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Medical Policy Manual

Topic: Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy

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Section: Surgery

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IMPORTANT REMINDER

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

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

DESCRIPTION

Stereotactic Radiosurgery (SRS)

Stereotactic radiosurgery (SRS) is a method of delivering high doses of ionizing radiation to small intracranial targets. In SRS, highly focused convergent beams are delivered so that only the desired target receives the prescribed dose while adjacent structures are spared due to a rapid dose fall-off. This differs from conventional radiotherapy, which involves exposing larger areas of intracranial tissue to relatively broad fields of radiation over a number of sessions.

In order to localize the treatment target and to achieve precise delivery of radiation, SRS relies on stereotactic guidance (using cerebral angiography, computerized tomography, and/or magnetic resonance imaging) and the use of a positioning frame to restrict head movement.

In SRS, radiation may be delivered in a single high dose session or in a few fractionated treatments (up to five), usually delivered over a period of several days. Fractionation allows delivery of a higher total dose of radiation, and it decreases the short and long-term side effects of radiation therapy.
The two main types of SRS are:

- Gamma-ray radiosurgery (Gamma Knife®)

- Linear-accelerator radiosurgery (e.g. LINAC and Cyberknife®).

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

Stereotactic Body Radiation Therapy (SBRT)

SBRT refers to the use of SRS-like technology for extracranial sites. Radiation may be delivered in a single high dose or a few fractionated treatments. SBRT is made possible by the recent availability of repositioning devices that can be used to restrict body movement.

Image-Guided Radiosurgery or Radiotherapy

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

Performance Status Measurement

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

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

ECOG Performance Status:	
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work

2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.

Note: Particle radiation can also be used without stereotactic guidance. In this setting, the use of particles is referred to as proton, helium, or neutron radiation *therapy*. This policy addresses only the use of gamma knife and the linear accelerator. Proton or helium ion radiation therapies are considered in separate medical policies. See cross-reference section below.

MEDICAL POLICY CRITERIA

I. Stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) using Gamma Knife®, LINAC, Cyberknife®, BrainLAB Novalis®, or TomoTherapy® units may be considered **medically necessary** for the following indications:

A. Acoustic neuromas (also known as Vestibular Schwannomas)

B. Craniopharyngiomas

C. Glomus jugulare tumors

D. Intracranial arteriovenous malformations

E. Intracranial chordomas and chondrosarcomas of the skull base

F. Lung metastases when all of the following criteria are met:

1. ≤3 metastatic lung lesions (oligometastases)

2. Adequate lung function

3. Clinical records from a cardiothoracic surgeon document at least one of the following:

a. The tumor is not resectable; or

b. The patient is not a good surgical candidate.

4. Karnofsky performance score ≥70

5. Life expectancy >6 months

6. Locally controlled primary tumor

7. No other metastatic disease

8. Targeted tumor diameter ≤5cm

G. Non-resectable, residual, or recurrent meningiomas

H. Pituitary adenomas

I. Primary neoplasms of the CNS, including but not limited to high-grade gliomas (initial treatment or treatment of recurrence)

J. Solitary or multiple brain metastases in patients who meet both of the following:

1. Karnofsky performance score ≥70 (or an ECOG score ≤2); AND

2. Life expectancy >6 months.

K. Spinal or vertebral body tumors (metastatic or primary) in patients who have received prior radiation therapy

L. Stage 1 non-small cell lung cancer (NSCLC) as defined by clinical stage grouping of either T1, N0, M0 or T2, N0, M0, when the patient is an unsuitable candidate for surgical resection.

M. Trigeminal neuralgia (also known as tic douloureux) refractory to medical management

II. Stereotactic radiosurgery and stereotactic body radiation therapy are considered **investigational** for all other indications including but not limited to:

A. Choroidal neovascularization (CNV)

B. Chronic pain

C. Epilepsy

D. Functional disorders other than trigeminal neuralgia

E. Refractory symptoms of essential tremor or Parkinson's disease

F. Treatment of extracranial sites (e.g. ovaries, primary and metastatic tumors of the liver, pancreas, kidney, adrenal glands, prostate, and pelvis), except for the cases of spinal tumors, stage 1 non-small cell lung cancer, and lung metastases as noted above

G. Uveal melanoma

Note: See separate policy, Medicine, Policy No. 49 for non-stereotactic applications of particle beam radiation therapy (i.e., proton or helium ion). See separate policy, Medicine, Policy No. 134 for intraocular radiation therapy for age-related macular degeneration (choroidal neovascularization (CNV).

SCIENTIFIC EVIDENCE

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

This policy groups together several different techniques for delivering stereotactic radiosurgery, i.e., the Gamma Knife, LINAC devices, and real-time image-guided devices (e.g.the Cyberknife® device, BrainLAB Novalis®, TomoTherapy®). 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 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 stereotactic radiosurgery 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 stereotactic radiosurgery and radiotherapy.

- Size of Lesion

  In terms of stereotactic radiosurgery, 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 most lesions the dose distributions produced by the gamma knife are essentially identical to those achievable with LINAC units. However, when targeting large volumes (i.e., greater than 25 cm^3), 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 Gamma Knife 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 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.

- 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 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, and limited clinical experience.

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 radiosurgery and radiotherapy.

Stereotactic Radiosurgery (SRS): **Literature Review**

The focus of the literature appraisal below is on the indications identified in the policy criteria as investigational (see above).

Brain Metastases

The published literature on SRS for the treatment of brain metastases suggests some benefit, including local control and acceptable treatment-related toxicity. However, the studies have methodological limitations, including but not limited to small study populations, retrospective and/or non-comparative designs, and very heterogeneous study populations (e.g., studies included patients with or without whole brain radiation therapy [WBRT], with or without surgical resection, and with differing extents of intracranial/extracranial disease and comorbidities).[1-19]

Whole Brain Radiation Therapy (WBRT) vs. WBRT with SRS

- In a 2014 Cochrane review, the efficacy and safety of surgery or SRS plus WBRT with that of surgery or SRS alone for treatment of brain metastases in patients with systemic cancer was compared. The authors concluded the evidence that adding upfront WBRT to surgery or SRS decreases any intracranial disease progression at one year was of low quality. There was no clear evidence of an effect on overall and progression free survival. Further, the authors concluded the impact of upfront WBRT on neurocognitive function, health related quality of life and neurological adverse events was undetermined due to the high risk of performance and detection bias, and inconsistency in the technology and methods used to measure and report results across studies.
- The 2010 Cochrane review assessed the efficacy of WBRT plus radiosurgery versus WBRT alone in the upfront treatment of adult patients with newly diagnosed brain metastases (single or multiple), resulting from any primary, extracranial cancer.[20] Analysis of all included patients (n=358, meta-analysis based on two trials) indicated 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. Furthermore, significantly longer overall survival was reported in the combined treatment group for patients with Karnofsky performance status score equal to or greater than 70, as well as patients with a single metastasis. The authors warn that given the unclear risk of bias in the included studies, the results of this analysis have to be interpreted with caution.
- In an update of the 2010 Cochrane review on (WBRT), authors assessed the efficacy of WBRT plus SRS versus WBRT alone in the treatment of brain metastases.[21] Since the last version of this review no new studies were found that met the inclusion criteria. As the review above, analysis of all included patients, SRS plus WBRT, did not show a survival benefit over WBRT alone. Authors concluded that given the unclear risk of bias in the included studies, the results of the analysis need to be interpreted with caution.

SRS for Curative vs. Palliative Treatment of Brain Metastases

The characteristics of patients most likely to derive better health outcomes from SRS compared with other treatment options are not clear, particularly in patients with active systemic disease where SRS is not used with curative intent. Specifically, conclusions cannot be drawn from the current evidence concerning whether there is added palliative benefit from SRS that cannot be achieved with other treatment modalities.

Chronic Pain

The studies of SRS and stereotactic body radiation therapy (SBRT) for treatment of chronic pain are extremely limited. Only two small case series have been published to date. This evidence is not sufficient to understand the safety and effectiveness of SBRT for treatment of chronic pain or to adequately describe the subpopulation of patients with chronic pain most likely to benefit from this treatment:

- A 1998 TEC Special Report identified two studies of patients who underwent radiosurgical thalamotomy for chronic pain (n=2 and n=42).[22] However, this evidence was not sufficient to support the use of SRS/SBRT for chronic pain.

- No additional studies of SRS/SBRT for the treatment of chronic pain were identified.

Epilepsy

- The 1998 BlueCross BlueShield Association Technology Evaluation Center (TEC) Assessment cited two studies of eleven and nine patients in which radiosurgery was used to treat epilepsy.[23] The assessment concluded that evidence was insufficient to permit conclusions about the effects of radiosurgery on epilepsy.
- The studies of SRS for treatment of epilepsy published to date are preliminary in nature and consist of a small number of case series with very small study populations (n<50), short follow-up times, and/or heterogeneous study populations.[24-35] Evidence from these studies is unreliable due to methodological limitations, such as non-random allocation of treatment and lack of adequate comparison groups. In addition, the available evidence from patients with epileptic lesions of various sizes and locations is unable to adequately show what factors are associated with favorable outcomes following SRS treatment.
- In a recent study, authors investigated gamma knife radiosurgery (RS) as an alternative to open surgery for mesial temporal lobe epilepsy (MTLE).[36] In this multicenter prospective trial, 24 patients with unilateral hippocampal sclerosis and concordant video-electroencephalography (EEG) findings were enrolled. Patients were randomized to low or high doses delivered to the amygdala, hippocampal head, and parahippocampal gyrus. Postoperative perimetry were obtained at 24 months after RS. Authors concluded that visual field defects (VFDs) appeared after RS in proportions similar to historical comparisons from open surgery for MTLE. The nature of VFDs was consistent with lesions of the optic radiations. The findings support the hypothesis that the mechanism of RS involves some degree of tissue damage and is not confined entirely to functional changes in neuromodulation. Additional prospective trials are necessary to determine the efficacy of anticonvulsant mechanisms of RS.

Parkinson's Disease and Essential Tremors

The preliminary studies of SRS for the treatment of refractory symptoms of essential tremor and Parkinson's disease are limited and report conflicting findings.[37-39] No further evidence has emerged

that may permit conclusions about the effectiveness of stereotactic radiosurgery on Parkinson's disease or other movement disorders. Specifically, radiofrequency ablation (RFA) or deep brain stimulation (DBS) are considered the therapies of choice for those with medically refractive disease and no evidence comparing SRS with deep brain stimulation or radiofrequency ablation is available.

- In the first prospective study on SRS for Parkinson's disease (PD), authors investigated the safety and optimally effective conditions for performing unilateral gamma knife (GK) thalamotomy for tremors of PD and essential tremor (ET).[40] Seventy-two patients (PD characterized by tremor, n = 59; ET, n = 13) were included in a systematic postirradiation 24-month follow-up study that was conducted at 6 institutions. Of 53 patients who completed 24 months of follow-up, 43 were evaluated as having excellent or good results (81.1%). Authors concluded that GK thalamotomy was an alternative treatment for intractable tremors of PD as well as for ET. This prospective trial was limited by a small sample size, the lack of an RFA and/or DBS control group for comparison, and the severity of PD was not well defined in the patient population. Additional prospective studies are necessary to determine the efficacy of SRS compared with RFA or DBS in the treatment of medically refractory PD.
- Kooshkabadi et al. investigated the techniques and results of SRS in 86 patients (mean age 71 years; number of procedures 88) who underwent a unilateral Gamma Knife thalamotomy (GKT) for tremor during a 15-year period (1996-2011).[41] Symptoms were related to essential tremor in 48 patients, Parkinson disease in 27 patients, and multiple sclerosis in 11 patients. The mean tremor score was 3.28 ± 0.79 before and 1.81 ± 1.15 after ($p < 0.0001$) GKT; the mean handwriting score was 2.78 ± 0.82 and 1.62 ± 1.04, respectively ($p < 0.0001$); and the mean drinking score was 3.14 ± 0.78 and 1.80 ± 1.15, respectively ($p < 0.0001$). After GKT, 57 patients (66%) showed improvement in all 3 scores, 11 patients (13%) in 2 scores, and 2 patients (2%) in just 1 score. In 16 patients (19%) there was a failure to improve in any score. The limitations of the study included a lack of a comparison group or control group, including patients that may have received best medical therapy or deep brain stimulation (DBS) and not all patients were followed-up at the same center where initial testing occurred.
- Young et al. described the safety and effectiveness of nucleus ventralis intermedius (VIM) thalamotomy performed with the Leksell Gamma Knife (GK) for the treatment of essential tremor (ET).[42] One hundred seventy-two patients underwent a total of 214 VIM thalamotomy procedures for the treatment of disabling ET. The authors described the results in 161 patients who underwent a total of 203 thalamotomies (119 unilateral and 42 bilateral). There were statistically significant decreases ($p < 0.0001$) in tremor scores for both writing and drawing. The authors concluded that GK may be appropriate for patients who are not ideal candidates for deep brain stimulation. Several complications post-surgery were reported that impacted the patients' functional levels.

Trigeminal Neuralgia: SRS as a Primary Treatment for Trigeminal Neuralgia

Evidence that shows effectiveness of SRS treatment for trigeminal neuralgia comes from the studies of patients with the disease refractory to medical management. This evidence does not allow conclusions concerning safety and efficacy of SRS as a primary treatment for trigeminal neuralgia.

Uveal melanoma

The literature on the use of SRS for uveal melanoma consists of case series; no studies directly comparing SRS with other, accepted radiation modalities used to treat uveal melanoma (brachytherapy, proton beam) are identified.

- A 2012 review article summarizes the literature on the use of SRS for uveal melanoma, with long-term tumor control rates using the Gamma Knife reported to be around 90%.[43] Initial studies using SRS for uveal melanoma reported secondary side effects from radiation to be common, however more recent studies have reported lower incidences with lower total radiation doses.
- The largest study to date consisted of 212 patients with choroidal melanoma, who were not suitable for brachytherapy or resection.[44] Patients in the study received different doses of radiation ranging from 50 Gy to 70 Gy, in 5 fractions over 7 days. Ophthalmologic examination was performed at baseline and every 3 months in the first 2 years, every 6 months until 5 years, and once a year until 10 years after SRS. The study included measurement of tumor dimension and height using standardized methods, assessment of visual acuity and routine ophthalmologic examinations. Local tumor control was 96% at 5 years, and 93% at 10 years. Thirty-two patients developed metastases, and 22 of these patients died during the follow-up period. Median visual acuity decreased from 0.55 at baseline to hand motion ($p<0.001$). The authors concluded that SRS was sufficient to achieve excellent local tumor control in patients with melanoma of the choroid, and that disease outcome and vision were comparable to that achieved with proton beam radiotherapy.
- Additional case series using SRS for uveal melanoma have suggested that it is a possible eye-sparing option for patients, with outcomes comparable to enucleation or other radiation modalities.[45-47]

Stereotactic Body Radiation Therapy (SBRT): Literature Appraisal

Adrenal Metastases

The evidence on SBRT for adrenal metastases consists of very small case series. This level of evidence is insufficient to demonstrate the impact of SBRT on patient health outcomes.

- Scorsetti described the feasibility, tolerability and clinical outcomes of SBRT in the treatment of adrenal metastases in 34 consecutive cancer patients.[48] Between 2004 and 2010, a total of 34 consecutive patients, accounting for 36 adrenal metastatic lesions, were treated with SBRT. All 34 patients were clinically and radiologically evaluated during and after completion of SBRT. The following outcomes were taken into account: best clinical response at any time, local control, time to systemic progression, time to local progression, overall survival and toxicity. Survival was estimated by the Kaplan-Meier method and factors potentially affecting outcomes were analyzed with Cox regression analysis. Total RT doses ranged from 20 Gy in 4 fractions to 45 Gy in 18 fractions (median dose: 32 Gy; median number of fractions: 4). All doses were prescribed to the 95% isodose line. No cases of Grade ≥ 3 toxicity were recorded. At a median follow-up time of 41 months (range, 12-75) 22 patients were alive. Three of 28 lesions (11%) showed complete response, 13/28 (46%) partial response, 10/28 (36%) stable disease and 2/28 (7%) progressed in the treated area. Local failure was observed in 13 cases. Actuarial local control rates at one and two years were 66% and 32%, respectively. Median time to local progression was 19 months. Median survival was 22 months.
- Holy presented initial institutional experiences with SBRT for adrenal gland metastases.[49] Between 2002 and 2009, 18 patients with a non-small cell lung cancer and adrenal metastasis received SBRT. An isolated adrenal metastasis was diagnosed in 13 patients, while 5 patients with multiple metastatic lesions had SBRT due to back pain. Depending on treatment intent and target size, the dose/fraction concept varied from 5 x 4 Gy to 5 x 8 Gy. Dose was given with an

isotropic convergent beam technique to a median maximum dose of 132% to the target's central part. The mean clinical (CTV) and planning target volume (PTV) was 89 cm^3 (5-260 cm^3) and 176 cm^3 (20-422 cm^3). A median progression-free survival time (PFS) of 4.2 months was obtained for the entire patient group, with a markedly increased PFS of 12 months in 13 patients suffering from an isolated metastasis of the adrenal gland. After a median follow-up of 21 months, 10 of 13 patients (77%) with isolated adrenal metastasis achieved local control. In these patients, median overall survival (OS) was 23 months.

- Casamassima evaluated a retrospective single-institution outcome after hypofractionated SBRT for adrenal metastases.[50] Between 2002 and 2009, 48 patients were treated with SBRT for adrenal metastases. The median age of the patient population was 62.7 years (range, 43-77 years). In the majority of patients, the prescription dose was 36 Gy in 3 fractions (70% isodose, 17.14 Gy per fraction at the isocenter). Eight patients were treated with single-fraction stereotactic radiosurgery and forty patients with multi-fraction stereotactic radiotherapy. Overall, the series of patients was followed up for a median of 16.2 months (range, 3-63 months). At the time of analysis, 20 patients were alive and 28 patients were dead. The 1- and 2-year actuarial overall survival rates were 39.7% and 14.5%, respectively. Forty-eight distant failures and 2 local failures were recorded, with a median interval to local failure of 4.9 months. The actuarial 1-year disease control rate was 9%; the actuarial 1- and 2-year local control rate was 90%.
- Chawla investigated the dosimetry and outcomes of patients undergoing SBRT for metastases to the adrenal glands.[51] A retrospective review of 30 patients who had undergone SBRT for adrenal metastases from various primary sites, including lung (n = 20), liver (n = 3), breast (n = 3), melanoma (n = 1), pancreas (n = 1), head and neck (n = 1), and unknown primary (n = 1) was performed. Of the 30 patients, 14 with five or fewer metastatic lesions (including adrenal) underwent SBRT, with the intent of controlling all known sites of metastatic disease, and 16 underwent SBRT for palliation or prophylactic palliation of bulky adrenal metastases. The prescribed dose ranged from 16 Gy in 4 fractions to 50 Gy in 10 fractions. The median dose was 40 Gy. Of the 30 patients, 24 had >3 months of follow-up with serial computed tomography. Of these 24 patients, 1 achieved a complete response, 15 achieved a partial response, 4 had stable disease, and 4 developed progressive disease. No patient developed symptomatic progression of their adrenal metastases. The 1-year survival, local control, and distant control rate was 44%, 55%, and 13%, respectively. No patient developed Radiation Therapy Oncology Group Grade 2 or greater toxicity. Local control was poor and most patients developed widespread metastases shortly after treatment.

Choroidal neovascularization (CNV)

The evidence for the role of SBRT for choroidal neovascularization (CNV) is limited to 1 RCT. At this time, it is not known which patient populations would most likely benefit from this treatment.

- INTREPID is a randomized sham-controlled double-masked trial with 230 patients that assessed the efficacy and safety of stereotactic radiotherapy (SRT) to treat neovascular AMD.[52] Both SRT and sham-control patients received ranibizumab as needed. After 1 year, treatment with either16-Gy or 24-Gy SRT reduced the number of ranibizumab treatments (median of 2 compared with 3.5 for sham-controls) with no significant differences from control in changes in visual acuity over the 1-year of follow-up. There were no safety concerns identified in the first 12 months; safety follow-up is continuing.

Kidney Cancer

The literature on SBRT for renal cell carcinoma consists only of very small case series. This level of evidence is not sufficient to understand the impact of SBRT on renal carcinoma-related health outcomes. In addition, this level of evidence limits comparisons between SBRT and more established treatment modalities for renal cell carcinoma.

- A 2012 systematic review on the use of stereotactic radiotherapy for primary renal cell carcinoma identified a total of 126 patients worldwide who had been treated using this modality.[53] A systematic search performed in January 2012 identified 7 retrospective studies and 3 prospective studies, which used a wide range of techniques, doses and dose fractionation schedules. Median or mean follow-up ranged from 9 months to 57.5 months. Local control was reported as 93.9% (range 84%-100%) and the rate of severe grade 3 or higher adverse events was 3.8% (range 0%-19%). The conclusions of the systematic review were that the current literature suggests that stereotactic radiotherapy for renal cell carcinoma can be delivered with good rates of local control and acceptable toxicity, but that there is insufficient evidence to recommend a consensus for dose fractionation or technique, and there is a need for further prospective studies.
- Beitler reported outcomes in nine patients with nonmetastatic renal cell carcinoma, 2 of which had bilateral renal cell cancers.[54] Patients were treated definitively with 40 Gy in 5 fractions using SBRT. With a median follow up of 26.7 months, 4 of the 9 patients were alive. The survivors had a minimum follow-up of 48 months. At presentation, all 4 of the survivors had tumors < or =3.4 cm in largest dimension, had clinically negative lymph nodes, and presented no clinical evidence of penetration of Gerota fascia or renal vein extension.

Lung Tumors

Lung Metastases

Published evidence suggests some benefit of SBRT in the treatment of lung metastases, including local control and acceptable treatment-related toxicity. However, the studies have methodological limitations, including, but not limited to small study populations and retrospective and/or non-comparative designs, which introduce significant bias. In addition, the studies have very heterogeneous study populations and the characteristics of patients most likely to derive better health outcomes from SBRT compared with other treatment options are not clear. The data is particularly unclear when SBRT is used for palliation rather than attempted cure. A review of the study eligibility criteria in the available published literature identified a small number of studies that did not have clearly defined eligibility criteria. For example, some retrospective reviews reported outcomes in all patients treated with SBRT in a certain time period, regardless of their pre-treatment clinical characteristics. However, in a majority of the studies the eligibility criteria were well-defined. Patient characteristics that were repeated across studies are reflected in the policy criteria concerning SBRT treatment for the treatment of lung metastases.[55-79]

Non-Small-Cell Lung Cancer (NSCLC)

- A number of studies of SBRT were identified in the treatment of NSCLC. 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.[80] 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.[81] 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. In a recent study, authors investigated SBRT as

an alternative to surgery for clinical stage I NSCLC in a retrospective study using two combined databases.[82] Authors reported that overall survival (OS) was similar in SBRT or surgery-treated patients after controlling for prognostic and patient selection factors. Authors concluded that randomized clinical trials are needed to better compare the effectiveness of these treatments.

- 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.[83] This paper cited a number of studies of SBRT for early stage lung cancer receiving a biologic equivalent dose of 100 Gy or more. Three of the studies cited reported five-year survival that ranged from 30% to 83%; in the largest series of 257 patients the five-year survival was 42%. Koto reported on a phase II study of 31 patients with Stage 1 non-small-cell lung cancer.[84] Patients received 45 Gy in 3 fractions, but those with tumors close to an organ at-risk received 60 Gy in eight fractions. With a median follow-up of 32 months, the three-year overall survival was 72%, disease-free survival was 84%. Five patients developed grade two or greater pulmonary toxicity. While comparative studies were not identified, older studies have reported three-year disease-specific survival rates of 49% for those with stage 1 disease.[85] SBRT 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.
- Evidence-based guidelines from the American College of Chest Physicians state, "There is growing evidence that SBRT provides greater local control than standard radiation therapy for high-risk and medically inoperable patients with NSCLC. The role of ablative therapies in the treatment of high-risk patients with stage I NSCLC is evolving."[86] Guidelines did not state a clear recommendation for SBRT treatment of NSCLC.

Pancreatic Cancer

The role of SBRT for pancreatic tumors has not been established. At this time, it is not known which patient populations would most likely benefit from this treatment. Although studies have shown promising local control rates, there have been no significant changes in patient survival when compared with historical data, and some studies have shown unacceptable toxicity and questionable palliative effect.

- Goyal reported outcomes with SBRT in patients with pancreatic adenocarcinoma who were found not to be candidates for surgical resection.[87] A prospective database of the first 20 consecutive patients receiving SBRT for unresectable pancreatic adenocarcinomas and a neuroendocrine tumor was reviewed. Mean radiation dose was 25 Gray (Gy) (range 22-30 Gy) delivered over 1-3 fractions. Chemotherapy was given to 68% of patients in various schedules/timing. Patients had a mean gross tumor volume of 57.2 cm(3) (range 10.1-118 cm(3)) before SBRT. The mean total gross tumor volume reduction at 3 and 6 mo after SBRT were 21% and 38%, respectively ($p < 0.05$). Median follow-up was 14.57 mo (range 5-23 mo). The overall rate of freedom from local progression at 6 and 12 mo were 88% and 65%. The probability of overall survival at 6 and 12 mo were 89% and 56%. No patient had a complication related to fiducial markers placement regardless of modality. The rate of radiation-induced adverse events was: grade 1-2 (11%) and grade 3 (16%). There were no grade 4/5 adverse events seen.
- Rwigema assessed the feasibility and safety of SBRT in patients with advanced pancreatic adenocarcinoma.[88] The outcomes of 71 patients treated with SBRT for pancreatic cancer between 2004 and 2009 were reviewed. Forty patients (56%) had locally unresectable disease, 11 patients (16%) had local recurrence following surgical resection, 8 patients (11%) had metastatic

disease, and 12 patients (17%) received adjuvant SBRT for positive margins. The median dose was 24 Gy (18-25 Gy), given in a single-fraction SBRT (n = 67) or fractionated SBRT (n = 4). Kaplan-Meyer survival analyses were used to estimate freedom from local progression (FFLP) and overall survival (OS) rates. The median follow-up among surviving patients was 12.7 months (4-26 months). The median tumor volume was 17 mL (5.1-249 mL). The overall FFLP rates at 6 months/1 year were 71.7%/48.5%, respectively. Among those with macroscopic disease, FFLP was achieved in 77.3% of patients with tumor size <15 mL (n = 22), and 59.5% for ≥15 mL (n = 37) (P = 0.02). FFLP was achieved in 73% following 24 to 25 Gy, and 45% with 18 to 22 Gy (P = 0.004). The median OS was 10.3 months, with 6 month/1 year OS rates of 65.3%/41%, respectively. Grade 1-2 acute and late GI toxicity were seen in 39.5% of patients. Three patients experienced acute grade 3 toxicities. SBRT is feasible, with minimal grade ≥3 toxicity. The overall FFLP rate for all patients was 64.8%, comparable to rates with external beam radiotherapy.

- Chang reported on the local control and toxicity of SBRT for patients with unresectable pancreatic adenocarcinoma.[89] Seventy-seven patients with unresectable adenocarcinoma of the pancreas received 25 gray (Gy) in 1 fraction. Forty-five patients (58%) had locally advanced disease, 11 patients (14%) had medically inoperable disease, 15 patients (19%) had metastatic disease, and 6 patients (8%) had locally recurrent disease. Nine patients (12%) had received prior chemoradiotherapy. Sixteen patients (21%) received between 45 to 54 Gy of fractionated radiotherapy and SBRT. Various gemcitabine-based chemotherapy regimens were received by 74 patients (96%), but 3 patients (4%) did not receive chemotherapy until they had distant failure. The median follow-up was 6 months (range, 3-31 months) and, among surviving patients, it was 12 months (range, 3-31 months). The overall rates of freedom from local progression (FFLP) at 6 months and 12 months were 91% and 84%, respectively. The 6- and 12-month isolated local recurrence rates were 5% and 5%, respectively. There was no difference in the 12-month FFLP rate based on tumor location (head/uncinate, 91% vs body/tail, 86%; p=.52). The progression-free survival (PFS) rates at 6 months and 12 months were 26% and 9%, respectively. The PFS rate at 6 months was superior for patients who had nonmetastatic disease versus patients who had metastatic disease (28% vs 15%; P = .05). The overall survival (OS) rates at 6 months and 12 months from SBRT were 56% and 21%, respectively. Four patients (5%) experienced grade > or = 2 acute toxicity. Three patients (4%) experienced grade 2 late toxicity, and 7 patients (9%) experienced grade > or = 3 late toxicity. At 6 months and 12 months, the rates of grade > or = 2 late toxicity were 11% and 25%, respectively.

Primary Hepatocellular Tumors (HCC) and Liver Metastases

Systematic Reviews Including both Primary and Metastatic Tumors of the Liver

- A 2012 systematic review by Tao assessed the efficacy and safety of SBRT for treating primary and secondary hepatic neoplasms.[90] The review included prospective clinical trials published in English. Fifteen studies involving 158 patients with primary tumors and 341 patients with metastases to the liver were included. Treatment was performed in 1-10 fractions to total doses of 18-60 Gy. However, most studies that were included reported outcomes for patients with both primary and metastatic disease, without separating out outcome data for primary tumors only. In addition, some studies reporting on outcomes for primary liver tumors included cholangiocarcinomas. Therefore, this evidence limits ability to draw specific conclusions concerning the safety and efficacy of SBRT for primary versus secondary hepatic tumors.

Primary HCC

- At Indiana University, in a phase I study, Cardenes et al. treated 17 HCC patients with Child-Turcotte-Pugh (CTP) CTP-A or CTP-B, 1-3 lesions and cumulative tumor diameter ≤6 cm.[91] Patients with CTP-A were treated in three fractions with the dose escalated from 12 to 16 Gy. For patients with CTP-B, the dose was modified to five fractions starting at 8 Gy per fraction and was not escalated because two patients treated at 3×14 Gy developed grade 3 hepatic toxicity. The one-year overall survival was 75% and there were no local failures during the median 24 months of follow-up. Building upon the phase I study, 36 patients with CTP-A disease were treated with 3×18 Gy and 24 patients with CTP-B disease were treated with 5×8 Gy.
- In an attempt to extend the use of SBRT to larger lesions, Shin et al. treated six patients with tumors >10 cm (median tumor volume 1288 ml, range 1008-1815 ml).[92] The 4×8–10 Gy regimen was relatively safe with only one case of grade 3 changes in transaminases. Following SBRT, 1 patient underwent lobectomy, 4 patients underwent TACE, and 1 patient did not undergo any further treatment due to disease progression and poor general condition. After a median follow-up of 25.39 months (8.1-56 months), three patients had died. Median survival was 10 months (3-56 months) and median progression free survival 6 months (2-21 months).
- Andolino evaluated the safety and efficacy of SBRT for the treatment of primary HCC.[93] From 2005 to 2009, 60 patients with liver-confined HCC were treated with SBRT: 36 Child-Turcotte-Pugh (CTP) Class A and 24 CTP Class B. The median number of fractions, dose per fraction, and total dose, was 3, 14 Gy, and 44 Gy, respectively, for those with CTP Class A cirrhosis and 5, 8 Gy, and 40 Gy, respectively, for those with CTP Class B. The records of all patients were reviewed, and treatment response was scored according to Response Evaluation Criteria in Solid Tumors v1.1. Toxicity was graded according to the Common Terminology Criteria for Adverse Events v4.0. Local control (LC), time to progression (TTP), progression-free survival (PFS), and overall survival (OS) were calculated according to the method of Kaplan and Meier. The median follow-up time was 27 months, and the median tumor diameter was 3.2 cm. The 2-year LC, PFS, and OS were 90%, 48%, and 67%, respectively, with median TTP of 47.8 months. Subsequently, 23 patients underwent transplant, with a median time to transplant of 7 months. There were no ≥Grade 3 nonhematologic toxicities. Thirteen percent of patients experienced an increase in hematologic/hepatic dysfunction greater than 1 grade, and 20% experienced progression in CTP class within 3 months of treatment. The authors concluded that SBRT is a safe, effective, noninvasive option for patients with HCC ≤6 cm, and that SBRT should be considered when bridging to transplant or as definitive therapy for those ineligible for transplant.
- Ibarra evaluated tumor response to SBRT in a combined multicenter database.[94] Patients with advanced HCC (n = 21) or intrahepatic cholangiocarcinoma (ICC, n = 11) treated with SBRT from four academic medical centers were entered into a common database. Statistical analyses were performed for freedom from local progression (FFLP) and patient survival. The overall FFLP for advanced HCC was 63% at a median follow-up of 12.9 months. Median tumor volume decreased from 334.2 to 135 cm(3) ($p < 0.004$). The median time to local progression was 6.3 months. The 1- and 2-years overall survival rates were 87% and 55%, respectively. The incidence of grade 1-2 toxicities, mostly nausea and fatigue, was 39.5%. Grade 3 and 4 toxicities were present in two and one patients, respectively.
- Price reported the results of a phase 1/2 trial which evaluated the radiological response in 26 patients with HCC who were not surgical candidates and were treated with SBRT between 2005 and 2008.[95] Eligibility criteria included solitary tumors ≤ 6 cm or up to 3 lesions with sum diameters ≤ 6 cm, and well-compensated cirrhosis. All patients had imaging before, at 1 to 3 months, and every 3 to 6 months after SBRT. Patients received 3 to 5 fractions of SBRT. Median SBRT dose was 42 Gray (Gy) (range: 24-48 Gy). Median follow-up was 13 months. Per Response Evaluation Criteria in Solid Tumors (RECIST), 4 patients had a complete response

(CR), 15 had a partial response (PR), and 7 achieved stable disease (SD) at 12 months. One patient with SD experienced progression marginal to the treated area. The overall best response rate (CR + PR) was 73%. In comparison, by European Association for the Study of the Liver (EASL) criteria, 18 of 26 patients had ≥ 50% nonenhancement at 12 months. Thirteen of 18 demonstrated 100% nonenhancement, being > 50% in 5 patients. Kaplan-Meier 1- and 2-year survival estimates were 77% and 60%, respectively. SBRT is effective therapy for patients with HCC with an overall best response rate (CR + PR) of 73%.

- Louis evaluated the feasibility, tolerance and toxicity of SBRT in 25 HCC patients who were not eligible for other treatment modalities.[96] All patients had liver cirrhosis with an Eastern Cooperative Oncology Group (ECOG) performance score of less than 2 and pre-treatment Child scores ranging from A5 to B9. A total dose of 45 Gy in three fractions of 15 Gy each was prescribed to the 80% isodose line (95% of the PTV received 45 Gy) and delivered to the target volume over 10-12 days. Overall, the treatment was well tolerated with two grade 3 acute toxicities and no acute grade 4 toxicities. Late toxicity was minimal; all observed late toxicities occurred within the first six months of follow-up. There were three hepatic recurrences at a distance from the initial target were observed. The actuarial 1- and 2-year local control rate was 95% (95% CI: 69-95%). At a median overall follow-up of 12.7 months (range, 1-24 months), six of the twenty-five (24%) patients have died. Overall actuarial survival at 1- and 2-years was 79% (95% CI: 52-92%) and 52% (95% CI: 19-78%), respectively.
- Kwon evaluated the long-term effect of SBRT for primary HCC in 42 patients ineligible for local ablation therapy or surgical resection.[97] Median tumor volume was 15.4 cc (3.0-81.8) and the median follow-up duration was 28.7 months (8.4-49.1). Complete response (CR) for the in-field lesion was initially achieved in 59.6% and partial response (PR) in 26.2% of patients. Hepatic out-of-field progression occurred in 18 patients (42.9%) and distant metastasis developed in 12 (28.6%) patients. Overall 1-year and 3-year survival rates were 92.9% and 58.6%, respectively. In-field progression-free survival at 1 and 3 years was 72.0% and 67.5%, respectively. Patients with smaller tumors had better in-field progression-free survival and overall survival rates (<32 cc vs. ≥32 cc, P <0.05). No major toxicity was encountered but one patient died with extrahepatic metastasis and radiation-induced hepatic failure.
- Bujold and others described the outcomes of prospective trials of SBRT for HCC.[98] A total of 102 patients were evaluated (Trial 1, 2004 to 2007: n = 50; Trial 2, 2007 to 2010: n = 52). Median overall survival was 17.0 months (95% CI, 10.4 to 21.3 months), for which only tumor vascular thrombosis (TVT) (HR = 2.47; P = .01) and being in Trial 2 (HR = 0.49; P = .01) were significant on multivariate analysis. Authors suggested that these study results provided strong rationale for studying SBRT for HCC in a randomized trial.

In a summary, current studies of SBRT for primary HCC include heterogenous treatment schedules, treatment planning techniques and patient populations. The optimal dose and fractionation scheme have not been established. Therefore, this evidence is not sufficient to establish safety and effectiveness of SBRT for treatment of primary HCC.

SBRT for Liver Metastases

- A 2012 review by Mendez summarizes the literature on the use of SBRT for liver metastases.[99] In general, the data are limited by the small numbers of patients in the studies, retrospective analyses, and the inclusion of mixed tumor types in the local control and survival analyses. In addition, differences in the systemic therapies administered after SBRT may have affected treatment outcomes. One of the largest studies included in the review is outlined below.
- Chang studied outcomes of SBRT for colorectal liver metastases in a pooled patient cohort from

3 institutions with colorectal liver metastases.[100] Patients were included if they had 1 to 4 lesions, received 1 to 6 fractions of SBRT, and had radiologic imaging ≥ 3 months post-treatment. Sixty-five patients with 102 lesions treated from 2003 to 2009 were retrospectively analyzed. Forty-seven (72%) patients had ≥ 1 chemotherapy regimen before stereotactic body radiotherapy, and 27 (42%) patients had ≥ 2 regimens. The median follow-up was 1.2 years (range, 0.3-5.2 years). The median dose was 42 gray (Gy; range, 22-60 Gy). One and two year local control rates were 67% and 55%, respectively. One and two year OS rates were 72% and 38%, respectively.

- Scorsetti and others evaluated the feasibility of high-dose SBRT in the treatment of unresectable liver metastases.[101] Patients with 1 to 3 liver metastases, with maximum individual tumor diameters less than 6 cm and a Karnofsky Performance Status of at least 70, were enrolled and treated by SBRT on a phase 2 clinical trial. Between February 2010 and September 2011, a total of 61 patients with 76 lesions were treated. The median overall survival rate was 19 months. Authors concluded that SBRT for unresectable liver metastases can be considered an effective, safe, and noninvasive therapeutic option; however this study was limited in size, SBRT was not compared to other treatment options, and the patients included in the population were heterogenous (varying number of tumors and tumor size).

In a summary, the role of SBRT in treatment of liver metastases is not clear. The optimal dose and fractionation have not been established. In addition, there is no consensus on the maximum size or number of lesions suitable for SBRT. The evidence on SBRT for liver metastases is limited by the small numbers of patients in the studies, retrospective analyses, and the inclusion of mixed tumor types in the local control and survival analyses.

Prostate Cancer

Generally, the current areas of research interest in relation to SBRT for prostate cancer appear to be investigating the effects of different SBRT regimens (e.g., daily vs. every other day, different dosage, fractionation) on disease outcome and treatment toxicity. The literature search failed to identify scientific studies comparing SBRT with established standards of care for irradiation of prostate cancer, such as IMRT or 3D CRT. The safety and efficacy of SBRT compared with the standard of care is limited to one study.

- Yu et al. compared the toxicity of IMRT and SBRT using a retrospective study design that included a national sample of Medicare beneficiaries age ≥ 66 years. The sample population consisted of 1,335 SBRT patients matched to 2,670 IMRT patients. The authors concluded there was a greater rate of GU toxicity for patients undergoing SBRT compared with IMRT, and suggested that prospective correlation with randomized trials is needed.
- In 2010 the Agency for Healthcare Research and Quality (AHRQ) updated their assessment of radiation treatments for clinically localized prostate cancer.[102] The AHRQ report noted, "Data on comparative effectiveness between different forms of radiation treatments (BT, EBRT, SBRT) are also inconclusive whether one form of radiation therapy is superior to another form in terms of overall or disease-specific survival." Conclusions reached regarding SBRT are based upon a single study by Katz and colleagues reviewed below. Data on the use of stereotactic body radiation therapy (SBRT) for localized prostate cancer remains limited, mostly consisting of very small (n<50 patients) case series or treatment planning studies.[103-111]
- One of the largest case series published reported on 304 patients (211 with high-risk disease, 81 with intermediate-risk and 12 with low-risk disease): with clinically localized prostate cancer. For the majority of patients, the follow-up was less than 2 years. Although low rate of

biochemical failure (n=4) and acute urinary and rectal toxicities were observed (grade II, approximately 4% of study population), the authors note that additional follow-up is needed in order to determine long-term biochemical control and maintenance of low toxicity.[112]

- The 6-year outcomes from the above trial were reported. Late urinary grade II complications were seen in 4% of patients treated with 35 Gy and 9% of patients treated with 36.25 Gy.[113] Five late grade III urinary toxicities occurred in patients treated with 36.25 Gy. Late grade II rectal complications were seen in 2% and 5% of patients treated with 35 Gy and 36.25 Gy, respectively. Initially, bowel and urinary QOL scores decreased, but returned to baseline levels. There was an overall 20% decrease in the sexual QOL score. For patients that were potent prior to SBRT, 75% remained potent. Actuarial 5-year biochemical recurrence-free survival was 97% for patients with low-risk disease, 90.7% for those with intermediate risk, and 74.1% for high-risk patients.

Spinal and Vertebral Body Tumors

While a variety of extracranial applications for SRS and SBRT have been proposed,[114] the most thoroughly studied has been the treatment of spinal cord lesions. The accumulating evidence suggests that stereotactic body radiation therapy (SBRT) may lead to improved health outcomes in patients with spinal or vertebral body tumors. The preponderance of evidence comes from studies of patients who received prior irradiation. The current evidence limits conclusions concerning SBRT safety and efficacy for initial treatment of these lesions. In addition, due to the lack of comparative studies, it is not known whether symptom relief occurs more rapidly or is more durable following SBRT compared with other radiation therapies, such as 3D CRT. Finally, there is the concern, perhaps theoretical, that the limited size of the SBRT field may result in more late recurrences at adjacent levels.

- 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.[14] The majority of patients were treated for pain control. 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 are limited due to lack of target immobilization. Axial and radicular pain improved in 74 of the 79 symptomatic patients. There was no acute radiation toxicity or new neurologic deficits. The authors concluded that the treatment was feasible and safe. Conventional external beam radiation therapy typically is delivered over a course of 10-20 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 cord lesions who were treated with the Cyberknife®.[115] Patients underwent a median of three treatments. Pain was improved, as measured by declining mean VAS score, and quality of life was maintained during the one year study period.
- Gerszten et al. published results on a series of 500 cases from a single institution (334 tumors had previously undergone external beam irradiation) using the CyberKnife system.[116] 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.[117] The actuarial one-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 supported the safety and effectiveness of SBRT in cases of metastatic spinal tumors. They added that they considered 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.

Clinical Practice Guidelines

The National Comprehensive Network (NCCN) guidelines include the following recommendations and/or statements concerning stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT):

Note: Unless indicated otherwise, all NCCN recommendations are category 2A: based upon lower level of evidence, there is uniform NCCN consensus that the intervention is appropriate.

Central Nervous System[118]

- Medulloblastoma and supratentorial PNET: On disease progression, options include chemotherapy alone, radiation alone (including SRS) and chemoradiation.
- Primary spinal cord tumors: If resection is not possible, conventional EBRT or SRS is the next option.
- Meningiomas:
    - If neurologic impairment is imminent, surgery (if accessible) or radiotherapy (EBRT or SRS) is feasible.
    - Following subtotal resection, radiation should be considered for small, asymptomatic grade II tumors and for large grade I and II tumors. SRS may be used in lieu of conventional radiation as adjuvant or primary therapy in asymptomatic cases.
- Brain metastases
    - Resectable tumors: Resection plus post-operative WBRT for 1-3 lesions or SRS plus WBRT if only 1 brain lesion is involved (category 1 evidence: based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate).
    - The choice between open resection and SRS depend on multiple factors such as tumor size and location. The best outcome for SRS is achieved for small, deep lesions at institutions with experienced staff. If the tumor is unresectable, WBRT and/or SRS can be used.
- Recurrent CNS disease:
    - If previously received WBRT or SRS, should not receive WBRT again.
    - If had previous SRS with a durable response for greater than 6 months, reconsider SRS if imaging supports active tumor and not necrosis. Patients with 1-3 recurrent tumors have the additional options of surgery or SRS.
- Metastatic spinal tumors: Patients experiencing intractable pain or rapid neurological decline during radiation therapy should consider surgery or SRS. SRS can be considered for patients with good performance and low overall tumor volume.

Colon Cancer[119]

Metastatic disease: “Radiotherapy can be considered in highly selected cases in which the patient has a limited number of liver of lung metastases (category 3: based upon any level of evidence, there is a major NCCN disagreement that the intervention is appropriate) or in the setting of a clinical trial. It should be delivered in a highly conformal manner and should not be used in place of surgical resection. The possible techniques can include 3D conformal radiotherapy, IMRT, or stereotactic body radiation therapy (SBRT) (category 3).”

Hepatobiliary Cancers[120]

- “All tumors irrespective of the location may be amenable to EBRT (SBRT or 3D-conformal radiation therapy.”

- “There is growing evidence for the usefulness of SBRT in the management of patients with unresectable HCC. SRBT can be considered as an alternative to the ablation/embolization techniques mentioned above or when these therapies have failed or are contraindicated.” The panel encourages prospective clinical trials evaluating the role of SBRT in patients with unresectable HCC.

- “SRBT is often used for patients with 1-3 tumors. 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 extra-hepatic disease or it should be minimal and addressed in a comprehensive management plan. Patients with Child-Pugh A category are preferred. Those with Child-Pugh B cirrhosis can be safely treated, but they may require dose modifications and strict dose constraint adherence. Child-Pugh C cirrhosis is a relative contraindication, and these patients should be considered for a clinical trial.”

Kidney Cancer[121]

For the treatment of primary kidney cancer, NCCN guidelines do not address the use of SBRT.

Non-Small Cell Lung Cancer (NSCLC)[122]

SBRT is recommended for early stage NSCLC patients (i.e., stage I) who are medically inoperable, older, or those who refuse surgery after thoracic surgery evaluation.

Pancreatic Adenocarcinoma[123]

“No standard total dose or dose per fraction has been established for SBRT; therefore, it should preferably be utilized as a part of a clinical trial” in unresectable/locally advanced (non-metastatic) pancreatic cancer.

Prostate Cancer[124]

Though SBRT is described as “an emerging treatment technique,” NCCN states the following: “Longer follow-up and prospective multi-institutional data are required to evaluate longer term results especially since late toxicity theoretically could be worse in hypofractionated regimens compared to conventional fractionation.”

Summary

Adrenal Metastases

The level of evidence on stereotactic body radiation therapy (SBRT) for adrenal metastases is insufficient to demonstrate the impact of SBRT on patient health outcomes. Therefore, the use of SBRT for adrenal metastases is considered investigational.

Brain Metastases

Current evidence on stereotactic radiosurgery (SRS) for the treatment of brain metastasis suggests some benefit, including local control and acceptable treatment-related toxicity. However, the studies have significant methodological limitations and the characteristics of patients most likely to derive better health outcomes from SRS compared with other treatment options are not clear, particularly in patients with active systemic disease where SRS is not used with curative intent. Specifically, due to limited evidence, conclusions cannot be drawn concerning whether there is added palliative benefit from SRS that cannot be achieved with other treatment modalities. Therefore, except in select patients with good prognosis (Karnofsky score ≥70 and life expectancy >6 months), SRS is considered investigational for the treatment of brain metastases.

Choroidal neovascularization (CNV)

There is insufficient evidence to determine if stereotactic radiotherapy improves health outcomes in the treatment of choroidal neovascularization (CNV). Therefore, SBRT for CNV is considered investigational.

Chronic Pain

The studies of stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) for treatment of chronic pain are extremely limited. This evidence is not sufficient to understand safety and effectiveness of SBRT for treatment of chronic pain or to adequately describe the subpopulation of patients with chronic pain most likely to benefit from this treatment. Therefore, SRS/SBRT for chronic pain is considered investigational.

Epilepsy

The studies of stereotactic radiosurgery (SRS) for treatment of epilepsy published to date are preliminary in nature and consist of a studies with very small study populations(less than 50 participants), short follow-up times, and/or heterogeneous study populations. In addition, the available evidence from patients with epileptic lesions of various sizes and locations is unable to adequately show what factors are associated with favorable outcomes following SRS treatment. Therefore, SRS for epilepsy is considered investigational.

Hepatocellular Cancer (HCC)

Current studies of stereotactic body radiation therapy (SBRT) for hepatocellular carcinoma (HCC) include heterogenous treatment schedules, treatment planning techniques, and patient populations. The optimal dose and fractionation scheme have not been established. Therefore, SBRT for HCC is considered investigational.

Liver Metastasis

The role of stereotactic body radiation therapy (SBRT) in treatment of liver metastases is not clear. The optimal dose and fractionation have not been established. In addition, there is no consensus on the maximum size or number of lesions suitable for SBRT. The evidence on SBRT for liver metastases is limited by the small numbers of patients in the studies, retrospective analyses, and the inclusion of mixed tumor types in the local control and survival analyses. Therefore, the use of SBRT for hepatic metastases is considered investigational.

Kidney Cancer

The literature on stereotactic body radiation therapy (SBRT) for renal cell carcinoma is limited. This level of evidence is not sufficient to understand the impact of SBRT on renal carcinoma-related health outcomes. In addition, this level of evidence limits comparisons between SBRT and more established treatment modalities for renal cell carcinoma. Therefore, the use of SBRT for kidney cancer is considered investigational.

Lung Metastases

Evidence on stereotactic body radiation therapy (SBRT) treatment of lung metastases has methodological limitations; however studies consistently suggest some benefit of SBRT in the treatment of lung metastases (e.g., local control and acceptable treatment-related toxicity) in a select group of patients. Outside this subgroup, there is limited understanding of safety and efficacy of SBRT for lung metastases. Therefore, except in the select group of patients (as defined in the policy criteria), SBRT of lung metastases is considered investigational.

Pancreatic Cancer

The role of stereotactic body radiation therapy (SBRT) for pancreatic tumors has not been established. At this time, it is not known which patient populations would most likely benefit from this treatment. Although studies have shown promising local control rates, there have been no significant changes in patient survival compared with historical data and some studies have shown unacceptable toxicity and questionable palliative effect. Therefore, the use of SBRT for pancreatic cancer is considered investigational.

Parkinson's Disease and Essential Tremors

The preliminary studies of stereotactic radiosurgery (SRS) for the treatment of refractory symptoms of essential tremor and Parkinson's disease are extremely limited and report conflicting findings. In addition, there is no evidence from these studies comparing SRS with deep brain stimulation or radiofrequency ablation, which are considered the therapies of choice for those with medically refractive disease. Due to inadequate evidence, conclusions cannot be drawn about the safety and effectiveness of SRS for these indications. Therefore, SRS for treatment of Parkinson's disease and essential tremors is considered investigational.

Primary Non-Small Cell Lung Cancer (NSCLC)

Although no evidence from comparative studies is available, the non-comparative studies have consistently shown that stereotactic body radiation therapy (SBRT) for patients with stage 1 non-small cell lung cancer (NSCLC) who are not surgical candidates have survival rates comparable to patients who have undergone surgical resection. Therefore, SBRT is considered medically necessary only for the patients with stage 1 NSCLC (showing no nodal or distant disease) who are not surgical candidates. SBRT for NSCLC is considered investigational in all other cases.

Prostate Cancer

Stereotactic body radiation therapy (SBRT) has not been compared in scientific studies with established standards of care for radiation of prostate cancer, such as intensity-modulated radiation therapy (IMRT) or 3D CRT. Therefore, the safety and efficacy of SBRT compared with the standards of care is not known. Evidence on SBRT for prostate cancer consists of single-arm studies reporting acute and late toxicity and comparison studies focusing on early PSA outcomes. Although studies have reported promising initial results including low toxicity rates, longer term follow-up is necessary in order to determine long-term toxicity, cancer control, and survival. Therefore, the use of SBRT for prostate cancer is considered investigational.

Spinal and Vertebral Body Tumors (Primary or Metastatic)

The accumulating evidence suggests that stereotactic body radiation therapy (SBRT) leads to improved health outcomes in patients with spinal or vertebral body tumors; however, the preponderance of the evidence comes from studies of patients who received prior irradiation. The current evidence limits conclusions concerning SBRT safety and efficacy for initial treatment of these lesions. In addition, due to the lack of comparative studies, it is not known whether symptom relief occurs more rapidly or is more durable following SBRT compared with other radiation therapies, such as 3D CRT. Finally, there is the concern, perhaps theoretical, that the limited size of the SBRT field may result in more late recurrences at adjacent spinal levels. Therefore, except in patients who have received prior radiation therapy, SBRT is considered investigational for treatment of spinal or vertebral body tumors.

Trigeminal Neuralgia

Evidence that shows effectiveness of stereotactic radiosurgery (SRS) for treatment of trigeminal neuralgia comes from the studies of patients with the disease refractory to (i.e., not adequately treated with) medical management. This evidence does not allow conclusions concerning safety and efficacy of SRS as a primary treatment for trigeminal neuralgia. Therefore, except in the patients with trigeminal neuralgia refractory to medical management, SRS is considered investigational.

Uveal Melanoma

The literature on the use of stereotactic radiosurgery (SRS) for uveal melanoma is limited; no studies directly comparing SRS with other, accepted radiation modalities used to treat uveal melanoma (brachytherapy, proton beam) are identified. The published literature is insufficient to demonstrate improved outcomes with the use of SRS over other accepted radiation modalities in the treatment of uveal melanoma.

REFERENCES

1. Kondziolka, D, Patel, A, Lunsford, LD, Kassam, A, Flickinger, JC. Stereotactic radiosurgery plus whole brain radiotherapy versus radiotherapy alone for patients with multiple brain metastases. *Int J Radiat Oncol Biol Phys*. 1999 Sep 1;45(2):427-34. PMID: 10487566
2. Weltman, E, Salvajoli, JV, Brandt, RA, et al. Radiosurgery for brain metastases: a score index for predicting prognosis. *Int J Radiat Oncol Biol Phys*. 2000 Mar 15;46(5):1155-61. PMID: 10725626
3. Chau, I, Webb, A, Cunningham, D, et al. An oxaliplatin-based chemotherapy in patients with relapsed or refractory intermediate and high-grade non-Hodgkin's lymphoma. *Br J Haematol*. 2001 Dec;115(4):786-92. PMID: 11843810
4. 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*. 2006 Jun 7;295(21):2483-91. PMID: 16757720
5. Muller-Beissenhirtz, H, Kasper, C, Nuckel, H, Duhrsen, U. Gemcitabine, vinorelbine and prednisone for refractory or relapsed aggressive lymphoma, results of a phase II single center study. *Ann Hematol*. 2005 Nov;84(12):796-801. PMID: 16041531
6. Sallah, S, Wan, JY, Nguyen, NP. Treatment of refractory T-cell malignancies using gemcitabine. *Br J Haematol*. 2001 Apr;113(1):185-7. PMID: 11328299
7. Dang, NH, Pro, B, Hagemeister, FB, et al. Phase II trial of denileukin diftitox for relapsed/refractory T-cell non-Hodgkin lymphoma. *Br J Haematol*. 2007 Feb;136(3):439-47. PMID: 17233846
8. Mey, UJ, Orlopp, KS, Flieger, D, et al. Dexamethasone, high-dose cytarabine, and cisplatin in combination with rituximab as salvage treatment for patients with relapsed or refractory aggressive non-Hodgkin's lymphoma. *Cancer Invest*. 2006 Oct;24(6):593-600. PMID: 16982464
9. Crump, M, Baetz, T, Couban, S, et al. Gemcitabine, dexamethasone, and cisplatin in patients with recurrent or refractory aggressive histology B-cell non-Hodgkin lymphoma: a Phase II study by the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG). *Cancer*. 2004 Oct 15;101(8):1835-42. PMID: 15386331
10. Lopez, A, Gutierrez, A, Palacios, A, et al. GEMOX-R regimen is a highly effective salvage regimen in patients with refractory/relapsing diffuse large-cell lymphoma: a phase II study. *Eur J Haematol*. 2008 Feb;80(2):127-32. PMID: 18005385
11. Niitsu, N, Kohori, M, Higashihara, M, Bessho, M. Phase II study of the irinotecan (CPT-11), mitoxantrone and dexamethasone regimen in elderly patients with relapsed or refractory peripheral T-cell lymphoma. *Cancer Sci*. 2007 Jan;98(1):109-12. PMID: 17052256
12. Scagliotti, GV, Park, K, Patil, S, et al. Survival without toxicity for cisplatin plus pemetrexed versus cisplatin plus gemcitabine in chemonaive patients with advanced non-small cell lung cancer: a risk-benefit analysis of a large phase III study. *Eur J Cancer*. 2009 Sep;45(13):2298-303. PMID: 19473833
13. Zinzani, PL, Magagnoli, M, Bendandi, M, et al. Therapy with gemcitabine in pretreated peripheral T-cell lymphoma patients. *Ann Oncol*. 1998 Dec;9(12):1351-3. PMID: 9932168
14. Aoyama, H, Tago, M, Kato, N, et al. Neurocognitive function of patients with brain metastasis who received either whole brain radiotherapy plus stereotactic radiosurgery or radiosurgery alone. *Int J Radiat Oncol Biol Phys*. 2007 Aug 1;68(5):1388-95. PMID: 17674975
15. Velasquez, WS, McLaughlin, P, Tucker, S, et al. ESHAP--an effective chemotherapy regimen in refractory and relapsing lymphoma: a 4-year follow-up study. *J Clin Oncol*. 1994 Jun;12(6):1169-76. PMID: 8201379
16. Zelenetz, AD, Hamlin, P, Kewalramani, T, Yahalom, J, Nimer, S, Moskowitz, CH. Ifosfamide, carboplatin, etoposide (ICE)-based second-line chemotherapy for the management of relapsed

and refractory aggressive non-Hodgkin's lymphoma. *Ann Oncol*. 2003;14 Suppl 1:i5-10. PMID: 12736224
17. Bogart, JA, Govindan, R. A randomized phase II study of radiation therapy, pemetrexed, and carboplatin with or without cetuximab in stage III non-small-cell lung cancer. *Clin Lung Cancer*. 2006 Jan;7(4):285-7. PMID: 16512986
18. Patel, JD, Bonomi, P, Socinski, MA, et al. Treatment rationale and study design for the pointbreak study: a randomized, open-label phase III study of pemetrexed/carboplatin/bevacizumab followed by maintenance pemetrexed/bevacizumab versus paclitaxel/carboplatin/bevacizumab followed by maintenance bevacizumab in patients with stage IIIB or IV nonsquamous non-small-cell lung cancer. *Clin Lung Cancer*. 2009 Jul;10(4):252-6. PMID: 19632943
19. Jalal, S, Waterhouse, D, Edelman, MJ, et al. Pemetrexed plus cetuximab in patients with recurrent non-small cell lung cancer (NSCLC): a phase I/II study from the Hoosier Oncology Group. *J Thorac Oncol*. 2009 Nov;4(11):1420-4. PMID: 19701110
20. Kim, SJ, Kim, K, Kim, BS, et al. Alemtuzumab and DHAP (A-DHAP) is effective for relapsed peripheral T-cell lymphoma, unspecified: interim results of a phase II prospective study. *Ann Oncol*. 2009 Feb;20(2):390-2. PMID: 19211502
21. Patil, CG, Pricola, K, Sarmiento, JM, Garg, SK, Bryant, A, Black, KL. Whole brain radiation therapy (WBRT) alone versus WBRT and radiosurgery for the treatment of brain metastases. *Cochrane Database Syst Rev*. 2012;9:CD006121. PMID: 22972090
22. Crawley, C, Szydlo, R, Lalancette, M, et al. Outcomes of reduced-intensity transplantation for chronic myeloid leukemia: an analysis of prognostic factors from the Chronic Leukemia Working Party of the EBMT. *Blood*. 2005 Nov 1;106(9):2969-76. PMID: 15998838
23. TEC Assessment 1998. "Special Report: SRS for Intracranial Lesions by Gamma Beam, Linear Accelerator, and Proton Beam Methods." BlueCross BlueShield Association Technology Evaluation Center, Vol. 13, Tab 28.
24. Regis, J, Bartolomei, F, Rey, M, Hayashi, M, Chauvel, P, Peragut, JC. Gamma knife surgery for mesial temporal lobe epilepsy. *J Neurosurg*. 2000 Dec;93 Suppl 3:141-6. PMID: 11143232
25. Schrottner, O, Eder, HG, Unger, F, Feichtinger, K, Pendl, G. Radiosurgery in lesional epilepsy: brain tumors. *Stereotact Funct Neurosurg*. 1998 Oct;70 Suppl 1:50-6. PMID: 9782235
26. Whang, CJ, Kwon, Y. Long-term follow-up of stereotactic Gamma Knife radiosurgery in epilepsy. *Stereotact Funct Neurosurg*. 1996;66 Suppl 1:349-56. PMID: 9032879
27. Gardner, SL, Carreras, J, Boudreau, C, et al. Myeloablative therapy with autologous stem cell rescue for patients with Ewing sarcoma. *Bone Marrow Transplant*. 2008 May;41(10):867-72. PMID: 18246113
28. Fernandez, HF, Kharfan-Dabaja, MA. Tyrosine kinase inhibitors and allogeneic hematopoietic cell transplantation for chronic myeloid leukemia: targeting both therapeutic modalities. *Cancer Control*. 2009 Apr;16(2):153-7. PMID: 19337201
29. Klingebiel, T, Boos, J, Beske, F, et al. Treatment of children with metastatic soft tissue sarcoma with oral maintenance compared to high dose chemotherapy: report of the HD CWS-96 trial. *Pediatr Blood Cancer*. 2008 Apr;50(4):739-45. PMID: 18286501
30. Vellodi, A, Young, E, New, M, Pot-Mees, C, Hugh-Jones, K. Bone marrow transplantation for Sanfilippo disease type B. *J Inherit Metab Dis*. 1992;15(6):911-8. PMID: 1293388
31. Druker, BJ, Guilhot, F, O'Brien, SG, et al. Five-year follow-up of patients receiving imatinib for chronic myeloid leukemia. *N Engl J Med*. 2006 Dec 7;355(23):2408-17. PMID: 17151364
32. Matthay, KK, Reynolds, CP, Seeger, RC, et al. Long-term results for children with high-risk neuroblastoma treated on a randomized trial of myeloablative therapy followed by 13-cis-retinoic acid: a children's oncology group study. *J Clin Oncol*. 2009 Mar 1;27(7):1007-13. PMID: 19171716

33. Fagioli, F, Biasin, E, Mereuta, OM, et al. Poor prognosis osteosarcoma: new therapeutic approach. *Bone Marrow Transplant*. 2008 Jun;41 Suppl 2:S131-4. PMID: 18545234
34. Chakrabarti, S, Buyck, HC. Reduced-intensity transplantation in the treatment of haematological malignancies: current status and future-prospects. *Curr Stem Cell Res Ther*. 2007 May;2(2):163-88. PMID: 18220901
35. Apperley, JF. Managing the patient with chronic myeloid leukemia through and after allogeneic stem cell transplantation. *Hematology Am Soc Hematol Educ Program*. 2006:226-32. PMID: 17124065
36. Hensley-Judge, H, Quigg, M, Barbaro, NM, et al. Visual field defects after radiosurgery for mesial temporal lobe epilepsy. *Epilepsia*. 2013 May 10. PMID: 23663063
37. Ohye, C, Shibazaki, T, Zhang, J, Andou, Y. Thalamic lesions produced by gamma thalamotomy for movement disorders. *J Neurosurg*. 2002 Dec;97(5 Suppl):600-6. PMID: 12507104
38. Kondziolka, D, Ong, JG, Lee, JY, Moore, RY, Flickinger, JC, Lunsford, LD. Gamma Knife thalamotomy for essential tremor. *J Neurosurg*. 2008 Jan;108(1):111-7. PMID: 18173319
39. Lim, SY, Hodaie, M, Fallis, M, Poon, YY, Mazzella, F, Moro, E. Gamma knife thalamotomy for disabling tremor: a blinded evaluation. *Arch Neurol*. 2010 May;67(5):584-8. PMID: 20457958
40. Ohye, C, Higuchi, Y, Shibazaki, T, et al. Gamma knife thalamotomy for Parkinson disease and essential tremor: a prospective multicenter study. *Neurosurgery*. 2012 Mar;70(3):526-35; discussion 35-6. PMID: 21904267
41. Kooshkabadi, A, Lunsford, LD, Tonetti, D, Flickinger, JC, Kondziolka, D. Gamma Knife thalamotomy for tremor in the magnetic resonance imaging era. *J Neurosurg*. 2013 Apr;118(4):713-8. PMID: 23373801
42. Young, RF, Li, F, Vermeulen, S, Meier, R. Gamma Knife thalamotomy for treatment of essential tremor: long-term results. *J Neurosurg*. 2010 Jun;112(6):1311-7. PMID: 19895197
43. Zehetmayer, M. Stereotactic photon beam irradiation of uveal melanoma. *Developments in ophthalmology*. 2012;49:58-65. PMID: 22042013
44. 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*. 2011 Sep 1;81(1):199-205. PMID: 20675066
45. Sarici, AM, Pazarli, H. Gamma-knife-based stereotactic radiosurgery for medium- and large-sized posterior uveal melanoma. *Graefes Arch Clin Exp Ophthalmol*. 2013 Jan;251(1):285-94. PMID: 22944897
46. Muller, K, Naus, N, Nowak, PJ, et al. Fractionated stereotactic radiotherapy for uveal melanoma, late clinical results. *Radiother Oncol*. 2012 Feb;102(2):219-24. PMID: 21864922
47. Furdova, A, Slezak, P, Chorvath, M, Waczulikova, I, Sramka, M, Kralik, G. No differences in outcome between radical surgical treatment (enucleation) and stereotactic radiosurgery in patients with posterior uveal melanoma. *Neoplasma*. 2010;57(4):377-81. PMID: 20429631
48. 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*. 2012 May;51(5):618-23. PMID: 22263925
49. Holy, R, Piroth, M, Pinkawa, M, Eble, MJ. Stereotactic body radiation therapy (SBRT) for treatment of adrenal gland metastases from non-small cell lung cancer. *Strahlenther Onkol*. 2011 Apr;187(4):245-51. PMID: 21424513
50. Casamassima, F, Livi, L, Masciullo, S, et al. Stereotactic radiotherapy for adrenal gland metastases: university of Florence experience. *Int J Radiat Oncol Biol Phys*. 2012 Feb 1;82(2):919-23. PMID: 21300473
51. Chawla, S, Chen, Y, Katz, AW, et al. Stereotactic body radiotherapy for treatment of adrenal metastases. *Int J Radiat Oncol Biol Phys*. 2009 Sep 1;75(1):71-5. PMID: 19250766

52. Jackson, TL, Chakravarthy, U, Kaiser, PK, et al. Stereotactic radiotherapy for neovascular age-related macular degeneration: 52-week safety and efficacy results of the INTREPID study. *Ophthalmology*. 2013 Sep;120(9):1893-900. PMID: 23490327
53. Siva, S, Pham, D, Gill, S, Corcoran, NM, Foroudi, F. A systematic review of stereotactic radiotherapy ablation for primary renal cell carcinoma. *BJU Int*. 2012 Dec;110(11 Pt B):E737-43. PMID: 23107102
54. Beitler, JJ, Makara, D, Silverman, P, Lederman, G. Definitive, high-dose-per-fraction, conformal, stereotactic external radiation for renal cell carcinoma. *Am J Clin Oncol*. 2004 Dec;27(6):646-8. PMID: 15577450
55. Salazar, OM, Sandhu, TS, Lattin, PB, et al. Once-weekly, high-dose stereotactic body radiotherapy for lung cancer: 6-year analysis of 60 early-stage, 42 locally advanced, and 7 metastatic lung cancers. *Int J Radiat Oncol Biol Phys*. 2008 Nov 1;72(3):707-15. PMID: 18455322
56. Norihisa, Y, Nagata, Y, Takayama, K, et al. Stereotactic body radiotherapy for oligometastatic lung tumors. *Int J Radiat Oncol Biol Phys*. 2008 Oct 1;72(2):398-403. PMID: 18374506
57. Brown, WT, Wu, X, Fowler, JF, et al. Lung metastases treated by CyberKnife image-guided robotic stereotactic radiosurgery at 41 months. *South Med J*. 2008 Apr;101(4):376-82. PMID: 18360342
58. Hof, H, Hoess, A, Oetzel, D, Debus, J, Herfarth, K. Stereotactic single-dose radiotherapy of lung metastases. *Strahlenther Onkol*. 2007 Dec;183(12):673-8. PMID: 18040611
59. Le, QT, Loo, BW, Ho, A, et al. Results of a phase I dose-escalation study using single-fraction stereotactic radiotherapy for lung tumors. *J Thorac Oncol*. 2006 Oct;1(8):802-9. PMID: 17409963
60. Nakagawa, K, Aoki, Y, Tago, M, Terahara, A, Ohtomo, K. Megavoltage CT-assisted stereotactic radiosurgery for thoracic tumors: original research in the treatment of thoracic neoplasms. *Int J Radiat Oncol Biol Phys*. 2000 Sep 1;48(2):449-57. PMID: 10974461
61. Uematsu, M, Shioda, A, Tahara, K, et al. Focal, high dose, and fractionated modified stereotactic radiation therapy for lung carcinoma patients: a preliminary experience. *Cancer*. 1998 Mar 15;82(6):1062-70. PMID: 9506350
62. Onimaru, R, Shirato, H, Shimizu, S, et al. Tolerance of organs at risk in small-volume, hypofractionated, image-guided radiotherapy for primary and metastatic lung cancers. *Int J Radiat Oncol Biol Phys*. 2003 May 1;56(1):126-35. PMID: 12694831
63. Guckenberger, M, Heilman, K, Wulf, J, Mueller, G, Beckmann, G, Flentje, M. Pulmonary injury and tumor response after stereotactic body radiotherapy (SBRT): results of a serial follow-up CT study. *Radiother Oncol*. 2007 Dec;85(3):435-42. PMID: 18053602
64. Wulf, J, Haedinger, U, Oppitz, U, Thiele, W, Mueller, G, Flentje, M. Stereotactic radiotherapy for primary lung cancer and pulmonary metastases: a noninvasive treatment approach in medically inoperable patients. *Int J Radiat Oncol Biol Phys*. 2004 Sep 1;60(1):186-96. PMID: 15337555
65. Milano, MT, Katz, AW, Schell, MC, Philip, A, Okunieff, P. Descriptive analysis of oligometastatic lesions treated with curative-intent stereotactic body radiotherapy. *Int J Radiat Oncol Biol Phys*. 2008 Dec 1;72(5):1516-22. PMID: 18495378
66. Milano, MT, Katz, AW, Muhs, AG, et al. A prospective pilot study of curative-intent stereotactic body radiation therapy in patients with 5 or fewer oligometastatic lesions. *Cancer*. 2008 Feb 1;112(3):650-8. PMID: 18072260
67. Rusthoven, KE, Kavanagh, BD, Burri, SH, et al. Multi-institutional phase I/II trial of stereotactic body radiation therapy for lung metastases. *J Clin Oncol*. 2009 Apr 1;27(10):1579-84. PMID: 19255320

68. Kim, MS, Yoo, SY, Cho, CK, et al. Stereotactic body radiation therapy using three fractions for isolated lung recurrence from colorectal cancer. *Oncology*. 2009;76(3):212-9. PMID: 19218825
69. Guckenberger, M, Wulf, J, Mueller, G, et al. Dose-response relationship for image-guided stereotactic body radiotherapy of pulmonary tumors: relevance of 4D dose calculation. *Int J Radiat Oncol Biol Phys*. 2009 May 1;74(1):47-54. PMID: 18977095
70. Coon, D, Gokhale, AS, Burton, SA, Heron, DE, Ozhasoglu, C, Christie, N. Fractionated stereotactic body radiation therapy in the treatment of primary, recurrent, and metastatic lung tumors: the role of positron emission tomography/computed tomography-based treatment planning. *Clin Lung Cancer*. 2008 Jul;9(4):217-21. PMID: 18650169
71. Nagata, Y, Negoro, Y, Aoki, T, et al. Clinical outcomes of 3D conformal hypofractionated single high-dose radiotherapy for one or two lung tumors using a stereotactic body frame. *Int J Radiat Oncol Biol Phys*. 2002 Mar 15;52(4):1041-6. PMID: 11958900
72. Wulf, J, Hadinger, U, Oppitz, U, Thiele, W, Ness-Dourdoumas, R, Flentje, M. Stereotactic radiotherapy of targets in the lung and liver. *Strahlenther Onkol*. 2001 Dec;177(12):645-55. PMID: 11789403
73. Hara, R, Itami, J, Kondo, T, et al. Stereotactic single high dose irradiation of lung tumors under respiratory gating. *Radiother Oncol*. 2002 May;63(2):159-63. PMID: 12063005
74. Blomgren, H, Lax, I, Naslund, I, Svanstrom, R. Stereotactic high dose fraction radiation therapy of extracranial tumors using an accelerator. Clinical experience of the first thirty-one patients. *Acta Oncol*. 1995;34(6):861-70. PMID: 7576756
75. Song, DY, Benedict, SH, Cardinale, RM, Chung, TD, Chang, MG, Schmidt-Ullrich, RK. Stereotactic body radiation therapy of lung tumors: preliminary experience using normal tissue complication probability-based dose limits. *Am J Clin Oncol*. 2005 Dec;28(6):591-6. PMID: 16317270
76. Yoon, SM, Choi, EK, Lee, SW, et al. Clinical results of stereotactic body frame based fractionated radiation therapy for primary or metastatic thoracic tumors. *Acta Oncol*. 2006;45(8):1108-14. PMID: 17118847
77. Aoki, M, Abe, Y, Kondo, H, et al. Clinical outcome of stereotactic body radiotherapy of 54 Gy in nine fractions for patients with localized lung tumor using a custom-made immobilization system. *Radiat Med*. 2007 Jul;25(6):289-94. PMID: 17634882
78. Fumagalli, I, Bibault, JE, Dewas, S, et al. A single-institution study of stereotactic body radiotherapy for patients with unresectable visceral pulmonary or hepatic oligometastases. *Radiat Oncol*. 2012;7:164. PMID: 23014094
79. Marcenaro, M, Vagge, S, Belgioia, L, et al. Ablative or palliative stereotactic body radiotherapy with helical tomotherapy for primary or metastatic lung tumor. *Anticancer Res*. 2013 Feb;33(2):655-60. PMID: 23393363
80. Timmerman, RD, Park, C, Kavanagh, BD. The North American experience with stereotactic body radiation therapy in non-small cell lung cancer. *J Thorac Oncol*. 2007 Jul;2(7 Suppl 3):S101-12. PMID: 17603304
81. Hof, H, Muenter, M, Oetzel, D, Hoess, A, Debus, J, Herfarth, K. Stereotactic single-dose radiotherapy (radiosurgery) of early stage nonsmall-cell lung cancer (NSCLC). *Cancer*. 2007 Jul 1;110(1):148-55. PMID: 17516437
82. 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*. 2013 Apr 19. PMID: 23605504
83. Nguyen, NP, Garland, L, Welsh, J, Hamilton, R, Cohen, D, Vinh-Hung, V. Can stereotactic fractionated radiation therapy become the standard of care for early stage non-small cell lung carcinoma. *Cancer Treat Rev*. 2008 Dec;34(8):719-27. PMID: 18657910

84. 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*. 2007 Dec;85(3):429-34. PMID: 18022720
85. Kupelian, PA, Komaki, R, Allen, P. Prognostic factors in the treatment of node-negative nonsmall cell lung carcinoma with radiotherapy alone. *Int J Radiat Oncol Biol Phys*. 1996 Oct 1;36(3):607-13. PMID: 8948345
86. Howington, JA, Blum, MG, Chang, AC, Balekian, AA, Murthy, SC. Treatment of stage I and II non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013 May;143(5 Suppl):e278S-313S. PMID: 23649443
87. Goyal, K, Einstein, D, Ibarra, RA, et al. Stereotactic body radiation therapy for nonresectable tumors of the pancreas. *J Surg Res*. 2012 May 15;174(2):319-25. PMID: 21937061
88. Rwigema, JC, Parikh, SD, Heron, DE, et al. Stereotactic body radiotherapy in the treatment of advanced adenocarcinoma of the pancreas. *Am J Clin Oncol*. 2011 Feb;34(1):63-9. PMID: 20308870
89. Chang, DT, Schellenberg, D, Shen, J, et al. Stereotactic radiotherapy for unresectable adenocarcinoma of the pancreas. *Cancer*. 2009 Feb 1;115(3):665-72. PMID: 19117351
90. Tao, C, Yang, LX. Improved radiotherapy for primary and secondary liver cancer: stereotactic body radiation therapy. *Anticancer Res*. 2012 Feb;32(2):649-55. PMID: 22287758
91. Cardenes, HR, Price, TR, Perkins, SM, et al. Phase I feasibility trial of stereotactic body radiation therapy for primary hepatocellular carcinoma. *Clin Transl Oncol*. 2010 Mar;12(3):218-25. PMID: 20231127
92. Shin, YJ, Kim, MS, Yoo, SY, et al. Pilot study of stereotactic body radiotherapy for huge hepatocellular carcinoma unsuitable for other therapies. *Tumori*. 2010 Jan-Feb;96(1):65-70. PMID: 20437860
93. Andolino, DL, Johnson, CS, Maluccio, M, et al. Stereotactic body radiotherapy for primary hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys*. 2011 Nov 15;81(4):e447-53. PMID: 21645977
94. Ibarra, RA, Rojas, D, Snyder, L, et al. Multicenter results of stereotactic body radiotherapy (SBRT) for non-resectable primary liver tumors. *Acta Oncol*. 2012 May;51(5):575-83. PMID: 22263926
95. Price, TR, Perkins, SM, Sandrasegaran, K, et al. Evaluation of response after stereotactic body radiotherapy for hepatocellular carcinoma. *Cancer*. 2012 Jun 15;118(12):3191-8. PMID: 22025126
96. Louis, C, Dewas, S, Mirabel, X, et al. Stereotactic radiotherapy of hepatocellular carcinoma: preliminary results. *Technology in cancer research & treatment*. 2010 Oct;9(5):479-87. PMID: 20815419
97. Kwon, JH, Bae, SH, Kim, JY, et al. Long-term effect of stereotactic body radiation therapy for primary hepatocellular carcinoma ineligible for local ablation therapy or surgical resection. Stereotactic radiotherapy for liver cancer. *BMC Cancer*. 2010;10:475. PMID: 20813065
98. 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*. 2013 May 1;31(13):1631-9. PMID: 23547075
99. Mendez Romero, A, Hoyer, M. Radiation therapy for liver metastases. *Current opinion in supportive and palliative care*. 2012 Mar;6(1):97-102. PMID: 22189625
100. Chang, DT, Swaminath, A, Kozak, M, et al. Stereotactic body radiotherapy for colorectal liver metastases: A pooled analysis. *Cancer*. 2011 Sep 1;117(17):4060-9. PMID: 21432842
101. Scorsetti, M, Arcangeli, S, Tozzi, A, et al. Is stereotactic body radiation therapy an attractive option for unresectable liver metastases? A preliminary report from a phase 2 trial. *Int J Radiat Oncol Biol Phys*. 2013 Jun 1;86(2):336-42. PMID: 23433800

102. Agency for Healthcare Research and Quality (AHRQ). Technology Assessment. Comparative evaluation of radiation treatments for clinically localized prostate cancer: an update. August 13, 2010. Project ID: CANT1209. [cited 06/17/2014]; Available from: http://www.cms.gov/Medicare/Coverage/CoverageGenInfo/downloads/id69ta.pdf
103. Madsen, BL, Hsi, RA, Pham, HT, Fowler, JF, Esagui, L, Corman, J. Stereotactic hypofractionated accurate radiotherapy of the prostate (SHARP), 33.5 Gy in five fractions for localized disease: first clinical trial results. *Int J Radiat Oncol Biol Phys*. 2007 Mar 15;67(4):1099-105. PMID: 17336216
104. Fuller, DB, Naitoh, J, Lee, C, Hardy, S, Jin, H. Virtual HDR CyberKnife treatment for localized prostatic carcinoma: dosimetry comparison with HDR brachytherapy and preliminary clinical observations. *Int J Radiat Oncol Biol Phys*. 2008 Apr 1;70(5):1588-97. PMID: 18374232
105. 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*. 2012 Aug 1;118(15):3681-90. PMID: 22170628
106. 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*. 2011 May 20;29(15):2020-6. PMID: 21464418
107. Freeman, DE, King, CR. Stereotactic body radiotherapy for low-risk prostate cancer: five-year outcomes. *Radiat Oncol*. 2011;6:3. PMID: 21219625
108. 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*. 2012 Jan 1;82(1):228-34. PMID: 21183287
109. King, CR, Brooks, JD, Gill, H, Presti, JC, Jr. Long-term outcomes from a prospective trial of stereotactic body radiotherapy for low-risk prostate cancer. *Int J Radiat Oncol Biol Phys*. 2012 Feb 1;82(2):877-82. PMID: 21300474
110. 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*. 2010 Oct 1;78(2):442-8. PMID: 20137864
111. Spratt, DE, Scala, LM, Folkert, M, et al. A comparative dosimetric analysis of virtual stereotactic body radiotherapy to high-dose-rate monotherapy for intermediate-risk prostate cancer. *Brachytherapy*. 2013 Apr 23. PMID: 23622710
112. Dallorso, S, Dini, G, Faraci, M, Spreafico, F. SCT for Wilms' tumour. *Bone Marrow Transplant*. 2008 Jun;41 Suppl 2:S128-30. PMID: 18545233
113. Katz, AJ, Santoro, M, Diblasio, F, Ashley, R. Stereotactic body radiotherapy for localized prostate cancer: disease control and quality of life at 6 years. *Radiat Oncol*. 2013 May 13;8(1):118. PMID: 23668632
114. Chang, SD, Adler, JR. Robotics and radiosurgery--the cyberknife. *Stereotact Funct Neurosurg*. 2001;76(3-4):204-8. PMID: 12378098
115. 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*. 2005 May;2(5):540-9. PMID: 15945428
116. Gerszten, PC, Burton, SA, Ozhasoglu, C, Welch, WC. Radiosurgery for spinal metastases: clinical experience in 500 cases from a single institution. *Spine (Phila Pa 1976)*. 2007 Jan 15;32(2):193-9. PMID: 17224814
117. 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*. 2007 Aug;7(2):151-60. PMID: 17688054

118. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Central Nervous System Cancers. v.1.2014. [cited 06/20/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/cns.pdf
119. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Colon Cancer. v.3.2014. [cited 08/04/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf
120. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Hepatobiliary Cancers. v.2.2014. [cited 08/04/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf
121. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Kidney Cancer v.3.2014. [cited 08/04/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf
122. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Non-Small Cell Lung Cancer. v.4.2014. [cited 06/20/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
123. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology™. Pancreatic Adenocarcinoma. v.2.2014. [cited 08/04/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf
124. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™: Prostate Cancer v.2.2014. [cited 06/17/2014]; Available from: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf

CROSS REFERENCES

Charged Particle (Proton or Helium Ion) Radiation Therapy, Medicine, Policy No. 49

Intraocular Radiation Therapy for Age-Related Macular Degeneration, Medicine, Policy No. 134

Electromagnetic Navigation Bronchoscopy, Surgery, Policy No. 179

CODES	NUMBER	DESCRIPTION
Coding for stereotactic radiosurgery typically consists of a series of CPT codes describing the individual steps required; medical radiation physics, clinical treatment planning, attachment of stereotactic head frame, treatment delivery and clinical treatment management.		
Treatment delivery:		
The codes used for treatment delivery will depend on the energy source used, typically either photons or protons. For photons (i.e. with a Gamma knife or LINAC device (including Cyberknife®) nonspecific radiation therapy treatment delivery CPT codes may be used based on the voltage of the energy source (i.e. codes 77402-77416). When proton beam therapy is used CPT codes 77520 thru 77525 are available.		
CPT	32701	Thoracic target(s) delineation for stereotactic body radiation therapy (SRS/SBRT), (photon or particle beam), entire course of treatment

CODES	NUMBER	DESCRIPTION
	77371	Radiation therapy delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; multi-source Cobalt 60 based
	77372	Radiation therapy delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; linear accelerator based
	77373	Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance, entire course not to exceed 5 fraction
	77402	Radiation treatment delivery, single treatment area, single port or parallel opposed ports, simple blocks or no blocks; up to 5 MeV
	77403	6-10 MeV
	77404	11-19 MeV
	77406	20 MeV or greater
	77407	Radiation treatment delivery, two separate treatment areas, three or more ports on a single treatment area, use of multiple blocks; up to 5 MeV
	77408	6-10 MeV
	77409	11-19 MeV
	77411	20 MeV or greater
	77412	Radiation treatment delivery, three or more separate treatment areas, custom blocking, tangential ports, wedges, rotational beam, compensators, special particle electron beam (e.g., electron or neutrons); up to 5 MeV
	77413	6-10 MeV
	77414	11-19 MeV
	77416	20 MeV or greater
	77435	Stereotactic body radiation therapy, treatment management, per treatment course, to 1 or more lesions, including image guidance, entire course not to exceed 5 fractions
HCPCS	G0251	Linear accelerator based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, maximum five sessions per course of treatment

CODES	NUMBER	DESCRIPTION
Note: Codes for treatment delivery primarily reflects the cost related to the energy source used, and not physician work.		
Clinical treatment management:		
CPT	77432	Stereotactic radiation treatment management of cerebral lesion(s) (complete course of treatment consisting of one session.)
	61796	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 simple cranial lesion
	61797	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional cranial lesion, simple (List separately in addition to code for primary procedure)
	61798	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 complex cranial lesion
	61799	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional cranial lesion, complex (List separately in addition to code for primary procedure)
	61800	Application of stereotactic headframe for stereotactic radiosurgery (List separately in addition to code for primary procedure)
	63620	Stereotactic radiosurgery (partical beam, gamma ray, or linear accelerator); 1 spinal lesion
	63621	Stereotactic radiosurgery (partical beam, gamma ray, or linear accelerator); each additional spinal lesion (List separately in addition to code for primary procedure)
HCPCS	G0173	Linear accelerator based stereotactic radiosurgery, complete course of therapy in one session
	G0339	Image guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session, or first session of fractionated treatment.
	G0340	Image guided robotic linear accelerator-based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, second through fifth sessions, maximum five sessions per course of treatment