Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy

Policy # 00045
Original Effective Date: 03/25/2002
Current Effective Date: 01/15/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:
- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Cranial Sites of Treatment
Based on review of available data, the Company may consider the use of stereotactic radiosurgery using a gamma or linear accelerator unit for the following indications to be eligible for coverage:

Patient Selection Criteria
Coverage for the use of stereotactic radiosurgery using a gamma or linear-accelerator will be considered when any of the following criteria are met:
- Arteriovenous malformations;
- Acoustic neuromas;
- Pituitary adenomas;
- Non-resectable, residual or recurrent meningiomas;
- Cranopharyngiomas;
- Glomus jugulare tumors;
- Solitary or multiple brain metastases in patients having good performance status and no active systemic disease (defined as extracranial disease that is stable or in remission);
- Primary malignancies of the central nervous system (CNS), including but not limited to high-grade gliomas (initial treatment or treatment of recurrence);
- Trigeminal neuralgia refractory to medical management.

Patient Selection Criteria when irradiation of more than three cranial lesions is planned
In addition to the above criteria, the candidate must have a Karnofsky scale rating of 80 or greater for coverage eligibility to be considered.

Note: The Karnofsky performance status scale is widely used to evaluate the functional status of cancer patients to determine their eligibility for clinical trials and their prognosis.

Karnofsky Performance Status Scale

<table>
<thead>
<tr>
<th>Karnofsky Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Moribund; fatal processes progressing rapidly</td>
</tr>
<tr>
<td>20</td>
<td>Very sick; active support treatment is necessary</td>
</tr>
<tr>
<td>30</td>
<td>Severely disabled; hospitalization is indicated</td>
</tr>
<tr>
<td>40</td>
<td>Disabled; requires special care and assistance</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>Requires considerable assistance and frequent medical care</td>
</tr>
<tr>
<td>60</td>
<td>Requires occasional assistance; able to care for most personal needs</td>
</tr>
<tr>
<td>70</td>
<td>Care for self; unable to carry on normal activity or do active work</td>
</tr>
<tr>
<td>80</td>
<td>Normal activity with effort, some signs or symptoms of disease</td>
</tr>
<tr>
<td>90</td>
<td>Able to carry on normal activity; minor signs or symptoms of disease</td>
</tr>
<tr>
<td>100</td>
<td>Normal; no complaints; no evidence of disease</td>
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</table>

Extracranial Sites of Treatment
Based on review of available data, the Company may consider the use of stereotactic body radiotherapy for the following indications to be eligible for coverage:

Patient Selection Criteria
Coverage eligibility for the use of stereotactic body radiotherapy will be considered when any of the following criteria are met:

- Medically inoperable non-small cell lung cancer or pulmonary metastases;
- Spinal or vertebral body tumors (metastatic or primary) in patients who have received prior radiation therapy;
- Liver malignancy
- Spinal or vertebral metastases that are radioresistant (e.g., renal cell carcinoma, melanoma and sarcoma)

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers stereotactic radiosurgery to be investigational when used to treat chronic pain, seizures and functional disorders other than trigeminal neuralgia.

Based on review of available data, the Company considers the use of stereotactic radiosurgery using a gamma or linear-accelerator or the use of stereotactic body radiotherapy when patient criteria are not met, to be investigational.

Background/Overview
Stereotactic Radiosurgery – The Technology
Stereotactic radiosurgery 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. Stereotactic radiosurgery entails delivering highly focused convergent beams in a single session so that only the desired target is radiated, sparing adjacent structures.

Two main methods of this technology exist: gamma-ray radiosurgery (Gamma Knife [GK] \(^\text{\textregistered}\) \(^\text{\texttrademark}\)) and LINAC radiosurgery. The differences in the various systems are summarized in the following table:
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<table>
<thead>
<tr>
<th>Device</th>
<th>Energy Source</th>
<th>Energy Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma Knife</td>
<td>201 separate cobalt-60 sources arranged in a steel shell; beams intersect on target</td>
<td>gamma rays, consisting of two photons with an average energy of 1.25MeV</td>
</tr>
<tr>
<td>Linear accelerator adapted for stereotactic use</td>
<td>single beam of x-rays, rotated to produce multiple intersecting beams</td>
<td>x-rays, consisting of photons with an average energy of 2MeV</td>
</tr>
</tbody>
</table>

As shown in the table, the GK and LINAC systems are similar in concept; both use multiple photon radiation beams or arcs that intersect at a stereotactically determined target, thus permitting higher doses of radiation delivery with sparing of surrounding normal tissues. The differences between them relate to how the energy is produced (i.e., through decaying cobalt or from x-rays) and the number of energy sources used (i.e., multiple energy sources in the GK versus one in the LINAC system).

The radiosurgical procedure is preceded by a process of localizing the target, which can be performed with one or more of the following techniques: cerebral angiography, computed tomography (CT) and magnetic resonance imaging (MRI). Stereotactic radiosurgery is typically performed in one session, usually requiring no more than an overnight stay. Stereotactic body radiation therapy (SBRT) refers to stereotactically guided radiation therapy applied over several days. This fractionated form of radiation therapy is made possible by the recent availability of noninvasive repositioning devices that can be used in lieu of a head frame. Stereotactic body radiation therapy 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.

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

Applications of Stereotactic Radiosurgery (SRS)
The most common applications of SRS include treatment of intracranial tumors and malignancies, including primary and metastatic tumors, acoustic neuromas and other benign intracranial tumors such as meningiomas or pituitary adenomas. Stereotactic radiosurgery has been used for trigeminal neuralgia that is resistant to other therapies. It is also an established treatment for arteriovenous malformations (AVMs). More recently, SRS has been investigated as a treatment of functional disorders, which are defined as conditions having no detectable organic cause. Examples of functional disorders include chronic pain. Stereotactic radiosurgery is also being studied for treatment of extracranial sites including lung tumors, liver tumors and spinal lesions.

Intracranial metastases have been considered ideal targets for radiosurgery due to their small spherical size and non-infiltrative borders. Brain metastases are a frequent occurrence, seen in 25%–30% of all patients.

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with cancer, particularly in those with lung, breast, or colon cancer or melanoma. The treatment of primary brain tumors such as gliomas is more challenging, due to their generally larger size and infiltrative borders.

Acoustic neuromas are benign tumors originating on the eighth cranial nerve, and they can be seen in association with neurofibromatosis. Although these tumors are benign, they are associated with significant morbidity and even death if their growth compresses vital structures. Treatment options include complete surgical excision using microsurgical techniques, but radiosurgery has also been used extensively, either as a primary treatment or as a treatment of recurrence after incomplete surgical resection. In fact, acoustic neuromas were one of the first indications for SRS, dating back to 1969.

Pituitary adenomas are benign tumors with symptoms that are related to hormone production (i.e., functioning adenomas) or to neurologic symptoms due to their impingement on surrounding neural structures. Treatment options for pituitary adenomas include surgical excision, conventional radiation therapy, or SRS. Surgical excision is typically offered to patients with functioning adenomas, since 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, treatment goals are to control growth; complete removal of the adenoma is not necessary. Conventional radiation therapy has been used in this setting with an approximate 90% success rate with few complications.

Arteriovenous malformations consist of a tangled network of vessels in which blood passes from arteries to veins without intervening capillaries. They range in size from small, barely detectable lesions to huge lesions that can occupy an entire hemisphere. Stereotactic radiosurgery 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, there is an ongoing but declining risk of hemorrhage. 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 neurological sequelae. Stereotactic radiosurgery is an important alternative in these patients.

Trigeminal neuralgia is a disorder of the fifth cranial (i.e., trigeminal) nerve that causes episodes of intense, stabbing pain in the face. 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, balloon compression and rhizotomy. Stereotactic radiosurgery has been investigated as an alternative to these neurosurgical treatments.

Seizure disorders are initially treated medically. Surgical treatment is only considered in those rare instances when the seizures have proven refractory to all attempts at aggressive medical management, when the seizures are so frequent and severe as to significantly diminish quality of life, and when the seizure focus can be localized to a focal lesion in a region of the brain that is amenable to resection. Stereotactic radiosurgery has been investigated as an alternative to neurosurgical resection. For chronic pain that is refractory to a variety of medical and psychological treatments, there are a variety of surgical
alternatives. Neurodestructive procedures include cordotomy, myelotomy, dorsal root entry zone (DREZ) lesions and SRS thalamotomy. Stereotactic radiosurgery targeting the thalamus has been considered an investigative alternative to these neurodestructive procedures.

Studies are also being conducted to evaluate SBRT for a number of extracranial sites. This approach is being studied to better target lesions (sparing surrounding normal structures) and to shorten the length of time needed to complete the treatments.

**Rationale/Source**

Challenges to an Evidence-Based Approach to Rapidly Evolving Technologies in Radiation Oncology

This policy groups together several different techniques for delivering SRS, i.e., the GK, LINAC devices, proton beam radiotherapy, and the CyberKnife device, i.e., an example of image-guided radiotherapy. However, from an evidence-based approach, it is extremely difficult to compare these different devices to determine if one device is superior to another for a particular indication. A literature search in May 2006 failed to identify any controlled trials directly comparing different devices in homogeneous groups of patients. In addition, the field of radiation oncology is rapidly evolving, with a current intense interest in emerging image-guided technology. A limited number of SRS options may be available in individual markets, and thus the choice among devices may be dictated primarily by geography. The following summarizes different variables related to SRS and radiotherapy.

- **Size of Lesion**

  In terms of SRS, the superiority of one energy source over another depends primarily on the dose distribution capabilities, which in turn depend on the target's volume, location, and shape. For small lesions (i.e., < 5 cm³), the dose distributions produced by the GK are essentially identical to those achievable with LINAC units. When the target lesion is nonspherical or of intermediate size (e.g., between 5 and 25 cm³), LINAC units may have an advantage over GK units, due to their ability to treat larger lesions without requiring multiple isocenters (which makes treatment planning difficult), and the ability to shape the dose using collimated fields. However, when targeting large volumes (i.e., > 25 cm³), charged particle units that use a small fixed number of beams have the best ability to shape dose distributions and thus offer some advantages over both LINAC and GK units.

- **Dose Fractionation**

  Standard radiobiologic principles suggest that fractionating radiation therapy (i.e., delivery in multiple sessions) will reduce both early and late toxicities to surrounding normal tissues. Radiosurgery (one treatment) or hypofractionation (limited number of treatments) may be considered when patient movement limits the use of conventional radiation therapy, or may be offered as a convenience to patients, particularly those that require rapid pain relief. These two clinical indications are also associated with different outcomes that must be considered as part of an evidence-based analysis. A more basic scientific issue is an underlying understanding of the radiosensitivity of surrounding normal tissues.
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- **Dose Escalation**

Novel forms of radiation therapy have been/are being proposed as ways to provide dose escalation. In this setting, clinical questions include whether or not dose escalation provides improved tumor control, which depends on the dose response rate of individual tumor types, and whether an increased dose is associated with increased toxicity to surrounding tissues.

- **Decreased Toxicity**

A variety of novel treatment planning and delivery approaches are designed to reduce toxicity. Evidence of reduced toxicity would require directly comparative studies. Many of the potential benefits of delivery systems have been based on modeling studies or studies with phantoms.

In summary, the lack of comparative studies of different techniques of radiation planning and delivery in homogeneous groups of patients limits any scientific analysis regarding the relative safety and efficacy of different systems for different clinical situations, i.e., reduction of fractionation, dose escalation, reduced toxicity or a combination of all three. Therefore the scientific evidence is inadequate to permit scientific conclusions regarding the superiority of one device over another. The following discussion focuses on different general applications of stereotactic applications in radiation therapy.

**Treatment of Brain Metastases**

Previous studies suggested that use of radiosurgery for brain metastases should be limited to patients with three or fewer lesions. A recent randomized trial compared whole-brain radiation therapy (WBRT) with WBRT plus radiosurgery boost to metastatic foci. It found that the significant advantage of radiosurgery boost over WBRT alone in terms of freedom from local failure did not differ among patients with 2, 3 or 4 metastases. Survival also did not depend on the number of metastases. As the number of metastases rises, so does the total volume of tissue receiving high-dose radiation, thus the morbidity risk of radiation necrosis associated with radiosurgery is likely to increase. For a large number of metastases, and for large volumes of tissue, this risk may be high enough to negate the advantage of radiosurgery plus WBRT over WBRT alone seen in patients with four or fewer metastases. Stereotactic radiosurgery centers commonly exclude patients with more than five metastases from undergoing radiosurgery. It is difficult to identify a specific limit on the number of metastases for which the use of SRS is advantageous. A large number of very small metastases may respond to radiosurgery as well as a small number of larger metastases. Recent literature suggests that radiosurgery is no longer justified for between 1 and 3 metastases.

**Treatment of Epilepsy**

The 1998 TEC Assessment cited 2 studies of 11 and 9 patients, in which radiosurgery was used to treat epilepsy. The subsequent literature search revealed three small studies on the use of radiosurgery for medically refractory epilepsy. Regis et al selected 25 patients with mesial temporal lobe epilepsy, of which 16 provided minimum 2-year follow-up. Seizure-free status was achieved in 13 patients, 2 patients were improved, and 3 patients had radiosurgery-related visual field defects. Schröttner et al included 26 patients with tumoral epilepsy, associated mainly with low-grade astrocytomas. Mean follow-up among 24 available patients was 2.25 years. Tumor location varied across patients. Seizures were simple partial in 6 (3 with generalization) and complex partial in 18 (5 with generalization, 1 gelastic). Seizures were eliminated or...
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nearly so in 13 patients. Little improvement was observed in 4 patients and none in 7. Whang and Kwon performed radiosurgery in 31 patients with epilepsy associated with non-progressive lesions. A minimum of 1-year follow-up was available in 23 patients, of whom 12 were seizure-free, 3 had antiseizure medications discontinued, 2 had seizures reduced in frequency, and 9 experienced no change. While the Regis series selected a fairly homogeneous clinical sample, the other two studies were heterogeneous. No confirmatory evidence is available on mesial temporal lobe epilepsy. The available evidence from patients with epileptic lesions of various sizes and locations is insufficient to show what factors are associated with favorable outcome. There is inadequate reporting of complications associated with radiosurgery. The studies published to date are preliminary in nature. The 1998 TEC Assessment observed that evidence was insufficient to permit conclusions about the effects of radiosurgery on epilepsy. Conclusions about the health outcome effects of radiosurgery await additional studies.

Treatment of Chronic Pain
The TEC Assessment from 1998 identified 2 reports, with 2 and 47 patients, who underwent radiosurgical thalamotomy for chronic pain. No new studies were found in the search of recent literature. Thus, the conclusions of the 1998 TEC Assessment have not changed.

Treatment of Extracranial Sites Including Spinal Cord Lesions
A variety of applications have been proposed for the CyberKnife device. Published data are limited for most extracranial sites, and thus this use is considered investigational.

The site most studied involves spinal lesions. In the largest case series, Gerszten and colleagues reported on the outcomes of 115 patients with spinal tumors of varying etiologies, i.e., benign, metastatic, single or multiple lesions, in a variety of locations, i.e., cervical, thoracic, lumbar, sacral, who were treated with the CyberKnife in a single session. The majorities of patients were treated for pain control and also had received prior external beam irradiation. The authors point out that radiation therapy of the spinal cord is limited by its low tolerance and that if a radiation dose could be targeted more accurately at the lesions, higher doses could be delivered in a single fraction. They further point out that conventional methods of delivering intensity modulated radiation therapy (IMRT) are limited due to lack of target immobilization. Axial and radicular pain improved in 74 of the 79 symptomatic patients. There were no acute radiation toxicities or new neurologic deficits. Conventional external beam radiation therapy typically is delivered over a course of 10 to 20 fractions. In contrast, in this study only one CyberKnife treatment session was used. In a 2005 study, Degen and colleagues reported on the outcomes of 51 patients with 72 spinal lesions who were treated with the CyberKnife. Patients underwent a median of three treatments. Pain was improved, as measured by declining mean visual analogue scale (VAS) score, and quality of life was maintained during the 1-year study period.

Stereotactic Radiotherapy
Stereotactic radiotherapy describes the delivery of multiple fractions over a course of several days. One research focus has been on the treatment of acoustic neuromas, where the most significant side effect is functional preservation of the facial and auditory nerve. For example, in a single-institution study, Meijer and colleagues reported on the outcomes of single fraction versus fractionated LINAC-based SRS in 129 patients with acoustic neuromas. Among these patients, 49 were edentate and thus could not be fitted with
a relocatable head frame that relies on dental impressions. This group was treated with a single fraction, while the remaining 80 patients were treated with a fractionated schedule. With an average follow-up of 33 months, there was no difference in outcome in terms of local tumor control, facial nerve preservation and hearing preservation. Chung and colleagues reported on the results of a single-institution case series of 72 patients with acoustic neuromas, 45 who received single fraction therapy and 27 who received fractionated therapy. Patients receiving single fraction treatment were functionally deaf, while those receiving fractionated therapy had useful hearing in the affected ear. After a median follow-up of 26 months, there was no tumor recurrence in either group. Chang reported that 74% of 61 patients with acoustic neuromas treated with CyberKnife using staged treatment who had serviceable hearing maintained serviceable hearing during at least 36 months of follow-up. Three separate single-institution case series reported on 87 patients with metastatic disease, 143 patients with astrocytomas and 36 patients with cerebral AVMs who were treated with fractionated stereotactic radiotherapy. While all reported promising outcomes, the lack of a control group receiving SRS severely limits interpretation.

Addendum, Brain Metastases:
Aoyama and colleagues recently reported on a randomized trial of SRS plus WBRT versus SRS alone for treatment of patients with 1 to 4 brain metastases. They found a 12-month intracranial tumor recurrence rate of 46.8% in the SRS plus WBRT group compared to 76.4% in the group that only received SRS. However, median survival times were not different at 7.5 and 8.0 months, respectively. They also found no differences in neurological functional preservation. In an accompanying editorial, Raizer comments that either treatment approach is a reasonable first step, recognizing that those who select SRS alone are more likely to need subsequent salvage radiation treatments. Raizer adds the additional comment that those who have a single brain metastasis from non-small cell lung cancer (NSCLC) or recursive partitioning analysis (RPA) class 1 patients should initially receive SRS and WBRT.

The policy was updated with a literature search in 2007. A number of articles were identified describing studies of SRS and radiotherapy of extracranial sites; some studies refer to this approach as SBRT.

Additional reports on the use of SRS for spinal tumors have been published. Gerszten recently published results on a series of 500 cases from a single institution (334 tumors had previously undergone external beam irradiation) using the CyberKnife system. In this series, the maximum intratumoral dose ranged from 12.5 to 25 Gy with a mean of 20 Gy. Long-term pain improvement occurred in 290 of 336 cases (86%). Long-term radiographic tumor control was demonstrated in 90% of lesions treated with radiosurgery as a primary treatment modality. Twenty-seven of 32 cases (84%) with a progressive neurologic deficit before treatment experienced at least some clinical improvement. Chang reported on phase I/II results of SBRT in 74 spinal lesions in 63 patients (55% had prior irradiation) with cancer. The actuarial 1-year tumor progression-free incidence was 84%. Pattern-of-failure analysis showed two primary mechanisms of failure: recurrence in the bone adjacent to the site of previous treatment; and recurrence in the epidural space adjacent to the spinal cord. The authors concluded that analysis of the data obtained in their study supports the safety and effectiveness of SBRT in cases of metastatic spinal tumors. They add that they consider it prudent to routinely treat the pedicles and posterior elements using a wide bone margin posterior to the diseased vertebrae because of the possible direct extension into these structures and for patients without a history of radiotherapy, more liberal spinal cord dose constraints than those used in the study. The
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Accumulating evidence suggests that SBRT can be used in patients with spinal or vertebral body tumors; the preponderance of the data is in patients who received prior irradiation. It is uncertain from the current literature about the outcomes of using SBRT in the initial treatment of these lesions. It is not certain if symptom relief occurs more rapidly or is more durable, since there have not been comparative studies of SBRT with other types of radiation therapy. In addition, there is the concern, perhaps theoretical, that the limited size of the SBRT field may result in more late recurrences at adjacent levels. Thus, at this time, SBRT of spinal (vertebral) lesions may be considered eligible for coverage only after prior radiation therapy.

A number of studies of SBRT were identified in the treatment of NSCLC. Reported studies generally involved small numbers of patients with limited follow-up and did not have a comparison group. Timmerman concluded that prospective trials using SBRT in North America have been able to identify potent tolerant dose levels and confirm their efficacy, but also noted that sometimes debilitating toxicity has been observed for patients with tumors near the central airways. Hof reported on outcomes (median follow-up 15 months) for 42 patients with stages I and II lung cancer who were not suitable for surgery and who were treated with stereotactic radiotherapy. In this series, at 12 months overall survival was 75% and disease-free survival was 70%. Better local control was noted with higher doses of radiation. Early preliminary results were also noted for this treatment approach with liver, renal and prostate cancer. Given these currently available published results, no changes are made in the coverage statements.

Since the last update, a number of additional articles have been published about SBRT, especially for the treatment of lung tumors. However, data on the use of SBRT in other non-CNS sites remains limited. One new citation was identified related to treatment planning in prostate cancer. Recent studies on use in liver cancers describe feasibility studies and interim analysis.

In terms of lung tumors, publications are reporting longer-term outcomes with SBRT for patients with early lung cancer who are not surgical candidates. These are patients with clinical stage 1 disease who currently might have been treated with conventional radiation therapy. These studies were summarized in a recent review by Nguyen. This paper cites a number of studies of SBRT for early-stage lung cancer receiving a biologic equivalent dose of 100Gy or more. Three of the studies cited reported 5-year survival that ranged from 30% to 83%; in the largest series of 257 patients the 5-year survival was 42%. Koto reported on a phase II study of 31 patients with Stage 1 NSCLC. Patients received 45Gy in 3 fractions, but those with tumors close to an organ at risk received 60Gy in 8 fractions. With a median follow-up of 32 months, the 3-year overall survival was 72%, disease-free survival was 84%. Five patients developed grade 2 or greater pulmonary toxicity. While comparative studies were not identified, older studies have reported 3-year disease-specific survival rates of 49% for those with stage 1 disease. Stereotactic body radiation therapy may not be appropriate for tumors in close proximity to the heart, mediastinum, or spinal cord. In addition, centrally located proximal tumors may be associated with increased toxicity.

Physician Specialty Society and Academic Medical Center Input
In response to requests, input was received from 2 physician specialty societies and 4 academic medical centers. While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or
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academic medical centers, unless otherwise noted. 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.

Based on the information reviewed above, SBRT may be considered eligible for coverage in patients with stage I NSCLC (not larger than 5 cm in diameter) showing no nodal or distant disease and who are not candidates for surgical resection because of co-morbid conditions. Stereotactic body radiation therapy has also been shown to improve outcomes (reduce pain) in patients with spinal (vertebral) tumors that recur after prior radiation therapy. Data for other extra-cranial uses of SBRT are limited; these clinical situations are still considered investigational.

None of the studies identified through the literature search led to a change in the coverage statements. Studies supported the use of SBRT in stage I NSCLC and in selected cases of spinal tumors, as noted in the current coverage statements. There was little new published data related to use of SBRT for cancers of the prostate, pancreas, or kidney. Studies that were identified, in general, were phase I/II research studies. Use of SBRT for liver tumors continues to generate much interest. The data on hepatocellular cancer (HCC), while still limited, is at a more advanced stage of research than are data for metastatic lesions involving the liver. Nevertheless, a recent review article summarized findings for use of SBRT in HCC. This article described the limited data (often reported only as response rates) for this application including information about toxic effects and concluded that in light of the short follow-up times for the studies of SBRT in HCC, SBRT should be regarded as an experimental treatment to be offered only in a trial setting.

Prostate Cancer
Data on use of SBRT for localized prostate cancer remains limited. Many reported series are quite small, i.e., fewer than 50 patients. One of the larger series published involved 304 patients, but follow-up was less than 2 years for the majority of patients. In this study, Katz and colleagues performed SBRT on 304 patients with clinically localized prostate cancer: Fifty received 5 fractions of 7 Gy (total dose 35 Gy) and 254 received 5 fractions of 7.25 Gy (total dose 36.25 Gy). At a median 30-month (range: 26-37 months) follow-up, there were no biochemical failures for the 35-Gy dose level. Acute grade II urinary and rectal toxicities occurred in 4% of patients with no higher grade acute toxicities. At a median 17-month (range: 8-27 months) follow-up, the 36.25-Gy dose level had 2 low- and 2 high-risk patients fail biochemically (biopsy showed 2 low- and 1 high-risk patients were disease-free in the gland). Acute grade II urinary and rectal toxicities occurred in 4.7% and 3.6% of patients, respectively. The authors concluded that the low toxicity was encouraging and that additional follow-up is needed to determine long-term biochemical control and maintenance of low toxicity.

Publications also describe delivering SBRT in either daily or every other day treatments and comment that disease outcome and adverse effects may vary depending on the regimen. In addition, clinicaltrials.gov lists a number of studies that are planned or active related to SBRT in prostate cancer, including studies to evaluate toxicity. Thus, given the limited amount of published data related to impact on overall outcome, this is considered investigational.
Liver Cancer
More recent evidence in published, peer reviewed scientific literature supports the use of SRBT for hepatocellular carcinoma, intraoperative cholangiocarcinoma, and hepatic metastases in patients who are not eligible for surgery. Several NCCN Guidelines support the use of cellular carcinoma or colon or rectal liver metastases.

Lung Cancer
There is now evidence in the published, peer reviewed scientific literature suggesting that SBRT is safe and effective in treating medically inoperable patients with NSCLC or pulmonary metastases. Several NCCN Guidelines support the use of SRBT for NSCLC and limited lung metastases.

Tumors Metastatic to Brain
Finally, SRS continues to be used in metastatic brain tumors. One of the current areas of discussion relates to the role for both SRS and WBRT in patients with small numbers of metastatic lesions (generally no more than 3 or 4 lesions). This aspect was discussed in a recent clinical review by Suh, who also noted that clinical trials are underway. In a 2010 analysis, a Cochrane review first noted that given the unclear risk of bias in the included studies, the results need to be interpreted with caution. The analysis of all included patients (3 trials) indicated that SRS plus WBRT did not show a survival benefit over WBRT alone; however, performance status and local control were significantly better in the SRS plus WBRT group. In a randomized trial of 58 patients published following the Cochrane review, Chang and colleagues concluded that patients treated with SRS plus WBRT were at a greater risk of a significant decline in learning and memory function by 4 months compared with the group that received SRS alone.

Current coverage statements regarding metastatic brain tumors are unchanged.

References
5. TEC Assessments 1998; Tab 28.
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Coding

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>32553, 37201, 61796, 61797, 61798, 61799, 61800, 63620, 63621, 77370, 77371, 77372, 77373, 77421, 77427, 77431, 77432, 77435</td>
</tr>
<tr>
<td>HCPCS</td>
<td>G0173, G0251, G0339, G0340</td>
</tr>
<tr>
<td>ICD-9 Diagnosis</td>
<td>All relative diagnoses</td>
</tr>
<tr>
<td>ICD-9 Procedure</td>
<td>92.30, 92.31, 92.33, 92.39, 93.21, 93.59</td>
</tr>
</tbody>
</table>

Policy History

Original Effective Date: 03/25/2002
Current Effective Date: 01/15/2014
03/21/2002 Medical Policy Committee review
03/25/2002 Managed Care Advisory Council approval
06/24/2002 Format revision
03/08/2004 Medical Director review
03/16/2004 Medical Policy Committee review. Format revision. No substance change to policy statement.
03/29/2004 Managed Care Advisory Council approval
03/01/2005 Medical Director review
04/27/2005 Medical Policy Committee review. Patient selection criteria changes address clinical parameters for use of stereotactic radiosurgery in the presence of three or fewer and greater than three lesions.
05/23/2005 Managed Care Advisory Council approval
07/07/2006 Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
08/02/2006 Medical Director review
08/09/2006 Medical Policy Committee approval. Background, rationale/source and references updated.

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Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy

Policy #  00045
Original Effective Date:  03/25/2002
Current Effective Date:  01/15/2014

09/05/2007  Medical Director review
09/19/2007  Medical Policy Committee approval. No change to coverage eligibility.
06/04/2008  Medical Director review
06/18/2008  Medical Policy Committee approval. Extracranial sites now eligible for coverage with criteria.
06/04/2009  Medical Director review
06/17/2009  Medical Policy Committee approval. Title changed to track BCBSA.
06/03/2010  Medical Policy Committee review
06/16/2010  Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/02/2011  Medical Policy Committee review
02/02/2012  Medical Policy Committee review
02/15/2012  Medical Policy Implementation Committee approval. Criteria revised to include inoperable non-small cell lung cancer or pulmonary metastases and liver malignancy.
01/03/2013  Medical Policy Committee review
01/09/2013  Medical Policy Implementation Committee approval. Craniopharyngiomas and Glomus jugulare tumors were added to the cranial site criteria. Spinal or vertebral metastases that are radioresistant (e.g., renal cell carcinoma, melanoma and sarcoma was added to the extracranial site criteria.
01/09/2014  Medical Policy Committee review
01/15/2014  Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date:  01/2015

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);

2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or

3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. in accordance with nationally accepted standards of medical practice;

B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.
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