



CIGNA MEDICAL COVERAGE POLICY

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Subject Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiation Therapy (SBRT)

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- Proton Beam Therapy for Intracranial and Skull Base Tumors
- Proton Beam Therapy for Lung Cancer
- Proton Beam Therapy for Ocular Melanoma, Ocular Hemangiomas and Macular Degeneration
- Proton Beam Therapy for Prostate Cancer

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Coverage Policy

CIGNA covers stereotactic radiosurgery including fractionated stereotactic radiotherapy and/or stereotactic body radiation therapy (e.g., Gamma Knife[®], CyberKnife[®], X-Knife[®], Peacock[®], Trilogy[™], TomoTherapy[®], Hi-Art[®], ONCOR[™], RapidArc[®]) as medically necessary for ANY of the following indications:

- arteriovenous malformation of the brain or spine
- primary brain tumor (e.g., glioma, meningioma, pituitary tumor, hemangioblastoma, acoustic neuroma [i.e. vestibular schwannoma], hypothalamic hamartoma)
- metastatic tumor to the brain
- symptomatic primary or metastatic spinal tumor (e.g., neurological impairment, pain)
- trigeminal neuralgia refractory to medical management
- nasopharyngeal cancer
- Parkinsonian or essential tremor that is refractory to medical management
- uveal melanoma (melanoma of the uveal tract [iris, ciliary body, and choroid])

- any of the following neoplasms if unresectable or the individual is a poor surgical candidate or declines surgery:
 - liver malignancy
 - non small-cell lung cancer (NSCLC) or pulmonary metastasis
 - renal cell carcinoma (RCC) tumor
- extracranial malignancy which is either in or adjacent to a previously irradiated volume, or located near a critical structure, where the risk of toxicity precludes use of another local modality

CIGNA does not cover stereotactic radiosurgery including fractionated stereotactic radiotherapy and/or stereotactic body radiation therapy for any other indication, including but not limited to the following, because it is considered experimental, investigational or unproven (this list may not be all-inclusive):

- behavioral health disorders (e.g., obsessive-compulsive disorder)
- breast cancer
- epilepsy
- pancreatic cancer
- prostate cancer

General Background

Stereotactic radiosurgery (SRS), a type of external beam radiation, targets a tumor from many different directions so the beams of radiation converge on the tumor. No actual incision is made in SRS. With SRS, high doses of radiation can be delivered with sub-millimeter accuracy because either a positioning frame is secured to the patient's skull or body; or, a stereotactic image-guidance system is utilized. In the scientific literature, the term stereotactic radiation therapy or stereotactic radiotherapy (SRT) usually refers to "fractionated" radiotherapy, when the total dose of stereotactic radiation is divided into several smaller doses. The primary advantage of fractionation is that it allows higher doses to be delivered to the tumor because of increased tolerance of the surrounding normal tissues to these smaller fractionated doses. The term "stereotactic body radiation therapy or radiotherapy" (SBRT) refers to the use of SRS or SRT at any extracranial site. Megavoltage photons and protons may be used for SBRT. This procedure may also be referred to as stereotactic ablative radiotherapy (SABR). During irradiation, multiple static beams or rotational fields of varying degrees of complexity are employed with or without beam intensity modulation (IMRT). Image-guided radiation therapy (IGRT) refers to an approach which may be applied to a number of radiation therapy techniques, in which modern imaging modalities, such as CT and MRI, have been directly incorporated into radiation delivery machines, allowing for frequent confirmation of the tumor and patient positioning throughout the course of treatment. IGRT can be performed to enhance either 3-dimensional conformal radiation therapy (3DCRT) or IMRT and is considered a necessary, integral component of SBRT.

SRS/SBRT may be used as an alternative to conventional surgery, or as an important adjunct in a multimodality treatment approach. SRS/SBRT may be used with or without other radiation techniques or chemotherapy. SRS/SBRT has potential advantages over open surgery in that it is not invasive and can more easily address inaccessible or multiple lesions. In addition, the border zone between the lesion and normal tissue may receive a radiation dose sufficient to decrease the risk of local recurrence. The primary disadvantage of SRS/SBRT is the lack of certainty of obliteration and delay in obliteration or tumor shrinkage. The primary risk of SRS/SBRT is radiation necrosis, which may occur months after treatment and is related to the dose delivered and the volume treated.

U.S. Food and Drug Administration (FDA)

There are numerous devices approved for delivering stereotactic radiation therapy. Examples include the Leksell Gamma Knife[®] Target System (Elekta Instruments AB., Sweden) which is FDA-approved for the stereotactic irradiation of intracranial structures. The CyberKnife[®] System for Stereotactic Radiosurgery/ Radiotherapy (Accuray Incorporated, Sunnyvale, CA) was approved by the FDA in 1999 for use in the head and neck above the cervico-thoracic junction. In 2001, CyberKnife with Dynamic Tracking Software (DTS) was approved to provide SRS for lesions, tumors, and conditions anywhere in the body when radiation treatment is indicated.

Literature Review

Arteriovenous Malformations, Tumors of the Brain, Spinal Tumors and Trigeminal Neuralgia: Data regarding the safety and efficacy of SRS for numerous conditions have been published in evidence-based, peer-reviewed journals and in textbooks. SRS has become a standard of care in the treatment of arteriovenous malformations (AVM's) of the brain or spine, primary brain tumors, brain metastases, trigeminal neuralgia refractory to medical management, and for patients with spinal tumors with compression or intractable pain.

The American Heart Association (AHA) supports the use of SRS for the management of intracranial arteriovenous malformations (Ogilvy, 2001).

The National Comprehensive Cancer Network[®] (NCCN[®]) Clinical Practice Guidelines in Oncology[™] central nervous system cancers guideline (v.2.2011) discusses the use of SRS for primary brain tumors, meningiomas, brain metastases and primary and metastatic spinal tumors. In primary spinal cord tumors, SRS is usually not a primary treatment but should be administered if symptoms persist after incomplete resection. At progression or recurrence, re-resection is the first choice. If this is not feasible, SRS is an option. Regarding metastasis to spine, dissemination to the spinal column is largely incurable. Treatment goals are palliation and improvement of quality of life through symptom control. EBRT is usually given, though patients experiencing intractable pain or rapid neurological decline during RT may consider SRS. Fractionated SRS allows precise delivery of high dose radiation while minimizing exposure of the surrounding cord. This is especially important in pre-irradiated patients.

The NCCN Guidelines[™] on kidney cancer (v.2.2011) notes under supportive care and metastatic RCC, that SBRT is an alternative to surgery for limited volume brain metastasis. The NCCN Guidelines[™] on melanoma (v.1.2011) notes under brain metastasis, consider definitive or palliative SRS. The NCCN Guidelines[™] on thyroid cancer (v.1.2011) note that SBRT is a preferred option for a solitary lesion of papillary, follicular, or Hurthle cell metastasis to the brain.

American Academy of Neurology (AAN) supports the use of SRS with Gamma knife for the treatment of trigeminal neuralgia refractory to medical management (Gronseth, et al., 2008).

Nasopharyngeal Cancer (NPC): Evidence in the published, peer-reviewed scientific literature indicates that SRS is safe and effective when used for the treatment of NPC. Studies reflect use of SRS both in previously untreated/newly diagnosed NPC as well as local recurrent or persistent NPC. SRS was used as a standalone therapy or after external beam radiation therapy or surgery. Study endpoints were successful local control and acceptable incidence of toxicity (Chan, et al., 2010; Hara, et al., 2007; Chua, et al., 2007; Chen, et al., 2006; Chua, et al., 2006; Low, et al., 2006; Le, et al., 2003).

Parkinson's Disease (PD) / Tremor: Evidence in the published, peer-reviewed scientific literature, although limited due to patient population, suggests that Gamma knife thalamotomy (GKT) as a safe and effective alternative treatment for PD and related movement disorders in patient who are refractory to medical management. The literature suggests GKT is as safe and effective as deep brain stimulation (DBS), and especially suited for patients who are not ideal candidates for DBS (Lim, et al, 2010; Young, et al., 2010; Ohye, et al., 2005; Young, et al., 2000).

The American Academy of Neurology states that unilateral SRS thalamotomy effectively treats contralateral limb tremor in essential tremor whereas bilateral SRS thalamotomy is associated with more frequent and often severe side effects (Zesiewicz, et al., 2005).

Uveal Melanoma: Melanoma of the uveal tract (iris, ciliary body, and choroid) is rare. In the past, enucleation (eye removal) was the accepted standard treatment for primary choroidal melanoma, and it remains the most commonly used treatment for large tumors. Alternative treatments, such as radiation therapy, transpupillary thermotherapy, photocoagulation, and cryotherapy have been developed in an attempt to spare the affected eye and possibly retain useful vision. Toktas et al. (2010) retrospectively reported on 35 patients, noting cumulative 1-year and 3-year local tumor growth control rates were 97% and 83%, respectively. The mean and median times to local tumor progression were 48.0 and 51.7 months, respectively. Modorati et al. (2009) retrospectively evaluated on 78 patients who underwent SRS. The median follow-up time was 31.3 months. A complication was reduction of visual acuity observed during follow-up. The authors reported a favorable eye retention rate of

89.7% (70/78 patients). Survival rate was 88.8% at 3 years and 81.9% at 5 years. Local tumor control was achieved in 91.0% of patients. Dieckmann et al. (2007) reported on 158 uveal melanoma patients who received fractionated SRS. Median follow-up was 33.4 months. Local tumor control, defined as continuous tumor regression or stable disease of the tumor, was achieved in 98% (155/158 patients). The observed side effects were reported comparable to other treatment options for the specific cohort studied. The literature suggests that SRS should be considered as an alternative treatment for uveal melanomas to enucleation in particular when other conservative treatments are not available or suitable.

Liver Cancer: Many patients who are not candidates for a surgical resection are frequently not able to undergo other less invasive approaches, such as cryosurgery, intra-arterial chemotherapy, radiofrequency ablation, ethanol injection, and laser-induced thermo-therapy as they are typically mutually exclusive. SBRT offers a noninvasive alternative that is not limited by the same set of restrictions placed upon the other competing modalities (e.g., intimate association with vascular structures). Evidence in the published, peer-reviewed scientific literature supports the use of SBRT in patients who are not eligible for surgery or other local treatment (Kwon, et al., 2010; Lee, et al., 2009; Tse, et al., 2008; Katz, et al., 2007; Baumann, et al., 2006; Hoyer, et al., 2006; Wulf, et al., 2006). Study populations included patients with primary hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma and hepatic metastases. The majority of studies endpoint was local control, and results indicated “good to excellent local control with acceptable toxicity.” One study with an endpoint of survival (median follow-up was 4.3 years) (Hoyer, et al., 2006) noted survival of patients treated with SBRT was comparable with patients of the poor prognostic group treated with surgical resection and patients treated with minimal invasive techniques.

The NCCN Guidelines™ on Hepatobiliary Cancers (v.1.2011) state all HCC tumors irrespective of location may be amenable to SBRT or external beam conformal radiation. SBRT is often used for 1-3 tumors with a cumulative diameter under six centimeters. SBRT can be considered for larger lesions if there is at least 800 cubic centimeters of uninvolved liver and liver radiation tolerance can be respected. There should be no extra-hepatic disease or it should be minimal. Radiotherapy can be considered an alternative to ablation/embolization techniques or when these therapies have failed. Limited data support the use of SBRT for patients with unresectable HCC disease characterized as extensive or otherwise not suitable for liver transplantation, and those with local disease who are not operable due to performance status and comorbidity.

The NCCN Guidelines™ on colon cancer (v.2.2011) and rectal cancer (3.2011) state in patients with a limited number of liver or lung metastases, radiotherapy can be considered (3D conformal, IMRT, SBRT). It should not be used in place of surgical resection.

Lung Cancer: Evidence in the published, peer-reviewed scientific literature suggests that SBRT is safe and effective in treating medically inoperable patients with non-small cell lung cancer (NSCLC) or pulmonary metastases. Retrospective and prospective studies address use of SBRT in patients with Stage I, Stage II, and non-specified NSCLC; and in patients with pulmonary metastases. Study endpoint was frequently local control and results indicated good to excellent local control with acceptable toxicity (Timmerman, et al., 2010; Kim, et al., 2010; Salazar, et al., 2008; Lagerwaard, et al., 2008; Koto, et al., 2007; Hof, et al., 2007; Onishi, et al., 2007; Baumann, et al., 2006; Zimmermann, et al., 2006; Okunieff, et al., 2006; Timmerman, et al., 2006). One study with a median follow-up of 38 months did address survival, and included operable patients. Onishi et al. (2007) retrospectively described the results of 257 patients, including nearly 100 patients who refused surgery. The overall 5-year survival rates of medically operable and inoperable patients were 64.8% and 35.0%, respectively. The overall 5-year survival rates of the biological effective dose (BED) 100 Gray (Gy) or more and less than 100 Gy subgroups were statistically significant ($p < 0.05$), 53.9% and 19.7%, respectively. The authors stated that all the patients completed the treatment with no particular complaints.

The NCCN Guidelines™ on NSCLC (v.3.2011) state that SBRT provides statistically significant higher 5-year survival than three-dimensional conformal radiation therapy (3DCRT) in Stage I NSCLC. It is one of the well-established treatments for inoperable Stage I NSCLC patients with node negative peripheral lesions. It can also be used for patients with limited lung metastases and for palliative therapy.

The NCCN Guidelines™ on colon cancer (v.2.2011) and rectal cancer (3.2011) state in patients with a limited number of liver or lung metastases, radiotherapy can be considered (3D conformal, IMRT, SBRT). It should not be used in place of surgical resection.

American Society for Therapeutic Radiology and Oncology (ASTRO) Emerging Technology Committee Report 'Stereotactic Body Radiotherapy (SBRT) For Lung Cancer' (2008) states "Tolerability of treatment and local-control has been excellent in single institutional reports in both the medically inoperable and operable settings. In the medically inoperable setting, we conclude that SBRT is an accepted treatment option for Stage I-II NSCLC. In the operable setting, we conclude more study and longer follow-up is necessary to ensure that results are equivalent to those of surgery."

Renal Cancer: SBRT has been studied in the management of renal cell carcinoma (RCC), either as an alternative to surgery to the primary site or as cytoreductive therapy directed toward metastatic sites. SBRT may be an alternative for patients medically unfit or otherwise unwilling to undergo nephrectomy. Although limited, studied address use of SBRT in patients with inoperable primary, local recurrence or metastatic renal cell carcinoma, noting a high degree of local control (90-98%) (Svedman, et al., 2006; Wersålla, et al., 2005).

Previously Irradiated/Critical Location: The scientific literature supports the cautious use of radiation therapy including SBRT for extracranial malignancies which are either in or near previously irradiated volumes, or located near critical structures where the risk of toxicity precludes use of other local modalities (e.g., breast) (Unger, et al., 2010; Würschmidt, et al., 2008; Joseph, et al., 2008; Jereczek-Fossa, et al., 2008).

Behavioral Health Disorders: There is a paucity of data evaluating the use of SRS in behavioral health disorders such as chronic severe depression or intractable severe obsessive-compulsive disorder (OCD).

Breast Cancer: Studies on the use of SBRT to treat primary or recurrent breast cancer are lacking. SRS may be used to treat brain metastases.

Epilepsy: Preliminary studies of epilepsy patients suggest SRS may offer a noninvasive alternative to open surgery; however, definitive conclusion about the efficacy of SRS in refractory temporal lobe epilepsy will require direct comparison of long-term seizure-free rates with conventional surgery such as temporal lobectomy (Barbaro, et al., 2009; Rheims, et al., 2008; Bartolomei, et al., 2008; Regis, et al., 2004).

Pancreatic Cancer: Evidence is mixed regarding both the safety and efficacy of SBRT in treating pancreatic malignancies. Some studies indicate there has been unacceptable toxicity when SBRT is used in the treatment of pancreatic cancer. Also, studies comparing safety and survival of SBRT to current established therapies are lacking.

Chang et al. (2009) reported on the use of SRS on 77 patients with unresectable pancreatic adenocarcinoma. The overall median follow-up was six months; and, among the patients who were alive at last follow-up, it was 12 months. The overall rates of freedom from local progression (FFLP) at six months and 12 months were 91% and 84%, respectively. At six months and 12 months, the rates of grade ≥ 2 late toxicity were 11% and 25%, respectively. 10% developed \geq grade 3 acute or late gastrointestinal toxicity. The authors noted that SRS provides excellent local control for patients with locally advanced pancreatic cancer but has an associated risk of complications, mainly with ulcer formation and duodenal stricture.

Rwigema et al (2011) retrospectively reported on 71 patients who underwent SBRT for pancreatic cancer; 40 (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 follow-up among surviving patients was 12.7 months (4-26 months). The overall freedom from local progression (FFLP) rates at 6 months/1 year was 71.7%/48.5%, respectively. 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.

In a retrospective analysis, Mahadevan et al. (2010) reported on 36 patients with non-metastatic locally advanced unresectable pancreatic cancer. These patients received SBRT followed by chemotherapy. The overall median follow-up was 24 months. Nine Grade 2 (25%) and five Grade 3 (14%) toxicities occurred. The median overall survival time was 14.3 months. Of the 36 patients, 28 (78%) eventually developed distant metastases. Six patients (17%) were free of progression at the last follow-up visit.

Schellenberg et al. (2008) conducted a small Phase II trial including 16 patients with locally advanced, nonmetastatic, pancreatic adenocarcinoma. A single fraction of SBRT was delivered between chemotherapy cycles. The median follow-up after SBRT was 9.1 months for all patients, with a median follow-up of 22.3 months for living patients. At last follow-up, three patients (19%) had experienced local recurrence at 14, 16, and 21 months after SBRT. Of the 15 patients alive ≥ 6 months after SBRT, seven (47%) experienced Grade 2 or greater GI toxicity, with two (13%) of the 15 experiencing Grade 3 or greater GI toxicity.

Hoyer et al. (2005) conducted a Phase II trial, including 22 patients with locally advanced and surgically nonresectable, histological-proven pancreatic carcinoma. Median follow-up was three months. Median time to local or distant progression was 4.8 months. Median survival time was 5.7 months, and only 5% were alive one year after treatment. Acute toxicity reported 14 days after treatment was pronounced. Four patients suffered from severe mucositis or ulceration of the stomach or duodenum and one of the patients had a non-fatal ulcer perforation of the stomach. The authors stated that SRS was associated with "poor outcome, unacceptable toxicity and questionable palliative effect and cannot be recommended for patients with advanced pancreatic carcinoma."

The NCCN Guidelines™ on pancreatic adenocarcinoma (v.1.2011) state under principles of radiation that SBRT is often delivered in 1-5 fractions ranging from 5 – 25 Gy per fraction.

Prostate Cancer: Currently there are several standard local treatment options for prostate cancer that include radical prostatectomy, prostate brachytherapy (seed implantation or high-dose-rate interstitial regimens), external-beam prostate irradiation alone (from a variety of radiation sources), and combinations of external-beam radiation and brachytherapy as a boost.

Preliminary, small prospective and retrospective studies have been published that report biochemical and toxicity results in patients with prostate cancer who were treated with SBRT, including some patients also treated with neoadjuvant hormonal therapy. Limitations of published studies included: small patient populations, short-term follow-up, limited statistical power, and lack of comparison of long-term survival rates to established prostate cancer treatments. Therefore, the safety and clinical utility of prostate SBRT, including the impact on long-term net health outcomes, remains unknown. Large, prospective long-term studies directly comparing SBRT with other established prostate cancer treatments are indicated.

Katz et al. (2010b) prospectively evaluated 304 prostate cancer patients for a median of 2.5 years (30 months). Included patients were determined as: low risk (Gleason Score ≤ 6 and prostate-specific antigen [PSA] ≤ 10 ng/ml [n=211, 69.4%]); intermediate risk (Gleason = 7 or PSA > 10 and PSA < 20 [n=81, 26.6%]); or high risk (Gleason ≥ 8 or PSA > 20 [n=12, 3.9%]). SBRT was delivered at two dose levels (total dose 35 Gy and total dose 36.25 Gy). Fifty-seven patients received neoadjuvant hormonal therapy. No patients experienced any Grade III or IV acute complications. Less than 5% of patients experienced any acute Grade II urinary or rectal toxicity. No significant differences in complication rates were observed for patients receiving the 35 Gy or 36.25 Gy doses. There were no biochemical failures for the 35 Gy dose level. Two low-risk and two high-risk patients, all treated with the higher dose, failed biochemically. None of the intermediate-risk patients failed biochemically. The two low-risk patients that failed biochemically were both shown free of disease in the gland by 12-core biopsy. For both dose levels at 17 months, bowel and urinary quality of life returned to baseline values; sexual quality of life decreased by 10%.

In a prospective trial, King, et al., (2011) followed 67 clinically localized low-risk prostate cancer patients for a median of 2.7 years. Low- to favorable-intermediate risk features, included a pre-biopsy PSA of 10 ng/mL or less, a biopsy Gleason Grade of 3+3 or 3+4, and a clinical Stage T1c or T2a/b. No patient received hormone therapy. There has been no Grade 4 rectal or urinary toxicity. No patients experienced complete urinary obstruction, persistent urinary bleeding, or incontinence, and no patients experienced persistent rectal bleeding or fecal incontinence. Low-grade toxicities were substantially less frequent with every other day versus every day dose regimen ($p = 0.001$ for gastrointestinal and $p = 0.007$ for genitourinary). The authors compared their toxicity rates (using the same scale) with those published in four IMRT randomized controlled trials, and stated their study demonstrated rates of urinary and rectal toxicities equal to or lower than those observed in the dose-escalated trials as well as in the hypofractionated studies". There were two PSA biopsy-proven failures with negative metastatic workup. Median PSA at follow-up was 0.5 ± 0.72 ng/mL. The 4-year Kaplan-Meier PSA relapse-free survival was 94%. For comparison, using a calculated nomogram, the authors noted 5-year range

in predicted biochemical relapse-free survival rates: after radical prostatectomy as 95%–98%; after 78 Gy external beam radiotherapy as 91%–94%; and after permanent brachytherapy as 80%–90%.

Bolzicco et al. (2010) evaluated 45 low-and intermediate-risk prostate cancer patients in a prospective study. Included were: 22 low risk patients (T1c-T2a, Gleason score ≤ 6 , PSA < 10 ng/ml) and 23 intermediate risk patients (T2b-2c, Gleason score 7, PSA 10-20). A total of 17 patients also received patients received androgen-deprivation therapy. The median follow-up was 20 months. Acute complications were mild, short-lived and no greater than Grade 2 by RTOG scale. Late toxicities consisted of one patient (2.2%) experiencing Grade 2 rectal, one patient (2.2%) Grade 3 and four patients (8.8%) with Grade 1 urinary toxicity. There was a significant PSA value reduction in patients with low baseline PSA value, (≤ 1 ng/ml), who had hormone therapy ($p=0.0068$). Also, the 14 low risk patients gave significantly better results of mean PSA value than did the 17 intermediate risk patients ($p=0.02$) at one year. No patient had biochemical failure at last follow-up.

In a prospective Phase I/II trial, Madsen et al. (2007) evaluated 40 patients with localized prostate cancer. In a median follow-up of 41 months, Madsen reported acute toxicity Grade 1-2 was 48.5% (GU) and 39% (GI); and one acute Grade 3 GU toxicity (a urinary obstruction that occurred after the first fraction of treatment). Late Grade 1-2 toxicity was 45% (GU) and 37% (GI). No late Grade 3 or higher toxicity was reported. The actuarial 48 month biochemical freedom from relapse was 70%.

Jereczek-Fossa et al. (2011) conducted a prospective study including 34 patients (38 lesions) with a single recurrence from prostate cancer (isolated recurrent primary, lymph node, or metastatic prostate cancer) and an interval between first diagnosis of prostate cancer and diagnosis of recurrent disease of greater than 23 months. Of the 38 lesions: 15 were reirradiated for local recurrence [P]; 4 reirradiated for anastomosis recurrence [A]; 16 treated for single lymph node recurrence [LN]; and 3 treated for single metastasis [M]). The median follow-up was 16.9 months. Acute toxicity included urinary events (3 Grade 1, 2 Grade 2, and 2 Grade 3 events) and rectal events (1 Grade 1 event). Late toxicity included urinary events (3 Grade 1, 2 Grade 2, and 2 Grade 3 events) and rectal events (1 Grade 1 event and 1 Grade 2 event). Biochemical response was observed in 32 of 38 evaluable lesions. PSA stabilization was seen for 4 lesions, and in 2 cases PSA progression was reported. The 30-month progression-free survival rate was 42.6%. Disease progression was observed for 14 lesions (5, 2, 5, and 2 in Groups P, A, LN, and M respectively).

In a retrospective study, Katz et al. (2010a) reported on 73 localized prostate cancer patients who received SBRT as a boost to EBRT including 36 pts received hormone therapy. Included were 41 intermediate risk (Gleason Score of ≥ 6 and ≤ 7 and a PSA greater than 10 ng/ml but ≤ 20 ng/ml) and 32 high risk (Gleason Score ≥ 8 or a PSA > 20 ng/ml) patients. Median follow-up was 2.75 years (33 months). Less than 7% Grade II and no higher grade acute toxicities occurred. Three intermediate-risk and 7 high-risk biochemical failures occurred; one high-risk patient died of his cancer. Three-year actuarial biochemical control rates were 89.5% and 77.7% for intermediate- and high-risk patients, respectively. The authors stated their results are comparable to results obtained in studies of HDR boost treatment, “where 3-year biochemical control rates for intermediate- and high-risk patients range from 90-95% and 75-92%, respectively”.

Freeman et al. (2011) retrospectively evaluated 41 low risk prostate cancer patients. This included patients with a pre-treatment PSA of 10 ng/mL or less, Gleason score of 3+3 or lower and clinical stage T1c or T2a/b. Patients with a Gleason score of 3+4 were included if present in 2 or fewer cores and involving less than 5 mm aggregate tumor length. No patient received hormone therapy. The median follow-up was 5 years. Acute side effects resolved within 1–3 months of treatment completion. There were no Grade 4 toxicities. No late Grade 3 rectal toxicity occurred, and only one late Grade 3 genitourinary toxicity occurred following repeated urologic instrumentation. The 5-year biochemical progression-free survival rate was 92.7%. Authors state this result compares favorably with that obtained with surgery, LDR or HDR brachytherapy.

In a retrospective review, Jabbari et al. (2010) reported on 38 patients with a performance status 0–1, followed for a median of 18.3 months. Of the 38, 20 low or low-intermediate risk disease patients received SBRT as monotherapy; 18 intermediate to high risk disease patients received SBRT boost post-EBRT and androgen deprivation therapy. Disease risk was described as follows: low risk (pre-treatment [p]PSA < 10 , GS 6, T1c, 2a); intermediate risk (pPSA $10 \leq 20$, GS 7 or T2b); high risk (pPSA > 20 , GS 8, or T2c, T3). The authors noted that SBRT monotherapy or boost for newly diagnosed localized cancer was well tolerated, with 42% and 11% of the 38 study patients reporting acute Grade 2GU and GI toxicity, respectively, and no Grade 3 or higher acute toxicity. Two patients experienced late Grade 3 GU toxicity. The authors stated favorably low PSA nadirs were

observed with a current median PSA nadir of 0.35 ng/ml for all patients (0.47 ng/ml for the monotherapy cohort; 0.10 ng/ml for the boost cohort).

American Society for Therapeutic Radiology and Oncology (ASTRO) Emerging Technology Committee Report ‘Stereotactic Body Radiotherapy (SBRT) For Primary Management of Early-Stage, Low- to Intermediate-Risk Prostate Cancer’ (Buyyounouski, et al., 2010) states “Preliminary results, primarily available only in abstract form and consisting of reports of clinical experiences from single institutions, show that SBRT for the prostate is technically feasible, with little reported acute morbidity. Very early results, of limited statistical power, suggest that treatment will induce an initial PSA response of a magnitude equivalent to that seen with conventionally fractionated radiotherapy.”

Summary

Evidence in the peer-reviewed scientific literature supports safety and efficacy of stereotactic radiosurgery (SRS), including fractionated stereotactic radiotherapy and stereotactic body radiotherapy (SBRT), for the treatment of: arteriovenous malformation of the brain or spine; primary or metastatic brain tumors; spinal tumors causing compression and/or intractable pain; trigeminal neuralgia refractory to medical management; nasopharyngeal cancer; Parkinsonian or essential tremor that is refractory to medical management; uveal melanoma; and liver cancer, lung cancer, and renal cell carcinoma if unresectable or the individual is a poor surgical candidate or declines surgery. SRS/SBRT may be indicated for extracranial malignancies where highly precise application of radiotherapy is required.

There is insufficient evidence addressing the safety and clinical utility of SRS/SBRT when used to treat other conditions, including but not limited to: behavioral health disorders, breast cancer, epilepsy, pancreatic cancer and prostate cancer. Studies comparing safety and survival rates of SBRT to current established therapies for pancreatic cancer and prostate cancer are lacking. Comparative data are not available regarding long-term disease control, survival, and chronic toxicity.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT®* Codes	Description
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 head frame for stereotactic radiosurgery (List separately in addition to code for primary procedure)
63620	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 spinal lesion
63621	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional spinal lesion (List separately in addition to code for primary procedure)
77371	Radiation treatment delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; multi-source Cobalt 60 based
77372	Radiation treatment 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 fractions
77432	Stereotactic radiation treatment management of cerebral lesion(s) (complete course of treatment consisting of one session)
77435	Stereotactic body radiation therapy, treatment management, per treatment course, to one or more lesions, including image guidance, entire course not to exceed 5 fractions

HCPCS Codes	Description
G0173	Linear accelerator based stereotactic radiosurgery, complete course of therapy In one session
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
G0339	Image guided robotic linear accelerator base 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

ICD-9-CM Diagnosis Codes	Description
140.0-149.9	Malignant Neoplasm of Lip, Oral Cavity, and Pharynx
150.0-159.9	Malignant neoplasm of digestive organs and peritoneum
160.0-169.9	Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
170.0-176.9	Malignant neoplasm of bone, connective tissue, skin and breast
179	Malignant neoplasm of uterus, part unspecified
180.0-189.9	Malignant neoplasm of genitourinary organs
190.0-199.2	Malignant neoplasm of other and unspecified sites
200.00-200.88	Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue
201.00-201.98	Hodgkin's disease
202.00-202.98	Other malignant neoplasms of lymphoid and histiocytic tissue
209.00-209.79	Neuroendocrine tumors
210.0-229.9	Benign neoplasms
230.0-234.9	Carcinoma in situ
235.0-238.3	Neoplasms of uncertain behavior
239.0-239.9	Neoplasms of unspecified nature
253.0	Acromegaly and gigantism
332.0	Paralysis agitans
350.1	Trigeminal neuralgia
747.81	Congenital anomaly of cerebrovascular system
V15.3	Personal history of irradiation, presenting hazards to health

Experimental/Investigational/Unproven/Not Covered:

ICD-9-CM Diagnosis Codes	Description

157.0-157.9	Malignant neoplasm of pancreas
174.0 – 174.9	Malignant neoplasm of female breast
175.0 – 175.9	Malignant neoplasm of male breast
185	Malignant neoplasm of prostate
301.4	Obsessive-compulsive personality disorder
345.00 - 345.91	Epilepsy

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	5/15/2008	0110	Stereotactic Radiosurgery
Great-West Healthcare	2/20/2007	07.350.01	Stereotactic Radiosurgery

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