiation Therapy Oncology Group (RTOG) Grade 3 acute CNS toxicity, and two experienced Grade 3 or higher late CNS toxicity, with one possible treatment-related death. No toxicity was observed with mean doses to the optic nerve/chiasm up to 47 Gy and maximum doses up to 55 Gy. Cumulative five-year local control, PFS, and OS were 93%, 88%, and 89%, respectively.

Section Summary

The evidence on IMRT for the treatment of benign brain tumors includes noncomparative trials and case series. Results are consistent with low radiation toxicity but have not demonstrated better tumor control or improved survival with IMRT vs other radiotherapy techniques. The dose-planning studies evaluating IMRT in patients with malignant tumors should generalize to patients with benign brain tumors because the benefit of minimizing radiation toxicity to sensitive brain areas is identical.

BRAIN METASTASES

A retrospective study, published by Zhou in 2014, was designed to evaluate the feasibility of WBRT plus simultaneous integrated boost (SIB) with IMRT for inoperable brain metastases of NSCLC.^[16] Twenty-nine NSCLC patients with 87 inoperable brain metastases were included. All patients received WBRT at a dose of 40 Gy and SIB boost with IMRT at a dose of 20 Gy concurrent with WBRT in the fourth week. Prior to each fraction of image-guided (IG) IMRT boost, on-line 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 one-year intracranial control rate (ICR), local brain failure rate (BFR), and distant BFR were 63%, 14%, and 19%, respectively. The two-year ICR, local BFR, and distant BFR were 42%, 31%, and 36%, respectively. Both median intracranial PFS and median OS were 10 months. Six-month, one-year, and two-year OS rates were 66%, 41%, and 14%. Patients with Score Index for Radiosurgery in Brain Metastases (SIR) greater than five, number of intracranial lesions less than three and history of epidermal growth factor receptor–tyrosine kinase inhibitor (EGFR-TKI) treatment had better survival. Radiation necrosis was observed in three (3.5%) lesions after radiotherapy. Grades 2 and 3 cognitive impairment with grade two radiation leukoencephalopathy were observed in

four (14%) and four (14%) patients. No dosimetric parameters were found to be associated with these late toxicities. Patients who received EGFR-TKI treatment had higher incidence of grades 2 to 3 cognitive impairment with grade 2 leukoencephalopathy. This evidence suggests WBRT plus SIB with IMRT is a tolerable treatment for NSCLC patients with inoperable brain metastases. However, the evidence does not allow conclusions as to its efficacy.

Edwards (2010) reported outcomes on the use of whole brain radiotherapy (WBRT) with an IMRT boost in 11 patients with metastatic disease to the brain ranging from 25-80 mm in maximum diameter.^[17] Patients were excluded if they had more than four metastases. Histologies of the metastases included primary lung (n=5), breast (n=4), colon (n=1), and kidney (n=1). There were no acute or subacute complications. All tumors showed response on a one-month post-radiotherapy scan. Median follow-up was four months. Four of the 11 patients died of systemic disease six to nine months after radiotherapy. The remaining patients were alive with no evidence of progression of the treated brain disease or local recurrence at two to nine months after radiotherapy. No brain complications occurred to date.

PRACTICE GUIDELINE SUMMARY

NATIONAL COMPREHENSIVE CANCER NETWORK (NCCN)

NCCN guidelines state that “when radiation is given to patients with low grade gliomas, it is administered with restricted margins. Every attempt should be made to decrease the radiation dose outside the target volume. This can be achieved with three-dimensional planning or IMRT.”^[18] With regard to meningiomas, NCCN guidelines state, “Stereotactic or image-guided therapy is recommended when using tight margins or when close to critical structures. Conformal radiation therapy (eg, 3D-CRT, IMRT, VMAT) is recommended to spare critical structures and uninvolved tissue.” NCCN guidelines do not address the use of IMRT in high-grade tumors or metastases of the CNS.

SUMMARY

There is enough research to show that IMRT may provide improved patient outcomes with less adverse events compared to other radiotherapy techniques. Therefore, IMRT may be considered medically necessary for the treatment of central nervous system tumors when the tumor is in close proximity to organs at risk when policy criteria are met or when there is prior radiation to the planned area. IMRT is considered not medically necessary when policy criteria are not met.

REFERENCES

1. Amelio, D, Lorentini, S, Schwarz, M, Amichetti, M. Intensity-modulated radiation therapy in newly diagnosed glioblastoma: a systematic review on clinical and technical issues. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. 2010;97:361-9. PMID: 20926149
2. Gupta, T, Wadasadawala, T, Master, Z, Phurailatpam, R, Pai-Shetty, R, Jalali, R. 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. *International journal of radiation oncology, biology, physics*. 2012;82:756-64. PMID: 21345610
3. Edwards, AA, Keggins, E, Plowman, PN. The developing role for intensity-modulated radiation therapy (IMRT) in the non-surgical treatment of brain metastases. *The British journal of radiology*. 2010;83:133-6. PMID: 20019176
 4. Amelio, D, Lorentini, S, Schwarz, M, Amichetti, M. Intensity-modulated radiation therapy in newly diagnosed glioblastoma: a systematic review on clinical and technical issues. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. 2010 Dec;97(3):361-9. PMID: 20926149
 5. Fuller, CD, Choi, M, Forthuber, B, et al. Standard fractionation intensity modulated radiation therapy (IMRT) of primary and recurrent glioblastoma multiforme. *Radiat Oncol*. 2007;2:26. PMID: 17629934
 6. Paulsson, AK, McMullen, KP, Peiffer, AM, et al. Limited margins using modern radiotherapy techniques does not increase marginal failure rate of glioblastoma. *Am J Clin Oncol*. 2014 Apr;37(2):177-81. PMID: 23211224
 7. Chen, YD, Feng, J, Fang, T, Yang, M, Qiu, XG, Jiang, T. Effect of intensity-modulated radiotherapy versus three-dimensional conformal radiotherapy on clinical outcomes in patients with glioblastoma multiforme. *Chinese medical journal*. 2013 Jun;126(12):2320-4. PMID: 23786946
 8. MacDonald, SM, Ahmad, S, Kachris, S, et al. Intensity modulated radiation therapy versus three-dimensional conformal radiation therapy for the treatment of high grade glioma: a dosimetric comparison. *Journal of applied clinical medical physics / American College of Medical Physics*. 2007;8(2):47-60. PMID: 17592465
 9. Narayana, A, Yamada, J, Berry, S, et al. Intensity-modulated radiotherapy in high-grade gliomas: clinical and dosimetric results. *International journal of radiation oncology, biology, physics*. 2006 Mar 1;64(3):892-7. PMID: 16458777
 10. Huang, E, Teh, BS, Strother, DR, et al. Intensity-modulated radiation therapy for pediatric medulloblastoma: early report on the reduction of ototoxicity. *International journal of radiation oncology, biology, physics*. 2002 Mar 1;52(3):599-605. PMID: 11849779
 11. Reddy, K, Damek, D, Gaspar, LE, et al. Phase II trial of hypofractionated IMRT with temozolomide for patients with newly diagnosed glioblastoma multiforme. *International journal of radiation oncology, biology, physics*. 2012 Nov 1;84(3):655-60. PMID: 22483738
 12. Milker-Zabel, S, Zabel-du Bois, A, Huber, P, Schlegel, W, Debus, J. Intensity-modulated radiotherapy for complex-shaped meningioma of the skull base: long-term experience of a single institution. *International journal of radiation oncology, biology, physics*. 2007 Jul 1;68(3):858-63. PMID: 17379447
 13. Mackley, HB, Reddy, CA, Lee, SY, et al. Intensity-modulated radiotherapy for pituitary adenomas: the preliminary report of the Cleveland Clinic experience. *International journal of radiation oncology, biology, physics*. 2007 Jan 1;67(1):232-9. PMID: 17084541
 14. Sajja, R, Barnett, GH, Lee, SY, et al. Intensity-modulated radiation therapy (IMRT) for newly diagnosed and recurrent intracranial meningiomas: preliminary results. *Technology in cancer research & treatment*. 2005 Dec;4(6):675-82. PMID: 16292888
 15. Uy, NW, Woo, SY, Teh, BS, et al. Intensity-modulated radiation therapy (IMRT) for meningioma. *International journal of radiation oncology, biology, physics*. 2002 Aug 1;53(5):1265-70. PMID: 12128128

16. Zhou, L, Liu, J, Xue, J, et al. Whole brain radiotherapy plus simultaneous in-field boost with image guided intensity-modulated radiotherapy for brain metastases of non-small cell lung cancer. *Radiat Oncol.* 2014;9:117. PMID: 24884773
17. Edwards, AA, Keggin, E, Plowman, PN. The developing role for intensity-modulated radiation therapy (IMRT) in the non-surgical treatment of brain metastases. *The British journal of radiology.* 2010 Feb;83(986):133-6. PMID: 20019176
18. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Central Nervous System Cancers. V.1.2018. [cited 9/10/2018]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/cns.pdf
19. BlueCross BlueShield Association Medical Policy Reference Manual "Intensity-Modulated Radiotherapy: Central Nervous System Tumors." Policy No. 8.01.59

CODES

NOTE: The correct code to use for image fusion performed to provide enhanced delineation of target and normal critical structures is CPT code 77399 (Unlisted procedure, medical radiation physics, dosimetry and treatment devices, and special services); however, it is considered part of the treatment planning.

Codes	Number	Description
CPT	77301	Intensity modulated radiotherapy plan, including dose volume histograms for target and critical structure partial tolerance specification
	77338	Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan (new code 1/1/10)
	77385	Intensity modulated radiation treatment deliver (IMRT), includes guidance and tracking, when performed; simple
	77386	;complex
HCPCS	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

Date of Origin: May 2010