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Medical Policy Manual Surgery, Policy No. 213

Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy of Intracranial, Skull Base, and Orbital Sites

Effective: August 1, 2019

Next Review: July 2020
Last Review: July 2019

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

Stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) or stereotactic ablative radiotherapy (SABR) are radiotherapy techniques that use highly focused radiation beams to treat both neoplastic and non-neoplastic conditions, in contrast to traditional external radiation beam therapy, which involves the use of relatively broad fields of radiation over a number of sessions that may occur over weeks to months.

MEDICAL POLICY CRITERIA

I. Stereotactic radiosurgery (SRS) and Stereotactic Body Radiation Therapy (SBRT), also known as Stereotactic Ablative Body Radiotherapy (SABR), may be considered **medically necessary** for initial treatment or treatment of recurrence for any of the following indications:

   A. Primary neoplasms of the CNS (See Policy Appendix I at the end of the policy), including but not limited to low grade gliomas and high-grade gliomas

   B. Metastatic lesion(s) to the CNS (solitary or multiple) in patients with a current Karnofsky performance score greater than or equal to 60 or a current ECOG score less than or equal to 2 (See Policy Guidelines)

C. Acoustic neuromas (Vestibular Schwannomas)

D. Arteriovenous malformations

E. Chordomas and chondrosarcomas of the skull base

F. Craniopharyngiomas

G. Epilepsy when the following criteria are met:

1. Seizures are ongoing despite treatment with at least two antiepileptic regimens; and
2. Documentation of clinical agreement of medical appropriateness from a neurosurgeon or multidisciplinary body of physician consultants.

H. Essential tremor or Parkinson's disease when the following criteria are met:

1. Symptoms are ongoing despite treatment with at least two drug regimens; and
2. Documentation of clinical agreement of medical appropriateness from a neurosurgeon or multidisciplinary body of physician consultants.

I. Hemangioblastoma within intracranial, skull base, and orbital sites

J. Hemangiopericytoma within intracranial, skull base, and orbital sites

K. Glomus jugulare and Glomus tympanicum tumors

L. Meningiomas, benign, atypical, or malignant

M. Pituitary adenomas

N. Trigeminal neuralgia (tic douloureux) refractory to medical management

O. Uveal melanoma

II. Stereotactic radiosurgery and stereotactic body radiation therapy (also known as Stereotactic ablative body radiotherapy) are considered **investigational** for all other intracranial, skull base, and orbital indications including but not limited to cavernous malformations, choroidal neovascularization (CNV), chronic pain, and functional disorders other than trigeminal neuralgia and essential tremor.

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

POLICY GUIDELINES

For the purposes of this policy, neoplasm is defined as “an abnormal mass of tissue that results when cells divide more than they should or do not die when they should. Neoplasms may be benign (not cancer), or malignant (cancer).”[1]

PERFORMANCE STATUS MEASUREMENT

Performance status is frequently used in oncology practice as a variable in determining prognosis and management strategies. Either the Karnofsky Performance Status (KPS) or the Eastern Cooperative Oncology Group (ECOG) Performance Status scoring systems may be used.

Karnofsky Performance Status

100	Normal, without symptoms
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort; some signs or symptoms of disease
70	Cares for self; unable to carry on normal activity or do active work
60	Requires occasional assistance; able to care for most personal needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospitalization is indicated
20	Very sick; active support treatment is necessary
10	Moribund; fatal processes progressing rapidly

ECOG Performance Status

0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.

FRACTIONATION

Fractionated stereotactic radiotherapy refers to when SRS or SBRT are performed in 1-10 treatments focused upon a specific site. SRS is commonly delivered in 1-5 fractions and SBRT or SABR is commonly delivered in 1-5 fractions but may be delivered in as many as 10 fractions.

DOSE CONSTRAINT REFERENCES

Radiation Therapy Oncology Group (RTOG) Radiation Dose Constraints

Available from: https://en.wikibooks.org/wiki/Radiation_Oncology/Toxicity/RTOG

Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC)

Available from: https://en.wikibooks.org/wiki/Radiation_Oncology/Toxicity/QUANTEC

LIST OF INFORMATION NEEDED FOR REVIEW

REQUIRED DOCUMENTATION:

The information below **must** be submitted for review to determine whether policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History/Physical and Chart notes, including requirements as outlined by the policy criteria, as applicable to the indication for treatment.
- As applicable, documentation of sites, size and number of lesions
- As applicable, documented ECOG score or Karnofsky performance score

CROSS REFERENCES

1. Charged-Particle (Proton) Radiotherapy, Medicine, Policy No. 49
2. Intensity Modulated Radiotherapy (IMRT) of the Central Nervous System (CNS), Head, Neck, and Thyroid, Medicine, Policy No. 164
3. Intensity Modulated Radiotherapy (IMRT) of the Thorax, Abdomen, and Pelvis, Medicine, Policy No. 165
4. Intensity Modulated Radiotherapy (IMRT) for Breast Cancer, Medicine, Policy No. 166
5. Intensity Modulated Radiotherapy (IMRT) for Tumors in Close Proximity to Organs at Risk, Medicine, Policy No. 167
6. Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy for Tumors Outside of Intracranial, Skull Base, or Orbital Sites, Surgery, Policy No. 214

BACKGROUND

Stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) rely on three-dimensional imaging to localize the therapy target. SRS and SRBT have been used for a range of malignant and non-malignant conditions. Because they are more targeted than traditional external radiation therapy, SRS and SRBT are often used for treatment at sites that are difficult to reach via surgery, located close to other vital structures, or subject to movement within the body. The term SBRT will be used to describe treatment also referred to as stereotactic ablative body radiotherapy (SABR).

SRS and SBRT (or SABR) employ similar technological "stereotactic" sophistication with elements of advanced pretreatment imaging for localization of target(s), patient immobilization, control of breathing associated tumor movement, focally targeted treatment planning, and daily image guidance to ensure precise delivery of high daily doses of radiation. As commonly used in the medical literature, SRS refers to intracranial treatments and SBRT refers to extracranial treatments. Alternatively, SRS and SBRT may be defined independent of whether treatment is directed to intra or extra cranial tumors volumes. According to this definition, when such treatment is given as a single fraction, it may be referred to as SRS, and when it is delivered in 2-10 fractions it may be referred to as SBRT or SABR.

The fractionation used for SRS and SBRT is referred to as “hypofractionated” because it is fewer treatments than those used for conventional external beam radiotherapy.” Fractionation of stereotactic radiotherapy aims to optimize the therapeutic ratio; that is the ratio between tumor control and late effects on normal tissues. The main advantage of fractionation is that it allows higher total doses to be delivered to the tumor because of increased tolerance of the surrounding healthy tissues to each individual, fractionated dose. In addition, some lesions such as large arteriovenous malformations may require more than one procedure to complete the obliteration process.

SRS and SBRT can be administered by several types of devices that are distinguished by their source of radiation, including particle beams (e.g., proton), gamma radiation from cobalt-60 sources, or high-energy photons from linear accelerator (LINAC) systems. The Gamma Knife and linear accelerator systems (including the Cyberknife®) are similar in concept; both use multiple photon radiation beams that intersect at a stereotactically determined target, thus permitting higher doses of radiation delivery with sparing of surrounding normal tissues. The differences between the two relate to how the energy is produced (i.e., through decaying cobalt-60 in the gamma knife devices, or from x-rays in the linear accelerator system) and the number of energy sources used (i.e., multiple energy sources in the gamma knife versus one in the linear accelerator system).

IMAGE-GUIDED RADIOSURGERY OR RADIOTHERAPY

Image-guided radiosurgery or radiotherapy is a relatively new development collectively describing units with real-time image guidance systems. Examples include the Cyberknife® device, BrainLAB Novalis®, TomoTherapy®, and LINAC with computerized tomography (CT).

REGULATORY STATUS

Several devices that use cobalt 60 radiation (gamma ray devices) for SRS have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The most commonly used gamma ray device is the GammaKnife (Elekta; approved May 1999). Gamma ray emitting devices that use cobalt 60 degradation are also regulated through the U.S. Nuclear Regulatory Commission.

A number of LINAC movable platforms that generate high-energy photons have been cleared for marketing by the FDA through the 510(k) premarket notification process including the Novalis Tx®

(Novalis, Westchester, IL); the TrueBeam STx (Varian Medical Systems, Palo Alto, CA, approved December 2012); and the CyberKnife® System (Accuray, Inc.; approved December 1998). LINAC-based devices may be used for intracranial and extracranial lesions.

Note: Particle radiation can also be used without stereotactic guidance. In this setting, the use of particles is referred to as proton, helium, or neutron radiation *therapy*. Proton or helium ion radiation therapies (RT), intraocular RT for age-related macular degeneration, and electromagnetic navigation bronchoscopy for placement of fiducial markers are considered in separate medical policies. See cross-reference section below.

EVIDENCE SUMMARY

The selection of variables used in the delivery of SRS and SBRT is complex and individualized, requiring selection of the device, radiation dose, and the size and shape of treatment margins All of these variables depend on the location, shape, and radiosensitivity of the target tissue and the function and radiosensitivity of the surrounding tissue. Trials that allow direct comparison of all of the possible variables involved in selecting specific SRS and SBRT methods do not broadly exist making it difficult to draw comparative effectiveness conclusions. Further, for many rare conditions, large comparative studies are unlikely. The evidence below will focus on indications with criteria and investigational indications.

Please note that the evidence review below does not compare specific radiation planning and delivery techniques.

TRIGEMINAL NEURALGIA

Tuleasca published a 2018 systematic review of SRS for trigeminal neuralgia to support the development of a guideline endorsed by the International Society of Stereotactic Radiosurgery (ISRS). A total of 65 studies met inclusion criteria, with a total of 6461 patients. One study was prospective and the remainder were retrospective. Crude rates of hypesthesia ranged from 0% to 68.8% (mean 21.7%, median 19%) for gamma knife surgery (GKS), from 11.4% to 49.7% (mean 27.6%, median 28.5%) for LINAC, and from 11.8% to 51.2% (mean 29.1%, median 18.7%) for CyberKnife radiosurgery. Other toxicities reported were dysesthesias, paresthesias, dry eye, deafferentation pain, and keratitis. Actuarial initial freedom from pain without

medication was reported to be 28.6% to 100% (mean 53.1%, median 52.1%), 17.3% to 76% (mean 49.3%, median 43.2%), and 40% to 72% (mean 56.3%, median 58%) for GKS, LINAC, and CyberKnife radiosurgery, respectively. Recurrence rates were reported as ranges of 0 to 52.2% (mean 24.6%, median 23%), 19% to 63% (mean 32.2%, median 29%), and 15.8% to 33% (mean 25.8%, median 27.2%) for GKS, LINAC, and CyberKnife radiosurgery, respectively. The authors concluded that although the evidence is limited, radiosurgery is a safe and effective therapy for drug-resistant trigeminal neuralgia.

In 2017, Gubian and Rosahl published a meta-analysis of the safety and efficacy of SRS and microsurgery for trigeminal neuralgia. PRISMA guidelines were followed. A total of 53 studies met inclusion criteria. Success rates initially and at last follow-up (>five years after intervention) were 71.1% and 63.8% for SRS and 86.9% and 84% for microsurgery, respectively. Mean percentage of recurrence at 36-months post-intervention was 25% for SRS and 11% for microsurgery (p=0.0015). The length of recurrence-free intervals was not significantly different between SRS and microsurgery (30.45 and 30.55 months, respectively; p=0.987). The difference in incidence of hearing loss was also not significant (SRS 1.51% vs microsurgery 0.74%), but facial dysesthesia was more frequent in the SRS group (2.3% versus 28.8% for microsurgery; p=0.02).

A 2011 Cochrane systematic review of 11 trials of neurosurgical interventions for trigeminal neuralgia found that there was very low-quality evidence for the efficacy of most neurosurgical procedures for trigeminal neuralgia because of the poor quality of the trials.[2] All procedures produced variable pain relief, but many resulted in sensory side effects. There were no studies of microvascular decompression which observational data suggests gives the longest pain relief. Only one study was identified that used radiosurgery. The trial was intended to determine if increasing the nerve length within the SRS treatment volume would change outcomes. The study was stopped before accrual was completed and it was noted that pain measurements using validated scales were not made either before or after surgery.

Other nonrandomized studies and case series have reported on the use of SRS for trigeminal neuralgia.[3-7]

Section Summary

Case series identify improvements in pain related to trigeminal neuralgia after treatment with SRS. Comparative studies that evaluate the use of SRS compared with alternative treatments for trigeminal neuralgia are lacking. Only one study specifically addressed the use of radiosurgery and it was stopped before accrual was completed.

Epilepsy

Barbaro (2018) published the results of the first randomized controlled trial comparing SRS for the treatment of pharmacoresistant unilateral mesial temporal lobe epilepsy to anterior temporal lobectomy (ATL), the ROSE trial.[8] A total of 37 (64%) patients achieved seizure remission, with 16 (52%) in SRS and 21 (78%) in ATL. Noninferiority of SRS compared to ATL was not demonstrated. SRS did not confer sparing of verbal memory deficits compared to ATL. QOL scores improved significantly in the SRS group at 24 months and remained steady at 36 months, in contrast to the ATL group in whom QOL score improvement was immediately noticeable at 12 months. Adverse events were anticipated cerebral edema and related symptoms for some SRS patients, and cerebritis, subdural hematoma, and others for ATL patients. These all resolved with appropriate protocol specified interventions.

A 2018 systematic review by Eekers reported on 16 studies including a total of 170 patients.[9] Methodological quality of the included studies was graded using a modified QUADAS checklist. Limitations of the reviewed studies include a lack of control groups and poorly defined exclusion criteria. SRS was reported to have a positive effect on seizure outcome, defined as the total percentage of radiotherapy-adapted Engel class (RAEC) I and II patients, in 12 studies. No favorable effect on seizure outcome was found in two studies, although these contained only two and three patients, respectively. Toxicities reported include radionecrosis, impaired cognitive functioning, and headache, nausea, and vomiting related to increased intracranial pressure and edema. Subsequent resection was reported in nine of the studies. In those studies, 20% of patients underwent subsequent resection. Reasons reported were persisting seizures, cyst formation, edema, intracranial hypertension, and radionecrosis. Authors concluded that there is only level 4 evidence of primary radiotherapy reducing seizure frequency in adult patients and that prospective randomized trials are needed to determine its value.

McGonigal (2017) performed a systematic review of SRS for drug-resistant epilepsy and assessed the level of evidence according to the PRISMA guidelines.[10] A total of 55 articles met inclusion criteria. Level 2 evidence (prospective studies) indicated that SRS may result in superior neuropsychological outcomes and quality of life compared to microsurgery for mesial temporal lobe epilepsy and that SRS has a better risk-benefit ratio for small hypothalamic harmatomas compared to surgical methods. Only Level 4 evidence (case reports, prospective observational studies, and retrospective case series) was available for the other indications and no Level 1 evidence was identified.

In 2016, Feng published a systematic review and meta-analysis of data from 13 studies on the use of SRS to treat mesial temporal lobe epilepsy.[11] They calculated approximately half of the patients were seizure free over a follow-up period that ranged from six months to nine years (pooled estimate, 50.9%; 95% CI, 38.1% to 63.6%), with an average of 14 months to seizure cessation (pooled estimate, 14.08 months; 95% CI, 11.95 to 12.22 months). Nine of 13 included studies reported data for adverse events, which included visual field deficits and headache (the two most common adverse events), verbal memory impairment, psychosis, psychogenic nonepileptic seizures, and dysphasia. Patients in the individual studies experienced adverse events at rates that ranged from 8%, for nonepileptic seizures, to 85%, for headache.

A 1998 TEC Assessment[12] cited two studies of 11 and 9 patients, respectively, in which radiosurgery was used to treat epilepsy. The subsequent literature search revealed three small studies on the use of radiosurgery for medically refractory epilepsy. Regis (2000)[13] selected 25 patients with mesial temporal lobe epilepsy, 16 of whom provided minimum two-year follow-up. Seizure-free status was achieved in 13 patients, two patients were improved, and three patients had radiosurgery-related visual field defects.

A study by Schrottner (1998)[14] included 26 patients with tumor-related epilepsy, associated mainly with low-grade astrocytomas. Mean follow-up among 24 available patients was 2.25 years. Tumor location varied across patients. Seizures were simple partial in six (three with generalization) and complex partial in 18 (five with generalization, one gelastic). Seizures were eliminated or nearly so in 13 patients. Little improvement was observed in four patients and none in seven. Whang and Kwon (1996)[15] performed radiosurgery in 31 patients with epilepsy associated with nonprogressive lesions. A minimum of one-year follow-up was available in 23 patients, 12 of whom were seizure-free (and three of whom had antiseizure medications

discontinued), two had seizures reduced in frequency, and nine experienced no change. While the Regis series selected a fairly homogeneous clinical sample, the other two studies were heterogeneous. No confirmatory evidence is available on mesial temporal lobe epilepsy. The available evidence from patients with epileptic lesions of various sizes and locations is insufficient to show what factors are associated with favorable outcome.

Section Summary

For individuals with epilepsy refractory to medical management, the evidence on the use of SRS as a treatment for epilepsy includes case reports in primary epileptic disorders and case reports for tumor-related epilepsy. For mesial temporal lobe epilepsy, there is a pilot prospective non-comparative intervention and a single RCT comparing SRS to anterior temporal lobectomy (ATL).

TREMOR AND PARKINSON DISEASE

SRS has been used for the treatment of tremor via stereotactic radiofrequency thalamotomy.

Martínez-Moreno published a systematic review of stereotactic radiosurgery for tremor in association with International Stereotactic Radiosurgery Society practice guidelines.[16] The systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. A total of 34 studies met inclusion criteria. Of these, 30 were retrospective noncomparative studies and 14 studies had fewer than 10 patients. Three studies were prospective and one was a retrospective comparative study. Rates of tremor reduction were similar across the included studies, with an average of 88%. The one comparative study reported similar tremor control rates between SRS, deep brain stimulation, and radiofrequency thermocoagulation. There were fewer permanent complications and longer latency to clinical response following SRS than the two other modalities. The authors concluded based on level IV evidence that SRS for tremor is well-tolerated and effective.

Raju (2017) assessed outcomes of SRS for medically refractory tremor associated with Parkinson disease (PD) in a retrospective analysis of 33 patients.[17] All patients underwent gamma knife thalamotomy. Median follow-up was 23 months (range, 9-144 months). A total of 31 patients (93.9%) experienced improvements in tremor and 23 patients (70.0%) had complete or nearly complete tremor arrest. Improvements in other PD symptoms were also observed, including one patient (3%) with improvements in bradykinesia, three patients (9%) with improvements in rigidity, and three patients (9%) who reduced their dosage of dopa after SRS.

In 2017, Niranjan reported a retrospective analysis of 73 patients who underwent gamma knife thalamotomy for intractable essential tremor during a 19-year period (1996-2015).[18] A median central dose of 140 Gy (range, 130-150 Gy) was delivered to the nucleus ventralis intermedius through a single 4-mm isocenter. The median time to last follow-up was 28 months (range, 6-152 months). Improvement in tremor occurred in 93.2% of patients as demonstrated with changes in the Fahn-Tolosa-Marin clinical tremor rating scale to score tremor, handwriting, drawing, and ability to drink fluids. Three (4%) patients experienced temporary adverse radiation effects.

In 2015, Witjas reported on outcomes of a French prospective single-blind study of Gamma Knife thalamotomy (GKT) for tremor.[19] Fifty patients (mean age, 74.5 years; 32 men) with

severe refractory tremor (36 essential, 14 parkinsonian) were treated with unilateral GKT at a prescription dose of 130 Gy. Neurologic and neuropsychological assessments including a single-blinded video assessment of the tremor severity performed by a movement disorders neurologist from another center were performed before and 12 months after treatment. The upper limb tremor score improved by 54.2% on the blinded assessment ($p<0.001$). All tremor components (rest, postural, intention) were improved. Activities of daily living were improved by 72.2%. Cognitive functions remained unchanged. Following GKT, the median delay of improvement was 5.3 months (range, 1-12 months). The only side effect was a transient hemiparesis associated with excessive edema around the thalamotomy in one patient.

Kooshkabadi (2013) reported outcomes for 86 patients with tremor treated over a 15-year period, including 48 with essential tremor, 27 with Parkinson disease, and 11 with multiple sclerosis.[20] Fahn-Tolosa-Marin tremor scores were used to compare symptoms pre- and post-procedure: the mean tremor score improved from 3.28 (pre-SRS) to 1.81 (post-SRS; $p<0.0001$), the mean handwriting score improved from 2.78 (pre-SRS) to 1.62 (post-SRS; $p<0.0001$), and the mean drinking score improved from 3.14 (pre-SRS) to 1.8 (post-SRS, $p<0.0001$). Complications included temporary hemiparesis in two patients, dysphagia in one patient, and sustained facial sensory loss in one patient.

Lim (2010) reported outcomes for a small cohort of 18 patients who underwent SRS treatment for essential tremor.[21] For the 14 patients with videotaped evaluations allowing blinded evaluation of tremor severity and at least six months of follow-up (N=11 with essential tremor and N=3 with Parkinson disease), Fahn-Tolosa-Marin Tremor Rating Scale activities of daily living scores improved significantly after SRS (mean change score 2.7 points; $p=0.03$). However, there was no significant improvement in other Fahn-Tolosa-Marin Tremor Rating Scale items ($p=0.53$ for resting tremor, $p=0.24$ for postural tremor, $p=0.62$ for action tremor, $p=0.40$ for drawing, $p>0.99$ for pouring water, $p=0.89$ for head tremor). Mild neurologic complications occurred in two patients (lip and finger numbness), and severe neurologic complications occurred in one patient (edema surrounding thalamic lesion with subsequent hemorrhage at the lesion site, with speech difficulty and hemiparesis.)

Ohye (2012) conducted a prospective study of SRS for tremor that included 72 patients, 59 with Parkinson disease and 13 with essential tremor).[22] Among 52 patients who had follow-up at 24 months, tremor scores measured using the unified Parkinson's Disease Rating Scale ($p<0.001$; approximate score decrease extrapolated from graph from 1.5 at baseline to 0.75 at 24-month follow-up). In addition, there was a statistically significant reduction in rigidity (repeated ANOVA, $p<0.001$), but there was no change in gait and slow movement ($p=0.789$ and $p=0.337$, respectively).

Young (2000) reported outcomes for a cohort of 158 patients with tremor who underwent SRS, including 102 patients with Parkinson disease, 52 with essential tremor, and four with tremor due to other conditions.[23] Among patients with a parkinsonian tremor, at latest follow-up (mean, 47 months), blinded assessments on unified Parkinson's Disease Rating Scale demonstrated improvements in several specific items, including overall tremor (from 3.3 pretreatment to 1.2 at last follow-up; $p<0.05$), action tremor (from 2.3 pretreatment to 1.3 at last follow-up; $p<0.05$). Statistically significant improvements were also seen in Parkinson's Disease Rating Scale rigidity scores, which were maintained in 74 patients for at least four years. Among patients with Essential tremor, blinded assessments were conducted using the Fahn-Tolosa-Marin Tremor Rating Scale. At one-year of follow-up, 92.1% of patients with essential tremor were completely or nearly tremor-free. Improvements were reported in

components of the Fahn-Tolosa-Marin Tremor Rating Scale, but statistical comparisons are not presented. Three patients developed new neurologic symptoms attributed to the SRS.

In 2008, Kondziolka reported outcomes for 31 patients who underwent SRS thalamotomy for disabling essential tremor.[24] Among 26 patients with follow-up data available, score on the Fahn-Tolosa-Marin tremor score improved compared with baseline from 3.7 (pre-SRS) to 1.7 (post-SRS; p<0.000) and score on the Fahn-Tolosa-Marin handwriting score improved compared with baseline from 2.8 (pre-SRS) to 1.7 (post-SRS; p<0.000). One patient developed transient mild right hemiparesis and dysphagia and one patient developed mild right hemiparesis and speech impairment.

Section Summary

The evidence related to the use of SRS for tremor consists of uncontrolled cohort studies, many of which report outcomes from the treatment of tremor of varying etiologies. Most studies report improvements in standardized tremor scores, although few studies used a blinded evaluation of tremor score, allowing for bias in assessment. No studies that compared SRS with alternative methods of treatment or a control group were identified. Limited long-term follow-up is available, making the long-term risk: benefit ratio of an invasive therapy uncertain. Due to inadequate evidence, conclusions cannot be drawn about the safety and effectiveness of SRS for these indications.

CHRONIC PAIN

Lu (2018) reported a systematic review and meta-analysis of neurosurgical treatments for glossopharyngeal neuralgia.[25] A total of 23 studies were included on nerve section (NS; 6 studies), microvascular decompression (MVD; 11 studies), and SRS (6 studies). The meta-analysis indicated that short-term and long-term pain relief rate was highest after NS (IR, 94%; 95% CI, 88%-98%; IR, 96%; 95% CI, 91%-99%). The short-term and long-term pain relief rate was lowest after SRS (three months postoperatively, IR, 80%; 95% CI, 68%-96%; IR, 82%; 95% CI, 67%-94%). The postoperative complication rate was highest and lowest following MVD (IR, 26%; 95% CI, 16%-38%) and SRS (IR, 0%; 95% CI, 0%-4%), respectively.

In 2017, Roberts and Pouratian performed a systematic review to evaluate the efficacy of SRS for chronic pain.[26] They identified six articles with 113 patients that underwent SRS and had at least a three month follow-up for nonmalignant pain or at least a one month follow-up for malignant pain. At least 35% of patients reported having significant pain relief, but 21% of patients reported adverse events.

Section Summary

The evidence related to the use of SRS for chronic pain is limited and there remains a lack of comparative studies and long-term outcomes. This evidence is not sufficient to understand the safety and effectiveness of SBRT for the treatment of chronic pain or to adequately describe the subpopulation of patients with chronic pain most likely to benefit.

ACOUSTIC NEUROMAS

SRS is widely used for the treatment of acoustic neuromas (vestibular schwannomas). In 2017, a systematic review by Persson reported on SRS vs fractionated radiotherapy for tumor control in vestibular schwannoma (VS) patients.[27] Patients with unilateral VS treated with radiosurgery were compared with patients treated using fractionated stereotactic radiotherapy

(FSRT). A meta-analysis was not performed because all of the identified studies were case series. Rates of adverse events were calculated; the risk for facial nerve deterioration was 3.6% for SRS and 11.2% for FSRT and for trigeminal nerve deterioration 6.0% for SRS and 8.4% for FSRT.

Badahshi (2014) reported a three-year local tumor control rate of 88.9% in a study of 250 patients with vestibular schwannoma who underwent SRS or fractionated SRS.[28] Williams (2013) reported rates of tumor progression-free survival (PFS) for patients with large vestibular schwannomas treated with SRS of 95.2% and 81.8% at three and five years, respectively.[29] For patients with small vestibular schwannomas treated with SRS, tumor PFS was 97% and 90% at three and five years, respectively. In a retrospective case series of 93 patients with vestibular schwannomas treated with SRS, 83 of whom had long-term follow-up, Woolf reported an overall control rate of 92% at a median follow-up of 5.7 years. A small study from 2006 that compared microsurgical resection (N=36) with SRS (N=46) for the management of small (<3 cm) vestibular schwannomas showed better hearing preservation at last follow-up in the SRS group ($p<0.01$) and no difference in tumor control between the groups (100% vs 96%, $p=0.50$).[30]

In the treatment of acoustic neuromas, the most significant adverse effect is loss of function of the facial and auditory nerve. For example, in a single-institution study, Meijer (2003) reported on the outcomes of single fraction versus fractionated linear accelerator (LINAC)-based SRS in 129 patients with acoustic neuromas.[31] Among these patients, 49 were edentate and thus could not be fitted with a relocatable head frame that relies on dental impressions. This group was treated with a single fraction, while the remaining 80 patients were treated with a fractionated schedule. With an average follow-up of 33 months, there was no difference in outcome in terms of local tumor control, facial nerve preservation, and hearing preservation.

Chung (2004) reported on the results of a single-institution case series of 72 patients with acoustic neuromas, 45 of whom received single-fraction therapy and 27 who received fractionated therapy.[32] Patients receiving single-fraction treatment were functionally deaf, while those receiving fractionated therapy had useful hearing in the affected ear. After a median follow-up of 26 months, there was no tumor recurrence in either group. Chang reported that 74% of 61 patients with acoustic neuromas treated with CyberKnife using staged treatment had serviceable hearing maintained during at least 36 months of follow-up.[33]

Section Summary

The evidence related to the use of SRS for acoustic neuroma (vestibular schwannoma) consists primarily of case series and cohort studies, which report high rates of freedom from tumor progression. Given that vestibular schwannoma is a slow-growing tumor with symptoms most often related to local compression, demonstration of slowing of progression is a reasonable outcome. A single comparative study was identified that demonstrated comparable tumor control outcomes between SRS and surgical therapy for small vestibular schwannomas.

NONACOUSTIC SCHWANNOMAS

Kharod (2018) analyzed the outcomes of 11 patients with benign nonacoustic schwannomas treated with SRS.[34] Median follow-up as 8.2 years for all patients and eight years for all living patients. Eight patients were treated with SRS along, one was treated with SRS after subtotal surgical resection, and two were treated with postoperative SRS after recurrence following

initial surgical resection. Five-year overall survival, disease-free survival, and local control rates were all 100% and there were no grade 2 to 5 treatment-related toxicities.

Sheehan (2015) published a multicenter case series study that evaluated 42 patients with facial nerve schwannomas undergoing SRS.[35] Prior resection was performed in 36% of cases. At a median follow-up of 28 months, tumor control was achieved in 90% of patients. The study authors reported that most patients treated with SRS had neurological preservation. Smaller tumors treated with SRS had better outcomes for nerve function.

Section Summary

The evidence related to the use of SRS for facial nerve schwannomas consists of case series, which report high rates of tumor control and nerve preservation. However, there remains a lack of comparative studies that evaluate long term outcomes including overall survival.

BRAIN METASTASES

Systematic Reviews

Fuentes (2018) published a systematic review of RCTs to compare surgery with SRS for patients with a single brain metastasis.[36] Risk of bias was assessed with the Cochrane tool. Two RCTs met inclusion criteria. These included 85 patients. Both included studies were closed early due to poor participant accrual. Meta-analysis was not possible due to heterogeneity between the studies. Certainty of evidence was rated as low or very low for the various outcomes. Neither RCT reported differences in overall survival between the interventions. There were also no differences in progression-free survival, quality of life, or adverse events.

Khan (2017) published a meta-analysis of comparing WBRT, SRS, and treatment with a combination of the two for brain metastases.[37] Five studies with a total of 763 patients met inclusion criteria and were included in the meta-analysis. Out of those, 26% received WBRT alone, 26% received SRS alone, and 48% received WBRT plus SRS. No significant differences between treatment groups were found for survival benefit or adverse events. However, combination therapy provided significantly better local control than WBRT alone (hazard ratio 2.05; 95% CI 1.36-3.09; p=0.0006) or SRS alone (hazard ratio 1.84; 95% CI: 1.26-2.70; p=0.002).

In 2017, Ghidini conducted a systematic review on CNS metastases from esophageal and gastric cancer.[38] The authors analyzed data from 37 studies that met the criteria for inclusion. SRS was found to result in better OS, with the caveat that the studies examined included combination therapies that could cause an overestimate of survival.

Roos (2011) examined the randomized evidence to treat brain metastases.[39] A search of MEDLINE, EMBASE, and Cochrane databases for published papers and abstracts on relevant randomized trials was undertaken. Fourteen randomized trials were identified, 11 final reports and 3 abstracts, investigating various combinations of surgery, SRS and WBRT. Most of the trials had significant limitations. Surgery and SRS improved LC, maintenance of performance status and survival for favorable prognosis patients with solitary brain metastases relative to WBRT alone, although the absolute survival benefit for the majority was modest. Limited data suggest similar outcomes from surgery and SRS, but few patients were truly suitable for both options. For multiple (two-four) brain metastases, SRS improved LC and functional outcome but not survival. Adjuvant WBRT also improved intracranial control but not survival; however,

the neurocognitive risk: benefit ratio of WBRT was controversial. Quality-of-life data were limited.

A 2011 review by Park (2011) on the use of SRS for brain metastases discussed the two randomized trials that demonstrated that the addition of single-dose SRS to WBRT improves local tumor control and maintenance of functional status for patients.[40] Also reviewed are three recent randomized trials comparing the outcomes for SRS alone versus SRS plus WBRT for limited brain metastases. All three trials indicated a lack of detriment in neurocognition or quality of life with the omission of WBRT, despite significantly worsened intracranial tumor control that would require additional salvage therapy in almost all patients.

A Cochrane systematic review by Patil (2010)[41] addressed the role for both SRS and WBRT in patients with small numbers of metastatic lesions (generally no more than three or four lesions), noted that given the unclear risk of bias in the included studies, the results need to be interpreted with caution. The evidence was rated as moderate quality. The analysis of all included patients (three trials) indicated that SRS plus WBRT did not show a survival benefit over WBRT alone; however, performance status and LC were significantly better in the SRS plus WBRT group. Additionally, a significant improvement in OS was reported in the combined analysis for some patient subgroups. This Cochrane systematic review was updated in 2012 and again in 2017.[42] Between those two updates, only one additional study was identified that met the inclusion criteria, but it was not included in the meta-analysis due to a lack of data.

Randomized Controlled Trials

Since publication of the systematic reviews, several RCTs have been published. Brown (2017) reported a multi-institution RCT comparing postoperative SRS to WBRT in 194 patients with resected brain metastases.[43] Patients were followed for a median of 11.1 months. Cognitive-deterioration-free survival was 3.7 months in the SRS group and 3.0 months in the WBRT group ($p<0.0001$). Cognitive deterioration at six months was present in 52% of patients in the SRS group and 85% of patients in the WBRT group ($p<0.00031$). Median OS was not significantly different between the SRS and WBRT groups (12.2 and 22.6 months, respectively). Two grade 3 or 4 adverse events were reported with a relative frequency greater than 4%, hearing impairment (3% of SRS-treated patients versus 9% of WBRT treated patients) and cognitive disturbance (3% of SRS-treated patients versus 5% of WBRT-treated patients). There were no treatment-related deaths.

Mahajan (2017) compared post-operative SRS to observation for completely resected brain metastases in a single center RCT.[44] A total of 132 patients were randomized, with a median follow-up of 11.1 months. Four patients were not included in the analysis due to ineligibility. Patients were included if they were over three years of age, had a Karnofsky Performance Score of 70 or greater, were able to have an MRI scan, and had complete resection of one to three brain metastases. The SRS group received treatment within 30 days of surgery. The primary endpoint, time to local recurrence in the resection cavity, was 43% in the observation group and 72% in the SRS group (hazard ratio 0.46 [95% CI 0.24-0.88]; $p=0.015$).

Some studies have suggested that use of radiosurgery for brain metastases should be limited to patients with three or fewer lesions. A randomized trial from Kondziolka (1999) compared WBRT with WBRT plus radiosurgery boost to metastatic foci.[45] Results stated that the significant advantage of radiosurgery boost over WBRT alone in terms of freedom from local failure did not differ among patients with two, three, or four metastases. Survival also did not depend on the number of metastases. As the number of metastases rises, so does the total

volume of tissue receiving high-dose radiation, thus the morbidity risk of radiation necrosis associated with radiosurgery is likely to increase. For a large number of metastases, and for large volumes of tissue, this risk may be high enough to negate the advantage of radiosurgery plus WBRT over WBRT alone seen in patients with four or fewer metastases. SRS centers commonly exclude patients with more than five metastases from undergoing radiosurgery.[46,47] It is difficult to identify a specific limit on the number of metastases for which the use of SRS is advantageous. A large number of very small metastases may respond to radiosurgery, as well as a small number of larger metastases.

In 2006, Aoyama reported on a randomized trial of SRS plus WBRT versus SRS alone for treatment of patients with one to four brain metastases.[48] They found a 12-month intracranial tumor recurrence rate of 46.8% in the SRS plus WBRT group compared with 76.4% in the group that only received SRS. However, median survival times were not different at 7.5 and 8.0 months, respectively. They also found no differences in neurologic functional preservation. In an accompanying editorial, Raizer commented that either treatment approach is a reasonable first step, recognizing that those who select SRS alone are more likely to need subsequent salvage radiation treatments.[49]

Nonrandomized Comparative Studies

In 2017 Bates reported a single institution experience of brain metastases treated with WBRT, SRS, or both.[50] A total of 25 consecutive patients were analyzed. Some patients received concurrent kinase inhibitor therapy. No significant differences were reported in OS or brain PFS between the radiation modalities and no association between concurrent kinase inhibitor therapy and OS or brain PFS was identified.

In 2013, Verma retrospectively reviewed patients receiving different radiotherapy modalities for brain metastases with or without tyrosine kinase inhibitor (TKI) therapy.[51] Among 34 patients (89 lesions) those receiving SRS and TKIs had six-month local control rates of 94.7% vs 73.7% in the group who received SRS without TKIs. The difference was not statistically significant (p=0.09).

Tian (2013) reported results from a retrospective, single-institution cohort study comparing neurosurgical resection to SRS for solitary brain metastases from non-small-cell lung cancer (NSCLC). Seventy-six patients were included, 38 of whom underwent neurosurgery.[52] Median survival was 14.2 months for the SRS group and 10.7 months for the neurosurgery group. In multivariable analysis, treatment mode was not significantly associated with differences in OS.

Noncomparative Studies

Noncomparative studies continue to evaluate the use of SRS without WBRT for the management of brain metastases and the role of SRS for the management of larger numbers of brain metastases[53-58] and for chemoradiation.[59]

Section Summary

For cases of brain metastases, evidence from RCTs and systematic reviews indicate that the use of SRS improves outcomes in the treatment of brain metastases. SRS appears to be feasible in the treatment of larger numbers (e.g., >10) of brain metastases, and outcomes after SRS treatment do not appear to be worse for patients with larger numbers of metastases, at least for patients with 10 or fewer metastases.

CAVERNOUS MALFORMATIONS

Wen (2019) performed a systematic review and meta-analysis of gamma knife radiosurgery for cavernous malformations.[60] A total of nine studies met inclusion criteria, representing 747 patients. All studies were retrospective, and one was case-controlled. The authors calculated the overall risk ratio (RR) of hemorrhage rate of pre-GKRS and post-GKRS (6.08 [95% CI, 5.04-7.35]), the RR comparing hemorrhage rate of pre-GKRS and the first two years postradiosurgery (3.03 [95% CI, 2.65-4.11]), and the overall RR (12.13 [95% CI, 1.73-85.07]) comparing pre-GKRS with two years after GKRS. There was no significant difference of the hemorrhage rate between the first two years following treatment and two years after treatment (RR = 2.81; 95% CI, 0.20-13.42). Adverse events reported in eight of the studies were cyst formation, edema, new lesions, and neurologic deficiency.

Phuong (2017) reported on a case series of 79 patients with symptomatic cerebral cavernomas treated with SRS.[61] Complete response, partial response, and stable disease (best response) were reported in 17%, 82%, and 2%, respectively, of the 60 patients with headache. Complete response, partial response, and stable disease were reported in 31%, 64%, and 5% of the 39 patients with seizures. Complete response, partial response, stable disease, progression, and pseudoprogression were reported in 6%, 75%, 15%, 1%, and 5% of all patients, respectively, with respect to the size of cavernomas at 15 months. Four patients developed recurrent seizures after one year and five patients experienced bleeding within two years after SRS.

In 2017, Lopez-Serrano reported a case series of 95 patients treated with SRS for cavernous malformations (CMs).[62] Patients, who had all experienced at least one bleeding incident before treatment, were followed for a median of 78 months after treatment. Hemorrhage rate was compared pretreatment (3.06%) to the first three-year latency interval (1.4%) and to the remainder of the follow-up (0.16%). Adverse events reported were four patients with new location-dependent neurological deficits and three patients with edema-related headache. All patients recovered from these events fully.

A 2014 case series by Lee reported on 31 patients who were treated with SRS for CMs.[63] Treatment followed a single symptomatic bleed in 31 patients (group A) and two or more symptomatic bleeds in 18 patients (group B). The annual hemorrhage rate following SRS within the first two years and after two years (up to a mean follow-up of 64 months) was 7.06% and 2.03% for group A and 9.84% and 1.50% for group B, respectively. Pretreatment hemorrhage rate was 38.36% for group B. Adverse events were reported in four patients, one of which was did not resolve during the trial.

Park (2013) reported a case series of 21 patients treated with SRS for symptomatic brainstem intra-axial CMs.[64] Mean follow-up was 32 months. Excluding the first hemorrhage, the hemorrhage rate before SRS was 39.5%. The annual rate after SRS was 8.2% for the first two years. One adverse event, permanent paresthesia in one patient, was reported.

A case series of 30 patients treated with SRS for single or multiple CMs was reported by Huang in 2006.[65] For six patients, radiosurgery was for residual lesions identified following craniotomy. Mean follow-up was 59.9 months. Of the 13 patients presenting with seizures, following SRS eight were seizure-free, three had rare episodes of seizures, and two continued to have seizures. Hemorrhage rate pretreatment for the 22 patients presenting initially as acute hemorrhage was 1.9%. For all 30 patients, posttreatment hemorrhage rate was 1.9%. Posttreatment edema was observed in two patients.

In 2002, Kim reported a case series of 22 patients with symptomatic CMs treated with SRS.[66] Of these, 11 were treated with LINAC and 11 with Gamma knife. Twenty patients had experienced at least one episode of bleeding and two presented with seizure but did not have evidence of recent bleeding. Four of the patients that had incidence of bleeding underwent microsurgery prior to radiosurgery. Median follow-up was 38.3 months. The hemorrhage rate was 35.5% per year pretreatment and 1.55% per year posttreatment. Neurological deterioration was reported in six patients, and of those, persisted in two. Magnetic resonance images taken at the last follow-up showed that the lesion was decreased in eleven patients, increased in one, and unchanged in 10 cases.

Section Summary

The evidence related to the use of SRS for cavernous malformations consists of case series, which have reported improvements in hemorrhage rates. However, there remains a lack of comparative studies that evaluate long term outcomes.

PRACTICE GUIDELINE SUMMARY

NATIONAL COMPREHENSIVE CANCER NETWORK

The National Comprehensive Network (NCCN) provides guidelines for cancer treatment by site that include the use of SRS and SBRT for certain cancers.[67]

Cancer Site	Tumor Type	Recommendation	Version
CNS	Adult intracranial and spinal ependymoma – spine or brain reoccurrence	• Resection with limited radiotherapy if no prior radiotherapy; consider use of SRS if geometrically favorable (category 2A) • If unresectable, radiotherapy if no prior radiotherapy; consider use of SRS if geometrically favorable (category 2A) • If progression, radiotherapy; consider use of SRS if geometrically favorable (category 2A)	1.2019
CNS	Adult medulloblastoma and supratentorial PNET – recurrent disease	If progression after localized recurrence and maximum safe resection (category 2A)	1.2019
CNS	Primary spinal cord tumors	If recurrence, radiotherapy including SRS if surgery is not possible (category 2A)	1.2019
CNS	Meningiomas	Observe (preferred for small asymptomatic tumors) or if accessible, surgery with or without RT (external beam or SRS; Recommendations based on WHO grade: Grade III – RT; Grade II with incomplete resection: RT; Grade II with complete resection – consider RT; Grade I: observation or consider RT for symptomatic patients) or RT (external beam or SRS)	1.2019
CNS	Limited Brain Metastases, primary treatment	• For newly diagnosed or stable systemic disease or reasonable systemic treatment options exist, SRS (preferred) or WBRT. SRS is preferred when safe, especially for low tumor volume, to both the resection cavity and any other non-resected brain metastases. WBRT is generally not recommended but may be appropriate in some rare clinical circumstances.	1.2019

Cancer Site	Tumor Type	Recommendation	Version
CNS	Limited Brain Metastases, recurrence	• If local recurrence and previous surgery only, surgery, single dose or fractionated stereotactic RT, or WBRT (category 2A) • If local recurrence and previous WBRT or SRS, surgery or single dose (category 2B) or fractionated SRS (category 2A) • If distant brain recurrence and limited brain metastases, surgery, single dose or fractionated stereotactic RT, WBRT, or consider chemotherapy	1.2019
CNS	Extensive Brain Metastases, primary treatment	WBRT or SRS (category 2A). SRS can be considered for patients with good performance status and low overall tumor volume and/or radioresistant tumors such as melanoma.	1.2019
CNS	Metastatic spine tumors	• If spinal cord compression, fracture or spinal cord instability, consider surgical stabilization or vertebral augmentation followed by RT (recommend SRS if oligometastases and radioresistant) • If no spinal cord compression, no fracture or spinal instability, RT (preferred) or chemotherapy or surgery. Consider surgery or SRS if deterioration during RT, intractable pain, or tumor progression (recommend SRS if oligometastases and radioresistant) (category 2A). • If progressive disease or recurrent disease and if previously treated with RT or surgery and RT, consider surgery or SRS (recommend SRS if oligometastases and radioresistant). Consider re-irradiation if recurrent. • If progressive disease or recurrent disease and previously treated with chemotherapy, consider RT (recommend SRS if oligometastases and radioresistant) (category 2A). • If spinal cord compression, steroids, followed by: o primary RT (recommend SRS if oligometastases and radioresistant) or o surgery, followed by RT or o In the absence of clinical myelopathy, primary chemotherapy if chemosensitive tumor	1.2019

NCCN Categories

- **Category 1:** Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- **Category 2A:** Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- **Category 2B:** Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- **Category 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

*All recommendations are category 2A unless otherwise noted.

AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

Central Nervous System

- Brain Metastases: SRS is recommended for the following:[68]
  - Single brain metastases (initial management):
    - If good prognosis (expected survival 3 months or more) and complete resection possible:
      - If brain metastasis ≤3-4 cm, options include SRS and WBRT (level of evidence: I), SRS alone (level of evidence: 1), and surgery with SRS/radiation boost with or without WBRT (level of evidence: 3)
      - If brain metastasis >3-4 cm, treatment options include surgery with SRS/radiation boost with or without WBRT (level of evidence: 3)
    - If good prognosis and not resectable:
      - If brain metastasis ≤3-4 cm, options include SRS and WBRT (level of evidence: I), SRS alone (level of evidence: 1).
  - For multiple brain metastases (initial management):
    - If good prognosis (expected survival 3 months or more) and brain metastasis ≤3-4 cm, options include SRS and WBRT (level of evidence: I), SRS alone (level of evidence: 1)

Glioblastoma

- "SRS and hypofractionated stereotactic RT appear to provide promising outcomes compared with chemotherapy, with median survival from reirradiation typically 8 to 12 months".[69]

AMERICAN ACADEMY OF NEUROLOGY

The American Academy of Neurology published evidence-based recommendations in the Treatment of Essential Tremor Practice Parameter in 2005 (updated in 2011).[70] It states "There is insufficient evidence regarding the surgical treatment of head and voice tremor and the use of gamma knife thalamotomy (Level U)."

CONGRESS OF NEUROLOGICAL SURGEONS

The Congress of Neurological Surgeons also published 2019 evidence-based guidelines on "Use of Stereotactic Radiosurgery in the Treatment of Adults With Metastatic Brain Tumors." These guidelines make the following level 3 recommendations regarding SRS:

- SRS is recommended as an alternative to surgical resection in solitary metastases when surgical resection is likely to induce new neurological deficits, and tumor volume and location are not likely to be associated with radiation-induced injury to surrounding structures.
- SRS should be considered as a valid adjunctive therapy to supportive palliative care for some patients with brain metastases when it might be reasonably expected to relieve focal symptoms and improve functional quality of life in the short term if this is consistent with the overall goals of the patient.
- After open surgical resection of a solitary brain metastasis, SRS should be used to decrease local recurrence rates.
- For patients with solitary brain metastasis, SRS should be given to decrease the risk of local progression.
- For patients with 2 to 4 brain metastases, SRS is recommended for local tumor control, instead of whole brain radiotherapy, when their cumulative volume is < 7 mL.

- The use of stereotactic radiosurgery alone is recommended to improve median overall survival for patients with more than 4 metastases having a cumulative volume < 7 mL.

INTERNATIONAL STEREOTACTIC RADIOSURGERY SOCIETY

The International Stereotactic Radiosurgery Society (ISRS) published practice guidelines for treatment of tremor based on a systematic review of the literature in 2018.[16] The guidelines include the following recommendations (level of evidence: IV):

- SRS is recommended for patients w/ tremor for whom medical therapy has failed & who are not candidates for invasive surgery.
- SRS should be considered even for patients w/ tremor for whom medical therapy has failed even if they are candidates for invasive surgery since SRS appears to have a lower level of complications.
- GKRS has been performed w/ a single 4-mm collimator, single-fraction maximum dose of 130–150 Gy & the lesion made in the VIM located using advanced imaging modalities & stereotactic atlases.

The ISRS also published a practice guideline for cavernous sinus meningiomas based on a systematic review of the literature. Based on level III evidence, the guidelines recommend SRS/SBRT "as a primary/upfront treatment option for an asymptomatic, or mildly symptomatic CS meningioma."

SUMMARY

There is enough research to show that use of stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) of intracranial, skull base, and orbital sites for initial treatment or treatment of recurrence improves health outcomes for the following conditions: primary neoplasms of the central nervous system; metastasis to CNS with adequate performance score; acoustic neuromas (vestibular schwannomas); arteriovenous malformations; chordomas and chondrosarcomas of the skull base; craniopharyngiomas; drug-resistant epilepsy when criteria are met; hemangioblastoma; hemangiopericytoma; glomus jugulare and glomus tympanicum tumors; meningiomas; pituitary adenomas; trigeminal neuralgia that is refractory to medical management; and uveal melanoma. In addition, clinical practice guidelines recommend the use of SRS or SBRT for many of these indications. Therefore, the use of SRS and SBRT may be considered medically necessary when policy criteria are met for these indications.

For all other tumors or indications when policy criteria are not met, there is not enough research to show that stereotactic radiosurgery (SRS) or stereotactic body radiation therapy (SBRT) of intracranial, skull base, and orbital sites leads to improved health outcomes. Therefore, SRS and SBRT of intracranial, skull base, and orbital sites is considered investigational when policy criteria are not met.

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CODES

NOTE: Coding for stereotactic radiosurgery typically consists of a series of CPT codes describing the individual steps required; medical radiation physics, clinical treatment planning, attachment of stereotactic head frame, treatment delivery and clinical treatment management.

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.

Treatment delivery:

The codes used for treatment delivery will depend on the energy source used, typically either photons or protons.

Codes	Number	Description
CPT	32701	Thoracic target(s) delineation for stereotactic body radiation therapy (SRS/SBRT), (photon or particle beam), entire course of treatment
	77371	Radiation therapy delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; multi-source Cobalt 60 based
	77372	Radiation therapy delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; linear accelerator based
	77373	Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance, entire course not to exceed 5 fraction
	77435	Stereotactic body radiation therapy, treatment management, per treatment course, to 1 or more lesions, including image guidance, entire course not to exceed 5 fractions

NOTE: Codes for treatment delivery primarily reflects the cost related to the energy source used, and not physician work.

Clinical treatment management:

CPT	77432	Stereotactic radiation treatment management of cerebral lesion(s) (complete course of treatment consisting of one session.)
	61796	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 simple cranial lesion
	61797	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional cranial lesion, simple (List separately in addition to code for primary procedure)
	61798	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 complex cranial lesion
	61799	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional cranial lesion, complex (List separately in addition to code for primary procedure)
	61800	Application of stereotactic headframe for stereotactic radiosurgery (List separately in addition to code for primary procedure)
	63620	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 spinal lesion
	63621	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional spinal lesion (List separately in addition to code for primary procedure)
HCPCS	G0339	Image guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session, or first session of fractionated treatment.
	G0340	Image guided robotic linear accelerator-based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, second through fifth sessions, maximum five sessions per course of treatment

APPENDIX I: WHO Classification of Tumors of the Central Nervous System	
Diffuse astrocytic astrocytic and oligodendroglial tumors	**Neuronal and mixed neuronal-glial tumors**
Diffuse astrocytoma	Dysembryoplastic neuroepithelial tumor
Glioblastoma	Gangliocytoma
Diffuse midline glioma	Ganglioglioma
Oligodendroglioma	Anaplastic ganglioglioma
Other astrocytic tumors	Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)
Pilocytic astrocytoma	Desmoplastic infantile astrocytoma and ganglioglioma
Pilomyxoid astrocytoma	Papillary glioneuronal tumor
Subependymal giant cell astrocytoma	Rosette-forming glioneuronal tumor
Pleomorphic xanthoastrocytoma	Central neurocytoma
Anaplastic pleomorphic xanthoastrocytoma	Extraventricular neurocytoma
Other gliomas	Cerebellar liponeurocytoma
Choroid plexus papilloma	Paraganglioma
Atypical choroid plexus papilloma	**Tumors of the pineal region**
Choroid plexus carcinoma	Pineocytoma
Milanotic schwannoma	Pineal parenchymal tumor of intermediate differentiation
Neurofibroma	Pineoblastoma
Atypical neurofibroma	Papillary tumor of the pineal region
Plexiform neurofibroma	**Embryonal tumors**
Perineurioma	Medulloblastomas
Hybrid nerve sheath tumors	Embryonal tumor with multilayered rosettes
Malignant peripheral nerve sheath tumor	Medulloepithelioma
Meningiomas	CNS neuroblastoma
Meningioma	CNS ganglioneuroblastoma
Meningothelial meningioma	CNS embryonal tumor
Fibrous meningioma	Atypical teratoid/rhabdoid tumor
Transitional meningioma	**Tumors of the cranial and paraspinal nerves**
Psammomatous meningioma	Schwannoma
Angiomatous meningioma	Osteochondroma
Microcystic meningioma	Osteosarcoma
Secretory meningioma	**Melanocytic tumors**
Lymphoplasmacyte-rich meningioma	Meningeal melanocytosis

APPENDIX I: WHO Classification of Tumors of the Central Nervous System	
Metaplastic meningioma	Meningeal melanocytoma
Chordoid meningioma	Meningeal melanoma
Clear cell meningioma	Meningeal melanomatosis
Atypical meningioma	**Lymphomas**
Papillary meningioma	Diffuse large B-cell lymphoma of the CNS
Rhabdoid meningioma	Immunodeficiency-associated CNS lymphomas
Anaplastic (malignant) meningioma	Intravascular large B-cell lymphoma
Mesenchymal, non-meningothelial tumors	T-cell and NK/T-cell lymphomas of the CNS
Solitary fibrous tumor/hemangiopericytoma	Anaplastic large cell lymphoma
Hemangioblastoma	MALT lymphoma of the dura
Hemangioma	**Histocytic tumors**
Epithelioid hemangioendothelioma	Langerhans cell histiocytosis
Angiosarcoma	Erdheim-Chester disease
Kaposi sarcoma	Rosai-Dorfman disease
Ewing sarcoma /PNET	Juvenile xanthogranuloma
Lipoma	Histiocytic sarcoma
Angiolipoma	**Germ cell tumors**
Hibernoma	Germinoma
Liposarcoma	Embryonal carcinoma
Desmoid-type fibromatosis	Yolk sac tumor
Myofibroblastoma	Choriocarcinoma
Inflammatory myofibroblastic tumor	Teratoma
Benign fibrous histiocytoma	Mixed germ cell tumor
Fibrosarcoma	**Tumors of the sellar region**
Undifferentiated pleomorphic sarcoma/malignant fibrous histiocytoma	Craniopharyngioma
Leiomyoma	Granular cell tumor of the sellar region
Leiomyosarcoma	Pituicytoma
Rhabdomyoma	Spindle cell oncocytoma
Rhabdomyosarcoma	**Ependymal tumors**
Chondroma	Subependymoma
Chondrosarcoma	Ependymomas
Osteoma	

Adapted from Louis (2016).[72]

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