

# Medical Policy



Nonprofit corporations and independent licensees  
of the Blue Cross and Blue Shield Association

**Joint Medical Policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and is therefore subject to change.**

---

**\*Current Policy Effective Date: 11/1/23**  
(See policy history boxes for previous effective dates)

## **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 disproportionately 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 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
- Trigeminal neuralgia refractory to medical management
- Pineal gland tumors
- Schwannomas
- Medulloblastoma supratentorial PNET
- Other tumors types when used to treat a previously irradiated field
- Uveal melanoma
  - For treatment of melanoma of the choroid

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, melanoma and sarcoma).
- Members with stage T1 or T2 a non-small cell lung cancer (not larger than 5 cm) showing no nodal or distant disease and who are not candidates for surgical resection
- In the treatment of primary and metastatic liver malignancies
- Low- or intermediate-risk localized prostate cancer\*\*
- For local treatment of advanced or recurrent pancreatic adenocarcinoma without evidence of distant metastasis
- Lung metastatic disease when all the following apply:
  - Single metastatic lesion measuring  $\leq 5$  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 (ex. 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 when all of the following conditions are met:
  - One to three metastatic lesions involving the lungs, liver or bone
  - Primary tumor is breast, colorectal, melanoma, non-small cell lung, prostate, renal cell, or sarcoma
  - Primary tumor is controlled
- Other tumors 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.*

\*\*SBRT using proton beam therapy is acceptable for low/intermediate prostate cancer.

**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 |

**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 ( $\geq 85\%$ ) 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 ( $p < 0.001$ ). 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 ( $p < 0.018$ ). (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 with:

- arteriovenous malformations;
- acoustic neuromas;
- craniopharyngiomas;
- glomus jugulare tumors;
- pituitary adenomas; nonresectable,
- residual, or recurrent meningiomas;
- solitary or multiple brain metastases;
- primary malignancies of the central nervous system; and
- trigeminal neuralgia refractory to medical management.

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 with:

- stage T1 or T2a NSCLC (not >5 cm) showing no nodal or distant disease and who are not candidates for surgical resection;
- spinal or vertebral body tumors (metastatic or primary)

- spinal or vertebral metastases that are radioresistant (e.g., renal cell carcinoma, melanoma, sarcoma); and
  - solid tumors, primary or metastatic, of the liver and prostate;
  - oligometastases
  - pancreatic adenocarcinoma
- 

## **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<sup>3</sup> 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        | <ul style="list-style-type: none"> <li>• Chondrosarcoma</li> <li>• Chordoma</li> <li>• Progressive Ewing sarcoma</li> <li>• Unresectable giant cell tumor</li> <li>• Osteosarcoma with positive margins or relapsed progressive disease</li> </ul> | <ul style="list-style-type: none"> <li>• Consider SRS to allow high-dose therapy while maximizing normal tissue sparing (category 2A)</li> <li>• Consider use of SRS, especially for oligometastases</li> </ul> | 3.2023  |



|               |  |  |        |
|---------------|--|--|--------|
|               | <ul style="list-style-type: none"> <li>• Oligometastases</li> </ul>  |  |        |
| CNS           | <ul style="list-style-type: none"> <li>• Adult low-grade infiltrative supratentorial astrocytoma/oligodendroglioma</li> <li>• Anaplastic gliomas/glioblastomas</li> <li>• Adult intracranial ependymoma</li> <li>• Adult medulloblastoma</li> <li>• Primary CNS lymphoma</li> <li>• Primary spinal cord tumors</li> <li>• Meningiomas</li> <li>• Limited brain metastases</li> <li>• Extensive brain metastases</li> <li>• Leptomeningeal metastases</li> <li>• Metastatic spine tumors</li> </ul> | 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   | <ul style="list-style-type: none"> <li>• 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 trial. RT should not be used in place of surgical resection.</li> <li>• 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.</li> </ul>   | 2.2023 |
| Head and Neck |  | The panel acknowledged that SBRT might be beneficial in the setting of re-irradiation, palliation, or older adults.  | 2.2023 |
| Hepatobiliary | <ul style="list-style-type: none"> <li>• Hepatocellular carcinoma</li> <li>• Gallbladder Cancer</li> </ul>   | <ul style="list-style-type: none"> <li>• Principles of locoregional therapy includes recommendations for SBRT</li> <li>• 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.</li> </ul>  | 1.2023 |
| Lung          | <ul style="list-style-type: none"> <li>• NSCLC</li> </ul>  | <ul style="list-style-type: none"> <li>• 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).</li> <li>• Close follow-up and salvage therapy for isolated local and/or locoregional recurrence after SABR have been shown to improve overall survival.</li> <li>• SABR is an appropriate option for patients with high surgical risk (e.g., age ≥ 75 years, poor lung function)</li> </ul> | 3.2023 |

|          |   |  |        |
|----------|---|--|--------|
|          |   | <ul style="list-style-type: none"> <li>• 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.</li> <li>• 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)</li> </ul>  |        |
| Pancreas | <ul style="list-style-type: none"> <li>• Pancreatic adenocarcinoma</li> </ul> | <p>Locally advanced disease</p> <ul style="list-style-type: none"> <li>• SBRT should be avoided if direct invasion of the bowel or stomach is identified on CT, MRI, and endoscopy</li> <li>• Data are limited to support specific RT recommendations for locally advanced disease. Options may include: <ul style="list-style-type: none"> <li>○ Chemoradiation, SBRT, or hypofractionated RT in selected patients who are not candidates for combination chemotherapy</li> <li>○ Induction chemotherapy followed by chemoradiation or SBRT in select patients (locally advanced without systemic metastases)</li> </ul> </li> <li>• SBRT should be delivered at an experienced, high-volume center with technology that allows for image-guided RT or on a clinical trial</li> </ul> <p>Recurrent pancreatic cancer</p> <ul style="list-style-type: none"> <li>• Data are limited to support specific RT recommendations for locally recurrent disease. Options for patients with recurrent, unresectable disease may include: <ul style="list-style-type: none"> <li>○ Induction chemotherapy followed by chemoradiation or SBRT (if not previously performed)</li> <li>○ Chemoradiation or SBRT in selected patients who are not candidates for induction chemotherapy</li> </ul> </li> <li>• SBRT should be delivered at an experienced, high-volume center with technology that allows for image-guided RT or in a clinical trial</li> </ul> | 2.2023 |
| Prostate | <ul style="list-style-type: none"> <li>• Prostate cancer</li> </ul>           | <ul style="list-style-type: none"> <li>• 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: <ul style="list-style-type: none"> <li>○ In patients with limited metastatic disease to the vertebra or paravertebral region</li> <li>○ when ablation is the goal</li> <li>○ In symptomatic patients where the lesion occurs in or immediately adjacent to a previously irradiated treatment field</li> <li>○ In patients with oligometastatic progression where progression-free survival is the goal.</li> </ul> </li> </ul>  | 2.2023 |

- SBRT combined with ADT can be considered when delivering longer courses of EBRT would present medical or social hardship for patients with:
  - Unfavorable intermediate risk
  - High risk
- SBRT can be considered when enrollment in clinical trials is encouraged for oligometastatic disease where durable local control is desirable

|                     |   |   |        |
|---------------------|---|---|--------|
| Kidney cancer       | <ul style="list-style-type: none"> <li>• Non-clear cell and clear renal carcinoma</li> </ul>  | <ul style="list-style-type: none"> <li>• SBRT may be considered for medically inoperable patients with stage 1 kidney cancer (category 2B) or stage II/III kidney cancer (both category 3)</li> <li>• Relapse or State IV: Metastasectomy or SBRT or ablative techniques for oligometastatic disease</li> </ul>   | 4.2023 |
| Cutaneous Melanoma  | <ul style="list-style-type: none"> <li>• Intact extracranial metastases</li> </ul>  | <ul style="list-style-type: none"> <li>• Principles of RT include recommendations for use of SBRT</li> <li>• SBRT may be considered for selected patients with oligometastasis</li> </ul>   | 2.2023 |
| Uveal melanoma      | <ul style="list-style-type: none"> <li>• Primary and recurrent intraocular tumors</li> </ul>  | <ul style="list-style-type: none"> <li>• SRS is the least often used and nonpreferred form of definite RT for primary and recurrent intraocular tumors</li> </ul>   | 1.2023 |
| Soft tissue sarcoma | <ul style="list-style-type: none"> <li>• Extremity/superficial trunk/head and neck</li> <li>• Retroperitoneal/intra-abdominal</li> </ul>  | <ul style="list-style-type: none"> <li>• If disseminated metastases: SBRT as a palliative option (category 2A)</li> <li>• For Stage IV with single organ and limited tumor bulk that are amenable to local therapy: SBRT with or without chemotherapy as an option</li> <li>• For metastatic disease with isolated regional disease or nodes: SBRT as an option</li> </ul>  | 2.2023 |
| Thyroid             | <ul style="list-style-type: none"> <li>• Iodine-refractory unresectable locoregional recurrent/persistent disease</li> <li>• Iodine-refractory soft tissue metastases</li> <li>• Iodine-refractory bone metastases</li> </ul> | <ul style="list-style-type: none"> <li>• Consider resection of distant metastases and/or EBRT/SBRT/IMRT/other local therapies when available for progressive and/or symptomatic metastatic lesions</li> <li>• Most recurrent tumors respond well to iodine therapy; or EBRT, SBRT, or IMRT</li> <li>• Consider surgical palliation and/or EBRT/SBRT other local therapies when available if symptomatic, or asymptomatic in weight-bearing sites</li> </ul> | 2.2023 |

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.

<sup>i</sup> 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.

<sup>ii</sup> 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 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.

For patients with early-stage NSCLC, ASTRO (2017) made the following recommendation:(208)

- 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)

For glioblastoma, ASTRO (2016) released the following guideline statement:

- "In younger patients with good performance status, focal reirradiation (e.g., stereotactic radiosurgery, hypofractionated stereotactic radiotherapy, brachytherapy) for recurrent glioblastoma may improve outcomes compared with supportive care or systemic therapy alone (LQE). Tumor size and location should be taken into account when deciding whether reirradiation would be safe (93% agreement, Low Quality Evidence; Weak recommendation)."

ASTRO made the following recommendation (2013) regarding the use of SBRT for prostate cancer:

- It is ASTRO's opinion that data supporting the use of SBRT for prostate cancer have matured to a point where SBRT could be considered an appropriate alternative for select patients with low to intermediate risk disease.

For brain metastases, ASTRO (2012) made the following recommendations related to the use of SRS:

- For single brain metastases (initial management):
  - If good prognosis (expected survival 3 months or more) and complete resection possible:
    - If brain metastasis  $\leq$  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  $\leq$  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  $\leq$  3-4 cm, options include SRS and WBRT (level of evidence: I), SRS alone (level of evidence: 1)

For palliative therapy for bone metastases, ASTRO made recommendations in 2011 and in a 2017 update:

- "Advanced RT [radiotherapy] techniques such as SBRT as the primary treatment for painful

spine bone lesions or for spinal compression should be considered in the setting of a clinical trial or with data collected in a registry given that insufficient data are available to routinely support this treatment currently.”

- “Advanced radiation techniques such as SBRT retreatment for recurrent pain in spine bone lesions may be feasible, effective, and safe, but the panel recommends that this approach should be limited to clinical trial participation or on a registry given limited data supporting routine use.”

### **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**

| <b>NCT No.</b>                                       | <b>Trial Name</b>  | <b>Planned Enrollment</b> | <b>Completion Date</b> |
|--|--|---------------------------|------------------------|
| <b><i>Ongoing stereotactic radiosurgery</i></b>      |  |                           |                        |
| <i>Central nervous system neoplasms</i>              |  |                           |                        |
| <i>Acoustic neuroma (vestibular schwannoma)</i>      |  |                           |                        |
| NCT02055859  | Cyberknife Radiosurgery for Patients with Neurinomas   | 102                       | May 2025               |
| <b><i>Brain metastases</i></b>                       |  |                           |                        |
| NCT01592968  | A Prospective Phase III Randomized Trial to Compare Stereotactic Radiosurgery Versus Whole Brain Radiation Therapy for $\geq 4$ 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               |
| <b><i>Glioma</i></b>                                 |  |                           |                        |
| NCT01464177  | Prospective Randomized Phase II Trial of Hypofractionated Stereotactic Radiotherapy in Recurrent Glioblastoma Multiforme   | 40                        | Oct 2021 (recruiting)  |
| <b><i>Ongoing stereotactic body radiotherapy</i></b> |  |                           |                        |
| <i>Non-small-cell lung cancer</i>                    |  |                           |                        |
| NCT05111197  | Local Ablative Stereotactic Radiotherapy for Residual Hypermetabolic Lesion in Patients With Locally Advanced or Metastatic Non-small Cell Lung Cancer Long-term   | 112                       | Jan 2025               |

|   |   |     |                       |
|---|---|-----|-----------------------|
|   | Responders to Immunotherapy : a Randomized, Multicenter, Open-label Phase III Study   |     |                       |
| NCT01968941                                       | A Randomized Trial of Medically-Inoperable Stage I Non-small Cell Lung Cancer Patients Comparing Stereotactic Body Radiotherapy Versus Conventional Radiotherapy  | 324 | Jun 2022              |
| <i>Hepatocellular carcinoma</i>                   |   |     |                       |
| NCT01730937                                       | Randomized Phase III Study of Sorafenib Versus Stereotactic Body Radiation Therapy Followed by Sorafenib in Hepatocellular Carcinoma  | 193 | Jun 2025              |
| <i>Prostate Cancer</i>                            |   |     |                       |
| 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) |
| NCT02064036                                       | Whole-Pelvic Radiotherapy With a Stereotactic Body Radiotherapy Boost and Long-Term Androgen Deprivation for Unfavorable- Intermediate and High Risk Localized Adenocarcinoma of the Prostate.                                    | 29  | Nov 2021 (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 cT1c - cT3a Prostate Cancer With a Low Risk of Nodal Metastases ( $\leq 20\%$ , 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) |
| <i>Kidney cancer</i>                              |   |     |                       |
| NCT03108703                                       | Assessment of Quality of Life and Outcomes in Patients Treated with Stereotactic Body Radiation Therapy (SBRT) for Primary Renal Cell Carcinoma (RCC)   | 30  | Dec 2021              |
| <i>Breast cancer</i>                              |   |     |                       |
| <b>Unpublished: Stereotactic Radiosurgery</b>     |   |     |                       |
| NCT02147028                                       | A Randomized Phase II Trial of Hippocampal Sparing Versus Conventional Whole Brain Radiotherapy After Surgical Resection or Radiosurgery in Favourable Prognosis Patients With 1-4 Brain Metastases                               | 23  | Feb 2021              |
| <b>Unpublished Stereotactic Body Radiotherapy</b> |   |     |                       |
| NCT01839994                                       | Phase III Clinical Trial on Conventionally Fractionated Conformal Radiotherapy (CFCRT) Versus CF-CRT Combined With High-dose-rate Brachytherapy or Stereotactic Body Radiotherapy for Intermediate and High-risk Prostate Cancer. | 350 | Dec 2018 (unknown)    |

NCT: national clinical trial.

<sup>a</sup> 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 or 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 hemangiomas.
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. 06/01/2015), 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 lesion 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 Treatment for Prostate Cancer  
Intensity Modulated Radiation Therapy (IMRT) of the Abdomen and Pelvis  
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

---

## References

1. China M, Vastani A, Hill CS, et al. Gamma Knife radiosurgery for cerebral arteriovenous malformations: a systematic review and meta-analysis. *Neurosurg Rev.* Jun 2022; 45(3): 1987-2004. PMID 35178626
2. Magro E, Gentric JC, Darsaut TE, et al. Responses to ARUBA: a systematic review and critical analysis for the design of future arteriovenous malformation trials. *J Neurosurg.* Feb 2017;126(2):486-494. PMID 27128584
3. Mau CY, Sabourin VM, Gandhi CD, et al. SLAM: Stereotactic Radiosurgery of Large Arteriovenous Malformations: meta-analysis of hemorrhage in high-grade Pollock-Flickinger arteriovenous malformations. *World Neurosurg.* Jan 2016;85:32-41. PMID 26325212
4. Mohr JP, Parides MK, Stapf C, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. *Lancet.* Feb 15, 2014;383(9917):614-621. PMID 24268105
5. Bowden G, Kano H, Tonetti D, et al. Stereotactic radiosurgery for arteriovenous malformations of the cerebellum. *J Neurosurg.* Mar 2014;120(3):583-590. PMID 24160482
6. Fokas E, Henzel M, Wittig A, et al. Stereotactic radiosurgery of cerebral arteriovenous malformations: long-term follow-up in 164 patients of a single institution. *J Neurol.* Aug 2013;260(8):2156-2162. PMID 23712798
7. Kano H, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, Part 6: multistaged volumetric management of large arteriovenous malformations. *J Neurosurg.* Jan 2012;116(1):54-65. PMID 22077447
8. Matsuo T, Kamada K, Izumo T, et al. Linear accelerator-based radiosurgery alone for arteriovenous malformation: more than 12 years of observation. *Int J Radiat Oncol Biol Phys.* Jul 1, 2014;89(3):576-583. PMID 24803036
9. Paul L, Casasco A, Kusak ME, et al. Results for a series of 697 AVMs treated by Gamma Knife: Influence of angiographic features on the obliteration rate. *Neurosurgery.* Jul 18, 2014;75(5):568-583; discussion 582-563; quiz 583. PMID 25050575

10. Potts MB, Sheth SA, Louie J, et al. Stereotactic radiosurgery at a low marginal dose for the treatment of pediatric arteriovenous malformations: obliteration, complications, and functional outcomes. *J Neurosurg Pediatr.* Jul 2014;14(1):1-11. PMID 24766309
11. Cohen-Inbar O, Lee CC, Xu Z, et al. A quantitative analysis of adverse radiation effects following Gamma Knife radiosurgery for arteriovenous malformations. *J Neurosurg.* Oct 2015;123(4):945-953. PMID 25909572
12. Ding D, Starke RM, Kano H, et al. Stereotactic radiosurgery for Spetzler-Martin Grade III arteriovenous malformations: an international multicenter study. *J Neurosurg.* Apr 15, 2016:1-13. PMID 27081906
13. Ding D, Starke RM, Kano H, et al. Radiosurgery for cerebral arteriovenous malformations in a randomized trial of unruptured brain arteriovenous malformations (ARUBA)-eligible patients: a multicenter study. *Stroke.* Feb 2016;47(2):342-349. PMID 26658441
14. Ding D, Xu Z, Yen CP, et al. Radiosurgery for cerebral arteriovenous malformations in elderly patients: effect of advanced age on outcomes after intervention. *World Neurosurg.* Sep 2015;84(3):795-804. PMID 25997797
15. Hanakita S, Shin M, Koga T, et al. Risk reduction of cerebral stroke after stereotactic radiosurgery for small unruptured brain arteriovenous malformations. *Stroke.* May 2016;47(5):1247-1252. PMID 27073242
16. Starke RM, Kano H, Ding D, et al. Stereotactic radiosurgery for cerebral arteriovenous malformations: evaluation of long-term outcomes in a multicenter cohort. *J Neurosurg.* Mar 4, 2016:1-9. PMID 26943847
17. El-Ghanem M, Kass-Hout T, Kass-Hout O, et al. Arteriovenous Malformations in the Pediatric Population: Review of the Existing Literature. *Interv Neurol.* Sep 2016;5(3-4):218-225. PMID 27781052
18. Tonetti D, Kano H, Bowden G, et al. Hemorrhage during pregnancy in the latency interval after stereotactic radiosurgery for arteriovenous malformations. *J Neurosurg.* Dec 2014;121 Suppl:226-231. PMID 25434957
19. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia.* Jul 2013;33(9):629-808. PMID 23771276
20. Zakrzewska JM, Akram H. Neurosurgical interventions for the treatment of classical trigeminal neuralgia. *Cochrane Database Syst Rev.* Sep 07 2011(9):Cd007312. PMID 21901707
21. Yen CP, Schlesinger D, Sheehan JP. Gamma Knife(R) radiosurgery for trigeminal neuralgia. *Expert Rev Med Devices.* Nov 2011;8(6):709-721. PMID 22029468
22. Dhople AA, Adams JR, Maggio WW, et al. Long-term outcomes of Gamma Knife radiosurgery for classic trigeminal neuralgia: implications of treatment and critical review of the literature. Clinical article. *J Neurosurg.* Aug 2009;111(2):351-358. PMID 19326987
23. Feng ES, Sui CB, Wang TX, et al. Stereotactic radiosurgery for the treatment of mesial temporal lobe epilepsy. *Acta Neurol Scand.* Dec 2016;134(6):442-451. PMID 26846702
24. Barbaro NM, Quigg M, Ward MM, et al. Radiosurgery versus open surgery for mesial temporal lobe epilepsy: the randomized, controlled ROSE trial. *Epilepsia.* Jun 2018;59(6):1198-1207. PMID 29600809
25. Quigg M, Barbaro NM, Ward MM et al. Visual field defects after radiosurgery versus temporal lobectomy for mesial temporal lobe epilepsy: Findings of the ROSE trial.. *Seizure.* 2018 Nov 9;63:62-67. PMID 30408713
26. Regis J, Bartolomei F, Rey M, et al. Gamma knife surgery for mesial temporal lobe epilepsy. *J Neurosurg.* Dec 2000;93 Suppl 3:141-146. PMID 11143232

27. Schrottnner O, Eder HG, Unger F, et al. Radiosurgery in lesional epilepsy: brain tumors. *Stereotact Funct Neurosurg.* Oct 1998;70 Suppl 1:50-56. PMID 9782235
28. Whang CJ, Kwon Y. Long-term follow-up of stereotactic Gamma Knife radiosurgery in epilepsy. *Stereotact Funct Neurosurg.* 1996;66 Suppl 1:349-356. PMID 9032879
29. Dallapiazza RF, Lee DJ, De Vloo P et al. Outcomes from stereotactic surgery for essential tremor.. *J. Neurol. Neurosurg. Psychiatry,* 2018 Oct 20;90(4). PMID 30337440
30. Raju SS, Niranjana A, Monaco EA et al. Stereotactic radiosurgery for medically refractory multiple sclerosis-related tremor.. *J. Neurosurg.,* 2017 Jul 1;128(4). PMID 28665251
31. Niranjana A, Raju SS, Kooshkabadi A, et al. Stereotactic radiosurgery for essential tremor: Retrospective analysis of a 19-year experience. *Mov Disord.* May 2017;32(5):769-777. PMID 28319282
32. Witjas T, Carron R, Krack P, et al. A prospective single-blind study of Gamma Knife thalamotomy for tremor. *Neurology.* Nov 3, 2015;85(18):1562-1568. PMID 26446066
33. Kooshkabadi A, Lunsford LD, Tonetti D, et al. Gamma Knife thalamotomy for tremor in the magnetic resonance imaging era. *J Neurosurg.* Apr 2013;118(4):713-718. PMID 23373801
34. Ohye C, Higuchi Y, Shibasaki T, et al. Gamma knife thalamotomy for Parkinson disease and essential tremor: a prospective multicenter study. *Neurosurgery.* Mar 2012;70(3):526-535; discussion 535-526. PMID 21904267
35. Lim SY, Hodaie M, Fallis M, et al. Gamma knife thalamotomy for disabling tremor: a blinded evaluation. *Arch Neurol.* May 2010;67(5):584-588. PMID 20457958
36. Kondziolka D, Ong JG, Lee JY, et al. Gamma Knife thalamotomy for essential tremor. *J Neurosurg.* Jan 2008;108(1):111-117. PMID 18173319
37. Young RF, Jacques S, Mark R, et al. Gamma knife thalamotomy for treatment of tremor: long-term results. *J Neurosurg.* Dec 2000;93 Suppl 3:128-135. PMID 11143229
38. Roberts DG, Pouratian N. Stereotactic radiosurgery for the treatment of chronic intractable pain: a systematic review. *Oper Neurosurg (Hagerstown).* Oct 1, 2017;13(5):543-551. PMID 28521018
39. Savardekar AR, Terrell D, Lele SJ, et al. Primary Treatment of Small to Medium ( 3 cm) Sporadic Vestibular Schwannomas: A Systematic Review and Meta-Analysis on Hearing Preservation and Tumor Control Rates for Microsurgery versus Radiosurgery. *World Neurosurg.* Apr 2022; 160: 102-113.e12. PMID 34838768
40. Persson O, Bartek J, Jr., Shalom NB, et al. Stereotactic radiosurgery vs. fractionated radiotherapy for tumor control in vestibular schwannoma patients: a systematic review. *Acta Neurochir (Wien).* Jun 2017;159(6):1013- 1021. PMID 28409393
41. Muzevic D, Legcevic J, Splavski B, et al. Stereotactic radiotherapy for vestibular schwannoma. *Cochrane Database Syst Rev.* Dec 16 2014(12):Cd009897. PMID 25511415
42. Badakhshi H, Muellner S, Wiener E, et al. Image-guided stereotactic radiotherapy for patients with vestibular schwannoma. A clinical study. *Strahlenther Onkol.* Jun 2014;190(6):533-537. PMID 24589920
43. Williams BJ, Xu Z, Salvetti DJ, et al. Gamma Knife surgery for large vestibular schwannomas: a single-center retrospective case-matched comparison assessing the effect of lesion size. *J Neurosurg.* Aug 2013;119(2):463-471. PMID 23706053
44. Woolf DK, Williams M, Goh CL, et al. Fractionated stereotactic radiotherapy for acoustic neuromas: long-term outcomes. *Clin Oncol (R Coll Radiol).* Dec 2013;25(12):734-738. PMID 23973046
45. Pollock BE, Driscoll CL, Foote RL, et al. Patient outcomes after vestibular schwannoma management: a prospective comparison of microsurgical resection and stereotactic radiosurgery. *Neurosurgery.* Jul 2006;59(1):77-85; discussion 77-85. PMID 16823303

46. Chang SD, Gibbs IC, Sakamoto GT, et al. Staged stereotactic irradiation for acoustic neuroma. *Neurosurgery*. Jun 2005;56(6):1254-1261; discussion 1261-1253. PMID 15918941
47. Chung HT, Ma R, Toyota B, et al. Audiologic and treatment outcomes after linear accelerator-based stereotactic irradiation for acoustic neuroma. *Int J Radiat Oncol Biol Phys*. Jul 15, 2004;59(4):1116-1121. PMID 15234046
48. Meijer OW, Vandertop WP, Baayen JC, et al. Single-fraction vs. fractionated linac-based stereotactic radiosurgery for vestibular schwannoma: a single-institution study. *Int J Radiat Oncol Biol Phys*. Aug 1, 2003;56(5):1390-1396. PMID 12873685
49. Chen Y, Li ZF, Zhang FX, et al. Gamma knife surgery for patients with volumetric classification of nonfunctioning pituitary adenomas: a systematic review and meta-analysis. *Eur J Endocrinol*. Oct 2013;169(4):487-495. PMID 23904281
50. Lee CC, Kano H, Yang HC, et al. Initial Gamma Knife radiosurgery for nonfunctioning pituitary adenomas. *J Neurosurg*. Mar 2014;120(3):647-654. PMID 24405068
51. Sheehan JP, Starke RM, Mathieu D, et al. Gamma Knife radiosurgery for the management of nonfunctioning pituitary adenomas: a multicenter study. *J Neurosurg*. Aug 2013;119(2):446-456. PMID 23621595
52. Lee CC, Yang HC, Chen CJ, et al. Gamma Knife surgery for craniopharyngioma: report on a 20-year experience. *J Neurosurg*. Dec 2014;121 Suppl:167-178. PMID 25434950
53. Hashizume C, Mori Y, Kobayashi T, et al. Stereotactic radiotherapy using Novalis for craniopharyngioma adjacent to optic pathways. *J Neurooncol*. Jun 2010;98(2):239-247. PMID 20422439
54. Hasegawa T, Kobayashi T, Kida Y. Tolerance of the optic apparatus in single-fraction irradiation using stereotactic radiosurgery: evaluation in 100 patients with craniopharyngioma. *Neurosurgery*. Apr 2010;66(4):688-694; discussion 694-685. PMID 20190668
55. Combs SE, Thilmann C, Huber PE, et al. Achievement of long-term local control in patients with craniopharyngiomas using high precision stereotactic radiotherapy. *Cancer*. Jun 1, 2007;109(11):2308-2314. PMID 17469176
56. Ong V, Bourcier AJ, Florence TJ, et al. Stereotactic Radiosurgery for Glomus Jugulare Tumors: Systematic Review and Meta-Analysis. *World Neurosurg*. Jun 2022; 162: e49-e57. PMID 35189418
57. Ivan ME, Sughrue ME, Clark AJ, et al. A meta-analysis of tumor control rates and treatment-related morbidity for patients with glomus jugulare tumors. *J Neurosurg*. May 2011;114(5):1299-1305. PMID 21029039
58. Wakefield DV, Venable GT, VanderWalde NA, et al. Comparative neurologic outcomes of salvage and definitive Gamma Knife radiosurgery for glomus jugulare: a 20-year experience. *J Neurol Surg B Skull Base*. Jun 2017;78(3):251-255. PMID 28593112
59. Ibrahim R, Ammori MB, Yianni J, et al. Gamma Knife radiosurgery for glomus jugulare tumors: a single-center series of 75 cases. *J Neurosurg*. May 2017;126(5):1488-1497. PMID 27392265
60. De Maria L, Terzi di Bergamo L, Conti A, et al. CyberKnife for Recurrent Malignant Gliomas: A Systematic Review and Meta-Analysis. *Front Oncol*. 2021; 11: 652646. PMID 33854978
61. El-Shehaby AM, Reda WA, Abdel Karim KM, et al. Gamma Knife radiosurgery for low-grade tectal gliomas. *Acta Neurochir (Wien)*. Feb 2015;157(2):247-256. PMID 25510647
62. Clark GM, McDonald AM, Nabors LB, et al. Hypofractionated stereotactic radiosurgery with concurrent bevacizumab for recurrent malignant gliomas: the University of Alabama at Birmingham experience. *Neurooncol Pract*. Dec 2014;1(4):172-177. PMID 26034629

63. Doodoo E, Huffmann B, Peredo I, et al. Increased survival using delayed gamma knife radiosurgery for recurrent high-grade glioma: a feasibility study. *World Neurosurg.* Nov 2014;82(5):e623-632. PMID 24930898
64. Cabrera AR, Cuneo KC, Desjardins A, et al. Concurrent stereotactic radiosurgery and bevacizumab in recurrent malignant gliomas: a prospective trial. *Int J Radiat Oncol Biol Phys.* Aug 1, 2013;86(5):873-879. PMID 23725997
65. Cuneo KC, Vredenburgh JJ, Sampson JH, et al. Safety and efficacy of stereotactic radiosurgery and adjuvant bevacizumab in patients with recurrent malignant gliomas. *Int J Radiat Oncol Biol Phys.* Apr 1, 2012;82(5):2018- 2024. PMID 21489708
66. Garsa A, Jang JK, Baxi S, et al. Radiation Therapy for Brain Metastases: A Systematic Review. *Pract Radiat Oncol.* Sep-Oct 2021; 11(5): 354-365. PMID 34119447
67. Liu Z, He S, Li L. Comparison of Surgical Resection and Stereotactic Radiosurgery in the Initial Treatment of Brain Metastasis. *Stereotact Funct Neurosurg.* 2020; 98(6): 404-415. PMID 32898850
68. Roos D. What is the randomised evidence for surgery and stereotactic radiosurgery for patients with solitary (or few) brain metastases?. *Int J Evid Based Healthc.* Mar 2011; 9(1): 61-6. PMID 21332664
69. Park HS, Chiang VL, Knisely JP, et al. Stereotactic radiosurgery with or without whole-brain radiotherapy for brain metastases: an update. *Expert Rev Anticancer Ther.* Nov 2011;11(11):1731-1738. PMID 22050022
70. Patil CG, Pricola K, Garg SK, et al. Whole brain radiation therapy (WBRT) alone versus WBRT and radiosurgery for the treatment of brain metastases. *Cochrane Database Syst Rev.* 2010(6):CD006121. PMID 20556764
71. Patil CG, Pricola K, Sarmiento JM, et al. Whole brain radiation therapy (WBRT) alone versus WBRT and radiosurgery for the treatment of brain metastases. *Cochrane Database Syst Rev.* Sep 12 2012(9):Cd006121. PMID 22972090
72. Patil CG, Pricola K, Sarmiento JM, et al. Whole brain radiation therapy (WBRT) alone versus WBRT and radiosurgery for the treatment of brain metastases. *Cochrane Database Syst Rev.* Sep 25 2017; 9: CD006121. PMID 28945270
73. Chang DT, Schellenberg D, Shen J, et al. Stereotactic radiotherapy for unresectable adenocarcinoma of the pancreas. *Cancer.* Feb 1 2009;115(3):665-672. PMID 19117351
74. Hartgerink D, Bruynzeel A, Eekers D, et al. A Dutch phase III randomized multicenter trial: whole brain radiotherapy versus stereotactic radiotherapy for 4-10 brain metastases. *Neurooncol Adv.* Jan-Dec 2021; 3(1):vdab021. PMID 33738451
75. Hartgerink D, Bruynzeel A, Eekers D, et al. Quality of life among patients with 4 to 10 brain metastases after treatment with whole-brain radiotherapy vs. stereotactic radiotherapy: a phase III, randomized, Dutch multicenter trial. *Ann Palliat Med.* Apr 2022; 11(4): 1197-1209. PMID 34806396
76. Kondziolka D, Patel A, Lunsford LD, et al. Stereotactic radiosurgery plus whole brain radiotherapy versus radiotherapy alone for patients with multiple brain metastases. *Int J Radiat Oncol Biol Phys.* Sep 1, 1999;45(2):427-434. PMID 10487566
77. Weltman E, Salvajoli JV, Brandt RA, et al. Radiosurgery for brain metastases: a score index for predicting prognosis. *Int J Radiat Oncol Biol Phys.* Mar 15, 2000;46(5):1155-1161. PMID 10725626
78. Yu C, Chen JC, Apuzzo ML, et al. Metastatic melanoma to the brain: prognostic factors after gamma knife radiosurgery. *Int J Radiat Oncol Biol Phys.* Apr 1, 2002;52(5):1277-1287. PMID 11955740
79. Aoyama H, Shirato H, Tago M, et al. Stereotactic radiosurgery plus whole-brain radiation therapy vs stereotactic radiosurgery alone for treatment of brain metastases: a randomized controlled trial. *JAMA.* Jun 7, 2006;295(21):2483-2491. PMID 16757720



80. Tian LJ, Zhuang HQ, Yuan ZY. A comparison between cyberknife and neurosurgery in solitary brain metastases from non-small cell lung cancer. *Clin Neurol Neurosurg*. Oct 2013;115(10):2009-2014. PMID 23850045
81. Yamamoto M, Serizawa T, Shuto T, et al. Stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901): a multi-institutional prospective observational study. *Lancet Oncol*. Apr 2014;15(4):387-395. PMID 24621620
82. Yomo S, Hayashi M. Upfront stereotactic radiosurgery in patients with brain metastases from small cell lung cancer: retrospective analysis of 41 patients. *Radiat Oncol*. Jul 08 2014;9(1):152. PMID 25005424
83. Rava P, Leonard K, Sioshansi S, et al. Survival among patients with 10 or more brain metastases treated with stereotactic radiosurgery. *J Neurosurg*. Aug 2013;119(2):457-462. PMID 23662828
84. Raldow AC, Chiang VL, Knisely JP, et al. Survival and intracranial control of patients with 5 or more brain metastases treated with gamma knife stereotactic radiosurgery. *Am J Clin Oncol*. Oct 2013;36(5):486-490. PMID 22706180
85. Parker T, Rigney G, Kallos J, et al. Gamma knife radiosurgery for uveal melanomas and metastases: a systematic review and meta-analysis. *Lancet Oncol*. Nov 2020; 21(11): 1526-1536. PMID 33152286
86. Guleser UY, Sarici AM, Ucar D, et al. Comparison of iodine-125 plaque brachytherapy and gamma knife stereotactic radiosurgery treatment outcomes for uveal melanoma patients. *Graefes Arch Clin Exp Ophthalmol*. Apr 2022; 260(4): 1337-1343. PMID 34735632
87. Eibl-Lindner K, Furweger C, Nentwich M, et al. Robotic radiosurgery for the treatment of medium and large uveal melanoma. *Melanoma Res*. Feb 2016;26(1):51-57. PMID 26484738
88. Furdova A, Sramka M, Chorvath M, et al. Stereotactic radiosurgery in intraocular malignant melanoma--retrospective study. *Neuro Endocrinol Lett*. Mar 2014;35(1):28-36. PMID 24625918
89. Zehetmayer M. Stereotactic photon beam irradiation of uveal melanoma. *Dev Ophthalmol*. 2012;49:58-65. PMID 22042013
90. Dunavoelgyi R, Dieckmann K, Gleiss A, et al. Local tumor control, visual acuity, and survival after hypofractionated stereotactic photon radiotherapy of choroidal melanoma in 212 patients treated between 1997 and 2007. *Int J Radiat Oncol Biol Phys*. Sep 1, 2011;81(1):199-205. PMID 20675066
91. Sarici AM, Pazarli H. Gamma-knife-based stereotactic radiosurgery for medium- and large-sized posterior uveal melanoma. *Graefes Arch Clin Exp Ophthalmol*. Jan 2013;251(1):285-294. PMID 22944897
92. Muller K, Naus N, Nowak PJ, et al. Fractionated stereotactic radiotherapy for uveal melanoma, late clinical results. *Radiother Oncol*. Feb 2012;102(2):219-224. PMID 21864922
93. Furdova A, Slezak P, Chorvath M, et al. No differences in outcome between radical surgical treatment (enucleation) and stereotactic radiosurgery in patients with posterior uveal melanoma. *Neoplasma*. 2010;57(4):377-381. PMID 20429631
94. Sahgal A, Myrehaug SD, Siva S, et al. Stereotactic body radiotherapy versus conventional external beam radiotherapy in patients with painful spinal metastases: an open-label, multicentre, randomised, controlled, phase 2/3 trial. *Lancet Oncol*. Jul 2021; 22(7): 1023-1033. PMID 34126044
95. Ito K, Sugita S, Nakajima Y, et al. Phase 2 Clinical Trial of Separation Surgery Followed by Stereotactic Body Radiation Therapy for Metastatic Epidural Spinal Cord

- Compression. *Int J Radiat Oncol Biol Phys*. Jan 01 2022; 112(1): 106-113. PMID 34715257
96. Gerszten PC, Ozhasoglu C, Burton SA, et al. CyberKnife frameless stereotactic radiosurgery for spinal lesions: clinical experience in 125 cases. *Neurosurgery*. Jul 2004;55(1):89-98; discussion 98-89. PMID 15214977
  97. Degen JW, Gagnon GJ, Voyadzis JM, et al. CyberKnife stereotactic radiosurgical treatment of spinal tumors for pain control and quality of life. *J Neurosurg Spine*. May 2005;2(5):540-549. PMID 15945428
  98. Sahgal A, Atenafu EG, Chao S, et al. Vertebral compression fracture after spine stereotactic body radiotherapy: a multi-institutional analysis with a focus on radiation dose and the spinal instability neoplastic score. *J Clin Oncol*. Sep 20, 2013;31(27):3426-3431. PMID 23960179
  99. Gerszten PC, Burton SA, Ozhasoglu C, et al. Radiosurgery for spinal metastases: clinical experience in 500 cases from a single institution. *Spine (Phila Pa 1976)*. Jan 15, 2007;32(2):193-199. PMID 17224814
  100. Chang EL, Shiu AS, Mendel E, et al. Phase I/II study of stereotactic body radiotherapy for spinal metastasis and its pattern of failure. *J Neurosurg Spine*. Aug 2007;7(2):151-160. PMID 17688054
  101. Zhang R, Kang J, Ren S, et al. Comparison of stereotactic body radiotherapy and radiofrequency ablation for early stage non-small cell lung cancer: a systematic review and meta-analysis. *Ann Transl Med*. Jan 2022; 10(2): 104. PMID 35282118
  102. Li C, Wang L, Wu Q, et al. A meta-analysis comparing stereotactic body radiotherapy vs conventional radiotherapy in inoperable stage I non-small cell lung cancer. *Medicine (Baltimore)*. Aug 21 2020; 99(34): e21715. PMID 32846789
  103. Solda F, Lodge M, Ashley S, et al. Stereotactic radiotherapy (SABR) for the treatment of primary non-small cell lung cancer; systematic review and comparison with a surgical cohort. *Radiother Oncol*. Oct 2013;109(1):1-7. PMID 24128806
  104. Harkenrider MM, Bertke MH, Dunlap NE. Stereotactic Body Radiation Therapy for Unbiopsied Early-stage Lung Cancer: A Multi-Institutional Analysis. *Am J Clin Oncol*. Aug 2014;37(4):337-342. PMID 23660597
  105. Allibhai Z, Taremi M, Bezjak A, et al. The impact of tumor size on outcomes after stereotactic body radiation therapy for medically inoperable early-stage non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. Dec 1, 2013;87(5):1064-1070. PMID 24210082
  106. Hof H, Muentner M, Oetzel D, et al. Stereotactic single-dose radiotherapy (radiosurgery) of early stage non-small-cell lung cancer (NSCLC). *Cancer*. Jul 1, 2007;110(1):148-155. PMID 17516437
  107. Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA*. Mar 17, 2010;303(11):1070-1076. PMID 20233825
  108. Stanic S, Paulus R, Timmerman RD, et al. No clinically significant changes in pulmonary function following stereotactic body radiation therapy for early-stage peripheral non-small cell lung cancer: an analysis of RTOG 0236. *Int J Radiat Oncol Biol Phys*. Apr 1, 2014;88(5):1092-1099. PMID 24661663
  109. Timmerman RD, Park C, Kavanagh BD. The North American experience with stereotactic body radiation therapy in non-small cell lung cancer. *J Thorac Oncol*. Jul 2007; 2(7 Suppl 3): S101-12. PMID 17603304
  110. Ijsseldijk MA, Shoni M, Siegert C, et al. Oncologic Outcomes of Surgery Versus SBRT for Non-Small-Cell Lung Carcinoma: A Systematic Review and Meta-analysis. *Clin Lung Cancer*. May 2021; 22(3): e235-e292. PMID 32912754

111. Zheng X, Schipper M, Kidwell K, et al. Survival Outcome After Stereotactic Body Radiation Therapy and Surgery for Stage I Non-Small Cell Lung Cancer: A Meta-Analysis. *Int J Radiat Oncol Biol Phys*. Jul 19, 2014. PMID 25052562
112. Nguyen NP, Garland L, Welsh J, et al. Can stereotactic fractionated radiation therapy become the standard of care for early stage non-small cell lung carcinoma. *Cancer Treat Rev*. Dec 2008;34(8):719-727. PMID 18657910
113. Koto M, Takai Y, Ogawa Y, et al. A phase II study on stereotactic body radiotherapy for stage I non-small cell lung cancer. *Radiother Oncol*. Dec 2007;85(3):429-434. PMID 18022720
114. Kupelian PA, Komaki R, Allen P. Prognostic factors in the treatment of node-negative non-small cell lung carcinoma with radiotherapy alone. *Int J Radiat Oncol Biol Phys*. Oct 1, 1996;36(3):607-613. PMID 8948345
115. Chang JY, Senan S, Paul MA, et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials. *Lancet Oncol*. Jun 2015; 16(6): 630-7. PMID 25981812
116. Yu JB, Soulos PR, Cramer LD, et al. Comparative effectiveness of surgery and radiosurgery for stage I non-small cell lung cancer. *Cancer*. Jul 15, 2015;121(14):2341-2349. PMID 25847699
117. Ezer N, Veluswamy RR, Mhango G, et al. Outcomes following Stereotactic Body Radiotherapy versus Limited Resection in Older Patients with Early-Stage Lung Cancer. *J Thorac Oncol*. Aug 2015;10(8):1201-1206. PMID 26200275
118. Crabtree TD, Puri V, Robinson C, et al. Analysis of first recurrence and survival in patients with stage I non-small cell lung cancer treated with surgical resection or stereotactic radiation therapy. *J Thorac Cardiovasc Surg*. Apr 2014;147(4):1183-1191; discussion 1191-1182. PMID 24507980
119. Port JL, Parashar B, Osakwe N, et al. A Propensity-Matched Analysis of Wedge Resection and Stereotactic Body Radiotherapy for Early Stage Lung Cancer. *Ann Thorac Surg*. Jul 29, 2014. PMID 25085557
120. Varlotto J, Fakiris A, Flickinger J, et al. Matched-pair and propensity score comparisons of outcomes of patients with clinical stage I non-small cell lung cancer treated with resection or stereotactic radiosurgery. *Cancer*. Aug 1, 2013;119(15):2683-2691. PMID 23605504
121. Reed GB, Jr., Cox AJ, Jr. The human liver after radiation injury. A form of veno-occlusive disease. *Am J Pathol*. Apr 1966;48(4):597-611. PMID 5327788
122. Sharma H. Role of external beam radiation therapy in management of hepatocellular carcinoma. *J Clin Exp Hepatol*. Aug 2014;4(Suppl 3):S122-125. PMID 25755603
123. Wang PM, Chung NN, Hsu WC, et al. Stereotactic body radiation therapy in hepatocellular carcinoma: Optimal treatment strategies based on liver segmentation and functional hepatic reserve. *Rep Pract Oncol Radiother*. Nov-Dec 2015; 20(6): 417-24. PMID 26696781
124. Shanker MD, Moodaley P, Soon W, et al. Stereotactic ablative radiotherapy for hepatocellular carcinoma: A systematic review and meta-analysis of local control, survival and toxicity outcomes. *J Med Imaging Radiat Oncol*. Dec 2021; 65(7): 956-968. PMID 34396706
125. Long Y, Liang Y, Li S, et al. Therapeutic outcome and related predictors of stereotactic body radiotherapy for small liver-confined HCC: a systematic review and meta-analysis of observational studies. *Radiat Oncol*. Apr 08 2021; 16(1): 68. PMID 33832536
126. Lee J, Shin IS, Yoon WS, et al. Comparisons between radiofrequency ablation and stereotactic body radiotherapy for liver malignancies: Meta-analyses and a systematic review. *Radiother Oncol*. Apr 2020; 145: 63-70. PMID 31923711

127. Tao C, Yang LX. Improved radiotherapy for primary and secondary liver cancer: stereotactic body radiation therapy. *Anticancer Res.* Feb 2012;32(2):649-655. PMID 22287758
128. Ji R, Ng KK, Chen W, et al. Comparison of clinical outcome between stereotactic body radiotherapy and radiofrequency ablation for unresectable hepatocellular carcinoma. *Medicine (Baltimore).* Jan 28 2022; 101(4): e28545. PMID 35089192
129. Bettinger D, Pinato DJ, Schultheiss M et al. Stereotactic Body Radiation Therapy as an Alternative Treatment for Patients with Hepatocellular Carcinoma Compared to Sorafenib: A Propensity Score Analysis.. *Liver Cancer*, 2019 Oct 12;8(4). PMID 31602371
130. Wahl DR, Stenmark MH, Tao Y, et al. Outcomes after stereotactic body radiotherapy or radiofrequency ablation for hepatocellular carcinoma. *J Clin Oncol.* Feb 10, 2016;34(5):452-459. PMID 26628466
131. Jacob R, Turley F, Redden DT, et al. Adjuvant stereotactic body radiotherapy following transarterial chemoembolization in patients with non-resectable hepatocellular carcinoma tumours of  $\geq 3$  cm. *HPB (Oxford).* Feb 2015;17(2):140-149. PMID 25186290
132. Zhong NB, Lv GM, Chen ZH. Stereotactic body radiotherapy combined with transarterial chemoembolization for huge ( $\geq 10$  cm) hepatocellular carcinomas: A clinical study. *Mol Clin Oncol.* Sep 2014;2(5):839-844. PMID 25054055
133. Bujold A, Massey CA, Kim JJ, et al. Sequential phase I and II trials of stereotactic body radiotherapy for locally advanced hepatocellular carcinoma. *J Clin Oncol.* May 1, 2013;31(13):1631-1639. PMID 23547075
134. Ibarra RA, Rojas D, Snyder L, et al. Multicenter results of stereotactic body radiotherapy (SBRT) for non-resectable primary liver tumors. *Acta Oncol.* Jan 23, 2012;51(5):575-583. PMID 22263926
135. Price TR, Perkins SM, Sandrasegaran K, et al. Evaluation of response after stereotactic body radiotherapy for hepatocellular carcinoma. *Cancer.* Oct 24, 2012;118 (12):3191-3198. PMID 22025126
136. Andolino DL, Johnson CS, Maluccio M, et al. Stereotactic body radiotherapy for primary hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys.* Nov 15, 2011;81(4):e447-453. PMID 21645977
137. Mahadevan A, Blanck O, Lanciano R, et al. Stereotactic Body Radiotherapy (SBRT) for liver metastasis – clinical outcomes from the international multi-institutional RSSearch(R) Patient Registry. *Radiat Oncol.* Feb 13 2018;13(1):26. PMID 29439707
138. Yuan ZY, Meng MB, Liu CL, et al. Stereotactic body radiation therapy using the CyberKnife((R)) system for patients with liver metastases. *Onco Targets Ther.* Jun 2014;7:915-923. PMID 24959080
139. Lanciano R, Lamond J, Yang J, et al. Stereotactic body radiation therapy for patients with heavily pretreated liver metastases and liver tumors. *Front Oncol.* May 2012;2:23. PMID 22645716
140. Chang DT, Swaminath A, Kozak M, et al. Stereotactic body radiotherapy for colorectal liver metastases: a pooled analysis. *Cancer.* Sep 1, 2011;117(17):4060-4069. PMID 21432842
141. Mazloom A, Hezel AF, Katz AW. Stereotactic body radiation therapy as a bridge to transplantation and for recurrent disease in the transplanted liver of a patient with hepatocellular carcinoma. *Case Rep Oncol.* Jan 2014;7(1):18-22. PMID 24575010
142. Sapisochin G, Barry A, Doherty M, et al. Stereotactic body radiotherapy vs TACE or RFA as a bridge to transplant in patients with hepatocellular carcinoma. An intention-to-treat analysis. *J Hepatol.* Jul 2017;67(1):92- 99. PMID 28257902

143. Mannina EM, Cardenes HR, Lasley FD, et al. Role of stereotactic body radiation therapy before orthotopic liver transplantation: retrospective evaluation of pathologic response and outcomes. *Int J Radiat Oncol Biol Phys.* Apr 1, 2017;97(5):931-938. PMID 28333015
144. Foerster R, Zwahlen DR, Buchali A, et al. Stereotactic Body Radiotherapy for High-Risk Prostate Cancer: A Systematic Review. *Cancers (Basel).* Feb 12 2021; 13(4). PMID 33673077
145. Jackson WC, Silva J, Hartman HE et al. Stereotactic Body Radiation Therapy for Localized Prostate Cancer: A Systematic Review and Meta-Analysis of Over 6,000 Patients Treated On Prospective Studies.. *Int. J. Radiat. Oncol. Biol. Phys.*, 2019 Apr 9;104(4). PMID 30959121
146. Kishan AU, Dang A, Katz AJ et al. Long-term Outcomes of Stereotactic Body Radiotherapy for Low-Risk and Intermediate-Risk Prostate Cancer.. *JAMA Netw Open*, 2019 Feb 9;2(2). PMID 30735235
147. Yu JB, Cramer LD, Herrin J, et al. Stereotactic body radiation therapy versus intensity-modulated radiation therapy for prostate cancer: comparison of toxicity. *J Clin Oncol.* Apr 20, 2014;32(12):1195-1201. PMID 24616315
148. Katz A, Ferrer M, Suarez JF. Comparison of quality of life after stereotactic body radiotherapy and surgery for early-stage prostate cancer. *Radiat Oncol.* 2012;7:194. PMID 23164305
149. Miszczyk L, Namysl-Kaletka A, Napieralska A et al. Stereotactic Ablative Radiotherapy for Prostate Cancer-The Treatment Results of 500 Patients and Analysis of Failures.. *Technol. Cancer Res. Treat.*, 2019 Aug 30;18:1533033819870815. PMID 31462169
150. Zelefsky MJ, Pinitpatcharalert A, Kollmeier M et al. Early Tolerance and Tumor Control Outcomes with High-dose Ultrahypofractionated Radiation Therapy for Prostate Cancer.. *Eur Urol Oncol*, 2019 Nov 2. PMID 31668713
151. Fuller DB, Falchook AD, Crabtree T et al. Phase 2 Multicenter Trial of Heterogeneous-dosing Stereotactic Body Radiotherapy for Low- and Intermediate-risk Prostate Cancer: 5-year Outcomes.. *Eur Urol Oncol*, 2019 Jun 4;1(6). PMID 31158102
152. King CR, Brooks JD, Gill H, et al. Long-term outcomes from a prospective trial of stereotactic body radiotherapy for low-risk prostate cancer. *Int J Radiat Oncol Biol Phys.* Feb 1, 2012;82(2):877-882. PMID 21300474
153. Freeman DE, King CR. Stereotactic body radiotherapy for low-risk prostate cancer: five-year outcomes. *Radiat Oncol.* 2011;6:3. PMID 21219625
154. McBride SM, Wong DS, Dombrowski JJ, et al. Hypofractionated stereotactic body radiotherapy in low-risk prostate adenocarcinoma: Preliminary results of a multi-institutional phase 1 feasibility trial. *Cancer.* Dec 13, 2011;118(15):3681-3690. PMID 22170628
155. Boike TP, Lotan Y, Cho LC, et al. Phase I dose-escalation study of stereotactic body radiation therapy for low- and intermediate-risk prostate cancer. *J Clin Oncol.* May 20, 2011;29(15):2020-2026. PMID 21464418
156. Bolzicco G, Favretto MS, Satariano N, et al. A single-center study of 100 consecutive patients with localized prostate cancer treated with stereotactic body radiotherapy. *BMC Urol.* 2013;13:49. PMID 24134138
157. Jabbari S, Weinberg VK, Kaprealian T, et al. Stereotactic body radiotherapy as monotherapy or post-external beam radiotherapy boost for prostate cancer: technique, early toxicity, and PSA response. *Int J Radiat Oncol Biol Phys.* Jan 1, 2012;82(1):228-234. PMID 21183287
158. Katz AJ, Santoro M, Ashley R, et al. Stereotactic body radiotherapy for organ-confined prostate cancer. *BMC Urol.* 2010;10:1. PMID 20122161

159. Katz AJ, Santoro M, Diblasio F, et al. Stereotactic body radiotherapy for localized prostate cancer: disease control and quality of life at 6 years. *Radiat Oncol.* 2013;8:118. PMID 23668632
160. Loi M, Wortel RC, Francolini G et al. Sexual Function in Patients Treated With Stereotactic Radiotherapy For Prostate Cancer: A Systematic Review of the Current Evidence.. *J Sex Med*, 2019 Jul 16;16(9). PMID 31303575
161. Wiegner EA, King CR. Sexual function after stereotactic body radiotherapy for prostate cancer: results of a prospective clinical trial. *Int J Radiat Oncol Biol Phys.* Oct 1, 2010;78(2):442-448. PMID 20137864
162. Chen LN, Suy S, Wang H, et al. Patient-reported urinary incontinence following stereotactic body radiation therapy (SBRT) for clinically localized prostate cancer. *Radiat Oncol.* 2014;9:148. PMID 24966110
163. Kim DW, Cho LC, Straka C, et al. Predictors of rectal tolerance observed in a dose-escalated phase 1-2 trial of stereotactic body radiation therapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* Jul 1, 2014;89(3):509-517.
164. King CR, Collins S, Fuller D, et al. Health-related quality of life after stereotactic body radiation therapy for localized prostate cancer: results from a multi-institutional consortium of prospective trials. *Int J Radiat Oncol Biol Phys.* Dec 1, 2013;87(5):939-945. PMID 24119836.
165. Yan M, Moideen N, Bratti VF, et al. Stereotactic body radiotherapy (SBRT) in metachronous oligometastatic prostate cancer: a systematic review and meta-analysis on the current prospective evidence. *Br J Radiol.* Dec 01 2020; 93(1116): 20200496. PMID 32822547
166. Phillips R, Shi WY, Deek M, et al. Outcomes of Observation vs Stereotactic Ablative Radiation for Oligometastatic Prostate Cancer: The ORIOLE Phase 2 Randomized Clinical Trial. *JAMA Oncol.* May 01 2020; 6(5): 650-659. PMID 32215577
167. De Bleser E, Jereczek-Fossa BA, Pasquier D et al. Metastasis-directed Therapy in Treating Nodal Oligorecurrent Prostate Cancer: A Multi-institutional Analysis Comparing the Outcome and Toxicity of Stereotactic Body Radiotherapy and Elective Nodal Radiotherapy.. *Eur. Urol.*, 2019 Jul 25;76(6). PMID 31331782
168. Petrelli F, Comito T, Ghidini A, et al. Stereotactic Body Radiation Therapy for Locally Advanced Pancreatic Cancer: A Systematic Review and Pooled Analysis of 19 Trials. *Int J Radiat Oncol Biol Phys.* Feb 01 2017; 97(2): 313-322. PMID 28068239
169. Groot VP, van Santvoort HC, Rombouts SJ, et al. Systematic review on the treatment of isolated local recurrence of pancreatic cancer after surgery; re-resection, chemoradiotherapy and SBRT.. *HPB (Oxford)*, 2017 Jan 10;19(2). PMID 28065427
170. Zhong J, Patel K, Switchenko J, et al. Outcomes for patients with locally advanced pancreatic adenocarcinoma treated with stereotactic body radiation therapy versus conventionally fractionated radiation. *Cancer.* Sep 15, 2017;123(18):3486-3493. PMID 28493288
171. Goyal K, Einstein D, Ibarra RA, et al. Stereotactic body radiation therapy for nonresectable tumors of the pancreas. *J Surg Res.* May 15 2012; 174(2): 319-25. PMID 21937061
172. Rwigema JC, Parikh SD, Heron DE, et al. Stereotactic body radiotherapy in the treatment of advanced adenocarcinoma of the pancreas. *Am J Clin Oncol.* Feb 2011;34(1):63-69. PMID 20308870
173. Taunk NK, Spratt DE, Bilsky M, et al. Spine radiosurgery in the management of renal cell carcinoma metastases. *J Natl Compr Canc Netw.* Jun 2015;13(6):801-809; quiz 809. PMID 26085394

174. Siva S, Pham D, Gill S, et al. A systematic review of stereotactic radiotherapy ablation for primary renal cell carcinoma. *BJU Int.* Dec 2012;110(11 Pt B):E737-743. PMID 23107102
175. Hannan R, Christensen M, Hammers H, et al. Phase II Trial of Stereotactic Ablative Radiation for Oligoprogressive Metastatic Kidney Cancer. *Eur Urol Oncol.* Apr 2022; 5(2): 216-224. PMID 34986993
176. Cheung P, Patel S, North SA, et al. Stereotactic Radiotherapy for Oligoprogression in Metastatic Renal Cell Cancer Patients Receiving Tyrosine Kinase Inhibitor Therapy: A Phase 2 Prospective Multicenter Study. *Eur Urol.* Dec 2021; 80(6): 693-700. PMID 34399998
177. Yamamoto T, Kadoya N, Takeda K, et al. Renal atrophy after stereotactic body radiotherapy for renal cell carcinoma. *Radiat Oncol.* May 26, 2016;11:72. PMID 27229710
178. Verma J, Jonasch E, Allen PK, et al. The impact of tyrosine kinase inhibitors on the multimodality treatment of brain metastases from renal cell carcinoma. *Am J Clin Oncol.* Dec 2013;36(6):620-624. PMID 22892430
179. Ranck MC, Golden DW, Corbin KS, et al. Stereotactic body radiotherapy for the treatment of oligometastatic renal cell carcinoma. *Am J Clin Oncol.* Dec 2013;36(6):589-595. PMID 22868242
180. Beitler JJ, Makara D, Silverman P, et al. Definitive, high-dose-per-fraction, conformal, stereotactic external radiation for renal cell carcinoma. *Am J Clin Oncol.* Dec 2004;27(6):646-648. PMID 15577450
181. Sohn S, Chung CK, Sohn MJ, et al. Stereotactic radiosurgery compared with external radiation therapy as a primary treatment in spine metastasis from renal cell carcinoma: a multicenter, matched-pair study. *J Neurooncol.* Aug 2014;119(1):121-128. PMID 24792488
182. Thibault I, Al-Omair A, Masucci GL, et al. Spine stereotactic body radiotherapy for renal cell cancer spinal metastases: analysis of outcomes and risk of vertebral compression fracture. *J Neurosurg Spine.* Nov 2014;21(5):711-718. PMID 25170656
183. Balagamwala EH, Angelov L, Koyfman SA, et al. Single-fraction stereotactic body radiotherapy for spinal metastases from renal cell carcinoma. *J Neurosurg Spine.* Dec 2012;17(6):556-564. PMID 23020208
184. Zelefsky MJ, Greco C, Motzer R, et al. Tumor control outcomes after hypofractionated and single-dose stereotactic image-guided intensity-modulated radiotherapy for extracranial metastases from renal cell carcinoma. *Int J Radiat Oncol Biol Phys.* Apr 1, 2012;82(5):1744-1748. PMID 21596489
185. Wang XS, Rhines LD, Shiu AS, et al. Stereotactic body radiation therapy for management of spinal metastases in patients without spinal cord compression: a phase 1-2 trial. *Lancet Oncol.* Apr 2012;13(4):395-402. PMID 22285199
186. Yamada Y, Bilsky MH, Lovelock DM, et al. High-dose, single-fraction image-guided intensity-modulated radiotherapy for metastatic spinal lesions. *Int J Radiat Oncol Biol Phys.* Jun 1, 2008;71(2):484-490. PMID 18234445
187. Gerszten PC, Burton SA, Ozhasoglu C, et al. Stereotactic radiosurgery for spinal metastases from renal cell carcinoma. *J Neurosurg Spine.* Oct 2005;3(4):288-295. PMID 16266070
188. Alongi F, Arcangeli S, Filippi AR, et al. Review and uses of stereotactic body radiation therapy for oligometastases. *Oncologist.* 2012;17(8):1100-1107. PMID 22723509
189. Tree AC, Khoo VS, Eeles RA, et al. Stereotactic body radiotherapy for oligometastases. *Lancet Oncol.* Jan 2013;14(1):e28-37. PMID 23276369

190. Corbin KS, Hellman S, Weichselbaum RR. Extracranial oligometastases: a subset of metastases curable with stereotactic radiotherapy. *J Clin Oncol*. Apr 10, 2013;31(11):1384-1390. PMID 23460715
191. Milano MT, Katz AW, Zhang H, et al. Oligometastases treated with stereotactic body radiotherapy: long-term follow-up of prospective study. *Int J Radiat Oncol Biol Phys*. Jul 1, 2012;83(3):878-886. PMID 22172903
192. Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial. *Lancet*. May 18 2019; 393(10185): 2051-2058. PMID 30982687
193. Palma DA, Olson R, Harrow S, et al. Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Cancers: Long-Term Results of the SABR-COMET Phase II Randomized Trial. *J Clin Oncol*. Sep 01 2020; 38(25): 2830-2838. PMID 32484754
194. Pastorino U, Buyse M, Friedel G, et al. Long-term results of lung metastasectomy: prognostic analyses based on 5206 cases. The International Registry of Lung Metastases. *J Thorac Cardiovasc Surg*. Jan 1997;113(1):37-49. PMID 9011700
195. Siva S, MacManus M, Ball D. Stereotactic radiotherapy for pulmonary oligometastases: a systematic review. *J Thorac Oncol*. Jul 2010;5(7):1091-1099. PMID 20479693
196. Norihisa Y, Nagata Y, Takayama K, et al. Stereotactic body radiotherapy for oligometastatic lung tumors. *Int J Radiat Oncol Biol Phys*. Oct 1, 2008;72(2):398-403. PMID 18374506
197. Rusthoven KE, Kavanagh BD, Cardenes H, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for liver metastases. *J Clin Oncol*. Apr 1, 2009;27(10):1572-1578. PMID 19255321
198. Tsao MN, Ven LI, Cheung P, et al. Stereotactic Body Radiation Therapy for Extracranial Oligometastatic Non-small-cell Lung Cancer: A Systematic Review. *Clin Lung Cancer*. Mar 2020; 21(2): 95-105.e1. PMID 31959533
199. Londero F, Grossi W, Morelli A, et al. Surgery versus stereotactic radiotherapy for treatment of pulmonary metastases. A systematic review of literature. *Future Sci OA*. Apr 15 2020; 6(5): FSO471. PMID 32518686
200. Ahmed KA, Barney BM, Macdonald OK, et al. Stereotactic body radiotherapy in the treatment of adrenal metastases. *Am J Clin Oncol*. Oct 2013;36(5):509-513. PMID 22781389
201. Scorsetti M, Alongi F, Filippi AR, et al. Long-term local control achieved after hypofractionated stereotactic body radiotherapy for adrenal gland metastases: A retrospective analysis of 34 patients. *Acta Oncol*. May 2012;51(5):618-623. PMID 22263925
202. Casamassima F, Livi L, Masciullo S, et al. Stereotactic radiotherapy for adrenal gland metastases: university of Florence experience. *Int J Radiat Oncol Biol Phys*. Feb 1, 2012;82(2):919-923. PMID 21300473
203. Holy R, Piroth M, Pinkawa M, et al. Stereotactic body radiation therapy (SBRT) for treatment of adrenal gland metastases from non-small cell lung cancer. *Strahlenther Onkol*. Apr 2011;187(4):245-251. PMID 21424513
204. Chawla S, Chen Y, Katz AW, et al. Stereotactic body radiotherapy for treatment of adrenal metastases. *Int J Radiat Oncol Biol Phys*. Sep 1, 2009;75(1):71-75. PMID 19250766
205. Napieralska A, Mischczyk L, Tukiendorf A, et al. The results of treatment of prostate cancer bone metastases after CyberKnife radiosurgery. *Ortop Traumatol Rehabil*. Jul 3 2014;16(3):339-349. PMID 25058109



206. Derdeyn CP, Zipfel GJ, Albuquerque FC, et al. Management of Brain Arteriovenous Malformations: A Scientific Statement for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke*. Aug 2017; 48(8): e200-e224. PMID 28642352
207. Vogelbaum MA, Brown PD, Messersmith H, et al. Treatment for Brain Metastases: ASCO-SNO-ASTRO Guideline. *J Clin Oncol*. Feb 10 2022; 40(5): 492-516. PMID 34932393
208. Videtic GMM, Donington J, Giuliani M, et al. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline. *Pract Radiat Oncol*. Sep 2017; 7(5): 295-301. PMID 28596092
209. Schneider BJ, Daly ME, Kennedy EB, et al. Stereotactic Body Radiotherapy for Early-Stage Non-Small-Cell Lung Cancer: American Society of Clinical Oncology Endorsement of the American Society for Radiation Oncology Evidence-Based Guideline. *J Clin Oncol*. Mar 01 2018; 36(7): 710-719. PMID 29106810
210. Apisarnthanarax S, Barry A, Cao M, et al. External Beam Radiation Therapy for Primary Liver Cancers: An ASTRO Clinical Practice Guideline. *Pract Radiat Oncol*. Jan-Feb 2022; 12(1): 28-51. PMID 34688956
211. Graber JJ, Cobbs CS, Olson JJ. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines on the Use of Stereotactic Radiosurgery in the Treatment of Adults With Metastatic Brain Tumors. *Neurosurgery*. Mar 01 2019; 84(3): E168-E170. PMID 30629225
212. Marchetti M, Sahgal A, De Salles AAF, et al. Stereotactic Radiosurgery for Intracranial Noncavernous Sinus Benign Meningioma: International Stereotactic Radiosurgery Society Systematic Review, Meta-Analysis and Practice Guideline. *Neurosurgery*. Oct 15 2020; 87(5): 879-890. PMID 32463867
213. Kotecha R, Sahgal A, Rubens M, et al. Stereotactic radiosurgery for non-functioning pituitary adenomas: meta-analysis and International Stereotactic Radiosurgery Society practice opinion. *Neuro Oncol*. Mar 05 2020; 22(3): 318-332. PMID 31790121
214. Lee CC, Trifiletti DM, Sahgal A, et al. Stereotactic Radiosurgery for Benign (World Health Organization Grade I) Cavernous Sinus Meningiomas-International Stereotactic Radiosurgery Society (ISRS) Practice Guideline: A Systematic Review. *Neurosurgery*. Dec 01 2018; 83(6): 1128-1142. PMID 29554317
215. Graffeo CS, Sahgal A, De Salles A, et al. Stereotactic Radiosurgery for Spetzler-Martin Grade I and II Arteriovenous Malformations: International Society of Stereotactic Radiosurgery (ISRS) Practice Guideline. *Neurosurgery*. Sep 01 2020; 87(3): 442-452. PMID 32065836
216. Singh R, Chen CJ, Didwania P, et al. Stereotactic Radiosurgery for Dural Arteriovenous Fistulas: A Systematic Review and Meta-Analysis and International Stereotactic Radiosurgery Society Practice Guidelines. *Neurosurgery*. Jul 01 2022; 91(1): 43-58. PMID 35383682
217. McGonigal A, Sahgal A, De Salles A, et al. Radiosurgery for epilepsy: Systematic review and International Stereotactic Radiosurgery Society (ISRS) practice guideline. *Epilepsy Res*. Nov 2017; 137: 123-131. PMID 28939289
218. Martinez-Moreno NE, Sahgal A, De Salles A, et al. Stereotactic radiosurgery for tremor: systematic review. *J Neurosurg*. Feb 01 2018; 1-12. PMID 29473775
219. Tuleasca C, Regis J, Sahgal A, et al. Stereotactic radiosurgery for trigeminal neuralgia: a systematic review. *J Neurosurg*. Apr 27 2018; 130(3): 733-757. PMID 29701555

220. Myrehaug S, Sahgal A, Hayashi M, et al. Reirradiation spine stereotactic body radiation therapy for spinal metastases: systematic review. *J Neurosurg Spine*. Oct 2017; 27(4): 428-435. PMID 28708043
221. Faruqi S, Chen H, Fariselli L, et al. Stereotactic Radiosurgery for Postoperative Spine Malignancy: A Systematic Review and International Stereotactic Radiosurgery Society Practice Guidelines. *Pract Radiat Oncol*. Mar-Apr 2022; 12(2): e65-e78. PMID 34673275
222. Reynolds MM, Arnett AL, Parney IF, et al. Gamma knife radiosurgery for the treatment of uveal melanoma and uveal metastases. *Int J Retina Vitreous*. 2017; 3: 17. PMID 28560050
223. Mathieu D, Kotecha R, Sahgal A, et al. Stereotactic radiosurgery for secretory pituitary adenomas: systematic review and International Stereotactic Radiosurgery Society practice recommendations. *J Neurosurg*. Mar 01 2022; 136(3): 801-812. PMID 34479203
224. Tsao MN, Sahgal A, Xu W, et al. Stereotactic radiosurgery for vestibular schwannoma: International Stereotactic Radiosurgery Society (ISRS) Practice Guideline. *J Radiosurg SBRT*. 2017; 5(1): 5-24. PMID 29296459
225. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. NCCN.org. [https://www.nccn.org/guidelines/category\\_1](https://www.nccn.org/guidelines/category_1). Accessed June 1, 2022.
226. Cabrera AR, Kirkpatrick JP, Fiveash JB, et al. Radiation therapy for glioblastoma: Executive summary of an American Society for Radiation Oncology Evidence-Based Clinical Practice Guideline. *Pract Radiat Oncol*. Jul-Aug 2016;6(4):217-225. PMID 27211230
227. Goodman KA. Stereotactic body radiation therapy for pancreatic cancer. *Cancer J*. 2016;22(4):290-5
228. National Comprehensive Cancer Network (NCCN). NCCN Guidelines for Treatment of Cancer by Site. Retrieved July 10, 2023 from: [https://www.nccn.org/professionals/physician\\_gls/default.aspx#site](https://www.nccn.org/professionals/physician_gls/default.aspx#site).
229. American Society for Therapeutic Radiation Oncology. Model Policy: Stereotactic Body Radiation Therapy (SBRT). April 17, 2013. Retrieved July 10, 2023 from: [http://www.astro.org/uploadedFiles/Main\\_Site/Practice\\_Management/Reimbursement/2013HPcoding%20guidelines\\_SBRT\\_Final.pdf](http://www.astro.org/uploadedFiles/Main_Site/Practice_Management/Reimbursement/2013HPcoding%20guidelines_SBRT_Final.pdf).
230. International Radio Surgery Association. Radiosurgery Practice Guideline Initiative – Stereotactic radiosurgery for patients with intracranial arteriovenous malformation (AVM); Radiosurgery practice guideline report #2-03; 2009; Retrieved July 10, 2023 from: <http://www.irsa.org/AVM%20Guideline.pdf>.
231. AIM Specialty Health. Clinical appropriateness guidelines: – Radiation oncology. March 13, 2022; <https://aimspecialtyhealth.com/wp-content/uploads/2021/12/Radiation-Therapy-excludes-Proton-03-13-22.pdf>. Accessed July 19, 2022.

*The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through July 2023, 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<br>Added procedure codes 77332-77334  |
| 11/1/17 | 8/15/17  | 8/15/17 | <ul style="list-style-type: none"> <li>• Routine maintenance</li> <li>• References and rationale updated</li> <li>• Updated to mirror BCBSA while maintaining divergence topics of primary and metastatic liver tumors, irradiated and unirradiated spinal tumors, and prostate cancer</li> </ul>   |
| 11/1/18 | 8/21/18  | 8/21/18 | <ul style="list-style-type: none"> <li>• Routine maintenance</li> <li>• ASTROs recommendation for SBRT use in low to intermediate risk for prostate cancer added to position statement with reference</li> </ul>  |
| 3/1/19  | 12/11/18 |         | <ul style="list-style-type: none"> <li>• Brain SRS aligned with AIM criteria to allow tx regardless of active extracranial systemic disease status</li> </ul>   |
| 1/1/20  | 10/15/19 |         | <ul style="list-style-type: none"> <li>• Routine maintenance</li> <li>• Rationale simplified</li> <li>• Uveal melanoma position statement changed to established based on BCBSA clinical input and AIM support</li> <li>• Pancreatic adenocarcinoma position statement changed to established based on AIM and Medicare support</li> <li>• Lung and bone mets adjusted to reflect AIM stance</li> </ul> |
| 11/1/20 | 8/18/20  |         | <ul style="list-style-type: none"> <li>• 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.</li> </ul>   |
| 11/1/21 | 8/17/21  |         | <ul style="list-style-type: none"> <li>• Routine maintenance</li> <li>• No change in policy status</li> </ul>   |
| 11/1/22 | 8/16/22  |         | <ul style="list-style-type: none"> <li>• Routine maintenance</li> </ul>   |

|         |         |  |  |
|---------|---------|--|--|
| 11/1/23 | 8/23/23 |  | <ul style="list-style-type: none"> <li>• Routine maintenance</li> <li>• No change in policy status</li> <li>• Vendor: eviCore</li> </ul> <p>Post JUMP:</p> <ul style="list-style-type: none"> <li>• Uveal melanoma - For treatment of melanoma of the choroid moved from Stereotactic body radiotherapy (extracranial) to Stereotactic radiosurgery (intracranial) under the Inclusions section.</li> <li>•Removed statement: Reference eviCore criteria for clinical preference from MPS. (ky)</li> </ul> |
|---------|---------|--|--|

Next Review Date: 3<sup>rd</sup> Qtr, 2024

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

**I. Coverage Determination:**

|  |  |
|--|--|
| <b>Commercial HMO (includes Self-Funded groups unless otherwise specified)</b> | Covered, policy guidelines apply   |
| <b>BCNA (Medicare Advantage)</b>   | Refer to the Medicare information under the Government Regulations section of this policy. |
| <b>BCN65 (Medicare Complementary)</b>  | 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.