

Stereotactic Body Radiation Therapy and Stereotactic Radiosurgery (for Ohio Only)

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[Instructions for Use](#)

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Related Policies

- [Intensity-Modulated Radiation Therapy \(for Ohio Only\)](#)
- [Proton Beam Radiation Therapy \(for Ohio Only\)](#)
- [Radiation Therapy: Fractionation, Image-Guidance, and Special Services \(for Ohio Only\)](#)

Application

This Medical Policy only applies to the state of Ohio. Any requests for services that are stated as unproven or services for which there is a coverage or quantity limit will be evaluated for medical necessity using Ohio Administrative Code 5160-1-01.

Coverage Rationale

Stereotactic radiation therapy including stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) for the brain, skull, or neck is proven and medically necessary under certain circumstances. For medical necessity clinical coverage criteria, refer to the InterQual® CP: Procedures, Stereotactic Radiosurgery, Brain, or Skull Base.

[Click here to view the InterQual® criteria.](#)

Stereotactic radiation therapy including stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) is considered proven and medically necessary for the following other indications:

- Chordoma and chondrosarcoma
- Craniopharyngioma
- [Definitive treatment](#) of the following:
 - Hepatocellular carcinoma without evidence of regional or distant metastasis
 - Non-small cell lung cancer when all the following criteria are met:
 - Stage I or stage IIA with negative mediastinal lymph nodes
 - Tumor size ≤ 5 cm
 - Individual is medically inoperable or refuses to have surgery after thoracic surgery evaluation
 - Pancreatic adenocarcinoma without evidence of distant metastasis
 - Prostate cancer without evidence of distant metastases
 - Renal cancer when all the following criteria are met:
 - Stage I
 - Individual is a non-optimal surgical candidate
- Extracranial [Oligometastatic Disease](#) when **all** the following criteria are met:

- Primary tumor type is any of the following:
 - Colorectal cancer
 - Melanoma
 - Non-small cell lung cancer
 - Prostate cancer
 - Renal cancer
 - Sarcoma
- Controlled primary tumor defined as at least 3 months since original tumor was treated definitively, with no progression at primary site
- Performance status KPS score \geq 70% or ECOG performance status of 0-2
- Life expectancy is at least 6 months
- Has a total of up to 3 metastatic lesions since diagnosis, and if the individual has previously received local therapy (e.g., SBRT, surgery, or radiofrequency ablation) for metastatic disease, the treated lesion(s) from that therapy are included in the total count of 3 lesions
- Each lesion is \leq 5 cm in size
- No evidence of malignant pleural effusion, leptomeningeal or peritoneal carcinomatosis
- All metastatic lesions are to be treated concurrently in a single episode of care
- SBRT must be completed in 5 fractions for an entire course of treatment regardless of number of lesions treated
- Glomus jugulare tumors
- Recurrent gliomas
- To treat a previously irradiated field
- Uveal melanoma

Stereotactic body radiation therapy (SBRT) for palliative treatment of bone metastases of the spine is proven and medically necessary when all the following criteria are met:

- Using 2 fractions or less
- Individual has no spinal cord compression or cauda equina compression

Definitions

Definitive Treatment: Radiation treatments for cancer with a curative intent (Landsteiner et al., 2023).

Oligometastatic Disease: Refers to a stage of disease where the cancer has spread beyond the site of the primary tumor but is not yet widely metastatic (Hellman 1995). Under the current policy, individuals with up to three metastatic lesions are considered to have Oligometastatic Disease. However, progression of a limited number of metastatic lesions in individuals with otherwise controlled widespread disease (Oligoprogression) is not considered Oligometastatic Disease under this policy.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
32701	Thoracic target(s) delineation for stereotactic body radiation therapy (SRS/SBRT), (photon or particle beam), entire course of treatment
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)

CPT Code	Description
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)
77301	Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications
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 cranial lesion(s) (complete course of treatment consisting of 1 session)
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

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HCPSC Code	Description
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
G0563	Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance and real-time positron emissions-based delivery adjustments to 1 or more lesions, entire course not to exceed 5 fractions

Description of Services

Stereotactic body radiation therapy (SBRT), also known as stereotactic ablative radiotherapy (SABR), is a method used to deliver external beam radiation therapy (EBRT) to a well-defined extracranial target in 5 fractions or less. It can deliver, with very high accuracy, substantially higher doses per treatment than those given in conventional fractionation while minimizing radiation exposure to adjacent normal tissue (Chao et al., 2020).

Stereotactic radiosurgery (SRS) is a non-surgical radiation therapy that is used to deliver a large dose of radiation with a high degree of precision and spatial accuracy, which can aid in preserving healthy tissue. SRS may be used to treat a variety of benign and malignant disorders involving intracranial structures, as well as select extracranial lesions. Although SRS ordinarily refers to a one-day treatment, physicians may suggest multiple stereotactic delivered treatments for tumors larger than one inch in diameter as the surrounding normal tissue exposed to the single high dose of radiation must be limited, and the volume of normal tissue treated increases proportionally to the tumor size. Safety can be improved and the normal tissue can be allowed to heal between treatments when delivering the radiation in a few sessions, as opposed to one. Fractionating the treatment allows for high doses to still be delivered within the target, while maintaining an adequate safety profile. This treatment is commonly referred to as fractionated stereotactic radiotherapy (FSRT), and normally refers to the delivery of two to five treatments of focused radiation which are not always given on consecutive days. [American College of Radiology (ACR), 2019].

Clinical Evidence

Chordoma and Chondrosarcoma

In a systematic review and meta-analysis, Maroufi et al. (2024) aimed to evaluate the safety and effectiveness of SRS in the management of skull based chordomas. Inclusion criteria included primary or recurrent skull based chordomas, treated with SRS as primary, adjunctive, or salvage treatment, and outcomes/complications associated with SRS were reports. Exclusion criteria were other lesions or locations, radiotherapy approaches other than SRS, lack of reported complications or outcomes, non-English studies, studies with less than 5 cases or not mentioning SRS timing, and non-original studies and case reports. Thirty-three retrospective cohorts and series (n = 714 individuals) published from 1991

to 2023 were included in the review. Individuals, predominantly male (57.37%) with a mean age of 46.54 years, exhibited a conventional chordoma subtype (74.77%) and primary lesions (77.91%), mainly in the clivus (98.04%). The mean lesion volume was 13.49 cm³, and 96.68% of individuals had undergone prior surgical attempts. Gamma Knife radiosurgery (GKRS) (88.76%) was the predominant SRS method. Radiologically, 27.19% of individuals experienced tumor regression, while 55.02% showed no signs of disease progression at the latest follow-up. Progression occurred after a mean of 48.02 months. Symptom improvement was noted in 27.98% of individuals. Radiosurgery was associated with a relatively low overall adverse event rate (11.94%), mainly cranial nerve deficits (8.72%). Meta-regression revealed that age and primary lesion type influenced symptom improvement, while factors like extent of resection, radiotherapy, and SRS type affected adverse event rates. The authors concluded that the majority of individuals treated with SRS achieved local tumor control and the safety and efficacy of SRS in the treatment of skull base chordomas is supported. Limitations include many included studies were retrospective in nature and limited long-term data.

Kano et al. (2015) conducted a multicentered retrospective evaluation to analyze the outcome of SRS for individuals with chondrosarcoma who underwent this treatment as part of a multimodality management. Forty-six individuals who underwent SRS for skull-based chondrosarcomas were identified at seven participating centers of the North American Gamma Knife Consortium (NAGKC). Thirty-six individuals had previously undergone tumor resections and five had been treated with fractionated radiation therapy. The median tumor volume was 8.0 cm³ (range 0.9-28.2 cm³), and the median margin dose was 15 Gy (range 10.5-20 Gy). At a median follow-up of 75 months after SRS, eight individuals were deceased. The actuarial OS after SRS was 89% at three years, 86% at five years, and 76% at 10 years. Local tumor progression occurred in 10 individuals. The rate of PFS after SRS was 88% at three years, 85% at five years, and 70% at 10 years. Prior radiation therapy was significantly associated with shorter PFS. Eight individuals required salvage resection, and three individuals (7%) developed AREs. Cranial nerve deficits improved in 22 (56%) of the 39 individuals who deficits before SRS. Clinical improvement after SRS was noted in individuals with abducens nerve paralysis (61%), oculomotor nerve paralysis (50%), lower cranial nerve dysfunction (50%), optic neuropathy (43%), facial neuropathy (38%), trochlear nerve paralysis (33%), trigeminal neuropathy (12%), and hearing loss (10%). Limitations include the retrospective nature of the study and length of follow up of less than 12 months for some individuals. The authors concluded that SRS provided a reasonable benefit-to-risk profile for those with residual or newly diagnosed small skull base chondrosarcomas and maximal safe resection should be the primary initial management. The authors additionally note SRS as a potent treatment option for small to medium-sized chondrosarcomas that is associated with improvement of cranial nerve function in selected cases, especially for individuals who present with diplopia related to abducens nerve palsy.

Hasegawa et al. (2007) conducted a case series analysis to evaluate outcomes of individuals with skull base chordomas and chondrosarcomas and treated with SRS, and to determine which tumors are appropriate for SRS as adjuvant therapy following maximum tumor resection. A total of 37 individuals (48 lesions) were treated using GKS; 27 had chordomas, seven had chondrosarcomas, and three had radiologically diagnosed chordomas. The mean tumor volume was 20 ml, and the mean maximum and marginal doses were 28 and 14 Gy, respectively. The mean follow-up period was 97 months from diagnosis and 59 months from GKS. The actuarial 5- and 10-year survival rates after GKS were 80% and 53%, respectively. The actuarial 5- and 10-year local tumor control (LTC) rates after single or multiple GKS sessions were 76% and 67%, respectively. All individuals with low-grade chondrosarcomas achieved good LTC. A tumor volume of less than 20 ml significantly affected the high rate of LTC ($p = 0.0182$). None of the individuals had AREs, other than one in whom facial numbness worsened despite successful tumor control. The authors concluded that as an adjuvant treatment after resection, GKS is a reasonable option for selected individuals harboring skull base chordomas or chondrosarcomas with a residual tumor volume of less than 20 ml. They also concluded that dose planning with a generous treatment volume to avoid marginal treatment failure should be made at a marginal dose of at least 15 Gy to achieve long-term tumor control.

Martin et al. (2007) conducted a case series analysis to evaluate the effect of SRS on local tumor control and survival in individuals with chordomas and chondrosarcomas. A total of 28 individuals with histologically confirmed chordomas ($n = 18$) or chondrosarcomas ($n = 10$) underwent GKRS either as primary or adjuvant treatment. Their ages ranged from 17 to 72 years (median 44 years). The most common presenting symptom was diplopia (26 individuals, 93%). In two individuals, SRS was the sole treatment. Twenty-six individuals underwent between one and five additional surgical procedures. Two underwent an initial transsphenoidal biopsy. The average tumor volume was 9.8 cm³. The median dose to the tumor margin was 16 Gy. Transient symptomatic AREs developed in only one patient. The actuarial local tumor control for chondrosarcomas at five years was $80 \pm 10.1\%$. For chordomas both the actuarial tumor control and survival was $62.9 \pm 10.4\%$. The authors concluded that SRS is an important option for skull base chordomas and chondrosarcomas either as primary or adjunctive treatment, and that multimodal management appears crucial to improve tumor control in most individuals.

Noël et al. (2003) conducted a single-center case series analysis to evaluate outcomes of individuals with chordomas or chondrosarcomas and treated with fractionated photon and proton radiation. Outcomes included local tumor control,

survival and treatment complications. A total of 67 individuals with a median age of 52 years (range, 14 to 85 years) were treated using the 201-MeV proton beam, 49 for chordoma and 18 for chondrosarcoma. Irradiation combined high-energy photons and protons. Photons represented two thirds of the total dose and protons one third. The median total dose delivered within gross tumor volume (GTV) was 67 Cobalt Gray Equivalents (CGE; range, 60 to 70 CGE). The median follow-up time was 29 months (range, four to 71 months). The 3-year (local control rates were 71% and 85% for chordomas and chondrosarcomas, respectively, and the 3-year OS rates 88% and 75%, respectively. Fourteen tumors (21.5%) failed locally (eight within the GTV, four within the clinical target volume [CTV], and two without further assessment). Seven individuals died from their tumor and one from a nonrelated condition (pulmonary embolism). The maximum tumor diameter and the GTV were larger in relapsing individuals, compared with the rest of the population: 56 mm vs. 44 mm ($p = 0.024$) and 50 ml vs. 22 ml ($p = 0.0083$), respectively. In univariate analysis, age ≤ 52 years at the time of radiotherapy ($p = 0.002$), maximum diameter < 45 mm ($p = 0.02$), and GTV < 28 ml ($p = 0.02$) impacted positively on local control. On multivariate analysis, only age was an independent prognostic factor of local control. The authors concluded that in those with chordomas and chondrosarcomas of the skull base and cervical spine, combined photon and proton radiation therapy offers excellent chances of cure, and that their results should be confirmed with longer follow-up.

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines regarding chordoma states specialized techniques such as SRS should be considered as clinically indicated in order to deliver high radiation doses while maximizing normal tissue sparing. Additionally, SRS has been evaluated for adjuvant treatment for chondrosarcoma of the skull base (NCCN, 2025).

Craniopharyngioma

Palavani et al. (2024) conducted a systematic review and meta-analysis to evaluate the efficacy and safety of fractionated stereotactic radiotherapy (FSRT) for individuals with craniopharyngioma. Ten studies ($n = 256$ patients) met the inclusion criteria which consisted of a sample size greater than four, effects of FSRT reported, and at least one the outcomes of interest reported (improvement in visual acuity or field, new-onset hypopituitarism, effectiveness, and tumor progression). The improvement in visual acuity was estimated at 45% (95% CI: 6-83%), while the improvement in the visual field was 22% (95% CI: 0-51%). Regarding endocrine function, the new-onset hypopituitarism rate was found to be 5% (95% CI: 0-11%). Relative to FSRT effectiveness, the pooled estimate of the complete tumor response rate was 17% (95% CI: 4-30%), and the tumor progression rate was 7% (95% CI: 1-13%). Also, a 3-year PFS rate of 98% (95% CI: 95-100%) was obtained. The authors concluded that FSRT may be a viable treatment option with notable benefits for tumor control and visual functions. The authors recommend further research to assess the clinical utility and associated risks. Limitations include the retrospective nature of many included studies and limited long-term data.

Lee et al. (2014a) conducted a single-center case series analysis to report long-term outcomes of individuals with craniopharyngioma and treated with RS, and to define the prognostic factors of craniopharyngioma. Individuals with craniopharyngioma were treated by GKS and then, all the individuals underwent clinical and endocrinological evaluations at an average of 6-month intervals. Individual demographics and clinical data including outcome of resection, adjuvant radiosurgical parameters, and imaging results were retrospectively reviewed from the center's database. Outcomes included tumor control, PFS, OS, complications and prognostic factors. A total of 137 consecutive individuals who underwent 162 sessions of GKS treatments were included in the analysis. The individuals' median age was 30.1 years (range, 1.5 to 84.9 years), and the median tumor volume was 5.5 ml (range, 0.2 to 28.4 ml). There were 23 solid (16.8%), 23 cystic (16.8%), and 91 mixed solid and cystic (66.4%) craniopharyngiomas. GKS was indicated for residual or recurrent craniopharyngiomas. The median radiation dose was 12 Gy (range, 9.5 to 16.0 Gy) at a median isodose line of 55% (range, 50% to 78%). At a median imaging follow-up of 45.7 months after GKS, the rates of tumor control were 72.7%, 73.9%, and 66.3% for the solid, cystic, and mixed tumors, respectively. The actuarial PFS rates plotted by the Kaplan-Meier method were 70.0% and 43.8% at five and 10 years after RS, respectively. After repeated GKS, the actuarial PFS rates were increased to 77.3% and 61.2% at five and 10 years, respectively. The OS rates were 91.5% and 83.9% at the 5- and 10-year follow-ups, respectively. Successful GKS treatment can be predicted by tumor volume ($p = 0.011$). Among the 137 individuals who had clinical follow-up, new-onset or worsened pituitary deficiencies were detected in 11 individuals (8.0%). Two individuals without tumor growth had a worsened visual field, and one individual had a new onset of third cranial nerve palsy. The authors concluded that their study results suggest that GKS is a relatively safe modality for the treatment of recurrent or residual craniopharyngiomas, and GKS is associated with improved tumor control and reduced in-field recurrence rates.

Niranjan et al. (2010) conducted a single-center case series analysis to evaluate outcomes of Gamma Knife SRS for residual or recurrent craniopharyngiomas and evaluate the factors that optimized the tumor control rates. A total of 46 individuals with craniopharyngiomas underwent 51 SRS procedures. The series included 22 males and 24 females, with a median age of 23.5 years (range, four to 77). The median tumor volume was 1.0 cm³ (range, 0.07 to 8.0). The median

prescription dose delivered to the tumor margin was 13.0 Gy (range, 9 to 20). The median maximal dose was 26.0 Gy (range, 20 to 50). The mean follow-up time was 62.2 months (range, 12 to 232). The OS rate after SRS was 97.1% at 5 years. The 3- and 5-year PFS rates (solid tumor control) were both 91.6%. The overall local control rate (for both solid tumor and cyst control) was 91%, 81%, and 68% at one, three, and five years, respectively. No individuals with normal pituitary function developed hypopituitarism after SRS. Two individuals developed homonymous hemianopsia owing to tumor progression after SRS. Among the factors examined, complete radiosurgical coverage was a significant favorable prognostic factor. The authors concluded that SRS is a safe and effective minimally invasive option for the management of residual or recurrent craniopharyngiomas, and that complete radiosurgical coverage of the tumor was associated with better tumor control.

Kobayashi et al. (2005) conducted a single-center case series analysis to evaluate long-term outcomes of individuals treated with GKS for residual or recurrent craniopharyngiomas after microsurgery, and the effects of dose reduction. A total of 107 individuals with craniopharyngiomas were treated with GKS, and 98 individuals were followed up for six to 148 months (mean 65.5 months). The mean tumor diameter and volume were 18.8 mm and 3.5 ml, respectively. The tumors were treated with a maximal dose of 21.8 Gy and a tumor margin dose of 11.5 Gy by using a mean of 4.5 isocenters. Final overall response rates were as follows: complete response 19.4%, partial response 67.4%, tumor control 79.6%, and tumor progression 20.4%. Reducing the tumor margin dose resulted in decreased therapeutic response and increased tumor progression, although the rate of visual and pituitary function loss also decreased. Among the factors examined, age (for adults) and the nature of the tumor (cystic or mixed) were statistically significant favorable and unfavorable prognostic factors, respectively. The actuarial 5- and 10-year survival rates were 94.1 and 91%, respectively. The PFS rates were 60.8 and 53.8%, respectively. Patient outcomes were reportedly excellent in 45 cases, good in 23, fair in four, and poor in three; 16 individuals died. Deterioration both in vision and endocrinological functions were documented as side effects in six individuals (6.1%). The authors concluded that stereotactic GKS is safe and effective, in the long term, as an adjuvant or boost therapy for residual or recurrent craniopharyngiomas after surgical removal and has minimal side effects.

Definitive Treatment of Hepatocellular Carcinoma (HCC) Without Evidence Regional or Distant Metastasis

Jang et al. (2020) conducted a multi-center, phase II, single-arm, open-label trial to evaluate the safety and efficacy of SBRT for individuals with HCC in a hepatitis B virus-endemic area. Eligible participants were aged ≥ 20 years who were diagnosed with unresectable HCC. Participants received SBRT with 45 to 60 Gy in three fractions. To evaluate gastroduodenal toxicity, esophagogastroduodenoscopy (EGD) was performed before and two months after SBRT. The primary endpoint was treatment-related severe toxicity at one year after SBRT. The secondary endpoints were the 2-year local control, PFS, and OS rates. A total of 74 participants were enrolled, and 65 eligible participants were analyzed. The median follow-up was 41 months (range, four to 69 months). One patient experienced radiation-induced liver disease with acute grade ≥ 3 toxicity 1 month after SBRT. In addition, one patient had a grade 3 esophageal ulcer with stenosis five months after SBRT. The actuarial rate of treatment-related severe toxicity at one year was 3%. The pre-SBRT and post-SBRT EGD findings were not significantly different among the 57 evaluable participants who underwent EGD. The 2-year and 3-year local control rates were 97% and 95%, respectively. The progression-free and OS rates were 48% and 84% at two years, respectively, and 36% and 76% at three years, respectively. The authors concluded that SBRT for individuals with HCC is well tolerated and is an effective treatment modality.

Wang et al. (2020) conducted a systematic review and meta-analysis aimed at comparing the safety and efficacy of radiofrequency ablation (RFA) with SBRT for HCC. Seven studies were identified from January 1990 to May 2020, for a total of 7,928 individuals, and included in the review. The results showed that SBRT was not inferior to RFA based on the pooled hazard ratios (HRs) for OS; however, the pooled HR for the local control rate showed the superiority of SBRT. Subgroup analysis showed that the pooled HR for the local control rate favored SBRT in individuals with tumors sized > 2 cm, but no significant difference was observed in individuals with tumors sized ≤ 2 cm. In addition, no significant differences in the incidence of late severe complications were observed between the SBRT and RFA groups. The authors concluded that SBRT had an OS equal to that with RFA, was well tolerated, and may be used as an alternative to RFA. Additionally, SBRT was superior to RFA in terms of local control of HCC, especially in those with tumors > 2 cm. Limitations include the retrospective nature of the studies included in the review, and the population in each study was different which may result in heterogeneity. The authors recommend future prospective randomized trials. (Wahl et al., (2016, previously cited in this policy, is included in this review).

Rim et al. (2019) conducted a systematic review and meta-analysis to evaluate the clinical feasibility and efficacy of SBRT for HCC. A search, using predetermine criteria, was performed using PubMed, Medline, Embase, and Cochrane Library databases. Primary endpoints were OS and local control and the secondary endpoint was grade ≥ 3 complications. A total of 32 studies, comprising 33 cohorts and consisting of 1,950 individuals were included in the meta-analysis. The majority (85%) of the studies used a retrospective design. Pooled 1-, 2-, and 3-year OS rates were 72.6% (95% CI, 65.7 to 78.6),

57.8% (50.9 to 64.4), and 48.3% (40.3 to 56.5), respectively. Pooled 1-, 2-, and 3-year local control rates were 85.7% (95% CI, 80.1 to 90.0), 83.6% (77.4 to 88.3), and 83.9% (77.6 to 88.6), respectively. The overall median tumor size was 3.3 cm (range, 1.6 to 8.6). Median radiation doses, calculated in equivalent dose in 2 Gy per fraction, ranged from 48 to 114.8 Gy (median 83.3 Gy). A subgroup comparison of tumor size showed significant differences for 1- and 2-year OS rates and 1-, 2-, and 3-year local control rates. In addition, radiation dose showed no difference for OS and a marginal difference for 1-year local control rate. Pooled rates of hepatic and gastrointestinal (GI) grade ≥ 3 complications were 4.7% (95% CI, 3.4 to 6.5) and 3.9% (2.6 to 5.6), respectively. Child-Pugh class was significantly correlated with hepatic complication of grade ≥ 3 ($p = 0.013$). The authors concluded that SBRT for HCC is a feasible option with excellent local control persisting up to three years. They reported that both OS and local control were affected by tumor size, and radiation dose marginally affected local control, and while severe complications were rare, liver function should be considered to prevent serious hepatic toxicity.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

In an ASTRO guideline for primary liver cancers, using external beam radiation therapy (EBRT) as a potential first-line treatment in patients with liver-confined HCC who are not candidates for curative therapy, as consolidative therapy after incomplete response to liver-directed therapies, and as a salvage option for local recurrences is strongly recommended. ASTRO conditionally recommends EBRT for patients with liver-confined multifocal or unresectable HCC, or those with macrovascular invasion, sequenced with systemic or catheter-based therapies. Additionally, the authors recommend future high-quality RCTs to further define the role of EBRT in HCC treatment (Apisarnthanarax et al., 2021).

International Stereotactic Radiosurgery Society (ISRS)

Bae et al. (2024) developed a guideline for the ISRS based on a systematic review and meta-analysis for liver-confined HCC to address appropriate patient management. The review included 17 observational studies between 2003 and 2019, a total of 1889 individuals, who underwent treatment for HCC with ≤ 9 SBRT fractions. The recommendations are as follows (not all-inclusive):

- Patients with HCC < 3 cm can be considered for SBRT with favorable local control and survival outcomes. SBRT to HCC ≥ 3 cm can be performed with the expectation of durable long-term local control.
- SBRT with 1-9 fractions is recommended for patients with liver-confined HCC. No specific recommendation for the optimal dose fractionation can be made.
- Classic radiation-induced liver disease is a rare event after SBRT to HCC with proper patient selection.

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for HCC states that SBRT can be considered as an alternative to ablation/embolization techniques or when these therapies have failed or are contraindicated. SBRT is typically given in 3-5 fractions and is often used for patients with 1-3 tumors (NCCN, 2024).

Definitive Treatment of Non-Small Cell Lung Cancer (NSCLC)

Ball et al. (2019) performed a phase 3, open-label RCT (TROG 09.02 CHISEL) comparing stereotactic ablative body radiotherapy (SABR) and standard fractionated radiotherapy in participants with stage I NSCLC in participants who were either inoperable or who had refused surgery to evaluate local control, OS, toxicity, and quality of life. Participants ($n = 101$) from 11 hospitals in Australia and three in New Zealand were randomly assigned to receive standard radiotherapy ($n = 35$) or SABR ($n = 66$). Inclusion criteria consisted of those 18 years or older with an ECOG score of 0 or 1, and a peripherally located tumor. Exclusion criteria included previous chemotherapy or radiotherapy and multiple primary tumors requiring radiotherapy. Five (7.6%) participants in the SABR group and two (6.5%) in the standard radiotherapy group did not receive treatment, and a further four in each group withdrew before study end. As of data cutoff (July 31, 2017), median follow-up for local treatment failure was 2.1 years (IQR 1.2–3.6) for participants randomly assigned to standard radiotherapy and 2.6 years (IQR 1.6–3.6) for participants assigned to SABR. 20 (20%) of 101 participants had progressed locally: nine (14%) of 66 participants in the SABR group and 11 (31%) of 35 participants in the standard radiotherapy group, and freedom from local treatment failure was improved in the SABR group compared with the standard radiotherapy group (hazard ratio 0.32, 95% CI 0.13–0.77, $p = 0.0077$). Median time to local treatment failure was not reached in either group. In participants treated with SABR, there was one grade 4 adverse event (dyspnea) and seven grade 3 adverse events (two cough, one hypoxia, one lung infection, one weight loss, one dyspnea, and one fatigue) related to treatment compared with two grade 3 events (chest pain) in the standard treatment group. The authors concluded that compared to standard radiotherapy, SABR had superior local control without an increase in major toxicity in those with inoperable peripherally located stage I NSCLC. Limitations include a large proportion of patient had previous cancer and small sample size. In 2023, Bucknell et al. conducted an analysis of the TROG 09.02 (CHISEL) phase 3 trial to compare pulmonary function tests and the 6-minute walk test after SBRT compared to conventional 3D-CRT at three

and 12 months after treatment. The authors concluded that there was no difference in reduced respiratory function between the two groups despite the higher biologically effective doses delivered to the tumor in SBRT.

Chang et al. (2015) conducted a pooled analysis of two clinical trials (STARS and ROSEL) that were halted due to slow recruitment. The STARS (NCT00840749) and ROSEL (NCT00687986) trials were open-label, randomized, phase III trials comparing SABR with surgery for individuals with stage I NSCLC. The primary outcome for this pooled analysis was OS according to treatment group (SABR vs. surgery) and secondary outcomes included recurrence-free survival, and grade 3 or worse acute or chronic toxicity. A total of 58 participants were enrolled with 31 participants randomized to SABR and 27 participants to surgery. Median follow-up was 40.2 months (IQR 23.0 to 47.3) for the SABR group and 35.4 months (18.9 to 40.7) for the surgery group. Six participants in the surgery group died compared with one patient in the SABR group. Estimated OS at three years was 95% (95% CI 85 to 100) in the SABR group compared with 79% (64–97) in the surgery group (HR, 0.14; 95% CI 0.017 to 1.190, log-rank $p = 0.037$). Recurrence-free survival at three years was 86% (95% CI 74 to 100) in the SABR group and 80% (65 to 97) in the surgery group (HR, 0.69; 95% CI 0.21 to 2.29, log-rank $p = 0.54$). In the surgery group, one patient had regional nodal recurrence and two had distant metastases; in the SABR group, one patient had local recurrence, four had regional nodal recurrence, and one had distant metastases. Three (10%) participants in the SABR group had grade 3 treatment-related adverse events (three participants with chest wall pain, two with dyspnea or cough, and one with fatigue and rib fracture). No participants given SABR had grade four events or treatment-related death. In the surgery group, one (4%) patient died of surgical complications and 12 (44%) participants had grade 3–4 treatment-related adverse events. Grade 3 events occurring in more than one patient in the surgery group were dyspnea (four participants), chest pain (four participants), and lung infections (two participants). The authors concluded that the results of this pooled analysis of STARS and ROSEL data suggest that SABR can be considered a treatment option in operable individuals needing a lobectomy, and that the equipoise suggested by the results justifies efforts for additional RCTs.

Haasbeek et al. (2010) conducted a single-center case series analysis to evaluate outcomes of stereotactic radiotherapy (SRT) in elderly individuals. Individuals diagnosed with stage IA/IB NSCLC and aged ≥ 75 years at the time of SRT were included. SRT was delivered using three fractionation schemes: fractions of 20Gy (for T1 tumors), five fractions of 12 Gy (for T1 tumors with broad contact with the chest wall and for T2 tumors), or eight fractions of 7.5 Gy (for tumors adjacent to the heart, large blood vessels, hilus, brachial plexus, or mediastinum). Individuals were followed routinely at three months, six months, one year, and annually thereafter. Outcomes included overall and disease-free survival, and actuarial local, regional, and distant failure rates. A total of 193 individuals aged ≥ 75 years were treated using SRT (118 T1 tumors, 85 T2 tumors). The median patient age was 79 years, 80% of individuals were considered medically inoperable, and 20% of individuals declined surgery. The median Charlson comorbidity score was four, and severe chronic obstructive pulmonary disease (Global Initiative for Chronic Obstructive Lung Disease Class III or greater) was present in 25% of individuals. Risk-adapted SRT schemes were used with the same total dose of 60 Gy in three fractions (33%), five fractions (50%), or eight fractions (17% of individuals), depending on the patient's risk for toxicity. SRT was well tolerated, and all but one patient completed treatment. Survival rates at one year and three years were 86% and 45%, respectively. Survival was correlated with performance score ($p = 0.001$) and pre-SRT lung function ($p = 0.04$). The actuarial local control rate at three years was 89%. Acute toxicity was rare, and late RTOG grade ≥ 3 toxicity was observed in $< 10\%$ of individuals. The authors concluded that SRT achieved high local control rates with minimal toxicity in individuals aged ≥ 75 years despite their significant medical comorbidities and that these results indicated that more active diagnostic and therapeutic approaches are justified in elderly individuals, and that SRT should be considered and discussed as a curative treatment alternative.

Timmerman et al. (2010) conducted a multi-center, phase II, single arm trial (RTOG 0236) to evaluate toxicity and efficacy of SBRT in a high-risk population of participants with early stage but medically inoperable lung cancer. Participants with biopsy-proven peripheral T1-T2, N0, M0 non-small cell tumors less than 5.0 cm in diameter and medical conditions precluding surgical treatment were included in the analysis. The prescription dose was 18 Gy per fraction in three fractions (54 Gy total) delivered in 1½-2 weeks. The primary endpoint was primary tumor control with OS, disease free survival (DFS), adverse events, involved lobe, regional, and disseminated recurrence as secondary endpoints. The study aimed to improve the two-year primary tumor control rate from 60% to 80%. A rate of 60% was chosen as the lowest acceptable primary tumor control rate after taking into consideration a $> 80\%$ primary tumor control rate seen in a previously published study (Timmerman 2006). A total of 59 participants accrued, of which 55 were evaluable (44 T1 and 11 T2 tumors) with a median follow-up of 34.4 months (range, 4.8 to 49.9 months). Only one patient had a primary tumor failure; the estimated 3-year primary tumor control rate was 97.6% (95% CI, 84.3% to 99.7%). Three participants had recurrence within the involved lobe; the 3-year primary tumor and involved lobe (local) control rate was 90.6% (95% CI, 76.0% to 96.5%). Two participants experienced regional failure; the local-regional control rate was 87.2% (95% CI, 71.0%, 94.7%). Eleven participants experienced disseminated recurrence; the 3-year rate of disseminated failure was 22.1% (95% CI, 12.3% to 37.8%). The rates of DFS and OS at three years were 48.3% (95% CI, 34.4% - 60.8%) and 55.8% (95% CI, 41.6% to 67.9%), respectively. The median OS was 48.1 months (95% CI, 29.6% to not reached). Protocol

specified treatment-related grade 3 adverse events were reported in seven participants (12.7%; 95% CI, 9.6% to 15.8%); grade 4 events were reported in two participants (3.6%; 95%CI, 2.7% to 4.5%). No grade 5 adverse events were reported. The authors concluded that individuals with inoperable NSCLC who received SBRT had a survival rate of 55.8% at three years and high rates of local tumor control compared to historical data.

Fakiris et al. (2009) conducted a single-center, phase II, single arm trial to report 50-month follow-up results from a phase I dose escalation trial in individuals with medically inoperable Stage I NSCLC (Timmerman 2003 and McGarry 2005). A total of 70 medically inoperable individuals who had clinically staged T1 (34 participants) or T2 (36 participants) (≤ 7 cm), N0, M0, biopsy-confirmed NSCLC received SBRT at a treatment dose of 60-66 Gy prescribed to the 80% isodose volume in three fractions. Median follow-up was 50.2 months (range, 1.4 to 64.8 months). Kaplan-Meier local control at three years was 88.1%. Regional (nodal) and distant recurrence occurred in six (8.6%) and nine (12.9%) participants, respectively. Median survival (MS) was 32.4 months and 3-year OS was 42.7% (95% CI, 31.1 to 54.3%). Cancer-specific survival at three years was 81.7% (95% CI, 70.0 to 93.4%). For participants with T1 tumors, MS was 38.7 months (95% CI, 25.3 to 50.2) and for T2 tumors MS was 24.5 months (95% CI, 18.5 to 37.4) ($p = 0.194$). Tumor volume (≤ 5 cc, 5–10 cc, 10–20 cc, > 20 cc) did not significantly impact survival: MS was 36.9 months (95% CI, 18.1 to 42.9), 34.0 (95% CI, 16.9 to 57.1), 32.8 (95% CI, 21.3 to 57.8), and 21.4 months (95% CI, 17.8 to 41.6), respectively ($p = 0.712$). There was no significant difference in survival between participants with peripheral vs. central tumors (MS 33.2 vs. 24.4 months, $p = 0.697$). Grade 3 - 5 toxicity occurred in five of 48 participants with peripheral lung tumors (10.4%) and in six of 22 participants (27.3%) with central tumors (Fisher's exact test, $p = 0.088$). The authors concluded that use of SBRT results in high rates of local control in medically inoperable individuals with Stage I NSCLC.

Onishi et al. (2007) reported updated results of a multi-center case series analysis conducted to determine the optimal small-volume stereotactic RT (SRT) dose that would limit toxicity and obtain local control in individuals with stage I NSCLC, whether the single-institution results were reproducible, and whether single high-dose stereotactic irradiation (STI) results were comparable to those of surgery. In the original study (Onishi 2004), the authors concluded that hypofractionated high-dose STI with BED < 150 Gy represents a feasible and beneficial method for obtaining curative treatment of individuals with Stage I NSCLC. The authors reported that local control and survival rates were better for BED ≥ 100 Gy than for BED < 100 Gy for all treatment methods and schedules. In addition, survival rates for STI in selected individuals (medically operable and BED ≥ 100 Gy) were excellent and reproducible among institutions, irrespective of specific treatment methods, and were potentially equivalent to those of surgery.

In the updated report, Onishi (2007) compared previously reported results for surgery and conventional RT with those for hypofractionated high-dose stereotactic RT (HypoFXSRT). In this retrospective study, 257 individuals with stage I NSCLC (median age, 74 years: 164 T1N0M0, 93 T2N0M0) were treated with HypoFXSRT alone at 14 institutions. Stereotactic three-dimensional treatment was performed using noncoplanar dynamic arcs or multiple static ports. A total dose of 18 to 75 Gy at the isocenter was administered in one to 22 fractions. The median calculated biological effective dose (BED) was 111 Gy (range, 57 to 180 Gy) based on $\alpha/\beta = 10$. For the comparison to surgery, the 5-year OS rates for individuals with stage IA and IB NSCLC and treated with surgery ranged from 61% to 72% and 40% to 50%, respectively (Mountain 2000, Naruke 2001 and Shirakusa 2002). During follow-up (median, 38 months), pulmonary complications of above grade 2 occurred in 14 individuals (5.4%). Local progression occurred in 36 individuals (14.0%), and the local recurrence rate was 8.4% for a BED of 100 Gy or more compared with 42.9% for less than 100 Gy ($p < 0.001$). The 5-year OS rate of medically operable individuals was 70.8% among those treated with a BED of 100 Gy or more compared with 30.2% among those treated with less than 100 Gy ($p < 0.05$). The authors concluded that when compared with conventional RT and surgery, HypoFXSRT is a safe and promising treatment modality, local control and survival rates are superior to those of conventional RT, HypoFXSRT should be a standard of care for medically inoperable individuals, and additional studies that randomly compare HypoFXSRT and surgery for medically operable individuals are needed.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's 2018 guideline, Stereotactic Body Radiotherapy for Early-Stage Non-Small Cell Lung Cancer, recommends that patients with stage I NSCLC should be evaluated by a thoracic surgeon, preferably within a multidisciplinary cancer care team, to determine operability. For patients with standard operative risk (i.e., with anticipated operative mortality of $< 1.5\%$) and stage I NSCLC, SBRT is not recommended as an alternative to surgery outside of a clinical trial setting. For patients with high operative risk (i.e., those who cannot tolerate lobectomy, but are candidates for sublobar resection) and stage I NSCLC, discussions about SBRT as a potential alternative to surgery are encouraged and patients should be informed that SBRT may have decreased risks from treatment in the short term however, outcomes longer than three years are not well-established (Schneider 2018).

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for NSCLC states that for stage I and selected node-negative stage IIA, SBRT has achieved good primary tumor control rates and OS that are higher than conventionally fractionated radiotherapy. NCCN recommends definitive SBRT for patients with stage I and II NSCLC who are medically inoperable, and SBRT may be a reasonable alternative to surgery for patients with potentially operable disease who are high risk, elderly, or refuse surgery after appropriate consultation (NCCN, 2024).

Definitive Treatment of Pancreatic Adenocarcinoma Without Evidence of Distant Metastasis

A systematic review and meta-analysis by Tchelebi et al. (2020) aimed to compare the efficacy and safety of SBRT to conventionally fractionated radiation therapy with concurrent chemotherapy (CFRT) for treatment of locally advanced pancreatic cancer. Twenty-one studies were included in the analysis, including 11 CFRT and nine SBRT studies for a total of 1147 individuals. The primary outcome was efficacy defined as a two-year OS. One-year OS and incidence of acute or late grade 3/4 toxicity were the secondary outcomes. For SBRT, the median dose was 30 Gy, and the most common regimen was 30 Gy/5 fractions. For CFRT, doses ranged from 45 to 54 Gy in 1.8- to 2.0-Gy fractions, with the majority of studies delivering 50.4 Gy in 28 fractions with concurrent Gemcitabine. The random effects estimate for 2-year OS was 26.9% (95% CI, 20.6%-33.6%) for SBRT versus 13.7% (95% CI, 8.9%-19.3%) for CFRT and was statistically significant in favor of SBRT. The random effects estimate for 1-year OS was 53.7% (95% CI, 39.3%-67.9%) for SBRT versus 49.3% (95% CI, 39.3%-59.4%) for CFRT, and was not statistically significant. The random effects estimate for acute grade 3/4 toxicity was 5.6% (95% CI, 0.0%-20.0%) for SBRT versus 37.7% (95% CI, 24.0%-52.5%) for CFRT and was statistically significant in favor of SBRT. The random effects estimate for late grade 3/4 toxicity was 9.0% for SBRT (95% CI, 3.3%-17.1%) versus 10.1% (95% CI, 1.8%-23.8%) for CFRT, which was not statistically significant. The authors concluded that for individuals with locally advanced pancreatic cancer, SBRT may provide a modest improvement in two-year OS with reduced rates of acute grade 3/4 toxicity and not change in one-year OS or late toxicity. Limitations include the phase one or two studies and retrospective nature of the SBRT studies, whereas the CFRT studies were all phase 2 or phase 3. The authors recommend future quality studies to evaluate SBRT for these individuals.

In a retrospective review, Zhong et al. (2017) compared SBRT with conventionally fractionated radiation therapy in locally advanced pancreatic cancer (LAPC) using the National Cancer Database. Individuals with cT2-4/N0-1/M0 adenocarcinoma of the pancreas diagnosed from 2004 to 2013 were included in the review. Radiation therapy delivered at ≥ 4 Gy per fraction was considered SBRT, and radiation therapy delivered at ≤ 2 Gy was deemed conventionally fractionated radiation therapy. Overall survival was the primary outcome. The total number of individuals included in the review was 8,450, conventionally fractionated radiation therapy = 7,819 and SBRT = 631. Receipt of SBRT was associated with superior OS in the multivariate analysis (hazard ratio, 0.84; 95% confidence interval, 0.75–0.93; $p < .001$). With propensity score matching, 988 individuals in all were matched, with 494 individuals in each cohort. Within the propensity-matched cohorts, the median OS (13.9 vs 11.6 months) and the 2-year OS rate (21.7% vs 16.5%) were significantly higher with SBRT versus conventionally fractionated radiation therapy. The authors concluded SBRT was superior to OS when compared with conventionally fractionated radiation therapy, and an additional benefit of SBRT was the shorter duration of treatment. Additionally, the authors recommend future randomized trials to evaluate these results. Limitations include the retrospective nature of the study and lack of control for the specific type of chemotherapy in propensity matching.

Herman et al. (2015) conducted a multi-center, phase II, single arm study to determine whether individuals treated with gemcitabine (GEM) administered with fractionated SBRT (in five fractions of 6.6 Gy, to a total 33.0 Gy) would achieve reduced late grade 2-4 GI toxicity compared with a historical cohort of individuals treated with GEM and a single 25-Gy fraction of SBRT. Participants with LAPC received up to three doses of GEM (1000 mg/m²) followed by a 1-week break and SBRT (33.0 Gy in five fractions). After SBRT, participants continued to receive GEM until disease progression or toxicity. Toxicity was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events [version 4.0] and the RTOG radiation morbidity scoring criteria. Participants completed the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30) and pancreatic cancer-specific QLQ-PAN26 module before SBRT and at four weeks and four months after SBRT. A total of 49 participants participated in the study with a median follow-up of 13.9 months (range, 3.9 to 45.2 months). The median age of the participants was 67 years and 84% had tumors of the pancreatic head. Rates of acute and late (primary endpoint) grade ≥ 2 gastritis, fistula, enteritis, or ulcer toxicities were 2% and 11%, respectively. The historical cohort rates for grade ≥ 2 acute and late toxicities were 19% and 47%, respectively (Schellenberg 2008). QLQ-C30 global QOL scores remained stable from baseline to after SBRT (67 at baseline, median change of 0 at both follow-ups; $p > 0.05$ for both). Participants reported a significant improvement in pancreatic pain ($p = 0.001$) 4 weeks after SBRT on the QLQ-PAN26 questionnaire. The median plasma carbohydrate antigen 19-9 (CA 19-9) level was reduced after SBRT (median time after SBRT, 4.2 weeks; 220 U/mL vs. 62 U/mL [$p < 0.001$]). The median OS was 13.9 months (95% CI, 10.2 to 16.7 months). Freedom from local disease

progression at one year was 78%. Four participants (8%) underwent margin-negative and lymph node-negative surgical resections. The authors concluded that fractionated stereotactic body radiotherapy with gemcitabine achieves favorable toxicity, QOL, and preliminary efficacy compared with historical data.

Mellon et al. (2015) conducted a single-center case series analysis to evaluate outcomes and toxicity of induction chemotherapy and SBRT for borderline resectable pancreatic cancer (BRPC) and LAPC. The center's internal database was queried to identify all individuals who received at least one dose of induction chemotherapy and SBRT for the treatment of BRPC or LAPC. After staging, medically fit individuals underwent chemotherapy for 2–3 months, with regimen at the discretion of the treating medical oncologist. Then, individuals received SBRT delivered in five consecutive daily fractions with median total radiation doses of 30 Gy to tumor and 40 Gy dose painted to tumor-vessel interfaces. That was followed by restaging imaging for possible resection. Outcomes included OS, event free survival (EFS), and locoregional control (LRC) rates. A total of 159 individuals, 110 with BRPC and 49 with LAPC, with median follow-up of 14.0 months were included in the analysis. The resection and margin negative (R0) rate for BRPC individuals who completed neoadjuvant therapy was 51% and 96%, respectively. Estimated median OS was 19.2 months for BRPC individuals and 15.0 months for LAPC individuals ($p = 0.402$). Median OS was 34.2 months for surgically resected individuals versus 14.0 months for unresected individuals ($p < 0.001$). Five of 21 (24%) individuals with LAPC received FOLFIRINOX chemotherapy underwent R0 resection. Among individuals with LAPC, FOLFIRINOX recipients underwent R0 resection more often than other chemotherapy recipients (5 of 21 vs. 0 of 28, $p = 0.011$). There was a trend for improved survival in individuals with LAPC who underwent resection ($p = 0.09$). For those not undergoing resection, 1-year LRC was 78%. Any grade ≥ 3 potentially radiation-related toxicity rate was 7%. The authors concluded that their results underscore the feasibility, safety, and effectiveness of neoadjuvant SBRT and chemotherapy for BRPC and LAPC.

Chuong et al. (2013) conducted a single-center, retrospective, case series analysis to evaluate outcomes of individuals with nonmetastatic pancreatic cancer and treated with induction chemotherapy followed by SBRT. SBRT was delivered over five consecutive fractions using a dose painting technique including 7-10 Gy/fraction to the region of vessel abutment or encasement and 5-6 Gy/fraction to the remainder of the tumor. Restaging scans were performed at four weeks, and resectable individuals were considered for resection. The primary endpoints were OS and PFS. A total of 73 individuals were evaluated, with a median follow-up of 10.5 months. Median doses of 35 Gy and 25 Gy were delivered to the region of vessel involvement and the remainder of the tumor, respectively. Thirty-two BRPC individuals (56.1%) underwent surgery, with 31 undergoing an R0 resection (96.9%). The median OS, 1-year OS, median PFS, and 1-year PFS for BRPC vs. LAPC individuals was 16.4 months vs. 15 months, 72.2% vs. 68.1%, 9.7 vs. 9.8 months, and 42.8% vs. 41%, respectively (all $p > 0.10$). BRPC individuals who underwent R0 resection had improved median OS (19.3 vs. 12.3 months; $p = 0.03$), 1-year OS (84.2% vs. 58.3%; $p = 0.03$), and 1-year PFS (56.5% vs. 25.0%; $p < 0.0001$), respectively, compared with all nonsurgical individuals. The 1-year local control in nonsurgical individuals was 81%. There was no acute grade ≥ 3 toxicity, and late grade ≥ 3 toxicity was minimal (5.3%). The authors concluded that SBRT safely facilitates margin-negative resection in individuals with BRPC pancreatic cancer while maintaining a high rate of local control in unresectable individuals, and these data support the expanded implementation of SBRT for pancreatic cancer.

Rajagopalan et al. (2013) conducted a single-center case series analysis to report outcomes of individuals with BRPC and LAPC who underwent surgery after neoadjuvant SBRT. Individuals were treated with SBRT followed by resection and chemotherapy was to the discretion of the medical oncologist and preceded SBRT for most individuals. A total of 12 individuals were included in the analysis. Most (92%) received neoadjuvant chemotherapy, and gemcitabine/capecitabine was most frequently prescribed ($n = 7$). Most individuals were treated with fractionated SBRT to 36 Gy/3 fractions ($n = 7$) and the remainder with single fraction to 24 Gy ($n = 5$). No grade 3 + acute toxicities attributable to SBRT were found. Two individuals developed post-surgical vascular complications and one died secondary to this. The mean time to surgery after SBRT was 3.3 months. An R0 resection was performed in 92% of individuals ($n = 11/12$). In 25% ($n = 3/12$) of individuals, a complete pathologic response was achieved, and an additional 16.7% ($n = 2/12$) demonstrated $< 10\%$ viable tumor cells. Kaplan-Meier estimated median progression free survival is 27.4 months. OS was 92%, 64% and 51% at 1-, 2-, and 3-years. The authors concluded that in individuals with BRPC and LAPC, treatment with neoadjuvant chemotherapy and SBRT followed by resection is safe and tolerated well, and a promising area for further exploration in this disease site.

Mahadevan et al. (2011) conducted single-center, retrospective, case series analysis to evaluate outcomes of individuals with LAPC who received a planned strategy of initial chemotherapy with restaging and then, for those individuals with no evidence of metastatic progression, treatment with SBRT. Individuals received GEM (1,000 mg/m² per week for 3 weeks then 1 week off) until tolerance, at least six cycles, or progression. Individuals without metastases after two cycles were treated with SBRT (tolerance-based dose of 24–36 Gy in three fractions) between the third and fourth cycles without interrupting the chemotherapy cycles. A total of 47 individuals were included in the analysis. Of those, 8 (17%) individuals were found to have metastatic disease after two cycles of GEM; the remaining 39 individuals received SBRT. The median follow-up for survivors was 21 months (range, six to 36 months). The median OS for all individuals who received SBRT

was 20 months, and the median PFS was 15 months. The local control rate was 85% (33 of 39 individuals); and 54% of individuals (21 of 39) developed metastases. Late Grade III toxicities such as GI bleeding and obstruction were observed in 9% (3/39) of individuals. The authors concluded that for those with locally advanced pancreas cancer, their strategy uses local therapy for those who are most likely to benefit from it and spares those individuals with early metastatic progression from treatment, and SBRT delivers such local therapy safely with minimal interruption to systemic chemotherapy, thereby potentially improving the outcome in these individuals.

Koong et al. (2004) conducted a phase I dose escalation study to determine the feasibility and toxicity of delivering SRS to participants with LAPC. Participants with ECOG performance status ≤ 2 received a single fraction of RS consisting of either 15 Gy, 20 Gy, or 25 Gy to the primary tumor. Acute GI toxicity was scored according to the RTOG criteria. Response to treatment was determined by serial high-resolution computed tomography scanning. A total of 15 participants were treated at the 3 dose levels (three participants received 15 Gy, five participants received 20 Gy, and seven participants received 25 Gy). At those doses, no grade 3 or higher acute GI toxicity was observed. This trial was stopped before any dose-limiting toxicity was reached, because the clinical objective of local control was achieved in all six evaluable participants treated at 25 Gy. The authors concluded that it is feasible to deliver SRS to those with locally advanced pancreatic cancer, and the recommended dose to achieve local control without significant acute GI toxicity is 25 Gy.

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for pancreatic adenocarcinoma states that as first-line therapy, SBRT may be used in select individuals with locally advanced disease without systematic metastases or those who are not candidates for combination therapy. As second-line therapy, SBRT may be used if not previously given and if the primary site is the sole site of progression (2024).

Definitive Treatment of Prostate Cancer Without Evidence of Distant Metastasis

Jackson et al. (2019) conducted a systematic review and meta-analysis to evaluate physician- and patient-reported outcomes after prostate SBRT. A search was conducted using Medline and EMBASE for original articles published between January 1990 and January 2018. The primary endpoints included 5-year overall biochemical recurrence-free survival (bRFS), physician-reported acute and late grade ≥ 3 toxicity for both genitourinary (GU) and GI domains, and patient-reported QOL using the Expanded Prostate Cancer Index Composite (EPIC). Secondary analyses included a meta-regression of the impact of covariables on bRFS and late toxicity. A total of 38 studies were included in the analysis, comprising 6,116 individuals. Twenty-two studies were clinical trials, of which one was a phase I trial that included 45 individuals, four were phase I/II trials that included 245 individuals, 17 were phase II or III trials that included 2,174 individuals and 16 were prospective observational studies, which included 3,652 individuals. The median follow-up period was 39 months (range, 12 to 115 months). Ninety-two percent, 78%, and 38% of studies included low, intermediate, and high-risk individuals, respectively. Overall, 5 and 7-year bRFS rates were 95.3% (95% CI, 91.3% to 97.5%) and 93.7% (95% CI, 91.4% to 95.5%), respectively. Estimated late grade ≥ 3 GU and GI toxicity rates were 2.0% (95% CI, 1.4% to 2.8%) and 1.1% (95% CI, 0.6% to 2.0%), respectively. By two years post-SBRT, EPIC urinary and bowel domain scores returned to baseline. Increasing dose of SBRT was associated with improved biochemical control ($p = 0.018$) but worse late grade ≥ 3 GU toxicity ($p = 0.014$). The authors concluded that prostate SBRT has substantial prospective evidence supporting its use as a standard treatment option, with favorable tumor control, patient-reported QOL, and levels of toxicity.

Widmark et al. (2019) conducted a multi-center, phase III, randomized, open-label non-inferiority trial to show that ultra-hypofractionation is non-inferior to conventional fractionation regarding failure-free survival without any significant differences in late normal tissue complications. Participants were men up to 75 years of age with histologically verified intermediate-to-high-risk prostate cancer and WHO performance status between 0 - 2. Participants were randomly assigned to ultra-hypofractionation (42.7 Gy in seven fractions, three days per week for 2.5 weeks) or conventional fractionated radiotherapy (78.0 Gy in 39 fractions, five days per week for eight weeks). No androgen deprivation therapy was allowed. The primary endpoint was time to biochemical or clinical failure. The prespecified non-inferiority margin was 4% at five years, corresponding to a critical HR limit of 1.338. Physician-recorded toxicity was measured according to the RTOG morbidity scale and patient-reported outcome measurements with the Prostate Cancer Symptom Scale (PCSS) questionnaire. A total of 1,200 participants were randomly assigned to conventional fractionation ($n = 602$) or ultra-hypofractionation ($n = 598$), of whom 1,180 (591 conventional fractionation and 589 ultra-hypofractionation) constituted the per-protocol population. Eighty-nine percent ($n = 1,054$) of participants were intermediate risk and 11% ($n = 126$) were high risk. Median follow-up time was 5.0 years (IQR 3.1 to 7.0). The estimated failure-free survival at five years was 84% (95% CI 80 to 87) in both treatment groups, with an adjusted HR of 1.002 (95% CI 0.758 to 1.325; $p = 0.99$). There was weak evidence of an increased frequency of physician-reported acute RTOG grade 2 or worse urinary toxicity in the ultra-

hypofractionation group at end of radiotherapy (158 [28%] of 569 participants vs. 132 [23%] of 578 participants; $p = 0.057$). There were no significant differences in grade 2 or worse urinary or bowel late toxicity between the two treatment groups at any point after radiotherapy, except for an increase in urinary toxicity in the ultra-hypofractionation group compared to the conventional fractionation group at 1-year follow-up (32 [6%] of 528 participants vs. 13 [2%] of 529 participants; ($p = 0.0037$). There were observed no differences between groups in frequencies at 5 years of RTOG grade 2 or worse urinary toxicity and bowel toxicity. Patient-reported outcomes revealed significantly higher levels of acute urinary and bowel symptoms in the ultra-hypofractionation group compared with the conventional fractionation group but no significant increases in late symptoms were found, except for increased urinary symptoms at 1-year follow-up, consistent with the physician-evaluated toxicity. The authors concluded that ultra-hypofractionated radiotherapy is non-inferior to conventionally fractionated radiotherapy for intermediate-to-high risk prostate cancer as it relates to failure-free survival and therefore, their results support the use of ultra-hypofractionation for radiotherapy of prostate cancer.

Clinical Practice Guidelines

American Urological Association (AUA)/American Society for Radiation Oncology (ASTRO)

The 2022 AUA/ASTRO guideline for localized prostate cancer strongly recommends utilization of dose escalation when EBRT is the primary treatment for individuals with prostate cancer. Additionally, clinicians should utilize available target localization, normal tissue avoidance, simulation, advanced treatment planning/delivery, and image-guidance procedures to optimize the therapeutic ratio of EBRT delivered for prostate cancer. This guideline was also endorsed by the Society of Urologic Oncology (Eastham et al., 2022).

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for prostate cancer states that SBRT is acceptable in practices with appropriate technology, physics, and clinical expertise (2024).

Definitive Treatment of Renal Cancer

Siva et al. (2024) conducted the FASTRACK II international, non-randomized clinical trial to evaluate the efficacy of SABR as a treatment alternative for individuals with primary renal cell cancer who are not suitable for surgery and have limited curative options. The phase 2 study took place in seven centers in Australia and one center in the Netherlands. Seventy participants 18 years of age or older with primary renal cell cancer (single lesion) confirmed by biopsy and an ECOG performance status of 0-2, who declined surgery or were medically inoperable, or at high risk of complications from surgery were included in the study. A multidisciplinary decision that treatment was warranted was also required. Exclusion criteria included tumors larger than 10cm, tumors abutting the bowel, previous high dose RT to an overlapping area, previous systemic treatment for renal cell cancer, and an estimated glomerular filtration rate (eGFR) of less than 30 mL/min per 1.73 m². Primary endpoint was local control. Before enrollment, 49 (70%) of 70 participants had documented serial growth on initial surveillance imaging. Forty-nine (70%) of 70 participants were male and 21 (30%) were female. Median tumor size was 4.6 cm (IQR 3.7–5.5). All participants enrolled had T1–T2a and N0–N1 disease. Twenty-three participants received single-fraction SABR of 26 Gy and 47 received 42 Gy in three fractions. Median follow-up was 43 months (IQR 38–60). Local control at twelve months from treatment commencement was 100% ($p < 0.0001$). Seven (10%) participants had grade 3 treatment-related adverse events, with no grade 4 adverse events observed. Grade 3 treatment-related adverse events were nausea and vomiting (three [4%] participants), abdominal, flank, or tumor pain (four [6%]), colonic obstruction (two [3%]), and diarrhea (one [1%]). No treatment-related or cancer-related deaths occurred. The authors concluded SABR can be considered a proven modality for inoperable participants with larger renal cell cancer tumors or in a location not amenable to thermal ablation. The authors recommend a future randomized trial. Study limitations include lack of randomization, small sample size, and lack of control group.

Clinical Practice Guidelines

International Society of Stereotactic Radiosurgery (ISRS)

An ISRS systematic review and guideline for SBRT for primary renal cell carcinoma developed by Siva et al. (2024) states surgery is the standard of care but SBRT can be an alternative for individuals who are medically inoperable, decline surgery, or are high risk. The summary of recommendations are as follows:

- Optimal dose regimens for SBRT in patients with primary renal cell carcinoma include 26 Gy in one fraction if the tumor is ≤ 4 –5 cm and 42–48 Gy in three fractions if the tumor is > 4 –5 cm, or potentially 40 Gy in five fractions if the dose constraints for OAR cannot be met for three fractions. (Strength of recommendation: moderate).
- A routine post-SBRT biopsy should not be performed to evaluate response and is only recommended in patients with imaging findings concerning for disease progression. (Strength of recommendation: strong).
- For patients with a solitary kidney, SBRT is an approach associated with both excellent local control and acceptable renal function preservation (except in patients with stages 4 and 5 chronic kidney disease); technical approaches to

reduce the volume of irradiated kidney, particularly in the intermediate dose-wash region, is recommended. (Strength of recommendation: strong).

- Optimal post-treatment follow-up schedule after SBRT for primary renal cell carcinoma includes cross-axial imaging of the abdomen, including both kidneys and adrenals every six months and surveillance scans including chest imaging at a minimum. (Strength of recommendation: moderate).

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for kidney cancer state SBRT should be considered as the primary radiation modality unless precluded by anatomic site, proximity to OARs, or previous treatment. For non-surgical candidates, definitive radiation using SBRT may be considered for individuals with T1 tumors (< 7 cm in diameter). Tumors abutting the bowel should be considered not amenable to SBRT and current data is insufficient to consider SBRT in tumors larger than 7 mm (NCCN, 2025).

Extracranial Oligometastatic Disease

Harrow et al. (2022) states the Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastases (SABR-COMET) trial was amended in 2016 to extend follow-up to 10 years, this report contains oncologic outcomes beyond five years. Ninety-nine participants with primary tumor sites in the lung (n = 18), breast (n = 18), colon (n = 18), prostate (n = 16), and other (n = 29), were randomized into two arms, palliative standard-of-care treatment versus SABR to all metastases plus standard-of-care. The primary endpoint was OS and secondary endpoints were PFS, toxicity, QOL and time to new metastases. Eight-year OS was 27.2% in the SABR arm versus 13.6% in the control arm. Eight-year PFS estimates were 21.3% versus 0.0%, respectively. Rates of grade ≥ 2 acute or late toxic effects were 30.3% versus 9.1%, with no new grade 3 to 5 toxic effects. FACT-G QOL scores declined over time in both arms, but there were no differences in QOL scores between arms. The use of systemic therapy overall was similar between arms, but participants in the SABR arm were less likely to require cytotoxic chemotherapy. The authors concluded SABR had significant improvements in OS and PFS. Additionally, there were no new safety signals detected with extended follow-up. Limitations include several participants who were either lost to follow-up or died before the last report, and the trial included multiple histologies which limits conclusions that can be made about specific histologies. The authors recommend future larger studies.

Marvaso et al. (2021) conducted a systemic review and meta-analysis to better define the role of SBRT in individuals with oligorecurrent prostate cancer. All prospective studies including prostate cancer individuals with nodal and/or bone oligometastases and one to five lesions were considered eligible. Six studies published between 2013 and 2020 were included in the review. Data from 445 individuals, of which 396 received SBRT (67 in randomized studies and 329 in observational studies) were incorporated. Five studies considered local PFS and reported values close to 100%, one study reported a value of 80% in the observational arm. Benefit in terms of biochemical PFS brought by SBRT was apparent in all studies. The difference in cumulative probabilities between the comparator arm and the interventional arm was maintained after 24 months from baseline. All studies but one considered toxicity among the endpoints of interest. Most events were classified as either G1 or G2, and the only G ≥ 3 adverse event was reported in one trial. The authors concluded that SBRT is safe and has an almost nonexistent toxicity risk that makes it the perfect candidate for the optimal management of individuals with oligometastatic prostate cancer. A limitation of the study noted by the authors is the absence of a control group comparing SBRT with an active treatment. (Ost et al., 2018, which was previously cited in this policy, was included in this systematic review and meta-analysis).

Palma et al. (2020) reported extended outcomes (greater than 40 months after completion of accrual) from the SABR-COMET trial. The SABR-COMET trial was a multi-center, randomized phase II, open-label, trial to assess standard of care palliative treatments with or without SABR in participants with a controlled primary tumor and up to five metastatic lesions (Palma 2012). Eligible participants were randomized to either standard of care palliative treatments (control group) or standard of care plus SABR to all sites of metastatic disease (SABR group). The control group received radiotherapy that was delivered according to the standard principles of palliative radiation. The recommended treatment fractionations depended upon the tumor location and indication, and prescribed doses ranged from 8 Gy in one fraction to 30 Gy in ten fractions. The SABR group received stereotactic radiation to all sites of metastatic disease, with the goal of achieving disease control while minimizing potential toxicities. The allowable doses ranged from 30–60 Gy in three to eight fractions, depending upon target size and location. Participants were seen every three months after randomization for the first two years, and every six months thereafter. A total of 99 participants were enrolled at ten centers; 33 were randomly assigned to the control group and 66 to the SABR group. The primary tumor types were breast (n = 18), lung (n = 18), colorectal (n = 18), prostate (n = 16), and other (n = 29). Ninety-three percent (92/99) of the participants had one to three metastases. In the initial report (Palma 2019), the use of SABR demonstrated a 13-month improvement in median OS after a median follow-up of 28 months. In the subsequent report of extended outcomes, the median follow-up period was 51 months.

(95% CI, 46 to 58 months). The primary outcome event, death (all cause), occurred in 24 (73%) of 33 participants in the control group and 35 (53%) of 66 participants in the SABR group. The median OS was 28 months (95% CI, 19 to 33) in the control group versus 41 months (26–not reached) in the SABR group (HR, 0.57, 95% CI, 0.30 to 1.10; $p = 0.090$). The 5-year OS rate was 17.7% in the control group (95% CI, 6% to 34%) vs. 42.3% in SABR group (95% CI, 28% to 56%; $p = 0.006$). The 5-year PFS rate was not reached in the control group (3.2%; 95% CI, 0% to 14% at 4 years with last patient censored) and 17.3% in the SABR group (95% CI, 8% to 30%; $p = 0.001$). There were no new grade 2-5 adverse events and no differences in QOL between arms. The authors concluded that with extended follow-up, participants with controlled primary tumors and one to five oligometastases who received SABR demonstrated a 22-month improvement in median OS compared with participants who received a standard-of-care approach alone, corresponding to an absolute survival benefit of 25% at five years. Furthermore, they reported that there were no new safety concerns detected during the extended follow-up period.

In 2019, Gomez et al., reported extended outcomes from a previously published multi-center, phase II, RCT. The original study (Gomez 2016) evaluated PFS after aggressive local consolidative therapy (LCT) versus maintenance therapy or observation (MT/O) for individuals with stage IV NSCLC with ≤ 3 metastases remaining after front line systemic therapy. That trial was closed early after it demonstrated an 8-month benefit in PFS for participants who received LCT compared to participants who received MT/O; the median PFS was 11.9 months in the LCT arm (90% CI, 5.72 to 20.90 months) versus 3.9 months in the MT/O arm ($p = 0.005$). The extended outcomes included PFS, OS, toxicity, and the appearance of new lesions. A total of 49 participants (LCT arm, $n = 25$; No LCT arm, $n = 24$) were included in this analysis. The median follow-up time was 38.8 months (range, 28.3 to 61.4 months), the PFS benefit was durable (median, 14.2 months [95% CI, 7.4 to 23.1 months] with LCT vs. 4.4 months [95% CI, 2.2 to 8.3 months] with MT/O; $p = 0.022$). There was an OS benefit in the LCT arm (median, 41.2 months [95% CI, 18.9 months to not reached] vs. 17.0 months [95% CI, 10.1 to 39.8 months] with MT/O; $p = 0.017$). No additional grade 3 or greater toxicities were observed. Survival after progression was longer in the LCT arm (37.6 months with LCT vs. 9.4 months with MT/O; $p = 0.034$). Of the 20 participants who experienced progression in the MT/O arm, nine received LCT to all lesions after progression, and the median OS was 17 months (95% CI, 7.8 months to not reached). The authors concluded that in individuals with oligometastatic NSCLC that did not progress after front-line systemic therapy, LCT prolonged PFS and OS compared to MT/O. (This study is included in the I ISRS guideline below).

Iyengar et al. (2018) conducted a single-center, phase II, randomized trial to determine if noninvasive SABR prior to maintenance chemotherapy in individuals with non–progressive limited metastatic NSCLC after induction therapy led to significant improvements in PFS. Participants were eligible if they were 18 years or older, had a KPS score of 70 or better, had biopsy-proven metastatic NSCLC (primary plus up to five metastatic sites with no more than three sites in the liver or lung) and the tumors did not possess EGFR-targetable or ALK-targetable mutations but did achieve a partial response or stable disease after induction chemotherapy. The primary end point was PFS; secondary end points included toxic effects, local and distant tumor control, patterns of failure, and OS. A total of 29 participants (nine women and 20 men) were enrolled; 14 participants with a median age of 63.5 years (range, 51.0-78.0 years) were allocated to the SABR-plus-maintenance chemotherapy arm, and 15 participants with a median age of 70.0 (range, 51.0-79.0 years) were allocated to the maintenance chemotherapy-alone arm. The SABR-plus-maintenance chemotherapy arm had a median of three metastases (range, 2-6) and the maintenance chemotherapy-alone arm had a median of two metastases (range, 2-5). The trial was stopped early after an interim analysis found a significant improvement in PFS in the SABR-plus-maintenance chemotherapy arm of 9.7 months vs. 3.5 months in the maintenance chemotherapy-alone arm ($p = 0.01$). Toxic effects were similar in both arms. There were no in-field failures with fewer overall recurrences in the SABR arm while those participants receiving maintenance therapy alone had progression at existing sites of disease and distantly. The authors concluded that consolidative SABR prior to maintenance chemotherapy appeared beneficial, nearly tripling PFS in those with limited metastatic NSCLC compared with maintenance chemotherapy alone, with no difference in toxic effects. The irradiation prevented local failures in original disease, the most likely sites of first recurrence. In addition, PFS for individuals with limited metastatic disease appears similar PFS in individuals with a greater metastatic burden, further supporting the potential benefits of local therapy in limited metastatic settings. (This study is included in the ISRS guideline below).

In 2017, Ruers et al., published updated outcomes from a previously conducted a multi-center phase II randomized trial. The original study investigated the possible benefits of radiofrequency ablation (RFA) in individuals with non-resectable colorectal liver metastases. A total of 119 participants with unresectable colorectal liver metastases (< 10 metastases and no extrahepatic disease) participated in the study. Fifty-nine participants were randomized to systemic treatment alone and 60 participants were randomized to systemic treatment plus aggressive local treatment by radiofrequency ablation \pm resection. The authors reported that the primary end point (30-month OS $> 38\%$) was met (Ruers 2012). In this updated report, the authors report long-term OS results. At a median follow up of 9.7 years, 92 of 119 (77.3%) participants had died: 39 of 60 (65.0%) in the combined modality arm and 53 of 59 (89.8%) in the systemic treatment arm. Almost all participants died of progressive disease (35 participants in the combined modality arm, 49 participants in the systemic

treatment arm). There was a statistically significant difference in OS in favor of the combined modality arm (HR, 0.58, 95% CI, 0.38 to 0.88, $p = 0.01$). Three-, five-, and eight-year OS were 56.9% (95% CI, 43.3% to 68.5%), 43.1% (95% CI, 30.3% to 55.3%), 35.9% (95% CI, 23.8% to 48.2%), respectively, in the combined modality arm and 55.2% (95% CI, 41.6% to 66.9%), 30.3% (95% CI, 19.0% to 42.4%), 8.9% (95% CI, 3.3% to 18.1%), respectively, in the systemic treatment arm. Median OS was 45.6 months (95% CI, 30.3 to 67.8 months) in the combined modality arm vs. 40.5 months (95% CI, 27.5 to 47.7 months) in the systemic treatment arm. The authors concluded that this randomized study demonstrated that aggressive local treatment could prolong OS in individuals with unresectable colorectal liver metastases.

Mokhles et al. (2016) conducted a systematic review and meta-analysis to evaluate evidence on the clinical effectiveness of intensive follow-up after curative surgery for primary colorectal cancer. The primary outcome was the OS difference between the existing monitoring strategy compared with a more intensive monitoring strategy (i.e., measurement of carcinoembryonic antigen and/or CT to detect asymptomatic metastatic disease earlier). Searches were conducted using MEDLINE (Ovid), Embase, the Cochrane Library and Web of Science, Scopus, CINAHL (EBSCO), PubMed publisher, Google Scholar, LILACS, SciELO and ProQuest for randomized comparisons of increased intensity monitoring compared with a contemporary standard policy after resection of primary colorectal cancer. Among 7,081 publications, there were 22 relevant articles, with 16 randomized comparisons and 11 that included survival data. More intensive monitoring advanced the diagnosis of recurrence by a median of ten (IQR 5 to 24) months. In ten of 11 studies, there was no demonstrable difference in OS. Seven RCTs, published from 1995 to 2016, randomly assigned 3,325 individuals to a monitoring protocol made more intensive by introducing new methods or increasing the frequency of existing follow-up protocols versus less invasive monitoring. No detectable difference in OS was associated with more intensive monitoring protocols (HR, 0.98, 95% CI 0.87 to 1.11). The authors concluded that based on pooled data from randomized trials, the anticipated survival benefit from surgical treatment resulting from earlier detection of metastases has not been achieved.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)/European Society for Radiotherapy and Oncology (ESTRO)

Iyengar et al. (2023), developed an ASTRO/ESTRO guideline that provides recommendations based on a systematic review of the literature regarding local therapy for the treatment and management of extracranial oligometastatic NSCLC. A summary of the guideline recommendations are as follows:

- For oligometastatic NSCLC, definitive local therapy is recommended only for patients having up to five distant metastases, diagnosed with appropriate imaging. Implementation remark: Despite some prospective trials including patients with up to five extracranial metastases, most patients enrolled had one to two treated oligometastatic lesions, which should be factored into decision-making. (Strength of recommendation: strong; quality of evidence: moderate).
- For patients with oligometastatic NSCLC, highly conformal RT approaches and minimally invasive techniques for surgery are recommended to minimize morbidity. (Strength of recommendation: strong; quality of evidence: moderate).
- For patients with oligometastatic NSCLC, a risk adapted approach using stereotactic RT (preferred), hypofractionated RT, or alternatively definitive chemoradiation based on the location and burden of disease is recommended. (Strength of recommendation: strong; quality of evidence: high).
- For patients with oligometastatic NSCLC, definitive local RT should use doses and fractionations which achieve durable local control. (Strength of recommendation: strong; quality of evidence: high).
- Implementation remarks:
 - Durable local control defined as minimum 85% local control at 2 years.
 - Higher BED10 (typically > 75 Gy) with SBRT alone is associated with optimal local control.
 - Lower BED10 (50-75 Gy range) is associated with acceptable local control, typically in the setting of combination systemic therapy and SBRT.

International Stereotactic Radiosurgery Society (ISRS)

Mayinger et al. (2023) developed a ISRS practice guideline related to SBRT for lung oligo-metastases. Thirty-five studies (27 retrospective-, five prospective, and three randomized trials) were included in the review that reported on treatment of > 3600 patients and > 4650 metastases. The authors concluded that SBRT is an effective local treatment modality with high local control rates and low risk of radiation-induced toxicities. A total of 21 practice recommendations covering the areas of staging & patient selection, SBRT treatment, and follow-up were developed and summarized below:

- For patients diagnosed with pulmonary oligometastatic disease and an indication for definitive local therapy after discussion in a multidisciplinary tumor board, SBRT and pulmonary metastasectomy are recommended as evidence-based local treatment modalities based on prospective randomized evidence. (Level of evidence: high; strength of recommendation: strong).

- For patients diagnosed with pulmonary oligometastatic disease and an indication for definitive local therapy after discussion in a multidisciplinary tumor board, the optimal patient-individual local treatment modality SBRT versus pulmonary metastasectomy should be discussed in a multidisciplinary setting and should consider the patients' preference. (Level of evidence: moderate; strength of recommendation: strong).
- For patients diagnosed with pulmonary oligometastatic disease and an indication for definitive local therapy, SBRT of a single pulmonary metastasis of peripheral location and maximum diameter of 5 cm is recommended as one of the standard of care treatment options based on a favorable safety and efficacy profile (Level of evidence: moderate; strength of recommendation: strong).
- For patients diagnosed with two to five pulmonary oligometastases and an indication for definitive local therapy, simultaneous SBRT can be considered if normal tissue constraints can be met. (Level of evidence: moderate; strength of recommendation: strong).
- For patients diagnosed with pulmonary oligometastatic disease and an indication for definitive local therapy, SBRT of pulmonary metastasis with ultracentral location is potentially associated with an increased risk of severe toxicity and the choice of SBRT as definitive local therapy should be carefully evaluated. (Level of evidence: moderate; strength of recommendation: strong).
- For patients diagnosed with oligometastatic disease and an indication for definitive local therapy of pulmonary metastases, SBRT in a single-fraction can be considered if pulmonary metastases are small, peripherally located, distant to critical serial organs at risk and without broad chest wall contact. (Level of evidence: high; strength of recommendation: strong).

Glomus Jugulare Tumors

Ong et al. (2022) performed a systematic review and meta-analysis to evaluate SRS as a treatment for glomus jugulare tumors (GJTs). An online search for articles was executed in March 2019 and the final analysis included 23 studies with a total of 460 patients. Average rates of tinnitus, hearing loss, and lower cranial nerve deficit as presenting symptoms were 56%, 56%, and 42%, respectively. Overall clinical status improvement rate after treatment was 47%. Rates of tinnitus, hearing loss, and lower cranial nerve improvement after treatment were 54%, 28%, and 22%, respectively. The mean follow-up time across studies was 47 months (range, 4-268 months). The aggregate tumor control rate at the time of follow-up was 95%. The authors concluded that the tumor control rate of 95% and 47% symptomatic improvement suggests that SRS may be a viable alternative to resection and a suitable treatment for GJTs. The authors recommend future studies to further evaluate the role of SRS in the management of GJTs. Limitations include study heterogeneity and lack of RCTs.

Sheehan et al. (2012) conducted a multi-center case series analysis to examine the outcomes of individuals with glomus tumors who underwent RS. A total of 134 patient procedures (132 unique individuals) were included in the study. Prior resection was performed in 51 individuals, and prior fractionated external beam radiotherapy was performed in six individuals. The individuals' median age at the time of RS was 59 years. Forty percent had pulsatile tinnitus at the time of RS. The median dose to the tumor margin was 15 Gy. The median duration of follow-up was 50.5 months (range, five to 220 months). Overall tumor control was achieved in 93% of individuals at last follow-up; actuarial tumor control was 88% at five years post RS. Absence of trigeminal nerve dysfunction at the time of RS ($p = 0.001$) and higher number of isocenters ($p = 0.005$) were statistically associated with tumor progression-free tumor survival. Individuals demonstrating new or progressive cranial nerve deficits were also likely to demonstrate tumor progression ($p = 0.002$). Pulsatile tinnitus improved in 49% of individuals who reported it at presentation. New or progressive cranial nerve deficits were noted in 15% of individuals; improvement in preexisting cranial nerve deficits was observed in 11% of individuals. None of the individuals died as a result of tumor progression. The authors concluded that GKS was a well-tolerated management strategy that provided a high rate of long-term glomus tumor control, symptomatic tinnitus improved in almost one-half of the individuals, and overall neurological status and cranial nerve function were preserved or improved in the majority of individuals after RS.

Guss et al. (2011) performed a systematic review and meta-analysis regarding management of glomus jugulare with RS. No limits were set on the date of publication or the duration of follow-up. The studies were determined eligible for inclusion if they were original research studies that reported the results of RS for glomus jugulare tumors. Nineteen studies with a total of 335 individuals were included in the meta-analysis. Data on 335 glomus jugulare individuals were extracted, including 278 who had received Gamma Knife and 57 who had received linear accelerator or CyberKnife. The results across all studies found 97% of individuals achieved tumor control, and 95% of individuals achieved clinical control. Eight studies reported a mean or median follow-up time of > 36 months. In these studies, 95% of individuals achieved clinical control and 96% achieved tumor control. The Gamma Knife, LINAC, and CyberKnife technologies all exhibited high rates of tumor and clinical control. Limitations noted include small sample size of the studies and the various treatments received (Gamma Knife, LINAC, or CyberKnife). The authors concluded that because of its high effectiveness,

radiosurgery should be considered for the primary management of GJTs. The authors recommend future prospective studies with larger participant numbers treated with RS as a primary treatment modality and longer follow-up.

Lim et al. (2001) conducted a single-center, retrospective, case series analysis to report their experience with the application of LINAC or CyberKnife modalities for the treatment of glomus jugulare tumors. A total of 13 individuals with 16 tumors were included in this analysis. All individuals were treated with frame-based LINAC or CKRS, with doses ranging from 1,400 to 2,700 cGy. Individuals were assessed for posttreatment side effects, which included hearing loss, tongue weakness, and vocal hoarseness. The individuals' most recent magnetic resonance (MR) images were also assessed for changes in tumor size. The median follow-up duration was 41 months and the mean follow-up period was 60 months. All tumors remained stable or decreased in size on follow-up MR images. All individuals had stable neurological symptoms, and one experienced transient ipsilateral tongue weakness and hearing loss, both of which subsequently resolved. One patient experienced transient ipsilateral vocal cord paresis; however, that individual had received previous external-beam radiation therapy. The authors concluded that their findings support RS as an effective and safe method of treatment for GJTs and results in low rates of morbidity.

Recurrent Gliomas

De Maria et al. (2021) performed a systematic review and meta-analysis to establish safety and efficacy of CyberKnife treatment for recurrent WHO grade III and IV, malignant gliomas of the brain. Thirteen studies (n = 398) from 2000 to 2021 were included. The primary outcomes were median OS, median PFS and median time to progression. Complications, local response, and recurrence were secondary outcomes. Overall survival from initial diagnosis and CyberKnife treatment was 22.6 months and 8.6 months. Median time to progression and median PFS were 6.7 months and 7.1 months. Median OS from CyberKnife treatment was 8.4 months for WHO grade IV gliomas, compared to 11 months for WHO grade III gliomas. Median OS from CyberKnife treatment was 4.4 months for individuals who underwent CyberKnife treatment alone, compared to 9.5 months for individuals who underwent CyberKnife treatment plus chemotherapy. No correlation was observed between median time to recurrence and median OS from CyberKnife. Rates of acute neurological and acute non-neurological side effects were 3.6% and 13%. Rates of corticosteroid dependency and radiation necrosis were 18.8% and 4.3%. The authors determined that using the CyberKnife System for reirradiation of recurrent malignant gliomas provided encouraging survival rates. For individuals with WHO grade III gliomas and individuals who undergo combined treatment with CyberKnife plus chemotherapy, there is a better survival trend. Complication rates were low. The authors recommend further research with larger prospective studies.

Gigliotti et al. (2018) conducted a case series analysis to evaluate the efficacy of SRS and FSRT as salvage therapy for recurrent high-grade glioma, and to examine the overall efficacy of treatment with LINAC-based RS and fractionated radiotherapy. A total of 25 individuals aged 23 to 74 years were re-irradiated with LINAC-based SRS and FSRT. Individuals were treated to a median dose of 25 Gy in 5 fractions. The median OS after (initial) diagnosis was 39 months with an actuarial 1-, 3-, and 5-year OS rates of 88%, 56%, and 30%, respectively. After treatment with SRS or FSRT, the median OS was nine months with an actuarial 1-year OS rate of 29%. Local control, assessed for 28 tumors, after six months was 57%, while local control after one year was 39%. Three individuals experienced LF. There was no evidence of toxicity noted after SRS or FSRT throughout the follow-up period. The authors concluded that SRS and FSRT remain a safe, reasonable, effective treatment option for re-irradiation following recurrent glioblastoma, and treatment volume may predict local control in the salvage setting.

Sharma et al. (2018) conducted a single-center, retrospective, case series analysis to evaluate the role of SRS in individuals with recurrent glioblastoma (GBMs). Individuals' electronic medical records were retrospectively reviewed to obtain demographic, imaging, and clinical data. OS and PFS from the date of salvage SRS were the primary and secondary endpoints, respectively. A total of 53 individuals with rGBM underwent salvage SRS targeting 75 lesions. The median tumor diameter and volume were 2.55 cm³ and 3.80 cm³, respectively. The median prescription dose was 18 Gy (range, 12 to 24 Gy) and the homogeneity index was 1.90 (range, 1.11 to 2.02). The median OS after salvage SRS was estimated to be 11.0 months (95% CI 7.1 to 12.2) and the median PFS after salvage SRS was 4.4 months (95% CI 3.7 to 5.0). A KPS score \geq 80 was independently associated with longer OS, while small tumor volume (< 15 cm³) and less homogeneous treatment plans (homogeneity index > 1.75) were both independently associated with longer OS (p = 0.007 and 0.03) and PFS (p = 0.01 and 0.002, respectively). Based on these factors, two prognostic groups were identified for PFS (5.4 vs. 3.2 months), while three were identified for OS (median OS of 15.2 vs. 10.5 vs. 5.2 months). The authors concluded that good performance, smaller tumor volumes, and treatment at higher homogeneity indices were associated with longer OS and/or PFS despite multiple prior treatments for rGBM, and that for individuals with rGBM and those clinical characteristics, SRS is a reasonable salvage treatment option.

Imber et al. (2017) conducted a single-center, retrospective, case series analysis to identify proper indications, efficacy, and anticipated complications of SRS for rGBM. Individuals with pathologically confirmed glioblastoma/gliosarcoma who received comprehensive or radiosurgical care at the center were included in the analysis. The partitioning

deletion/substitution/addition algorithm to identify potential predictor covariate cut points and Kaplan-Meier and proportional hazards modeling to identify factors associated with post-SRS and postdiagnosis survival. A total of 174 individuals with glioblastoma (median age, 54.1 years) underwent SRS a median of 8.7 months after initial diagnosis. Seventy-five percent had one treatment target (range, 1 to 6), and median target volume and prescriptions were 7.0 cm³ (range, 0.3 to 39.0 cm³) and 16.0 Gy (range, 10 to 22 Gy), respectively. Median OS was 10.6 months after SRS and 19.1 months after diagnosis. Kaplan-Meier and multivariable modeling revealed that younger age at SRS, higher prescription dose, and longer interval between original surgery and SRS are significantly associated with improved post-SRS survival. Forty-six individuals (26%) underwent salvage craniotomy after SRS, with 63% showing radionecrosis or mixed tumor/necrosis vs 35% showing purely recurrent tumor. The necrosis/mixed group had lower mean isodose prescription compared with the tumor group (16.2 vs. 17.8 Gy; $p = 0.003$) and larger mean treatment volume (10.0 vs. 5.4 cm³; $p = 0.009$). The authors concluded that GKRS may benefit a subset of focally recurrent individuals, particularly those who are younger with smaller recurrences. The authors also stated that higher prescriptions are associated with improved post-SRS survival and do not seem to have greater risk of symptomatic treatment effect.

Maranzano et al. (2011) conducted a single-center case series analysis to evaluate long-term outcomes in individuals with rGBM and re-irradiated with RS or fractionated stereotactic radiotherapy. A total of 22 individuals were treated with RS or FSRT for 24 lesions of recurrent glioblastoma. The male/female ratio was 14:8, median age 55 years (range, 27 to 81), and median KPS90 (range, 70 to 100). The majority of the cases (77%) was in recursive partitioning analysis classes III or IV. RS or FSRT was chosen according to lesion size and location. Median time between primary radiotherapy and re-irradiation was 9 months. Median doses were 17 Gy and 30 Gy, whereas median cumulative normalized total dose was 141 Gy and 98 Gy for RS and fractionated stereotactic radiotherapy, respectively. All individuals that accepted RS had a cumulative normalized total dose of more than 100 Gy, whereas only a few (44%) of FSRT individuals had a cumulative normalized total dose exceeding 100 Gy. Median follow-up from re-irradiation was 54 months. At the time of analysis, all individuals had died. After re-irradiation, one (4%) lesion was in partial remission, 16 (67%) lesions were stable, and the remaining seven (29%) were in progression. Median duration of response was six months, and median survival from re-irradiation 11 months. Three of 13 (23%) individuals that accepted RS developed asymptomatic brain radionecrosis. The cumulative normalized total dose for the three individuals was 122 Gy, 124 Gy, and 141 Gy, respectively. In one case, the volume of the lesion was large (14 cc), and in the other two the interval between the first and second cycle of radiotherapy was short (five months). The authors concluded that re-irradiation with RS and FSRT is feasible and effective in individuals with recurrent glioblastoma, and apart from the importance of an accurate patient selection, cumulative radiotherapy dose and a correct indication for RS or FSRT must be considered to avoid brain toxicity.

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines state that recurrence of glioma can be managed with reirradiation and should be performed with highly focused techniques such as SRS for lower volume disease (NCCN, 2024).

Uveal Melanoma

In a systematic review and meta-analysis, Parker et al. (2020) evaluated the clinical outcomes of individuals with uveal melanomas or intraocular metastases treated with GKRS. The primary outcomes analyzed were local tumor control and tumor regression. Fifty-two studies were eligible for systematic review, 1,010 individuals had uveal melanoma and three with intraocular metastasis. The authors found that 840 of 898 individuals (0.96, 95% CI 0.94-0.97; $I^2 = 16\%$) from 19 studies had local control, and 378 of 478 individuals (0.81, 0.70-0.90; $I^2 = 83\%$) from 16 studies experienced tumor regression. The authors concluded GKRS is an effective primary method of treating uveal melanomas and intraocular metastases, with reliable tumor control rates and a similar efficacy and survival profile to outcomes for plaque brachytherapy and charged particle therapy. The authors recommend future research focusing on generating level 1 evidence (RCTs) of the efficacy of GKRS in treating ocular tumors, measuring overall complication rates of GKRS, providing consistent reporting of visual acuity measurements after GKRS, and evaluating low-dose regimens to reduce radiation-induced side-effects and subsequent vision loss. (Fakiris et al. (2007) previously cited in this policy is included in this review).

Yazici et al. (2017) conducted a multi-center, retrospective, case series analysis to evaluate treatment outcomes of individuals with uveal melanoma and treated with SRS or fractionated stereotactic radiation therapy (FSRT). Treatment was administered with CyberKnife. Primary endpoints were local recurrence-free survival (LRFS) and enucleation-free survival. Secondary endpoints included OS, DFS, distant metastasis-free survival (DMFS), visual acuity, and late treatment toxicity. Local control was defined as the lack of tumor progression (i.e., an increase in tumor volume). Complete response was defined as the disappearance of the tumor, and partial response as a > 50% decrease in the tumor volume. A total of 181 individuals (182 uveal melanomas) who underwent SRS/FSRT were included in the analysis. The median patient age was 54 years (range, 18 to 82 years) and 104 (58%) were male. The median tumor diameter and

thickness was 10 mm (range, 2 to 12 mm) and 8.0 mm (range, 1.5 to 18 mm), respectively. According to Collaborative Ocular Melanoma Study criteria, tumor size was small in 1%, medium in 49.5%, and large in 49.5% of the individuals. Seventy-one tumors received < 45 Gy, and 111 received ≥ 45 Gy. Median follow-up time was 24 months (range, 2 to 79 months). Complete and partial response was observed in eight and 104 eyes, respectively. The rate of 5-year OS was 98%, DFS 57%, LRFS 73%, DMFS 69%, and enucleation-free survival 73%. There was a significant correlation between tumor size and DFS, SRS/FSRT dose and enucleation-free survival; and both were prognostic for LRFS. Enucleation was performed in 41 eyes owing to progression in 26 and complications in 11. The authors concluded that using SRS/FSRT, better control of large tumors was achieved with ≥ 45 Gy in three fractions. They also recommend increasing the radiation dose, as well as limiting the maximum eye and lens dose to 50 Gy and 15 Gy, respectively, to increase the eye retention rate, and that additional studies with longer follow-up should be conducted.

Dieckmann et al. (2003) conducted a case series analysis to evaluate local tumor control and radiogenic side effects after fractionated LINAC based SRS for uveal melanoma. A total of 90 individuals with uveal melanoma and treated at a LINAC with 6 MV were included in the analysis. The head was immobilized with a modified stereotactic frame system (BrainLAB). For stabilization of the eye position a light source was integrated into the mask system in front of the healthy or the diseased eye. A mini-video camera was used for on-line eye movement control. Tumors included in the study were either located unfavorably with respect to macula and optical disc (< 3 mm distance) or presented with a thickness > 7.0 mm. Median tumor volume was 305 +/-234 mm³ (range, 70 to 1,430 mm³), and mean tumor height was 5.4 +/-2.3 mm (range, 2.7 to 15.9 mm). Total doses of 70 (single dose 14 Gy @ 80% isodose) or 60 Gy (single dose 12 Gy @ 80% isodose) were applied in five fractions within 10 days. The first fractionation results in total dose (2 Gy) of 175 Gy for tumor and 238 Gy for normal tissue, corresponding values for the second fractionation schedule are 135 and 180 Gy, respectively. After a median follow-up of 20 months (range, 1 to 48 months) local control was achieved in 98% (n = 88). The mean relative tumor reductions were 24%, 27%, and 37% after 12, 24 and 36 months. Three individuals (3.3%) developed metastases. Secondary enucleation was performed in seven individuals (7.7%). Long term side effects were retinopathy (25.5%), cataract (18.9%), optic neuropathy (20%), and secondary neovascular glaucoma (8.8%). The authors concluded that fractionated LINAC based stereotactic photon beam therapy in conjunction with a dedicated eye movement control system is a highly effective method to treat unfavorably located uveal melanoma, and that total doses of 60 Gy (single dose 12 Gy) are considered to be sufficient to achieve good local tumor control.

Clinical Practice Guidelines

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for uveal melanoma states SRS is the least often used form of definitive radiotherapy of primary or recurrent intraocular tumors. SRS planning, fiducial marker use and tumor localization are generally consistent with particle beam therapy approaches (NCCN, 2024).

Palliative Treatment of Bone Metastases of the Spine

In an open-label, multicenter, randomized controlled phase 2/3 trial conducted by Sahgal et al. (2021), the efficacy of SBRT versus conventional external beam radiotherapy (cEBRT) in individuals with painful spinal metastasis was compared. Participants (n = 229) were randomized to receive either SBRT (24 Gy in two daily fractions) or cEBRT (20 Gy in five daily fractions). Primary outcome was complete response rate for pain at the treated site three months after radiotherapy. Inclusion criteria included individuals aged 18 and older with MRI-confirmed painful spinal metastasis (pain score ≥ 2 on the Brief Pain Inventory), involving no more than three consecutive vertebral segments, an ECOG performance status of 0-2, and a Spinal Instability Neoplasia Score of less than 12. Those with neurologically symptomatic spinal cord or cauda equina compression were excluded. At three months, 40 (35%) of 114 participants in the SBRT group, and 16 (14%) of 115 participants in the cEBRT group had a complete response for pain (p = 0.0002). This significant difference was maintained in multivariable-adjusted analyses (p = 0.0003). The most common grade 3–4 adverse event was grade 3 pain (five [4%] of 115 participants in the cEBRT group vs five (5%) of 110 participants in the SBRT group). No treatment-related deaths were observed. The authors concluded that SBRT at a dose of 24 Gy in two fractions is superior to cEBRT at a dose of 20 Gy in five fractions in improving complete pain relief in those with painful spinal metastases and may be a more effective palliative treatment option. Limitations include that the open-label design could introduce bias, small sample size, and short follow-up duration.

The single institution, non-blinded, randomized phase II trial by Sprave et al. (2018) compared the effectiveness of palliative SBRT and 3D-CRT for managing pain for individuals with previously untreated spinal bone metastasis. The primary objective was to evaluate pain relief in participants (n = 55) with histologically or radiologically confirmed painful spinal metastases following treatment with either SBRT or 3DCRT. Pain relief was measured using the visual analog scale (VAS) at three and six months post-treatment. Participants were randomly assigned to receive either single-fraction SBRT (24 Gy) or 3D-CRT (30 Gy in 10 fractions). At three months both groups showed pain reduction but the SBRT group experienced a faster decrease in pain scores (p = 0.01). However, there was no significant difference in VAS

scores between the groups at three months ($p = 0.13$). At six months, the SBRT group reported significantly lower pain scores compared to the 3D-CRT group ($p = 0.002$). Pain response at three months showed a trend towards better pain response in the SBRT group ($p = 0.057$). At six months, the pain response in the SBRT group was significantly better ($p = 0.003$). There were no significant differences in opioid usage observed between the groups at three months ($p = 0.761$) and six months ($p = 0.174$). No participants in the SBRT group had severe (grade ≥ 3) toxicities. The authors concluded that SBRT provided faster and more lasting pain relief compared to 3D-CRT for individuals with spinal metastases and may be a more effective option for managing pain in these individuals. Limitations include small study size, trial was non-blinded and conducted at a single institution, and short follow-up period.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's guideline on palliative radiation therapy for symptomatic bone metastases (Alcorn et al., 2024) provides recommendations using consensus-building methodology based on a systematic review by AHRQ (Skelly et al., 2023). The authors note that developing the most favorable RT regimen requires an assessment including prognosis, any previous RT doses, normal tissue risks, quality of life, and patient values and goals. Per the guideline:

- For patients with symptomatic spine bone metastases, including those causing compression of the spinal cord or cauda equina, RT is recommended to improve ambulatory status, sphincter function, and reduce pain. Implementation remark: Before initiating RT, evaluation for spine stability and surgery are necessary. (Strength of recommendation: strong; quality of evidence: high).
- In patients with spine bone metastases causing compression of the spinal cord or cauda equina who are not eligible for initial surgical decompression and are treated with conventional palliative RT, 800 cGy in 1 fraction, 1600 cGy in 2 fractions, 2000 cGy in 5 fractions, or 3000 cGy in 10 fractions are recommended. (Strength of recommendation: strong; quality of evidence: high).
- For patients with symptomatic bone metastases treated with SBRT, 1200 to 1600 cGy in 1 fraction (nonspine) and 2400 cGy in 2 fractions (spine) are recommended. (Strength of recommendation: strong; quality of evidence: moderate).
- For patients with symptomatic bone metastases with ECOG PS 0-2, receiving no surgical intervention, and absent neurological symptoms, SBRT is conditionally recommended over conventional palliative RT. Implementation remark: Other factors to consider include life expectancy, tumor radiosensitivity, and metastatic disease burden. (Strength of recommendation: conditional; quality of evidence: moderate).

National Comprehensive Cancer Network (NCCN)

Per NCCN guidelines regarding radiation therapy for metastatic spinal tumors, stereotactic approaches such as SRS and SBRT may be preferred for those where ablation of the tumor is a goal of treatment, life expectancy is three months or more, the tumors are radioresistant (e.g., renal cell, melanoma, sarcoma, hepatocellular, some colorectal, and NSCLC cases), and in certain individuals for optimal pain relief (NCCN, 2024).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

The FDA has approved a number of devices for use in SBRT and SRS. Refer to the following website for more information (use product codes MUJ and IYE): <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>. (Accessed October 8, 2024)

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Policy History/Revision Information

Date	Summary of Changes
04/01/2025	Applicable Codes <ul style="list-style-type: none"> Added HCPCS code G0563

Date	Summary of Changes
	Supporting Information <ul style="list-style-type: none">Archived previous policy version CS180OH.C

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state (Ohio Administrative Code [OAC]), or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state (OAC), or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state (OAC), or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state (OAC), or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare uses InterQual® for the primary medical/surgical criteria, and the American Society of Addiction Medicine (ASAM) for substance use, in administering health benefits. If InterQual® does not have applicable criteria, UnitedHealthcare may also use UnitedHealthcare Medical Policies, Coverage Determination Guidelines, and/or Utilization Review Guidelines that have been approved by the Ohio Department for Medicaid Services. The UnitedHealthcare Medical Policies, Coverage Determination Guidelines, and Utilization Review Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.