Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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Title: Stereotactic Radiosurgery and Stereotactic Body Radiotherapy

Description/Background

Stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) are 3-dimensional conformal radiotherapy methods that deliver highly focused, convergent radiotherapy beams on a target that is defined with 3-dimensional imaging techniques with the ability to spare adjacent radiosensitive structures. SRS primarily refers to such radiotherapy applied to intracranial lesions. SBRT refers to therapy generally applied to other areas of the body. Both techniques differ from conventional external-beam radiotherapy, which involves exposing large areas of tissue to relatively broad fields of radiation over multiple sessions.

BACKGROUND

Conformal Radiotherapy

Stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) are techniques that use highly focused, conformal radiation beams to treat both neoplastic and non-neoplastic conditions. Although SRS and SBRT may be completed with one session (single fraction), SRS typically refers to a single-session procedure to ablate the target lesion. However, either technique may require additional sessions (typically not >5) over a course of days, referred to as fractionated radiotherapy.

Platforms available for SRS and SBRT are distinguished by their source of radiation; they include gamma radiation from cobalt 60 sources; high-energy photons from LINAC systems; and particle beams (e.g., protons). Particle beam therapy is not covered in this policy.

SRS and SBRT have been used for a range of malignant and nonmalignant conditions. A comprehensive review that encompasses all potential uses is beyond the scope of this evidence review. Thus, a brief discussion follows of common applications of SRS and SBRT for which published evidence has been identified in database searches.

Disparity Awareness

Studies have demonstrated that there are socioeconomic disparities with regard to access to radiation therapy, particularly for patients in ethnic minority groups and those living in rural areas. In the United States, certain racial/ethnic groups continue to be at an increased risk of developing or dying from particular cancers. Black men have the highest rate of new cancer diagnoses and Black men and women experience the highest rate of cancer-related death. American Indians and Alaska Natives are disproportionally affected by kidney cancer and also have higher death rates from this cancer when compared to other racial/ethnic groups.

Regulatory Status

Several devices that use cobalt 60 radiation (gamma ray devices) for SRS have been cleared for marketing by FDA through the 510(k) process. The most commonly used gamma ray device is the Gamma Knife® (Elekta, Stockholm; approved May 1999; product code IWB), which is a fixed device used only for intracranial lesions. Gamma ray emitting devices that use cobalt 60 degradation are also regulated through the U.S. Nuclear Regulatory Commission.

A number of linear-accelerator unit (LINAC) movable platforms that generate high-energy photons have been cleared for marketing by FDA through the 510(k) premarket notification process. Examples include the Novalis Tx® (Novalis, Westchester, IL); the TrueBeam STx (Varian Medical Systems, Palo Alto, CA; approved December 2012; product code IYE); and the CyberKnife® Robotic Radiosurgery System (Accuray, Sunnyvale, CA; approved December 1998; product code MUJ). LINAC-based devices may be used for intracranial and extracranial lesions.

Medical Policy Statement

The safety and effectiveness of stereotactic radiosurgery and stereotactic body radiotherapy* using gamma-ray or linear-accelerator units are established and are considered useful therapeutic options when indicated.

** Platforms available for SRS and SBRT are distinguished by their source of radiation; they include gamma radiation from cobalt 60 sources; high-energy photons from LINAC systems; and particle beams (e.g., protons). Particle beam (e.g., proton therapy) is NOT covered in this policy.*

Inclusionary and Exclusionary Guidelines

Inclusions:

Stereotactic radiosurgery (**intracranial**) using a gamma-ray or linear-accelerator unit (LINAC) is considered established for the following indications:

- Arteriovenous malformation
- Acoustic neuromas
- Pituitary adenomas
- Non-resectable, residual or recurrent meningiomas
- Craniopharyngiomas
- Glomus jugulare tumors
- Solitary or multiple brain metastases in patients having good performance status

- Primary or recurrent malignancies of the central nervous system (CNS), including but not limited to high-grade gliomas
- Epilepsy refractory to medical management and/or invasive neurosurgical treatment
- Parkinson's disease refractory to medical management and/or invasive neurosurgical treatment
- Essential tremor refractory to medical management and/or invasive neurosurgical treatment
- Familial tremor classifications with major systemic disease refractory to medical management and/or invasive neurosurgical treatment
- Trigeminal neuralgia refractory to medical management and/or invasive neurosurgical treatment
- Inoperable primary spinal tumor with compression or intractable pain
- Pineal gland tumors
- Schwannomas
- Medulloblastoma supratentorial PNET
- Hemangioblastoma
- Uveal melanoma
- Other tumor types when used to treat a previously irradiated field

Stereotactic **body** radiotherapy **(extracranial)** is considered established for the following indications:

- Spinal or vertebral body tumors that include:
  - Metastatic or primary
  - Irradiated or unirradiated
- Spinal or vertebral metastases that are radioresistant (e.g., renal cell carcinoma, hepatocellular carcinoma, melanoma and sarcoma).
- Individuals with stage I, node-negative stage IIA (no larger than 5 cm), or T3N0 (T3 based on size) non-small cell lung cancer (NSCLC) showing no nodal or distant disease and who are not candidates for surgical resection
- Individuals with stage I or node-negative stage IIA limited-stage small-cell lung cancer (LSSCLC)
- In the treatment of primary and metastatic liver malignancies
- Low- or intermediate-risk localized prostate cancer. High-risk prostate cancer when not treating the pelvic lymph nodes.
- For local treatment of advanced or recurrent pancreatic adenocarcinoma without evidence of distant metastasis and for preoperative treatment in borderline resectable cases.
- Lung metastatic disease when **all** the following apply:
  - Single metastatic lesion measuring ≤ 5 cm
  - Extrapulmonary disease is stable or volume of disease is low with remaining treatment options when **one** of the following apply:
    - Intent is either curative or palliative (e.g. Lesion is close to a major vessel and standard treatment could lead to hemoptysis or hemorrhage)
    - Treatment of a previously irradiated field

- Bone metastatic disease when **both** of the following apply:
  - Treatment of a previously irradiated field

- Re-treatment with external beam radiation therapy would result in significant risk of spinal cord injury

- Oligometastatic disease
  - For an individual with non-small cell lung cancer who meets **all** of the following criteria:
    - Has had or will undergo curative treatment of the primary tumor (based on T and N stage)
    - Has 1 to 3 metastases in the synchronous setting
  - For an individual with colorectal cancer who meets **all** of the following criteria:
    - Has had or will undergo curative treatment of the primary tumor
    - Presents with 1 to 3 metastases in the lung or liver in the synchronous setting
    - For whom surgical resection is not possible
  - For an individual who meets the following criteria:
    - A clinical presentation of one to three metastatic lesions involving adrenal gland, lung, liver, lymph nodes, renal, spine or bone metastases when **all** of the following conditions are met:
      - Primary tumor is breast, colorectal, melanoma, non-small cell lung, prostate, renal cell, or sarcoma
      - Disease free interval of > 3 months from the initial diagnosis
      - Primary tumor received curative therapy and is controlled

- Locoregional recurrence in an individual without evidence of distant metastases: Cervical Cancer for the following:
  - History of previous radiation to the same or abutting region and inability to deliver therapeutic doses of radiation with other techniques.

- Kidney Cancer
  - For inoperable individuals with stage I kidney cancer.

- Other tumor types when used to treat a previously irradiated field.

Stereotactic radiosurgery or stereotactic body radiotherapy using fractionation is considered established when used for indications listed above.

Note:
- *Fractionated SRS refers to SRS or SBRT performed more than once on a specific site*
- *SBRT is commonly delivered over 3 to 5 fractions*
- *SRS is most often single-fraction treatment; however multiple fractions may be necessary when lesions are near critical structures.*

Exclusions:
Stereotactic radiosurgery and body radiotherapy are considered experimental/investigational for all other diagnoses not specified above.

CPT/HCPCS Level II Codes ***(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)***

Established codes:

32701	61781	61782	61783*	61796	61797
61798	61799	61800	63620	63621	77261
77332	77333	77334	77370	77371	77372
77373	77402	77407	77412	77432	77435
G0339	G0340	G6003	G6004	G6005	G6006
C9795					

* This code is not separately reimbursable.

Other codes (investigational, not medically necessary, etc.):

N/A

Note: The above code(s) may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.

Rationale

Evidence on the use of stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) consisting primarily of case series, registry data and early phase trials, with a limited number of randomized controlled trials (RCTs), nonrandomized comparative trials, and expert opinion.

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 which depend on the location, shape, and radio-sensitivity of the target tissue and the function and radio-sensitivity of the surrounding tissue. Several ongoing questions exist in the evaluation of SRS and SBRT, related to most appropriate choices of:

- Radiotherapy delivery device based on the size and shape of the target lesion.
- Dose fractionation.
- Methods to reduce toxicity.

Trials that would allow direct comparison of all of the possible variables involved in selecting specific SRS and SBRT methods do not currently exist. Therefore, the available evidence is inadequate to permit scientific conclusions about specific radiation planning and delivery techniques, including the specific number of fractions and methods of dose escalation or toxicity reduction. Therefore, the following discussion groups together several different techniques for delivering SRS and SBRT and does not attempt to compare specific radiation planning and delivery techniques.

The following conclusions are based on a review of the evidence, including, but not limited to, published evidence and clinical expert opinion, via a clinical input process.

STEREOTACTIC RADIOSURGERY (INTRACRANIAL)

The purpose of SRS is to use a focused radiotherapy technique to treat intracranial and other brain lesions that are relatively inaccessible surgically and that are often located near eloquent or radiosensitive areas.

Non-Neoplastic Intracranial Conditions Treated With SRS

Arteriovenous Malformations

An arteriovenous malformation (AVM) comprises a tangled network of vessels in which blood passes from arteries to veins without intervening capillaries. AVMs range in size from small, barely detectable lesions to large lesions that can occupy an entire hemisphere. SRS incites an inflammatory response in the vessels, which results in ongoing fibrosis with eventual complete obliteration of the lesion over a course of months to years. This latency period is variable, depending on the size of the AVM and the dose distribution of the radiosurgery. During this latency period, an ongoing but declining risk of hemorrhage is present. In contrast, surgical excision provides an immediate effect on the risk of hemorrhage. Total surgical extirpation of the lesion, if possible, is the desired form of therapy to avoid future hemorrhage. However, a small subset of AVMs because of their size or location cannot be excised without serious neurologic sequelae. SRS is an important alternative in selected patients.

The evidence on the use of SRS for unruptured AVM consists primarily of noncomparative cohort studies and systematic reviews, which demonstrate relatively high rates of complete obliteration of AVM after SRS, in the range of 40% to 70%. Isolating the effect of the SRS therapy in and of itself can be challenging, as many patients are treated with more than 1 therapy, including endovascular treatments and surgery. Recently, an RCT that compared medical therapy with various interventions in the treatment for AVM showed no significant improvement in outcomes with interventional therapy. However, given that the interventional studies included a variety of therapies, it is difficult to assess whether 1 particular component of the intervention has or lacks benefit. Several important aspects of management of AVM with or without SRS remain the subject of inquiry. Patient selection factors such as agreement on the exact definition of “unruptured” (no prior evidence of intracranial hemorrhage or mild intracranial hemorrhage associated with, e.g., seizure leading to investigation and diagnosis), size and location of lesions (eloquent areas) remain the subject of debate and impact potential candidacy for medical management vs intervention. The differentiation of focal neurologic deficits presumably due to limited intracranial hemorrhage from postintervention effects is under study. The evidence for management of special populations; pediatrics and pregnant women is limited to case reports.(1-18)

Trigeminal Neuralgia

Trigeminal neuralgia is a disorder of the fifth cranial (i.e., trigeminal) nerve that causes episodes of intense, stabbing pain in the face. The International Classification of Headache Disorders has defined classical trigeminal neuralgia as both idiopathic and related to vascular compression. Painful trigeminal neuropathy is caused by other conditions; post herpetic, posttraumatic, secondary to multiple sclerosis plaque or a space occupying lesion.(19)

Although trigeminal neuralgia is initially treated medically, in a substantial number of cases, drug treatment is either ineffective or the adverse effects become intolerable. Neurosurgical options include microvascular decompression, which involves craniotomy, peripheral neurectomy or rhizotomy. Rhizotomy is a technique to percutaneously isolate the nerve and apply ablation techniques such as balloon compression, radiofrequency ablation or chemical injection. SRS of the proximal trigeminal nerve root has been investigated as an alternative to

these neurosurgical treatments. There is a latency period of approximately one month for the effect to be observed.

Case series identify improvements in pain related to trigeminal neuralgia after treatment with SRS. Comparative studies that evaluated the use of SRS compared with alternative treatments for trigeminal neuralgia were reviewed in a systematic review without meta-analysis and were judged to be of poor quality. Only 1 study specifically addressed the use of radiosurgery, and it was stopped before accrual was completed.(19-22)

Epilepsy

Seizure disorders are initially treated medically and may require more than 1 pharmacologic agent. Surgical treatment is only considered in those instances when the seizures have proven refractory to all attempts at aggressive medical management, when the frequency and severity of the seizures significantly diminish quality of life, and when the seizure focus can be localized to a focal lesion in a region of the brain accessible to resection. When surgery is required the clinical standard of care is anterior temporal lobectomy. The purpose of SRS is to use a focused radiotherapy technique to ablate epileptogenic foci when seizures have become drug-resistant or medication-related adverse events are intolerable and to potentially avoid complications associated with surgical intervention.

The literature on the use of SRS as a treatment for epilepsy includes case reports on primary epileptic disorders as well as tumor-related epilepsy. Evidence on the use of SRS for epilepsy treatment is limited by the lack of RCTs comparing SRS with other therapies for epilepsy treatment.(23-28)

Tremor and Movement Disorders

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

The evidence related to the use of SRS for tremor includes a systemic review and uncontrolled cohort studies, many of which report outcomes from the treatment of tremor of varying etiologies. There is a retrospective analysis of a single-center experience. 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 comparing 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.

Chronic Pain

The TEC Assessment (1999) identified 2 reports evaluating radio surgical thalamotomy for chronic pain.

Roberts and Pouratian (2017) reported the results of a systematic review of the data in six studies (total n =113 patients) of SRS as an intervention for chronic pain.(38) Outcomes were reported on the basis of radiation target (pituitary or thalamus) and pain etiology (malignant or

nonmalignant). Clinical success was reported to be achieved in 51% of pituitary SRS, at least 23% of thalamic SRS, 39% of nonmalignant pain patients, and at least 33% of malignant pain patients. Adverse events were noted in 21% of patients; the majority related to hormonal deficits from pituitary SRS.

The evidence related to the use of SRS for chronic pain includes a systematic review of noncomparative studies. The relevant outcomes are symptoms and treatment-related morbidity. Clinical expert opinion input reported that intracranial SRS for treatment of chronic pain (other than associated with trigeminal neuralgia) was not an appropriate alternative to other surgical interventions. The evidence is insufficient to determine the effects of the technology on health outcomes.

Neoplastic Conditions Treated with SRS
Benign neoplastic intracranial conditions include acoustic neuroma, pituitary adenoma, craniopharyngioma, and glomus jugulare tumor. Treatment options include conservative therapies (e.g., surveillance, medical therapy), radiotherapy, and surgical intervention. SRS is typically used when conservative medical treatment has failed and as an alternative to open neurosurgical intervention.

Benign Neoplastic Lesions

Acoustic Neuromas
Acoustic neuromas, also called vestibular schwannomas, are benign tumors originating on the eighth cranial nerve, sometimes associated with neurofibromatosis, which can be linked to significant morbidity and even death if their growth compresses vital structures. The tumors arise from the Schwann cell sheath surrounding either the vestibular or cochlear branches of the eighth cranial nerve. Treatment options include complete surgical excision using microsurgical techniques.

SRS is widely used to treat acoustic neuromas (vestibular schwannomas). 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 generally using fractionated SRS. One systematic review found that SRS and microsurgery are comparable treatments for primary management of small to medium (<3 cm) vestibular schwannomas with regard to hearing preservation at 65 months; microsurgery was favored over SRS for tumor control at 70 months (98% vs 92%), while SRS was favored over microsurgery for reducing the proportion of patients with facial nerve dysfunction at 12 months (2% vs 10%) Given that vestibular schwannoma is a slow-growing tumor with symptoms most often related to local compression, demonstration of slowing of progression is a valid outcome. A single comparative study was identified that demonstrated comparable tumor control outcomes between SRS and surgical therapy for small vestibular schwannomas. A Cochrane review did not identify any RCTs.(39-48)

Pituitary Adenomas
Pituitary adenomas are benign tumors with symptoms related to hormone production (i.e., functioning adenomas) or to neurologic symptoms due to their impingement on surrounding neural structures. Surgical treatment options for pituitary adenomas include surgical excision, conventional radiotherapy, or SRS. Surgical excision is typically offered to patients with functioning adenomas, because complete removal of the adenoma leads to more rapid control of autonomous hormone production. The effects of SRS on hormone production are delayed or incomplete. In patients with nonfunctioning adenomas, the treatment goal is to control

growth; complete removal of the adenoma is not necessary. Conventional radiotherapy has been used in this setting with an approximate 90% success rate with few complications.

Noncomparative studies have demonstrated high rates of tumor control (≥ 85%) for pituitary adenomas with SRS treatment, with better tumor control with smaller lesions. Comparative studies evaluating the treatment of pituitary adenomas with SRS vs surgery or traditional radiotherapy do not exist.(49-51)

Craniopharyngiomas

Craniopharyngiomas are benign tumors that arise from pituitary embryonic tissue at the base of the gland. However, because of proximity to the optic pathways, pituitary gland, and hypothalamus, they may cause severe and permanent damage to these critical structures and can even be life-threatening. Total surgical resection is often difficult.

The evidence related to the use of SRS for craniopharyngioma consists primarily of case series and cohort studies, which report high rates OS.(52-55)

Glomus Jugulare Tumors

A glomus jugulare tumor is a rare, benign tumor arising in the skull temporal bone that involves middle and inner ear structure. No consensus exists on optimal management to control tumor burden while minimizing treatment-related morbidity.

SRS has been used for the treatment of other primary brain tumors, including gliomas, meningiomas, and primitive neuroectodermal tumors (i.e., medulloblastoma, pineoblastoma). Treatment of primary brain tumors such as gliomas is more challenging, due to their generally larger size and infiltrative borders.

The evidence review related to the use of SRS for glomus jugulare tumors includes 2 systematic reviews, neither of which compared SRS to other treatment modalities and recently published case series. Available data suggests that SRS is associated with improved patient outcomes.(56-59)

Section Summary: Benign Neoplastic Intracranial Lesions

The published evidence for the use of SRS to treat a subgroup of uncommon benign neoplastic intracranial lesions (acoustic neuroma, pituitary adenoma, craniopharyngioma, and glomus jugulare tumors) remains limited to systematic reviews of nonrandomized observational studies, other nonrandomized observational studies, and case series. These reports would suggest that long-term outcomes of fractionated radiosurgery for these benign neoplasms are associated with good local control and, acceptable treatment-related side effects. The likelihood of high quality systematically acquired evidence is low due to the rarity of the conditions. Clinical input continues to support an individualized approach to the use of SRS for these tumors with the recognition that outcomes are affected by factors such as the location of the tumor and type of SRS used (hypofractionated, fractionated or single session treatment). Thus, for the subpopulation of patients with uncommon benign neoplastic intracranial tumors (acoustic neuroma, pituitary adenoma craniopharyngioma, and glomus jugulare tumors) SRS would provide a clinically meaningful improvement in net health outcome.

SRS for Malignant Neoplastic Intracranial Lesions

Treatment of primary brain tumors such as gliomas are more challenging, due to their generally larger size and infiltrative borders. Intracranial metastases are considered ideal targets for radiosurgery due to their small spherical size and non-infiltrative borders. Brain metastases are a frequent occurrence, seen in 25% to 30% of all patients with cancer, particularly in those with cancer of the lung, breast, or colon, melanoma and kidney. Whole brain radiotherapy (WBRT) is considered the standard of care in the treatment of brain metastases, and the addition of SRS to WBRT has been shown to improve survival and local tumor control in selected patients. SRS offers the additional ability to treat tumors with relative sparing of normal brain tissue in a single fraction.

Primary or Recurrent Gliomas or Astrocytomas
Direct evidence is not available to compare radiotherapy methods for primary or recurrent gliomas or astrocytomas. Evidence from heterogeneous observational studies has demonstrated high rates of local control and survival using SRS to treat gliomas in the primary and recurrent setting. The tumors are very aggressive and there are limited treatment options. In 2018, clinical input continued to support that SRS for the treatment of recurrent glioma may be appropriate, although there is not an anticipated impact on OS survival. The standard of care for initial therapy of primary glioma after surgical resection is chemoradiation with temozolomide and conventional radiotherapy.(60-65)

Brain Metastases
For brain metastases, evidence from RCTs and systematic reviews have indicated that 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 ten or fewer metastases.(66-84)

Uveal melanoma
The purpose of SRS is to use a focused radiotherapy technique to treat certain malignant tumors that are relatively inaccessible surgically and that are often located near eloquent or radiosensitive areas.

Melanoma of the uvea (choroid, ciliary body, and iris) is the most common, primary, malignant, intraocular tumor in adults. Uveal melanoma is diagnosed mostly at older ages, with a progressively rising, age-specific, incidence rate that peaks near the age of 70 years.

Uveal melanomas can arise in the anterior (iris) or the posterior (ciliary body or choroid) uveal tract. Melanomas of the posterior uveal tract generally have a more malignant, histologic appearance; are detected later; and metastasize more frequently than iris melanomas.

A number of factors influence prognosis. The most important factors include the following: cell type, tumor size, location of the anterior margin of the tumor, degree of ciliary body involvement, presence of secondary glaucoma and extraocular extension. Extraocular extension, recurrence, and metastasis are associated with an extremely poor prognosis, and long term survival is limited. The five-year mortality rate associated with metastasis from the ciliary body or choroidal melanoma is approximately 30%, compared with a rate of 2% to 3% for iris melanomas.

The evidence for use of SRS to treat uveal melanoma is limited to case series. The condition is rare with poor clinical outcomes and treatment options. There are currently no active clinical

trials to evaluate SRS to treat uveal melanoma and, therefore, there are limited prospects for accumulating additional high quality data. Clinical input reported that the use of SRS to treat uveal melanoma could provide patients with low-risk disease (based on tumor size using the Collaborative Ocular Melanoma Study (COMS) definition of small and medium) an option to avoid or postpone enucleation with preservation of some visual acuity and functional abilities.(85-93)

STEREOTACTIC BODY RADIOTHERAPY (EXTRACRANIAL)

Extracranial Metastatic Tumors Treated With SBRT

Spinal Tumors - Primary and Metastatic

Metastatic tumors to the spine have historically been treated with conventional radiotherapy. The need for retreatment is high due to morbidity from metastatic disease (e.g., pain, myelopathy, spinal cord compression), but radiotherapy to the spine is often limited due to concern for radiation myelopathy and other adverse radiation effects. SBRT to the spine has been most widely studied in patients requiring re-irradiation, but interest has also developed in the use of SBRT for the initial treatment of spinal tumors.

SBRT has been shown to improve outcomes (reduce pain) in patients with spinal (vertebral) tumors in numerous observational trials and an RCT that compared SBRT to EBRT in patients with painful spinal metastases. Most of the literature addresses metastases that recur after prior radiotherapy. Repeat administration of conventional radiation therapy increases the risk of treatment-related myelopathies. Nonrandomized study results are sufficient to determine that SBRT improves outcomes (reduces pain) in patients with spinal (vertebral) tumors. In addition, in 2018, clinical expert opinion input reported that SBRT is an important treatment option for patients whose spinal tumors have had prior radiotherapy because of the ability to spare the spinal cord and escalate tumor dose. Thus, for individuals with primary or metastatic spinal or vertebral body tumors in patients who have received prior spinal radiotherapy, SBRT would provide a clinically meaningful improvement in net health outcome.(94-100)

Clinical input reported that SRS is an important treatment option for patients whose spinal tumors have had prior radiotherapy because of the ability to spare the spinal cord and dose escalate tumor. Thus, for individuals with primary or metastatic spinal or vertebral body tumors in patients who have received prior spinal radiotherapy, SBRT would provide a clinically meaningful improvement in net health outcome.

Non-small Cell Lung Cancer (NSCLC)

SBRT has been studied for the treatment of lung cancers, specifically non-small-cell lung cancer (NSCLC), with the greatest focus on inoperable stage I NSCLC.

Although no direct comparative evidence is available, evidence suggests that survival rates may be similar for SBRT and surgical resection for patients with stage T1 and T2a NSCLC tumor (not >5 cm in diameter) who show no nodal or distant disease and who are not candidates for surgical resection because of comorbid conditions. Additionally, SBRT was associated with improved survival and a reduced risk of adverse events as compared to conventional radiotherapy and RFA in inoperable NSCLC. In patients with operable stage I

NSCLC, long-term OS and DFS were improved with lobar resection as compared to SBRT and, for the majority of comparisons, sublobar resection was better than SBRT. (101-120)

Primary and Metastatic Hepatocellular Carcinoma
Surgical resection is the preferred treatment of hepatocellular carcinoma, although at the time of diagnosis, less than 20% of patients are amenable to definitive surgical management due to advanced local disease or comorbidities. These patients may be candidates for local ablative therapies, including radiofrequency ablation and chemoembolization. Radiation may be considered as an alternative to local ablative/embolization therapies or if these therapies fail.

Radiation-induced liver disease is an important complication of radiotherapy and is secondary to endothelial injury and thrombotic sequelae. The disease typically occurs four to eight weeks after completion of radiotherapy but has been described as early as two weeks and as late as seven months post-radiation. It is a major factor that limits radiation dose escalation and reirradiation for tumors situated proximate to the liver.(121-122)

The liver is the most common site of metastatic spread of colorectal cancer (CRC). Evidence has shown that surgical resection of limited liver metastases can result in long-term survival in select patients. However, only 10% to 20% of patients with metastatic CRC to the liver are surgical candidates. In patients who are not candidates for surgery, a variety of locally ablative techniques have been developed, the most common of which are RFA and TACE.

There are no RCTs reported on the use of SBRT for HCC. Studies have used heterogeneous treatment schedules, treatment planning techniques, patient populations, and outcome measures. The optimal dose and fractionation scheme are unknown. Although promising local control rates of 71% to 100% at 1 year have been reported, there are only retrospective cohorts reporting on the use of SBRT in conjunction with or as an alternative to established treatment modalities, including systemic therapy, RFA, and TACE. Similar short-term lesion-control rates have been reported for metastatic liver disease. Palliative treatment, including for larger lesions (>3 cm), has also been reported. The use of SBRT, either alone or in conjunction with other liver-directed therapies, is emerging as a bridge to transplant.(123-141)

In 2010, Blue Cross Blue Shield of Michigan obtained input from an experienced external panel of academic clinicians familiar with this technology in the challenges of caring for this patient population. Their extensive clinical expertise supported that these technologies were important tools in the treatment of selected extra-cranial tumors. Stereotactic radiosurgery may be capable of treating extracranial targets with submillimeter accuracy, according to the company's website and the published experience. It also tracks the tumor motion during the treatment using implanted fiducial markers. Stereotactic radiosurgery is indicated as standard treatment for clinical situations where obtaining local control is critical to the success of treatment and cannot be attained by less complex treatment.

Prostate Cancer
Evidence on the use of SBRT in prostate cancer consists of systematic reviews of prospective and retrospective studies, a single RCT, and single arm assessments of acute and late toxicity and early PSA outcome data retrospectively compared with historical controls. Studies have shown promising results on the use of SBRT in prostate cancer with low toxicity rates. As with other treatment modalities for prostate cancer, completion of randomized controlled trials is not likely. Many perspective case series and retrospective cohort studies involving

subjects with prolonged life expectancies and localized low-risk or intermediate-risk prostate cancer consistently associate SBRT with an acceptable toxicity profile and tumor control which is comparable to other radiation techniques. In the ORIOLE study, SBRT was associated with a significant improvement in disease progression and median PFS as compared to observation in men with recurrent hormone-sensitive prostate cancer and 1 to 3 metastases with a similar toxicity profile.(131-167)

ASTRO (2013) updated its recommendation to support of the use of SBRT for prostate cancer, as an appropriate alternative, for patients with low to intermediate risk.(226)

Pancreatic Cancer
Combined chemoradiotherapy plays a significant role in the treatment of locally advanced pancreatic cancer. Noncomparative observational and retrospective studies of SBRT have reported increased patient survival compared with historical data.

Initial experience with single fraction SBRT for unresectable pancreatic cancer resulted in favorable local control rates but high rates of late gastrointestinal complications. Subsequent studies using fractionated SBRT have shown lower rates of late toxicity. A recent retrospective review of locally advanced pancreatic cancer cases in the National Cancer Database (NCDB) compared outcomes between 7,819 patients treated with conventional radiation with outcomes in 631 patients treated with SBRT. Two year overall survival was 16.3% with conventional radiation versus 20.3% in patients treated with SBRT ($p<.001$). This benefit was maintained in the propensity matched analysis. Another retrospective study compared outcomes in the NCDB between chemo alone, chemo plus EBRT, chemo plus IMRT and chemo plus SBRT. Median overall survival results were 9.9 months, 10.9 months, 12 months and 13.9 months respectively. For the match propensity cohort, overall survival was superior with SBRT versus chemotherapy alone ($p<.018$).(73, 168-172, 227-229)

Primary and Metastatic Renal Cell Carcinoma
Localized renal cell carcinoma is conventionally treated surgically; local ablative methods may also be an option. Primary renal cell carcinoma is treated with partial or total nephrectomy when surgery is feasible. Patients may also receive systemic therapy with TKI therapy and supportive care. Local ablative methods may also be an option. RCC has been considered relatively radioresistant. However, the renal parenchyma, vasculature, and collecting system are considered radiosensitive.

The literature on the use of SBRT for renal cell carcinoma consists of small case series, a systematic review of cases series, and other observational studies. which have generally reported high rates of local control that may be particularly important for brain and spinal metastases. However, the impact of SBRT on patient outcomes cannot conclusively be derived from this evidence. There are no RCTs that have evaluated SBRT for primary RCC or metastatic lesions to the brain or spine that permit comparisons between SBRT and current established treatment modalities for RCC.(99, 173-187)

Oligometastases
Oligometastases are defined as isolated sites of metastasis, with the entire burden of disease being recognized as a finite number of discrete lesions that can be potentially cured with local therapies.

In general, the indications for SBRT for oligometastases are the same as for metastasectomy. Recently proposed specific criteria for the use of SBRT in patients with oligometastases include: a controlled primary, favorable histology, limited metastatic disease, metachronous appearance of metastases, young age, and good performance status.

Management of metastatic solid tumors has historically focused on systemic treatment with palliative intent. However, surgical treatment of oligometastatic disease is now common practice in some clinical settings. Although cure may be possible in some patients with oligometastatic disease, the aim of SBRT in this setting is mainly to achieve local control and delay progression, which also may postpone the need for further treatment.
The evidence related to the use of SBRT for the management of oligometastases to multiple sites, including the lungs, adrenal glands, and bones (other than spine) consists of relatively small, noncomparative studies that confirm clinically important rates of local control. Systemic therapy is most frequently the preferred therapy for patients with metastatic disease of these selected tumor types. SBRT used to treat oligoprogression has the potential for a patient to be maintained on the same line of systemic therapy, delaying the need for another line of therapy that is likely to be less effective. Clinical input also reported that SBRT may represent the singular option for some patients with oligometastatic disease that includes one or both adrenal glands in patients who are poor surgical and RFA candidates. Thus, for this specific subpopulation, SBRT would provide a clinically meaningful improvement in net health outcome. (188-205)

SUMMARY OF EVIDENCE

Stereotactic Radiosurgery

For individuals who have non-neoplastic intracranial conditions (e.g., arteriovenous malformations, trigeminal neuralgia), non-neoplastic neurologic conditions (e.g., epilepsy, tremor and movement disorders, chronic pain), benign neoplastic intracranial lesion(s) (e.g., acoustic neuromas, pituitary adenoma, meningiomas, craniopharyngioma, glomus jugulare tumors), and malignant neoplastic intracranial lesion(s) (e.g., gliomas, astrocytomas, brain metastases), or uveal melanoma who receive SRS, the evidence includes randomized controlled trials (RCTs), nonrandomized retrospective cohort studies, and observational studies or case series. Relevant outcomes are overall survival, symptoms, and treatment-related morbidity. General limitations of the body of evidence include, but are not limited to, a lack of trials that directly compare SRS and comparators, patient heterogeneity within and between studies, and failure to use standardized methods to collect and report outcomes (benefits and harms). There are several contextual factors to consider, such as: SRS offers a noninvasive, highly precise radiotherapy alternative to surgery (particularly important for patients unable to undergo resection due to the presence of underlying comorbidities), intracranial lesions often are difficult to access surgically (and may be associated with a high risk for devastating adverse sequelae), intracranial lesions typically are located adjacent to vital organs and structures that are highly susceptible to radiation toxicities, and the accuracy and precision of SRS in this context make this technique a viable alternative to standard, nonconformal external beam radiotherapy. Finally, given the rarity of many of the conditions under review, direct comparative trials are unlikely. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome for patients

For individuals in the subgroup of uncommon benign neoplastic intracranial lesions (acoustic neuroma, pituitary adenoma, craniopharyngioma, and glomus jugulare tumors) the published

evidence for the use of SRS remains limited to systematic reviews of nonrandomized observational studies, other nonrandomized observational studies, and case series. The relevant outcomes are symptoms and treatment-related morbidity. These reports would suggest that long-term outcomes of fractionated radiosurgery for these benign neoplasms are associated with good local control and, acceptable treatment related side effects. The likelihood of high-quality systematically acquired evidence is low due to the rarity of the conditions and the published evidence is insufficient to determine the effects of the technology on health outcomes.

In 2018, Blue Cross Blue Shield Association (BCBSA) received clinical expert opinion input which continued to support an individualized approach to the use of SRS for these tumors with the recognition that outcomes are affected by factors such as the location of the tumor and type of SRS used (hypofractionated, fractionated or single-session treatment). Thus, for the subpopulation of patients with uncommon benign neoplastic intracranial tumors (acoustic neuroma, pituitary adenoma craniopharyngioma, and glomus jugulare tumors), SRS would provide a clinically meaningful improvement in net health outcome. The evidence is sufficient to determine the impact of the technology results in a meaningful improvement in the net health outcome.

Stereotactic Body Radiotherapy
For individuals who have benign or malignant extracranial lesion(s) (e.g., extracranial primary and metastatic tumors) who receive SBRT, the evidence includes a few randomized controlled trials, nonrandomized cohort studies, and case series. Relevant outcomes are overall survival, symptoms, and treatment-related morbidity. Limitations of the evidence include a lack of comparative trials, heterogeneity between patients and treatment schedules and planning techniques, and failure to use standardized methods to collect and report outcomes. The evidence is sufficient to determine the effects of the technology on health outcomes for patients.

Supplemental Information

CLINICAL INPUT RECEIVED THROUGH PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS

2018 Input
In response to requests, Blue Cross Blue Shield Association received clinical input from five respondents, including 2 specialty society-level responses, one of which included multiple specialty societies, and 3 physician-level responses either identified by specialty societies or an academic medical center, while this policy was under review in 2018.

Evidence from clinical input is integrated within each section as summarized and the Summary of Evidence

2013 Input

In response to requests, Blue Cross Blue Shield Association received input from 3 physician specialty societies (6 reviewers) and 6 academic medical centers, for a total of 12 reviewers, while this policy was under review in 2013. Input was provided on content related to both stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT). Support for the use of SBRT for hepatocellular carcinoma, prostate cancer, and oligometastases, and the use of SRS for uveal melanoma was mixed.

2011 Input

In response to requests, Blue Cross Blue Shield Association received input from 6 physician specialty societies (8 reviewers) and 4 academic medical centers, for a total of 12 reviewers, while this policy was under review in 2011. Input was provided on content related to both SRS and SBRT. There was general agreement with the policy statements for the use of stereotactic radiosurgery in treating the neoplasms/conditions listed in the policy statements. In addition, there was support to expand the policy statements on the use of stereotactic radiosurgery to include craniopharyngiomas and glomus jugulare tumors.

There was general support for the use of SBRT in spinal tumors and early-stage NSCLC; there was also support to expand the use of SBRT in the spine to include metastatic radioresistant tumors. Support for the use in primary and metastatic lesions of the liver, pancreas, adrenal and kidney was mixed. There was little support for the use of SBRT in prostate cancer.

2008 Input

In response to requests, Blue Cross Blue Shield Association received input from two physician specialty societies and four academic medical centers while this policy was under review in 2008. The input uniformly supported use of this technology in the treatment of NSCLC and spinal tumors after prior radiation therapy. There was also support for use in some patients with liver (metastatic and primary) cancer and as first-line treatment of spinal tumors. There was little support for its use in cases of prostate cancer.

PRACTICE GUIDELINES AND POSITION STATEMENTS

American Heart Association Scientific Statement

The American Heart Association and American Stroke Association (2017) published a scientific statement on the management of brain arteriovenous malformations (AVMs).(206) The statement concludes that the available literature supports the use of stereotactic radiosurgery for small- to moderate volume brain AVMs that are generally 12 cm^3 or less in volume or located in deep or eloquent regions of the brain.

American Society of Clinical Oncology

In 2021, the American Society of Clinical Oncology (ASCO), Society for Neuro Oncology (SNO), and the American Society for Radiation Oncology (ASTRO) published a guideline that addresses the role of surgery, radiation therapy, and systemic therapy in the treatment of patients with brain metastases secondary to nonhematologic solid tumors.(207) The following recommendations regarding the use of SRS in this population were made in this guideline:

- "SRS alone (as opposed to WBRT [whole brain radiotherapy] or combination of WBRT and SRS) should be offered to patients with one to four unresected brain metastases, excluding small-cell carcinoma."
    - "Qualifying Statement: The inclusion criteria of the randomized trials that underly this recommendation were generally tumors of less than 3 or 4 cm in diameter and did not include radioprotectant strategies of memantine or hippocampal avoidance"
- "SRS alone should be offered to patients with 1 to 2 resected brain metastases if the surgical cavity can be safely treated and considering the extent of remaining intracranial disease."
    - "Qualifying Statement: The randomized trials upon which this recommendation is based were of single fraction SRS and conventional WBRT (without radioprotectant strategies of memantine or hippocampal avoidance)"
- "SRS, WBRT, and the combination of SRS plus WBRT are all reasonable options for patients with more than 4 unresected or more than 2 resected brain metastases and better performance status (e.g., [Karnofsky Performance Status] KPS ≥70). SRS may be preferred for patients with better prognosis or where systemic therapy that is known to be active in the CNS [central nervous system] is available."

National Comprehensive Cancer Network Guidelines

National Comprehensive Cancer Network (NCCN) provides guidelines for cancer treatment by site that include the use of SRS and SBRT for certain cancers.(225) Guidelines addressing SRS and SBRT are summarized in Table 1.

Table 1. Recommendations for SRS and SBRT

Cancer Site	Tumor Type	Recommendations	Version
Bone	• Chondrosarcoma • Chordoma • Progressive Ewing sarcoma • Unresectable giant cell tumor • Osteosarcoma with positive margins or relapsed progressive disease • Oligometastases	• Consider SRS to allow high-dose therapy while maximizing normal tissue sparing (category 2A) • Consider use of SRS/SBRT, especially for oligometastases	2.2024
CNS	• Adult low-grade infiltrative supratentorial astrocytoma/oligodendroglioma • Anaplastic gliomas/glioblastomas • Adult intracranial ependymoma • Adult medulloblastoma • Primary CNS lymphoma • Primary spinal cord tumors • Meningiomas • Limited brain metastases • Extensive brain metastases • Leptomeningeal metastases • Metastatic spine tumors	Principles of RT including consideration of SRS or SBRT are applied to each of the listed tumors (category 2A)	1.2023
Colon	Oligometastases to liver or lung	• Resection is preferred over locally ablative treatment. However, IGRT and SBRT may be considered in patients with a limited number of liver or lung metastases in highly selected cases or in the setting of a clinical	1.2024

		trial. RT should not be used in place of surgical resection. • IMRT clinical situations such as reirradiation of previously treated patients with recurrent disease or unique anatomical situations where IMRT facilitates the delivery of recommended target volume doses while respecting accepted normal tissue dose-volume constraints.	
Head and Neck		The panel acknowledged that SBRT might be beneficial in the setting of re-irradiation, palliation, or older adults.	3.2024
Hepatobiliary	• Hepatocellular carcinoma • Gallbladder Cancer	• Principles of locoregional therapy includes recommendations for SBRT • SBRT can be considered as an alternative to ablation/embolization techniques for HCC or when these therapies have failed or are contraindicated. SBRT could be considered for larger lesions or more extensive disease, if there is sufficient uninvolved liver and liver radiation tolerance can be respected. There should be no extrahepatic disease or it should be minimal and addressed in a comprehensive management plan.	2.2023
Lung	• NSCLC	• SBRT (also known as SABR) has achieved good primary tumor control rates and overall survival, higher than conventionally fractionated radiotherapy. Although SABR is not proven equivalent to lobectomy, some prospective series have demonstrated similar overall and cancer specific survival (Stage 1, selected node-negative Stage IIA). • Close follow-up and salvage therapy for isolated local and/or locoregional recurrence after SABR have been shown to improve overall survival. • SABR is an appropriate option for patients with high surgical risk (e.g., age ≥ 75 years, poor lung function) • SABR is most commonly used for tumors up to 5 cm in size, though selected larger isolated tumors can be treated safely if normal tissue constraints are respected. • Definitive RT to limited oligometastases, particularly SABR, is an appropriate option when it can be delivered safely to the involved sites (Stage IV, advanced/metastatic)	3.2024
Pancreas	• Pancreatic adenocarcinoma	Locally advanced disease • SBRT should be avoided if direct invasion of the bowel or stomach is identified on CT, MRI, and endoscopy • Data are limited to support specific RT recommendations for locally advanced disease. Options may include: ○ Chemoradiation, SBRT, or hypofractionated RT in selected patients who are not candidates for combination chemotherapy	1.2024

		○ Induction chemotherapy followed by chemoradiation or SBRT in select patients (locally advanced without systemic metastases) • SBRT should be delivered at an experienced, high-volume center with technology that allows for image-guided RT or on a clinical trial Recurrent pancreatic cancer • Data are limited to support specific RT recommendations for locally recurrent disease. Options for patients with recurrent, unresectable disease may include: ○ Induction chemotherapy followed by chemoradiation or SBRT (if not previously performed) ○ Chemoradiation or SBRT in selected patients who are not candidates for induction chemotherapy • SBRT should be delivered at an experienced, high-volume center with technology that allows for image-guided RT or in a clinical trial	
Prostate	• Prostate cancer	• Principles of RT identifies SBRT as acceptable in practices with appropriate technology, physics, and clinical expertise. SBRT for metastases can be considered in the following circumstances: ○ In patients with limited metastatic disease (eg, oligometastatic) to the vertebra or paravertebral region ○ when ablation is the goal ○ In symptomatic patients where the lesion occurs in or immediately adjacent to a previously irradiated treatment field ○ In patients with oligometastatic progression where progression-free survival is the goal. • SBRT can be considered when enrollment in clinical trials is encouraged for oligometastatic disease where durable local control is desirable	3.2024
Kidney cancer	• Non-clear cell and clear renal carcinoma	• SBRT may be considered for medically inoperable patients with stage 1 kidney cancer (category 2B) or stage II/III kidney cancer (both category 3) • Relapse or State IV: Metastasectomy or SBRT or ablative techniques for oligometastatic disease	3.2024
Cutaneous Melanoma	• Intact extracranial metastases	• Principles of RT include recommendations for use of SBRT • SBRT may be considered for selected patients with oligometastasis	2.2023
Uveal melanoma	• Primary and recurrent intraocular tumors	• SRS is the least often used and nonpreferred form of definite RT for primary and recurrent intraocular tumors	1.2023
Soft tissue sarcoma	• Extremity/superficial trunk/head and neck	• If disseminated metastases: SBRT as a palliative option (category 2A)	3.2023

	• Retroperitoneal/intra-abdominal	• For Stage IV with single organ and limited tumor bulk that are amenable to local therapy: SBRT with or without chemotherapy as an option • For metastatic disease with isolated regional disease or nodes: SBRT as an option	
Thyroid	• Iodine-refractory unresectable locoregional recurrent/persistent disease • Iodine-refractory soft tissue metastases • Iodine-refractory bone metastases	• Consider resection of distant metastases and/or EBRT/SBRT/IMRT/other local therapies when available for progressive and/or symptomatic metastatic lesions • Most recurrent tumors respond well to iodine therapy; or EBRT, SBRT, or IMRT • Consider surgical palliation and/or EBRT/SBRT other local therapies when available if symptomatic, or asymptomatic in weight-bearing sites	2.2024

ADT: androgen-deprivation therapy; CNS: central nervous system; EBRT: external-beam radiotherapy; HCC: hepatocellular carcinoma; IGRT: image-guided radiotherapy; IMRT: intensity-modulated radiotherapy; NSCLC: non-small cell lung cancer; RT: radiotherapy; SABR: stereotactic ablative radiotherapy; SBRT: stereotactic body radiotherapy; SRS: stereotactic radiosurgery.

[i] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed July 19, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org.

[ii] NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

American Society for Radiation Oncology

The American Society for Radiation Oncology (ASTRO) has guidelines on the treatment of a number of conditions, several of which include SRS or SBRT.

In 2017, the American Society for Radiation Oncology (ASTRO) published an evidence-based guideline on SBRT in patients with early-stage NSCLC. The guideline concluded that "SBRT has an important role to play in treating early-stage NSCLC, particularly for medically inoperable patients with limited other treatment options." Additionally, the document noted that "lower quality evidence led to conditional recommendations on use of SBRT for tumors >5 cm, patients with prior pneumonectomy, T3 tumors with chest wall invasion, synchronous multiple primary lung cancer, and as a salvage therapy after prior radiation therapy." Of note, the ASCO reviewed the ASTRO guideline in 2018 and determined that "the recommendations from the ASTRO guideline...are clear, thorough, and based on the most relevant scientific evidence." (209)

In 2022, ASTRO published an evidence-based guideline on indications and techniques for external beam radiation therapy (EBRT) in patients with primary liver cancers.(210) SBRT (also referred to as ultra hypofractionation delivered in ≤5 fractions) was among the EBRT techniques discussed for patients with confirmed HCC and intrahepatic cholangiocarcinoma (IHC). The choice of regimen is based on tumor location, underlying liver function, and available technology.

In 2019, ASTRO published an evidence-based guideline on radiation therapy for pancreatic cancer. (231) Recommendations are based on a ranking of evidence quality with a corresponding strength of recommendation rating scheme. Quality of evidence is based on the body of evidence available for a particular key question and includes consideration of number of studies, study design, adequacy of sample sizes, consistency of findings across studies, and generalizability.

In 2022, ASTRO published an evidence-based guideline on radiation therapy for brain metastases. (232) Recommendations are based on a ranking of evidence quality with a corresponding strength of recommendation rating scheme. Quality of evidence is based on the body of evidence available for a particular key question and includes consideration of number of studies, study design, adequacy of sample sizes, consistency of findings across studies, and generalizability.

International RadioSurgery Association Guidelines

The International Radiosurgery Association published consensus-based guidelines in 2009 on the treatment of brain or dural AVMs. The guidelines include a clinical pathway that incorporates patients' choice, AVM location and volume, and presence of residual AVM after repeat treatment to guide decisions about SRS use.(230)

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable.

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently unpublished trials that might influence this review are listed in Table 3.

Table 3. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing stereotactic radiosurgery			
Central nervous system neoplasms			
Acoustic neuroma (vestibular schwannoma)			
NCT02055859	Cyberknife Radiosurgery for Patients with Neurinomas	102	May 2025
Brain metastases			
NCT01592968	A Prospective Phase III Randomized Trial to Compare Stereotactic Radiosurgery Versus Whole Brain Radiation Therapy for >/= 4 Newly Diagnosed Non-Melanoma Brain Metastases	100	Sep 2023
NCT00950001	Efficacy of Post-Surgical Stereotactic Radiosurgery for Metastatic Brain Disease: A Randomized Trial	132	Aug 2020
NCT01644591	A Phase II Trial to Determine Local Control and Neurocognitive Preservation After Initial Treatment With Stereotactic Radiosurgery (SRS) for Patients With >3 Melanoma Brain Metastases	49	Aug 2025
NCT01503827	Whole Brain Radiotherapy Following Local Treatment of Intracranial Metastases of Melanoma - A Randomised Phase III Trial	220	Jun 2022
NCT04891471	WHOle Brain Irradiation and STEreotactic Radiosurgery for Five or More Brain Metastases (WHOBISTER): a Prospective Comparative Study of Neurocognitive Outcomes, Level of Autonomy in Daily Activities and Quality of Life	100	Sep 2025
Ongoing stereotactic body radiotherapy			
Non-small-cell lung cancer			
NCT05111197	Local Ablative Stereotactic Radiotherapy for Residual Hypermetabolic Lesion in Patients With Locally Advanced or Metastatic Non-small Cell Lung Cancer Long-term Responders to Immunotherapy : a Randomized, Multicenter, Open-label Phase III Study	112	Jan 2025
Hepatocellular carcinoma			

NCT01730937	Randomized Phase III Study of Sorafenib Versus Stereotactic Body Radiation Therapy Followed by Sorafenib in Hepatocellular Carcinoma	193	Jun 2025
Prostate Cancer			
NCT05209243	Phase III Study of Stereotactic Body Radiation Therapy (SBRT) Plus Standard of Care in Castration Sensitive Oligometastatic Prostate Cancer Patients	266	Mar 2026
NCT04983095	Metastasis Directed Stereotactic Body Radiotherapy for Oligo Metastatic Hormone Sensitive Prostate Cancer	114	Dec 2029 (recruiting)
NCT01508390	Phase II Study of Hypofractionated Stereotactic Body Radiation Therapy as a Boost to the Prostate for Treatment of Localized, Non-Metastatic, High Risk Prostate Cancer	30	Dec 2027 (recruiting)
NCT01794403	A Randomized Study of Radiation Hypofractionation Via Extended Versus Accelerated Therapy (HEAT) For Prostate Cancer	456	Mar 2023 (recruiting)
NCT02470897	A Phase I/II Study of Stereotactic Body Radiotherapy (SBRT) for Prostate Cancer Using Simultaneous Integrated Boost and Urethral-Sparing IMRT Planning	160	Dec 2026
NCT01764646	Stereotactic Body Radiation Therapy for –T1c - cT3a Prostate Cancer With a Low Risk of Nodal Metastases (≤ 20%, Roach Index): a Novalis Circle Phase II Prospective Randomized Trial	170	Sep 2025
NCT01985828	Prospective Evaluation of CyberKnife® as Monotherapy or Boost Stereotactic Body Radiotherapy for Intermediate or High Risk Localized Prostate Cancer	72	Dec 2026 (recruiting)
NCT03367702	Phase III IGRT and SBRT vs IGRT and Hypofractionated IMRT for Localized Intermediate Risk Prostate Cancer	622	Dec 2030 (recruiting)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

Government Regulations

National:

The Centers for Medicare and Medicaid Services does not have a National Coverage Determination for stereotactic radiosurgery/radiotherapy.

Local:

LCD – Carrier Wisconsin Physicians Service Ins. Co– MI
Cranial Stereotactic Radiosurgery (SRS) and Cranial Stereotactic Radiotherapy (SRT) (L30318) (Rev. Eff. 05/01/2015), **Retired 09/30/2015**

Indications:
Stereotactic Radiosurgery (SRS)
Stereotactic radiosurgery (SRS) is a method of delivering high doses of ionizing radiation to small intracranial targets. The technique differs from conventional radiotherapy, which involves exposing large areas of intracranial tissue to relatively broad fields of radiation over a number of sessions. SRS entails delivering highly focused convergent beams in a single session so that only the desired target is radiated, sparing adjacent structures. SRS is strictly defined as radiation therapy delivered via stereotactic guidance with ~1 mm targeting accuracy to a cranial lesion in a single fraction.

Stereotactic radiosurgery works the same as all other forms of radiation treatment. It does not remove the tumor or lesion, but it distorts the DNA of the tumor cells. The cells then lose their ability to reproduce and retain fluids. The tumor reduction occurs at the rate of the normal growth rate of the specific tumor cell. In lesions such as AVMs (a group of abnormal blood vessels in the brain), radiosurgery causes the blood vessels to thicken and close off. The shrinking of a tumor or closing off of a vessel occurs over a period of time. For benign tumors and vessels, this will usually be 18 months to two years. For malignant tumors and metastatic tumors, results may be seen as soon as a couple of months as these cells are very fast-growing.

In certain cases whole-brain radiation is administered prior to and/or following this procedure. Stereotactic radiation amounts may be reduced or the procedure may be contraindicated if the lesion is within 5 mm of the brainstem or optic chiasm.

Indications for SRS

Intracranial lesions under the following conditions:

1. Primary central nervous system malignancies, generally under 5 cm and as a boost treatment for larger cranial, base of skull, or spinal lesions that have been treated initially with external beam radiation therapy or surgery (e.g., grade III and IV gliomas, oligodendrogliomas, sarcomas, chondrosarcomas, chordomas, and nasopharyngeal of paranasal sinus malignancies).
2. Primary and secondary tumors involving the brain or spine parenchyma, meninges/dura, or immediately adjacent bony structures.
3. Benign brain and spinal tumors such as cranial meningiomas, acoustic neuromas, other schwannomas, pituitary adenomas, pineal cytomas, craniopharyngiomas, glomus tumors, and hemangioblastomas.
4. Cranial arteriovenous malformations and hemangiomas.
5. Trigeminal neuralgia not responsive to medical management.
6. Metastatic brain lesions, generally limited in number, with stable systemic disease, Karnofsky Performance Status of 50 or greater or expected to return to 70 or greater with treatment, and otherwise reasonable survival expectations or an Eastern Cooperative Oncology Group (ECOG) performance status of 2 or less or expected to return to 2 or less with treatment.
7. Relapse in a previously irradiated cranial or spinal field where the additional stereotactic precision is required to avoid unacceptable vital tissue radiation.
8. Essential tremor: coverage is limited to the patient who cannot be controlled with medication, has major systemic disease or coagulopathy, and who is unwilling or unsuited for open surgery. Coverage is further limited to unilateral thalamotomy. Gamma Knife pallidotomy remains non-covered and will be denied.

Limitations for SRS

SRS is not considered medically necessary under the following circumstances

1. Treatment for anything other than a severe symptom or serious threat to life or critical functions.
2. Treatment unlikely to result in functional improvement of clinically meaningful disease stabilization, not otherwise achievable.
3. In patients, with more than three (3) primary or metastases lesions SRS is inappropriate and consideration should be given to whole brain irradiation.
4. Patients with widespread cerebral or extra cranial metastases with limited life expectancy unlikely to gain clinical benefit within their remaining life.

5. Patients with poor performance status (Karnofsky Performance Status less than 40 or an ECOG Performance greater than 3).

Stereotactic Radiotherapy (SRT)
Stereotactic radiotherapy (SRT) refers to stereotactically guided radiation therapy applied over a period of days or weeks. This fractionated form of radiation therapy is made possible by the recent availability of noninvasive repositioning devices (removable masks and frames) that can be used in lieu of a head frame. Stereotactic radiotherapy is based on the basic radiobiologic principle that fractionation decreases the short and long-term side effects of radiation therapy. In some settings, this permits higher total dosage to be given. This is a newer technology and therefore the indications supported by literature are less than for SRS.

Indications for SRT:
For many of the indications listed, surgery is the first choice of treatment. Where this is not possible due to size or location of lesion SRT may be a first line choice. It can also be an adjunct post-surgery to treat areas that were non-resectable. Fractionated stereotactic radiosurgery is frequently used for brain tumors that are close to the optic chiasm (e.g., pituitary tumors) or for tumors that have normal nerves passing through their centers (e.g., acoustic neuromas and meningiomas of the cavernous sinus or skull base).

Fractionated cranial stereotactic radiotherapy is considered medically necessary for treatment of intracranial tumors in hard-to-reach locations, tumors with very unusual shapes, or for tumors located in such close proximity to a vital structure (e.g., optic nerve or hypothalamus) that even a very accurate high-dose single fraction of stereotactic radiosurgery could not be tolerated.

Current indications for SRT include:
Benign Lesions
1. Arteriovenous Malformations
2. Pituitary Adenoma
3. Vestibular schwannoma
4. Meningioma

Also, for benign neoplasms that were previously treated with conventional radiotherapy.
1. Craniopharyngiomas
2. Pineocytomas
3. Low grade astrocytic and ganglioneuronal tumors
4. Hemangioblastomas
5. Nonacoustic schwannomas.

Malignant Lesions
1. Lesions within 5 mm of the optic nerves or chiasms
2. Recurrent malignant gliomas
3. Brain metastasis
4. Base of skull
5. Certain types of recurring malignancies - head and neck cancers, such as cancer of the tonsil, larynx, tongue, sinus, and mouth

Non-Covered Conditions
All other uses of stereotactic radiosurgery are considered investigational/not medically

necessary including, but not limited to, treatment of chronic pain, psychoneurosis, Parkinson's and epilepsy. Arteriovenous malformations may cause seizures. In this case coding for the AVM would be appropriate. If and when literature supports coverage of SRS for treatment of certain lesions responsible for epilepsy we can reconsider. There are restrictions on coverage on other movement disorders.

LCD – Carrier Wisconsin Physicians Service Ins. Co – MI
Stereotactic Body Radiation Therapy (L28366) (Rev. Eff. 061/01/2015), **Retired 09/30/2015**

Stereotactic body radiation therapy (SBRT) is a treatment that couples a high degree of anatomic targeting accuracy and reproducibility with very high doses of extremely precise, externally generated, ionizing radiation, thereby maximizing the cell-killing effect on the target(s) while minimizing radiation-related injury in adjacent normal tissues.

The adjective "stereotactic" describes a procedure during which a target lei ion is localized relative to a known three-dimensional reference system that allows for a high degree of anatomic accuracy and precision. Examples of devices used in SBRT for stereotactic guidance may include a body frame with external reference markers in which a patient is positioned securely, a system of implanted fiducial markers that can be visualized with low-energy (kV) x-rays, and CT-imaging-based systems used to confirm the location of a tumor immediately prior to treatment.

All SBRT is performed with at least one form of image guidance to confirm proper patient positioning and tumor localization. To minimize intra-treatment tumor motion associated with respiration or other motion, some form of motion control or "gating" should be used.

SBRT may be fractionated (up to 5 fractions). Each fraction requires an identical degree of precision, localization and image guidance. Since the goal of SBRT is to intensify the potency of the radiotherapy by completing an entire course of treatment within an extremely accelerated time frame, any course of radiation treatment extending beyond five fractions is not considered SBRT and is not to be billed using these codes.

This LCD addresses only CPT codes 77373 and 77435. Other radiation oncology services (professional and technical) are coded separately and are addressed in the separate LCDs: Radiation Oncology: External Beam/Teletherapy and Intensity Modulated Radiation Therapy. All other acceptable uses of CPT codes 77373 and 77435 are described in the companion LCD, Stereotactic Radiosurgery.

When billing for SBRT *delivery*, it is not appropriate to bill more than one treatment delivery code on the same day of service, even though some types of delivery may have elements of several modalities (for example, a stereotactic approach with IMRT). *Only one* delivery code is to be billed.

Indications

A. SBRT for lung, liver, kidney, and, or pancreas neoplasms:
SBRT is covered for primary and metastatic tumors of the **lung, liver, kidney, or pancreas** when and only when each of the following criteria are met, and each specifically documented in the medical record:

1. The patient's general medical condition (notably, the performance status) justifies aggressive treatment to a primary cancer or, for the case of metastatic disease, justifies aggressive local therapy to one or more discreet deposits of cancer within the context of efforts to achieve total clearance or clinically beneficial reduction in the patient's overall burden of systemic disease. Typically, such a patient would have also been a potential candidate for alternate forms of intense local therapy applied for the same purpose (e.g., surgical resection, radiofrequency ablation, cryotherapy, etc).
2. Other forms of radiotherapy, including but not limited to external beam and IMRT, cannot be as safely or effectively utilized, and
3. The tumor burden can be completely targeted with acceptable risk to critical normal structures
4. If the tumor histology is germ cell or lymphoma, effective chemotherapy regimens have been exhausted or are otherwise not feasible.
5. Other forms of focal therapy, including but not limited to radiofrequency ablation and cryotherapy, cannot be as safely or effectively utilized.

B. SBRT for Prostate Neoplasms

SBRT of the prostate is covered as monotherapy for patients with low risk and low/intermediate risk prostate cancer when:

1. The patient's general medical condition (notably, the performance status) justifies aggressive treatment to a primary cancer. Typically, such a patient would have also been a potential candidate for alternate forms of intense local therapy applied for the same purpose.
2. Other forms of radiotherapy, including but not limited to external beam and IMRT or seed implantation, cannot be as safely or effectively utilized, and
3. The tumor burden can be completely targeted with acceptable risk to critical normal structures

C. Other Neoplasms:

Lesions of bone, breast, uterus, ovary and other internal organs not listed above are not covered for primary definitive SBRT as literature does not support an outcome advantage over other conventional radiation modalities but may be appropriate for SBRT in the setting of recurrence after conventional radiation modalities.

D. Other Indications for SBRT:
Except as above, any lesion with a documented necessity to treat using a high dose per fraction of radiation. When using high radiation doses per fraction, high precision is required to avoid surrounding normal tissue exposure.

Lesions which have received previous radiotherapy or are immediately adjacent to previously irradiated fields, where the additional precision of stereotactic radiotherapy is required to avoid unacceptable tissue radiation will be covered when other conditions of coverage are met (see Limitations below) and this necessity is documented in the medical record.

Limitations:
Coverage will be denied for each of the following:
1. Treatment unlikely to result in clinical cancer control and/or functional improvement.

2. Patients with wide-spread cerebral or extra-cranial metastases
3. Patients with poor performance status (Karnofsky Performance Status less than 40), or ECOG Performance Status greater than 3) - see Performance Status scales below.

Karnofsky Performance Scale (Perez and Brady, p 225)

100 Normal; no complaints, no evidence of disease
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 to do active work
60 Requires occasional assistance but is able to care for most needs
50 Requires considerable assistance and frequent medical care
40 Disabled; requires special care and assistance
30 Severely disabled; hospitalization is indicated although death not imminent
20 Very sick; hospitalization necessary; active supportive treatment is necessary
10 Moribund, fatal processes progressing rapidly
0 Dead

ECOG Performance Status (Am. J. Clin. Oncol. 5:649-655, 1982)

0 Fully active, able to carry on all pre-disease performances 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 housework, office work
2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.
4 Completely disables. Cannot carry on any self-care. Totally confined to bed or chair
5 Dead

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Charged Particle (Proton or Helium Ion) Radiation Therapy for Neoplastic Conditions
Focal Treatments for Prostate Cancer
Intensity Modulated Radiation Therapy (IMRT) of the Abdomen, Pelvis, and Chest
Intensity Modulated Radiation Therapy (IMRT) of the Breast and Lung
Intensity Modulated Radiation Therapy (IMRT): Central Nervous System Tumors
Intensity-Modulated Radiation Therapy (IMRT) of the Prostate
Intensity-Modulated Radiation Therapy (IMRT): Cancer of the Head and Neck or Thyroid

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through March 27, 2024, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/1/08	3/5/08	5/1/08	Joint policy established
5/1/09	2/10/09	2/10/09	Routine maintenance
3/1/11	12/14/10	1/4/11	Routine maintenance; CPT code 61795 deleted; added CPT codes 61781, 61782 and 61783
11/1/12	8/21/12	8/21/12	Extensive changes made to description and rationale sections; title changed from “Stereotactic Radiosurgery, Particle Beam Radiation and Linear Accelerator with or without Robotic Arm” to current title; added G0251 to policy; revised Inclusion and Exclusion sections to reflect rationale; added “adrenal gland” to exclusions and to policy statement; removed “colon” from exclusion criteria and from policy statement.
3/1/13	12/11/12	12/31/12	Added new code 32701, effective 1/1/13
7/1/14	4/8/14	4/15/14	Routine maintenance; added uveal melanoma as a non-covered indication.
11/1/15	8/18/15	9/16/15	Added low- or intermediate-risk localized prostate cancer as a covered indication; added tremor as a non-covered indication; in title, changed “radiation therapy” to “radiotherapy”; added statement to MPS: “Stereotactic radiosurgery is considered experimental/ investigational for the treatment of seizures and functional disorders, other than trigeminal neuralgia, including chronic pain, and tremor. Its effectiveness in these clinical indications has not been scientifically determined.” 2015 code updates incorporated into policy

11/1/16	8/16/16	8/16/16	Routine maintenance Added procedure codes 77332-77334
11/1/17	8/15/17	8/15/17	• Routine maintenance • References and rationale updated • Updated to mirror BCBSA while maintaining divergence topics of primary and metastatic liver tumors, irradiated and unirradiated spinal tumors, and prostate cancer
11/1/18	8/21/18	8/21/18	• Routine maintenance • ASTROs recommendation for SBRT use in low to intermediate risk for prostate cancer added to position statement with reference
3/1/19	12/11/18		• Brain SRS aligned with AIM criteria to allow tx regardless of active extracranial systemic disease status
1/1/20	10/15/19		• Routine maintenance • Rationale simplified • Uveal melanoma position statement changed to established based on BCBSA clinical input and AIM support • Pancreatic adenocarcinoma position statement changed to established based on AIM and Medicare support • Lung and bone mets adjusted to reflect AIM stance
11/1/20	8/18/20		• Added to inclusions per AIM stance: pineal gland tumors, schwannoma tumors, medulloblastoma supratentorial PNETs and other tumor types when used to treat a previously irradiated field. Exclusions updated to allow for above additions.
11/1/21	8/17/21		• Routine maintenance • No change in policy status
11/1/22	8/16/22		• Routine maintenance

11/1/23	8/23/23		• Routine maintenance • No change in policy status • Vendor: eviCore Post JUMP: • Uveal melanoma - For treatment of melanoma of the choroid moved from Stereotactic body radiotherapy (extracranial) to Stereotactic radiosurgery (intracranial) under the Inclusions section. •Removed statement: Reference eviCore criteria for clinical preference from MPS. (ky)
7/1/24	5/10/24		• This policy is coming early as code update – informational to add code C9795 eff 1/1/24 per code update as EST. This review will be the annual review for this policy and it will continue to come to JUMP in April now. • Added *This code is not separately reimbursable to code 61783. • Aligned JUMP policy Inclusions section with eviCore Radiation Oncology clinical guidelines V1.0.2024 DRAFT effective 4.1.2024 • Many updates were made to the inclusions and exclusions section based on eviCore policy above. Vendor: eviCore (ky)

Next Review Date: 2nd Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: STEREOTACTIC RADIOSURGERY AND STEREOTACTIC BODY RADIOTHERAPY

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered, policy guidelines apply
BCNA (Medicare Advantage)	Refer to the Medicare information under the Government Regulations section of this policy.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.