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

Note: This policy applies to individuals 19 years of age and older. Stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) are covered without further review for individuals younger than 19 years of age.

Stereotactic radiation therapy including SRS and 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 SRS and SBRT is considered proven and medically necessary for the following other indications:

- Bone metastasis (non-spine) when all the following criteria are met:
  - Symptomatic
  - Up to five fractions
- Chordoma and chondrosarcoma
- Craniopharyngioma
- Definitive treatment of the following:
  - Hepatocellular carcinoma without evidence of regional or distant metastasis
  - Intrahepatic bile duct cancer (cholangiocarcinoma) for unresectable tumors
  - Non-small cell lung cancer when all the following criteria are met:
    - Stage I or stage IIA with negative mediastinal lymph nodes
    - Tumor size is less than or equal to five centimeters

        - Individual is medically inoperable or has made a decision not to pursue surgery after an appropriate consultation
    - Pancreatic adenocarcinoma without evidence of distant metastasis
    - Prostate cancer without evidence of distant metastases (see criteria below for oligometastatic disease)
    - Renal cancer when all the following criteria are met:
        - Stage I
        - Individual is a non-optimal surgical candidate
    - Small cell lung cancer when **all** the following criteria are met:
        - Stage I or node negative stage IIA
        - Lesion is medically inoperable, or the 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 three months since original tumor was treated definitively, with no progression at primary site
    - KPS score greater than or equal to 70% or ECOG performance status of zero to two
    - Life expectancy is at least six months
    - Has a total of up to five metastatic lesions
    - Each lesion is less than or equal to five centimeters 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 five fractions for an entire course of treatment regardless of number of lesions treated
- Glomus jugulare tumors
- Neurologic conditions (epilepsy, Parkinson's disease, essential tremor) that are refractory to medical treatment and/or invasive surgical interventions
- Recurrent gliomas
- Spinal lesions when one of the following criteria are met:
    - Palliative treatment of symptomatic spinal bone metastasis when all the following criteria are met (for oligometastatic disease, refer to the criteria above):
        - Using five fractions or less
        - Individual has no spinal cord compression or cauda equina compression
    - Primary spinal lesions that cannot be treated with surgical resection or 3D conformal techniques
- To treat a previously irradiated field
- Uveal melanoma

Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service. Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the services requested.

The patient's medical record must contain documentation that fully supports the medical necessity for the requested services. This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures. Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available upon request.

Definitions

Definitive Treatment: Radiation treatments for cancer with a curative intent (NCCN, 2025; Landsteiner et al., 2023). The National Cancer Institute (NCI) defines curative intent therapy as a treatment designed to eliminate a disease or illness, aiming for a full recovery while maintaining a satisfactory quality of life (QOL). In cancer care, the suitability of a curative approach depends on the specific type and stage of cancer (NCI, 2025).

Oligometastatic Disease (OMD): The oligometastatic disease state was first defined by Hellman in 1995 and refers to a stage of disease where cancer has spread beyond the site of origin but is not yet widely metastatic. In such a state of limited metastatic disease burden, it is hypothesized that eradication of all sites of metastatic disease could result in long-term survival, or even cure, in a subgroup of individuals (Palma et al, 2012).

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)
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

HCPCS 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 five 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

International Stereotactic Radiosurgery Society (ISRS)

Tuleasca et al. (2025) performed a systematic review and meta-analysis of the literature related to planned subtotal resection for large VSs followed by SRS to the residual tumor to summarize outcomes and provide treatment recommendations. Twelve series met inclusion criteria reporting on treatment outcomes for 677 patients. Overall tumor control was 89.9%, with tumor stability observed in 43.9% and tumor reduction in 39.9% post-SRS. Facial nerve functional preservation immediately after microsurgery was 88.0%, improving to 94.4% at last follow-up. Cochlear functional preservation immediately after microsurgery was 58.8%, decreasing to 57.4% at last follow-up. The authors concluded that the cranial nerve sparing approach with planned subtotal microsurgical resection and SRS to the residual tumor resulted in a highly satisfactory outcome of facial and cochlear functional preservation and achieved a high rate of tumor control. For management of large VSs with combined microsurgery and SRS, the ISRS recommends:

- Nerve-sparing intracapsular microsurgical resection with facial nerve preservation. Strength of recommendation: strong; level of evidence: III.
- Upfront SRS should be considered as opposed to observation due to the potential to optimize long-term local control and within three to six months following subtotal resection. Strength of recommendation: conditional; level of evidence: III.
- Radiation therapy (RT) alone can be used as upfront treatment in patients with medical comorbidities precluding upfront surgery. Strength of recommendation: strong; level of evidence: III.
- A first post-operative MRI should be performed within three to six months to determine residual disease and an evaluation for post-operative SRS. Strength of recommendation: strong; level of evidence: III.

Bone Metastasis (Non-Spine)

Nguyen et al. (2019) conducted a phase II RCT that compared pain relief from high-dose single-fraction SBRT with conventional multifraction radiotherapy (MFRT) in individuals with mostly non-spine bone metastases. The primary endpoint was pain response. Secondary endpoints were quality of life (QOL) and symptom burden, narcotic use post-treatment, toxic effects, local control of irradiated metastases, and overall survival (OS). Inclusion criteria included those age 18 or older with a diagnosis of cancer and painful bone metastases with more than three months life expectancy. Concurrent treatment of three radiation fields or less was allowed. Prior radiation to the site, untreated spinal cord compression, pathologic fracture at the site, and previous radioactive isotope therapy within 30 days of randomization were the study exclusions. One hundred and sixty participants were randomized to receive either SBRT or MFRT. In this phase II portion of a phase II/III noninferiority trial of 96 men and 64 women, 81 participants received SBRT and 79 received MFRT. Among evaluable participants who received treatment per protocol, the single-fraction group had more pain responders than the MFRT group (complete response + partial response) at two weeks [34 of 55 (62%) versus 19 of 52 (36%)] ($p = .01$), three months [32 of 44 (73%) versus 17 of 35 (49%)] ($p = .04$), and nine months [17 of 22 (77%) versus 12 of 26 (46%)] ($p = .04$). A subdistribution hazard ratio (HR) of 0.71 (95% CI, 0.36-1.39) indicated that SBRT had 29% less risk of failure relative to the MFRT after considering death as a competing risk. The upper 95% CI for subdistribution HR was less than the noninferiority margin of 1.5, indicating that SBRT was noninferior to MFRT. No differences were found in treatment-related toxic effects or QOL scores after SBRT versus MFRT. The authors concluded

that high-dose, single-fraction SBRT appeared to be an effective option for treating those with painful bone metastases. Among those evaluated, SBRT showed higher rates of pain response (both complete and partial) compared to MFRT and should be considered for individuals with a relatively long expected survival. Limitations comprised the inclusion of metastases from various types of primary cancer and the attrition rate rose with increasing follow-up time due to the nature of having metastatic cancer. The authors recommended larger phase III studies.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's guideline on palliative RT 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, QOL, and patient values and goals. Per the guidelines:

- 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.
- For patients with symptomatic bone metastases treated with SBRT, 1200 to 1600 centigray (cGy) in one fraction (nonspine) and 2400 cGy in two fractions (spine) are recommended. Implementation remark: Other established SBRT dose and fractionation regimens (e.g., two to five fractions) with similar biological effective doses (BEDs) may be an option based on patient tumor and normal tissue factors, and physician experience. Strength of recommendation: strong; quality of evidence: moderate.
- For patients with symptomatic bone metastases with ECOG PS zero to two, 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.
- For patients with symptomatic nonspine bone metastases that would benefit from reirradiation to the same site, single-fraction (800 cGy in one fraction) or multifraction conventional palliative RT (2000 cGy in five fractions or 2400 cGy in six fractions) are recommended. Strength of recommendation: strong; quality of evidence: moderate.

National Comprehensive Cancer Network (NCCN)

Per NCCN guidelines, SRS or SBRT may be considered for metastatic bone disease, especially for oligometastases. (NCCN, 2025).

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 five 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 cubic centimeters (cm^3), 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 included 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 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 RT. The median tumor volume was 8.0 cm^3 (range 0.9-28.2 cm^3), 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 RT 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 noted 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 Gamma Knife surgery (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 five- and 10-year survival rates after GKS were 80% and 53%, respectively. The actuarial five- and 10-year local tumor control rates after single or multiple GKS sessions were 76% and 67%, respectively. All individuals with low-grade chondrosarcomas achieved good local tumor control. A tumor volume of less than 20 ml significantly affected the high rate of local tumor control ($p = 0.0182$). 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 cm^3. The median dose to the tumor margin was 16 Gy. Transient symptomatic AREs developed in only one individual. The actuarial local tumor control for chondrosarcomas at five years was 80 ±10.1%. For chordomas both the actuarial tumor control and survival was 62.9 ±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.

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 individuals) 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: six-83%), while the improvement in the visual field was 22% (95% CI: zero-51%). Regarding endocrine function, the new-onset hypopituitarism rate was found to be 5% (95% CI: zero-11%). Relative to FSRT effectiveness, the pooled estimate of the complete tumor response rate was 17% (95% CI: four-30%), and the tumor progression rate was 7% (95% CI: one-13%). Also, a three-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 recommended further research to assess the clinical utility and associated risks. Limitations included 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 six-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 increased to 77.3% and 61.2% at five and 10 years, respectively. The OS rates were 91.5% and 83.9% at the five- 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 GKRS 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 cm^3 (range, 0.07 to 8.0). The median prescription dose delivered to the tumor margin was 13.0 Gy (range, nine 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 five years. The three- and five-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.

Definitive Treatment of Hepatocellular Carcinoma (HCC) Without Evidence of Regional or Distant Metastasis/Intrahepatic Bile Duct Cancer

In a randomized, open-label, controlled trial, Xi et al. (2025) evaluated the safety and efficacy of radiofrequency ablation (RFA) compared to SBRT in the treatment of recurrent HCC with small solitary nodules (≤ 5 cm). The inclusion criteria consisted of individuals (age 18-75) with recurrent small HCC without extrahepatic metastasis or vascular invasion at recurrence, KPS score of 90 or more, and liver function of Child-Ough class A. Concomitant severe dysfunction of other systems and contraindications for SBRT or RFA were the primary exclusion criteria. Local progression-free survival (LPFS) was the main endpoint. Secondary endpoints were PFS, OS, local control rate, and safety. Eighty-three participants were assigned to the SBRT group and 83 were assigned to the RFA group. After a median follow-up time of 42.8 and 42.9 months in the SBRT and RFA groups, respectively, SBRT demonstrated a significantly better LPFS than that of RFA [HR, 0.45 (95% CI, 0.24 to 0.87); $p = 5.014$]. The two-year LPFS rates were 92.7% (95% CI, 87.3 to 98.5) with SBRT and 75.8% (95% CI, 67.2 to 85.7) with RFA. The median PFS time of the SBRT and RFA groups was 37.6 (95% CI, 26.0 to 49.2) and 27.6 (95% CI, 20.3 to 34.8) months, respectively [HR, 0.76 (95% CI, 0.50 to 1.15); $p = 5.190$]. Nine participants in the SBRT group and 10 in the RFA group died during the follow-up. The two-year OS rates were 97.6% (95% CI, 94.3 to 100.0) in the SBRT group and 93.9% (95% CI, 88.9 to 99.2) in the RFA group [HR, 0.91 (95% CI, 0.37 to 2.22); $p = 5.830$]. The incidences of both acute and late adverse events were comparable between the groups ($p = 5.436$ and $p = 5.715$, respectively). The authors concluded that in individuals with small, single recurrent HCC, SBRT provided better LPFS than RFA, especially in HCC ≤ 2 cm. Additionally, PFS, OS, and safety were similar between the two treatments. Limitations included the single-center nature of the study and small sample size.

Bisello et al. (2021) conducted a systematic review to evaluate the efficacy and safety of SBRT as treatment for individuals with intrahepatic cholangiocarcinoma. Inclusion criteria consisted of studies in English that had at least 10 participants with inoperable, non-metastatic, primary, or recurrent intrahepatic cholangiocarcinoma. Studies regarding SBRT were included even if preceded or followed by systemic treatments or other local therapies. Studies on adjuvant SBRT after radical surgery were excluded. Overall survival was the primary endpoint, and local control, PFS, and

treatment related toxicity were the secondary endpoints. Six studies (n = 145 individuals) met inclusion criteria. SBRT was frequently used as a salvage treatment, since 28.6-66.7% of individuals received previous systemic or local treatments. The median SBRT dose was 45 Gy delivered in three to five fractions. The median follow-up was 16 months, and median OS time was 14 months. In one of the included studies, SBRT was significantly superior in terms of OS compared with both chemoradiation and transarterial radio embolization (TARE). The one-year local control rate was 85% in one study, and one-year PFS rates were 50 and 68% in two studies, respectively. Toxicity was generally not reported in detail or was reported including other sites of biliary cancers. The meta-analysis was not conducted. The authors concluded that SBRT yields comparable outcomes to other treatments, with the added benefit of a brief and non-invasive therapy and should be considered for selected individuals with intrahepatic cholangiocarcinoma. Limitations included that there was limited evidence available regarding the effectiveness of SBRT in intrahepatic cholangiocarcinoma, small sample sizes, and the retrospective design of most of the studies.

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 two-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 participant experienced radiation-induced liver disease with acute grade ≥ 3 toxicity one month after SBRT. In addition, one participant 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 two-year and three-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 was an effective treatment modality.

Wang et al. (2020) conducted a systematic review and meta-analysis aimed at comparing the safety and efficacy of 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 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 2cm. 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 included the retrospective nature of the studies in the review, and the population in each study was different which may result in heterogeneity. The authors recommended 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 one-, two-, and three-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 one-, two-, and three-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 one- and two-year OS rates and one-, two-, and three-year local control rates. In addition, radiation dose showed no difference for OS and a marginal difference for one-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 for 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)

The ASTRO guideline for primary liver cancers provided evidence-based recommendations for treatment of HCC and IHC with EBRT. The recommendations are as follows (not all-inclusive):

- Use of EBRT as a potential first-line treatment in those with liver-confined HCC who are not candidates for curative therapy and catheter-based therapies are being considered, EBRT is a potential first-line single therapy option. Strength of recommendation- strong; quality of evidence- moderate.
- For those with liver-confined HCC and incomplete response to thermal ablation or catheter-based therapies, EBRT is recommended as a consolidative treatment option. Strength of recommendation: strong; quality of evidence: moderate.
- EBRT is recommended as a salvage treatment option for those with locally recurrent HCC after surgery, thermal ablation, or catheter-based therapies. Strength of recommendation: strong; quality of evidence: low.
- For those with liver-confined HCC, for whom EBRT is recommended, dose-escalated ultra- or moderately hypofractionated EBRT is recommended, with choice of regimen based on tumor location, underlying liver function, and available technology. Strength of recommendation: strong; quality of evidence: moderate.
- For patients with unresectable IHC, induction chemotherapy followed by consolidation with EBRT, alone or in combination with chemotherapy, is recommended. Implementation remark: For patients who are not candidates for induction chemotherapy, EBRT alone or in combination with chemotherapy should be considered. Strength of recommendation: strong; quality of evidence: moderate.

Additionally, the authors recommended future high-quality RCTs to further define the role of EBRT in HCC and IHC treatment (Apisarnthanarax et al., 2022).

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 one to nine 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 biliary tract cancers (intrahepatic cholangiocarcinoma) state that SBRT is preferred for unresectable tumors if dose constraints can be met. Image-guided RT is recommended when SBRT is used to improve accuracy and reduce toxicity (NCCN, 2025).

The NCCN guidelines for HCC state 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 three to five fractions and is often used for those with one to three tumors. The treatment of intrahepatic tumors with hypofractionation using photons or protons is a viable option. However, it is recommended to undergo this treatment at centers with specialized experience (NCCN, 2025).

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

Zhang et al. (2022) conducted a systematic review and meta-analysis of individuals with inoperable early-stage NSCLC to compare local control, OS, and toxicities between SBRT and RFA. Articles published in English in peer-reviewed journals, individuals with stage I NSCLC who were not a candidate for surgery, and the studies that reported on clinical outcomes were eligible for the review. Case reports, comments, editorials, reviews, studies with less than 15 individuals treated with SBRT or less than five individuals treated with RFA, SBRT studies with fraction number > 8 and fraction dose ≤ 8 Gy, and studies involving other treatments were excluded. Eighty-seven SBRT studies (12,811 patients) and 18 RFA studies (1,535 patients) met the eligibility criteria. For SBRT, the local control rates (with 95% CI) at one, two, three, and five years were 98% (97-98%), 95% (95-96%), 92% (91-93%), and 92% (91-93%), respectively, which were significantly higher than those for RFA [75% (69-82%), 31% (22-39%), 67% (58-76%), and 41% (30-52%), respectively] ($p < 0.01$). There were no significant differences in short-term OS between SBRT and RFA [one-year OS rate: 87% (86-88%) versus 89% (88-91%), $p = 0.07$; two-year OS rate: 71% (69-72%) versus 69% (64-74%), $p = 0.42$]. Regarding long-term OS, the three- and five-year OS rates for SBRT were 58% (56-59%) and 39% (37-40%), respectively, which were significantly ($p < 0.01$) superior to those for RFA [48% (45-51%) and 21% (19-23%), respectively]. The most common complication of SBRT was radiation pneumonitis (grade ≥ 2), making up 9.1% of patients treated with SBRT, while pneumothorax was the most common complication of RFA, making up 27.2% of patients treated with RFA. The authors concluded that SBRT demonstrates superior local control and long-term OS rates compared to RFA, while short-term OS rates remain similar. The authors suggested large-scale RCTs are needed to further compare the efficacy of SBRT and RFA. Limitations

included the heterogeneity of the studies, and the included studies were published between 2000 to 2020 and SBRT and RFA may have evolved during that time-frame.

Ball et al. (2019) performed a phase III, 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 QOL. 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 zero or one, 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 (HR 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 participant who had previous cancer and small sample size. In 2023, Bucknell et al. conducted an analysis of the TROG 09.02 (CHISEL) phase III trial to compare pulmonary function tests and the six-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 versus 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 participant 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 participant had regional nodal recurrence and two had distant metastases; in the SABR group, one participant 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%) participant died of surgical complications and 12 (44%) participants had grade 3–4 treatment-related adverse events. Grade 3 events occurring in more than one participant 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 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 individual's risk for toxicity. SRT was well tolerated, and all but one individual 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 one and a half to two 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 participant had a primary tumor failure; the estimated three-year primary tumor control rate was 97.6% (95% CI, 84.3% to 99.7%). Three participants had recurrence within the involved lobe; the three-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 three-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 three-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 versus central tumors (MS 33.2 versus 24.4 months, p = 0.697). Grade 3 to 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 the 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 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 BED was 111 Gy (range, 57 to 180 Gy) based on α/β = 10. For the comparison to surgery, the five-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 five-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, 2025).

National Institute for Health and Care Excellence

NICE developed a guideline for the diagnosis and management of lung cancer that states for those with stage I - IIA (T1a -T2b, N0, M0) NSCLC in whom lobectomy is contraindicated or declined, radical radiotherapy may be offered with SABR or sublobar resection (NICE, 2019; updated 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 (CFRT) with concurrent chemotherapy 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 ¾ toxicity were the secondary outcomes. For SBRT, the median dose was 30 Gy, and the most common regimen was 30 Gy/five 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 two-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 one-year OS was 53.7% (95% CI, 39.3%-67.9%) for SBRT versus49.3% (95% CI, 39.3%-59.4%) for CFRT and was not statistically significant. The random effects estimate for acute grade 3/4 toxicity was5.6% (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 ¾ toxicity and no change in one -year OS or late toxicity. Limitations included the phase one or two studies and retrospective nature of the SBRT studies, whereas the CRFT studies were all phase II or phase III. The authors recommended future quality studies to evaluate SBRT for these individuals.

In a retrospective review, Zhong et al. (2017) compared SBRT with CFRT 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 RT delivered at ≤ 2 Gy was deemed CFRT Overall survival was the primary outcome. The total number of individuals included in the review was 8,450, CFRT = 7,819 and SBRT = 631. Receipt of SBRT was associated with superior OS in

the multivariate analysis (HR, 0.84; 95% CI, 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 versus 11.6 months) and the 2-year OS rate (21.7% versus 16.5%) were significantly higher with SBRT versus CFRT. The authors concluded SBRT was superior to OS when compared with CFRT, and an additional benefit of SBRT was the shorter duration of treatment. Additionally, the authors recommended future randomized trials to evaluate these results. Limitations included 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/m^2) followed by a one-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 zero at both follow-ups; p > 0.05 for both). Participants reported a significant improvement in pancreatic pain (p = 0.001) four 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 versus 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 SBRT 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 two to three 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 (five of 21 versus zero 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, one-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, one-year OS, median PFS, and one-year PFS for BRPC versus LAPC individuals was 16.4 months versus 15 months, 72.2% versus 68.1%, 9.7 versus 9.8 months, and 42.8% versus 41%, respectively (all p > 0.10). BRPC individuals who underwent R0 resection had improved median OS (19.3 versus 12.3 months; p = 0.03), one-year OS (84.2% versus 58.3%; p = 0.03), and one-year PFS (56.5% versus 25.0%; p < 0.0001), respectively, compared with all nonsurgical individuals. The one-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 = seven). Most individuals were treated with fractionated SBRT to 36 Gy/3 fractions (n = seven) and the remainder with single fraction to 24 Gy (n = five). 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 = three of 12) of individuals, a complete pathologic response was achieved, and an additional 16.7% (n = two of 12) demonstrated < 10% viable tumor cells. Kaplan-Meier estimated median progression free survival is 27.4 months. OS was 92%, 64%, and 51% at one-, two-, and three-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.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

The ASTRO guideline developed by Palta et al. (2019) for pancreatic cancer recommends (not all-inclusive):

- Following surgical resection of pancreatic cancer, adjuvant SBRT is only recommended on a clinical trial or multi-institutional registry. Strength of recommendation: strong; quality of evidence: very low.
  For patients with borderline resectable pancreatic cancer and select locally advanced pancreatic cancer appropriate for downstaging prior to surgery, a neoadjuvant therapy regimen of systemic chemotherapy followed by multifraction SBRT is conditionally recommended. Strength of recommendation: conditional; quality of evidence: low.
- For patients with locally advanced pancreatic cancer not appropriate for downstaging to eventual surgery, a definitive therapy regimen of systemic chemotherapy followed by either conventionally fractionated RT with chemotherapy, dose-escalated chemoradiation, or multifraction SBRT without chemotherapy is conditionally recommended. Strength of recommendation: conditional; quality of evidence: low.

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for pancreatic adenocarcinoma state 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 subsequent therapy, SBRT may be used if not previously given and if the primary site is the sole site of progression (NCCN, 2025).

Definitive Treatment of Prostate Cancer Without Evidence of Distant Metastasis

In 2024, ECRI released a revised analysis of SBRT for localized prostate cancer that included evidence from two systematic reviews, three RCTs and two nonrandomized comparison studies. The analysis gave a favorable rating regarding the safety and efficacy of SBRT compared to other treatments for localized prostate cancer. All studies consistently found minimal differences between treatments, except that prostatectomy patients experienced significantly higher rates of erectile dysfunction compared to SBRT patients.

A phase III RCT (PACE-B) conducted by van AS (2024) assessed non-inferiority of five-fraction SBRT compared to conventionally or moderately hypofractionated radiotherapy for biochemical or clinical failure. Participants (n = 874) were randomized into two groups (CRT = 441, SBRT = 433) in 38 centers. Inclusion criteria included those 18 years or older, with prostate adenocarcinoma, WHO performance status of zero to two, with a life expectancy of five or more years. Participants had T1 or T2 disease low or intermediate risk. Those with Gleason grade four or higher disease, history of previous pelvic radiotherapy or treatment for prostate cancer, bilateral hip prostheses, or any NCCN high risk factors were excluded. Androgen deprivation therapy was not permitted. Median age was 69.8 years, median PSA 8.0 ng/mL, NCCN risk group was 9.3% low, 90.7% intermediate. After 74.0 months median follow-up, five-year biochemical/clinical failure free-rate (95% CI) was CRT: 94.6% (91.9%, 96.4%) versus SBRT: 95.8% (93.3%, 97.4%). SBRT was non-inferior to CRT with an unadjusted HR 0.73 (90% CI: 0.48, 1.12; p-value for non-inferiority 0.004). To five years, cumulative rate of late RTOG grade two or worse genitourinary toxicity was CRT: 18.3% (95% CI 14.8, 22.5%) versus SBRT: 26.9% (95% CI 22.8, 31.5%) (p < 0.001) and for gastrointestinal toxicity was CRT: 10.2% (95% CI 7.7, 13.5%) versus SBRT: 10.7% (95% CI 8.1, 14.2%) (p = 0.94). The authors concluded that for those with low/intermediate risk localized prostate cancer, SBRT (five-fraction) is non-inferior to CRT for biochemical/clinical failure and is an effective treatment option which offered similar efficacy with greater convenience for individuals.

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 five-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, five and seven-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 –zero to two. 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 five 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 versus 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 one-year follow-up [32 (6%) of 528 participants versus 13 (2%) of 529 participants; (p = 0.0037)]. There were no observed 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 one-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 supported 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 2025 NCCN guidelines for prostate cancer states that SBRT is acceptable for treatment of primary prostate cancer across all risk groups and for locoregional and/or distant metastases in practices with appropriate technology, physics, and clinical expertise. Metastasis-direct therapy with SBRT is recommended for the following:

- For limited metastatic disease (e.g., oligometastatic) when ablation is the goal.

- With limited progression (e.g., oligoprogression) or limited residual disease on otherwise effective systemic therapy (e.g., consolidation) where PFS is the goal.
- In a symptomatic patient where the lesion occurs in or immediately adjacent to a previously irradiated treatment field.
- At physician discretion for more durable control of pain than achieved with typical palliative regimens used in some randomized trial data, which should be considered particularly in prostate cancer where natural history of advanced disease can be very long.

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 II 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 zero to two, 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. The 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 four to six 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 future randomized trials. Study limitations include lack of randomization, small sample size, and lack of control group.

Suleja et al. (2024) conducted a systematic review and meta-analysis to evaluate the current evidence for treatment of individuals with localized renal cell carcinoma (RCC) using SBRT. Studies that assessed safety and clinical effectiveness in those with localized RCC using SBRT in single-arm trials or compared with other standard-of care therapies and reported on local control, renal function preservation, PFS, OS and rates of grade ≥ 3 adverse events were included in the review. A total of 13 prospective single-arm studies (308 individuals, 312 renal lesions) published between 2015 and 2024 were included in the meta-analysis. The most common clinical stages observed were T1a and T1b. The median diameter of the irradiated tumors ranged between 1.9 and 5.5 cm in individual studies. Grade ≥ 3 adverse effects were reported in 15 patients, and their estimated rate was 0.03 (95% CI: 0.01-0.11; n = 291). One- and two-year local control rates were 0.98 (95% CI: 0.95-0.99; n = 293) and 0.97 (95% CI: 0.93-0.99; n = 253), while one- and two-year OS rates were 0.95 (95% CI: 0.88-0.98; n = 294) and 0.86 (95% CI: 0.77-0.91; n = 224). There was no statistically significant heterogeneity, and the estimations were consistent after excluding studies at a high risk of bias in a sensitivity analysis. The authors concluded that the short-term outcomes indicate that SBRT has a low rate of high-grade adverse effects, excellent local control, and is an effective treatment option for certain individuals with localized RCC who are inoperable or those who decline surgery. The authors noted that long-term data from RCTs is needed, and surgical treatment remains the standard of care in operable individuals. Limitations included short-term follow-ups and a lack of RCTs. Siva et al. 2024 is included in this systematic review and meta-analysis.

Clinical Practice Guidelines

International Society of Stereotactic Radiosurgery (ISRS)

An ISRS systematic review and guideline for SBRT for primary RCC 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 RCC 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 organs at risk (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, are recommended. Strength of recommendation: strong

- Optimal post-treatment follow-up schedule after SBRT for primary RCC 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

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 or 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).

Definitive Treatment of Small Cell Lung Cancer (SCLC)

Safavi et al. (2021) conducted a systematic review and meta-analysis to evaluate and summarize oncologic and toxicity outcomes for those with inoperable T1-2N0M0 SCLC. Inclusion criteria consisted of peer-reviewed journal articles that assessed less than or equal to eight fractions of SABR for T1-2N0M0 SCLC. Excluded from the analysis were reviews, editorials, commentaries, guidelines, prefaces, case series with fewer than five patients, and studies published in languages other than English. Eleven retrospective studies were included in the review and seven were included in the meta-analysis. Inoperability was noted as the indication for SABR in 94% (75-100%) of individuals. Median follow-up and tumor size were 19.5 months (11.9-32) and 24 mm (19-29), respectively. Chemotherapy and PCI use rates were 44.1% (95% CI, 27.0-61.9%) and 13.8% (95% CI, 0.4-41.2%), respectively. Local control was 97.3% (95% CI, 92.3-99.8%) at one year and 95.7% (95% CI, 74.2-100.0%) at two years. Overall survival was 86.3% (95% CI, 74.4-94.9%) at one year and 63.7% (95% CI, 45.7-79.9%) at two years. Nodal and distant recurrence rates were 17.8% (95% CI, 7.5-31.2%) and 26.9% (95% CI, 7.4-53.0%), respectively. The rates of grade 1, grade 2, and grade 3 toxicity (CTCAE) were 12.6% (95% CI, 6.7-19.9%), 6.7% (95% CI, 3.3-11.2%), and 1.4% (95% CI, 0.0-5.3%), respectively. No grade 4 or 5 events were observed across the studies. The authors concluded that for inoperable early-stage, node-negative SCLC, SABR is locally effective with limited toxicity. Limitations included the retrospective nature of the included studies and small sample sizes. The authors suggested conducting future prospective studies to assess the use of SABR for individuals with higher risks of toxicity with surgery or combined chemoradiation.

In 2018, Verma et al. compared SBRT to conventionally fractionated RT for individuals (n = 2,107) with inoperable stage I SCLC. The National Cancer Database was searched (2004 to 2014) for histologically-confirmed T1-2N0M0 SCLC. Inclusion criteria included those with newly-diagnosed, T1-2N0M0 SCLC that received chemotherapy. Those who had surgery, were not receiving EBRT, and/or lacked survival/follow-up information, or received chemotherapy starting less than three months before or less than two months after RT were excluded. Of 2,107 patients, 7.1% underwent SABR/chemotherapy, and 92.9% received CFRT/chemotherapy. The median (interquartile range) dose of SABR was 50 (48-54) Gy in four (three to five) fractions, and 55.8 (45-60) Gy in 30 (30-33) fractions for CFRT. Patients receiving SABR/chemotherapy were more often older, had T1 disease, treated at academic/integrated network facilities, and managed in more recent years ($p < 0.05$ for all). Respective median survival figures were 29.2 versus 31.2 months ($p = 0.77$), which persisted following propensity matching (25.4 versus 34.3 months, $p = 0.85$). On multivariable analysis, radiotherapeutic technique was not associated with OS ($p = 0.95$). According to the authors, for those with stage I SCLC, SABR combined with chemotherapy provided statistically similar outcomes to CFRT combined with chemotherapy. The authors noted that RCTs for this relatively rare scenario would likely have inadequate accrual, and these retrospective data should be strongly considered when advocating for SABR/chemotherapy as the preferred treatment option for this patient group.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

Simone II et al. (2020) developed an ASTRO guideline for RT of SCLC which strongly recommends definitive thoracic RT early in the course of treatment for limited stage SCLC. Furthermore, SBRT or conventional fractionation received a strong recommendation (quality of evidence: moderate) for those with stage I or II node negative disease who are medically inoperable with chemotherapy delivery before or after SBRT.

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for SCLC indicate that the principals of SBRT for SCLC are similar to those for NSCLC. For individuals with stage I-IIA (T1-2, N0, M0) who are medically inoperable, or not surgical candidates may be considered for SBRT to the primary tumor followed by adjuvant systemic therapy. NCCN states that for those SCLC and a small number of BMs, SRS may be appropriate; and SRS is preferred for individuals who develop BMs after PCI (NCCN, 2025).

Neurologic Conditions (Epilepsy, Parkinson's Disease, Essential Tremor)

Dong et al. (2025) performed a systematic review and meta-analysis comparing five surgical methods, open and minimally invasive, used for treatment of individuals with drug-resistant epilepsy. Inclusion criteria consisted of those diagnosed with drug-resistant epilepsy, who were treated with anterior temporal lobectomy (ATL), selective amygdalohippocampectomy (SAH), laser interstitial thermal therapy (LITT), radiofrequency thermocoagulation (RFT), or GKRS and had availability of mean, SD, 95% CI, or median IQR for seizure-free. Studies were excluded if the individual was under 18 years of age, had follow-up of less than one year, lacked qualitative data, had fewer than 10 people, or were case reports, technical notes, repetitive literature, unrelated topics, or articles without full text. A total of 62 studies met inclusion criteria for a total of 5958 individuals. The analysis results indicate that ATL and SAH are the best choice for treating drug-resistant mesial temporal lobe epilepsy in adults. During the overall follow-up period, the seizure free rates for ATL, SAH, LITT, RFT, and GKRS were 62%, 70%, 58%, 47%, and 57%, respectively. Only three studies addressed GKRS, therefore a subgroup analysis based on follow-up time was not performed. The authors concluded that among the surgical treatments included in this review, ATL and SAH were the best in both overall and long-term follow-up. However, the authors note that when choosing a specific treatment, specific situations such as type and location of epileptic seizures should be considered, and a treatment plan developed to maximize effectiveness and reduce risks. Limitations included the limited number of RCTs and lack of unified outcome measures across different studies reduced the ability to analyze adverse effect data, QOL, and cognitive function. The authors recommended future high-quality long-term follow-up studies.

Bilski et al. (2024) conducted a systematic review to evaluate four treatment modalities received by individuals with essential tremors that did not achieve a treatment response to medical management. The methods compared were deep brain stimulation (DBS), SRS, radiofrequency thalamotomy (RF), and focused ultrasound thalamotomy (FUS). Inclusion criteria consisted of prospective and retrospective clinical trials with published results in the English language. Twenty-two studies were included in the review. The results confirm the high efficacy and safety of the SRS procedure in treating drug-resistant intention tremors. The study results present a high response rate reaching 80% and achievement of manual task improvement, lessening of the tremor and increase in the QOL of the majority of the operated individuals. After SRS, a considerable number of individuals showed improvements in activities such as tremor, writing, drawing, and drinking. The authors concluded that SRS is safe and effective for the treatment of ET. Limitations included the small sample sizes of the included studies.

A systematic review and single-arm meta-analysis conducted by Goncalves et al. (2024) aimed to evaluate the efficacy, safety, and long-term impact of SRS, including GKRS, in ET, focusing on tremor control and related adverse effects. Inclusion criteria consisted of randomized and non-randomized studies of four or more participants who had ET and underwent GKRS. Reviews, case reports, letters, comments, and studies not performed only on those with ET were excluded. The main outcomes assessed included the proportion of successful treatments, instances of technical failure, and the frequency of postoperative complications. Treatment was deemed successful if the individual experienced either complete or near-complete resolution of tremors, or demonstrated a positive response or noticeable improvement. As secondary outcomes, the study evaluated the mean difference (MD) scores in specific components of the Fahn-Tolosa-Marin (FTM) clinical rating scale for tremor; specifically, those related to tremor severity, handwriting, drawing, and drinking tasks. Twelve studies with a total of 414 individuals were included in the review, The treatment success rate with SRS was 86.6%. Conversely, the overall failure rate was 13.4%. Post-procedure complications were observed in 9.7% of patients. A meta-analysis of five studies revealed a statistically significant reduction of tremor from the FTM scale after treatment with GKRS (MD -2.1; 95% CI -2.5 to -1.6; $p < 0.01$; $I^2 = 81\%$). A meta-analysis of eight studies revealed a statistically significant reduction in writing tremor from the FTM scale after treatment with GKRS (MD-1.7; 95% CI -2.3 to -1.2; $p < 0.01$; $I^2 = 93\%$). A meta-analysis of six studies revealed a statistically significant reduction in drawing tremor from the FTM scale after treatment with GKRS (MD -1.9; 95% CI -2.5 to -1.4; $p < 0.01$; $I^2 = 80\%$). Finally, a meta-analysis of three studies revealed a statistically significant reduction in drinking tremor from the FTM scale after treatment with GKRS (MD -1.6; 95% CI -1.9 to -1.3; $p < 0.01$; $I^2 = 11\%$).The authors concluded that GKRS for ET had a high overall success rate and low failure rate and was a safe and effective treatment for managing this patient-population. Limitations included the nature of the retrospective studies included in the review, small sample sizes, and lack of tremor data after six and 12 months.

Barbaro et al (2018) conducted a RCT that compared SRS to ATL for the treatment of individuals with pharmacoresistant unilateral MTLE. Adults 18 years or more who were eligible for open surgery had at least three focal-onset seizures in three months with impairment of consciousness occurring during anticonvulsant administration and no neurological or visual deficits were the inclusion criteria. Pregnancy, supratentorial MRI abnormalities, diabetes mellitus, use of vigabatrin, psychiatric diagnoses that could hinder accurate seizure assessment, significant comorbidities, poor compliance, or current drug abuse were the exclusion criteria. The primary outcomes assessed were seizure remission, verbal memory (VM), and QOL at 36-month follow-up. A total of 58 participants (31 in SRS, 27 in ATL) were treated. Sixteen (52%) SRS and 21 (78%) ATL participants achieved seizure remission. Mean VM changes from baseline for 21 English-speaking,

dominant-hemisphere participants did not differ between groups; consistent worsening occurred in 36% of SRS and 57% of ATL participants. Quality of life improved with seizure remission. Adverse events were anticipated cerebral edema and related symptoms for some SRS participants, and cerebritis, subdural hematoma, and others for ATL participants. The authors concluded that ATL offered an advantage over SRS in terms of the proportion of individuals who achieved seizure remission. Both SRS and ATL demonstrated effectiveness and safety as treatment options for MTLE. SRS serves as a viable alternative for participants who have contraindications or are reluctant to undergo open surgery. Limitations included small sample sizes.

Eekers et al. (2018) performed a systematic review to determine the efficacy and treatment-related side effects of SRS for individuals with drug-resistant focal epilepsy. Sixteen studies (n = 170 individuals) were included in the review. Twelve of the 16 studies described a positive effect of radiotherapy on seizure frequency reduction, with 98 of the patients (on average 58%, range 25%-95%) reporting no or rare seizures [defined as radiotherapy-adapted Engel class (RAEC) I and II). In total, 20% (34 individuals) of the individuals needed subsequent surgery due to radionecrosis, cysts formation, edema, and intracranial hypertension or remaining seizures. A dose-effect model was fitted to the available response data in an attempt to derive a relationship between prescribed dose and RAEC frequency. The authors concluded that for those with drug-resistant focal non-neoplastic epilepsy, radiotherapy is a possible treatment option with a favorable effect on seizure outcome. Limitations included a low level of evidence with the absence of control groups.

McGonigal et al. (2017) conducted a systematic review to establish an ISRS guideline for the use of SRS in treating individuals with epilepsy. Fifty-five articles were included in the review; no Level 1 evidence was available. The review consisted of two Level 2 prospective trials specific to mesial temporal lobe epilepsy and two prospective trials with criteria relating to epilepsy associated with hypothalamic hamartoma. For remaining indications including corpus callosotomy as palliative treatment, epilepsy related to cavernous malformation and extra-temporal epilepsy, only Level 4 data was available (case report, prospective observational study, or retrospective case series). The authors concluded that SRS was an effective treatment for controlling seizures in mesial temporal lobe epilepsy that may lead to better neuropsychological outcomes and improved QOL for specific individuals compared to traditional microsurgery. Additionally, SRS offers a more favorable risk-benefit ratio for treating small hypothalamic hamartomas than surgical methods. Limitations included the retrospective nature of the majority of articles included in the review. A formal ISRS guideline was unable to be developed due to lack of non-randomized prospective trials.

Clinical Practice Guidelines

International Stereotactic Radiosurgery Society (ISRS)

Martínez-Moreno et al. (2018) published a systematic review to summarize the current literature and provide consensus guidelines for the ISRS. A total of 34 studies, three prospective, one retrospective comparative and thirty retrospective, were included in the review. The one retrospective comparative study evaluating DBS, RFT, and SRS reported similar tremor control rates, more permanent complications after DBS and RFT, more recurrence after RFT, and a longer latency period to clinical response with SRS. Similar tremor reduction rates in most of the reports were observed with SRS thalamotomy (mean 88%). Clinical complications were rare and usually not permanent (range 0%-100%, mean 17%, median 2%). Follow-up in general was too short to confirm long-term results No meta-analysis was performed. The authors concluded that SRS for tremor is well-tolerated and effective for the treatment of medically refractory tremor. Limitations included small sample sizes and the retrospective nature of most of the studies. The recommendations for management of tremor are as follows (all are level IV evidence):

- SRS is recommended for patients with tremor for whom medical therapy has failed & who are not candidates for invasive surgery.
- SRS should be considered even for patients with tremor for whom medical therapy has failed even if they are candidates for invasive surgery since SRS appears to have a lower level of complications.
- GKRS has been performed with a single 4-mm collimator, single-fraction maximum dose of 130-150 Gy and the lesion made in the ventral intermediate nucleus located using advanced imaging modalities and stereotactic atlases.

Definitive Treatment of Small Cell Lung Cancer (SCLC)

Safavi et al. (2021) conducted a systematic review and meta-analysis to evaluate and summarize oncologic and toxicity outcomes for those with inoperable T1-2N0M0 SCLC. Inclusion criteria consisted of peer-reviewed journal articles that assessed less than or equal to eight fractions of SABR for T1-2N0M0 SCLC. Excluded from the analysis were reviews, editorials, commentaries, guidelines, prefaces, case series with fewer than five patients, and studies published in languages other than English. Eleven retrospective studies were included in the review and seven were included in the meta-analysis. Inoperability was noted as the indication for SABR in 94% (75-100%) of individuals. Median follow-up and tumor size were 19.5 months (11.9-32) and 24 mm (19-29), respectively. Chemotherapy and PCI use rates were 44.1% (95% CI, 27.0-61.9%) and 13.8% (95% CI, 0.4-41.2%), respectively. Local control was 97.3% (95% CI, 92.3-99.8%) at one year and 95.7% (95% CI, 74.2-100.0%) at two years. Overall survival was 86.3% (95% CI, 74.4-94.9%) at one year

and 63.7% (95% CI, 45.7-79.9%) at two years. Nodal and distant recurrence rates were 17.8% (95% CI, 7.5-31.2%) and 26.9% (95% CI, 7.4-53.0%), respectively. The rates of grade 1, grade 2, and grade 3 toxicity (CTCAE) were 12.6% (95% CI, 6.7-19.9%), 6.7% (95% CI, 3.3-11.2%), and 1.4% (95% CI, 0.0-5.3%), respectively. No grade 4 or 5 events were observed across the studies. The authors concluded that for inoperable early-stage, node-negative SCLC, SABR is locally effective with limited toxicity. Limitations included the retrospective nature of the included studies and small sample sizes. The authors suggested conducting future prospective studies to assess the use of SABR for individuals with higher risks of toxicity with surgery or combined chemoradiation.

In 2018, Verma et al. compared SBRT to conventionally fractionated RT for individuals (n = 2,107) with inoperable stage I SCLC. The National Cancer Database was searched (2004 to 2014) for histologically-confirmed T1-2N0M0 SCLC. Inclusion criteria included those with newly-diagnosed, T1-2N0M0 SCLC that received chemotherapy. Those who had surgery, were not receiving EBRT, and/or lacked survival/follow-up information, or received chemotherapy starting less than three months before or less than two months after RT were excluded. Of 2,107 patients, 7.1% underwent SABR/chemotherapy, and 92.9% received CFRT/chemotherapy. The median (interquartile range) dose of SABR was 50 (48-54) Gy in four (three to five) fractions, and 55.8 (45-60) Gy in 30 (30-33) fractions for CFRT. Patients receiving SABR/chemotherapy were more often older, had T1 disease, treated at academic/integrated network facilities, and managed in more recent years ($p < 0.05$ for all). Respective median survival figures were 29.2 versus 31.2 months ($p = 0.77$), which persisted following propensity matching (25.4 versus 34.3 months, $p = 0.85$). On multivariable analysis, radiotherapeutic technique was not associated with OS ($p = 0.95$). According to the authors, for those with stage I SCLC, SABR combined with chemotherapy provided statistically similar outcomes to CFRT combined with chemotherapy. The authors noted that RCTs for this relatively rare scenario would likely have inadequate accrual, and these retrospective data should be strongly considered when advocating for SABR/chemotherapy as the preferred treatment option for this patient group.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

Simone II et al. (2020) developed an ASTRO guideline for RT of SCLC which strongly recommends definitive thoracic RT early in the course of treatment for limited stage SCLC. Furthermore, SBRT or conventional fractionation received a strong recommendation (quality of evidence: moderate) for those with stage I or II node negative disease who are medically inoperable with chemotherapy delivery before or after SBRT.

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines for SCLC indicate that the principals of SBRT for SCLC are similar to those for NSCLC. For individuals with stage I-IIA (T1-2, N0, M0) who are medically inoperable, or not surgical candidates may be considered for SBRT to the primary tumor followed by adjuvant systemic therapy. NCCN states that for those SCLC and a small number of BMs, SRS may be appropriate; and SRS is preferred for individuals who develop BMs after PCI (NCCN, 2025).

Extracranial Oligometastatic Disease

Gooijer et al. (2025) published a systematic review that evaluated efficacy following pulmonary metastasectomy and SBRT in those with oligometastatic colorectal lung metastases. Clinical trials and observational studies published between 2000 and 2023 that assessed outcomes (OS, PFS, or local recurrence rate) after metastasectomy or SBRT were included in the review. Overall survival, PFS, and local recurrence rate were assessed and compared between both groups. A total of 141 studies on metastasectomy (n = 29932) and 16 studies on SBRT (n = 1381) were included in the final analysis. The pooled five-year OS was 52.2% (CI: 49.8–54.5) and 45.0% (CI: 31.2-58.9) following metastasectomy and SBRT, respectively ($p = 0.213$). The pooled five-year PFS was 35.1% (CI: 32.2-38.1) following metastasectomy and 11.7% (CI: 0-38.2) following SBRT ($p < 0.001$). The pooled LRR was 10.5% (CI: 5.5-15.5) following metastasectomy and 28.1% (CI: 20.8-35.4) following SBRT ($p < 0.001$). The average Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) score of the included studies was low. According to the authors, those with oligometastatic colorectal lung metastases may achieve comparable OS whether treated with surgical metastasectomy or SBRT. However, PFS and local recurrence rates tend to favor surgical resection. A meta-analysis was not done because the outcome measures were too similar across studies, and the known prognostic factors were not evenly balanced between the two groups. Limitations include the non-randomized comparison of the two local treatment strategies. The authors recommend future RCTs comparing surgery and SBRT in this patient population.

Persson et al. (2024) conducted a systematic review and meta-analysis of RCTs to evaluate the efficacy and safety of SBRT as metastasis-directed therapy (MDT) for individuals with oligometastatic prostate cancer (OMPC) compared to those with no MDT. Primary outcomes were OS and grade 3 or greater toxicity. Systemic therapy-free survival, QOL, grade 5 toxicity, LC and PFS were secondary outcomes. Seven phase II RCTs with 559 participants were included in the review. Four trials included multiple types of primary cancer. Outcome definitions were heterogeneous except for OS and

toxicity. For OS, only one study reported events in both arms. Meta-analysis of the grade ≥ 3 toxicity results from two trials showed no difference (pooled RR 0.78, 95% CI 0.37-1.65, p = 0.52). Four trials reported significantly longer PFS, with a pooled HR of 0.31 (95% CI 0.21-0.45, p < 0.00001). Risk of bias was of some concerns or high. The quality of evidence was low or moderate. The authors concluded that phase II trials have demonstrated promising enhancements in PFS for various OMPC states without significant toxicity; however, OS comparisons remain inconclusive. Limitations of the study included small sample sizes and varying patient groups and treatment approaches. The authors suggested that future phase III trials are needed and should include larger sample sizes, blinding, and improved adherence to assigned interventions.

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 recommended 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 five-year OS rate was 17.7% in the control group (95% CI, 6% to 34%) versus 42.3% in SABR group (95% CI, 28% to 56%; p = 0.006). The five-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 eight-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 versus 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) versus 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 versus 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).

Sutera et al. (2019) conducted a phase II multicenter trial to assess outcomes, toxicity, and QOL of individuals with oligometastatic cancer who were prospectively treated with SABR. Participants were 18 years of age or older, with oligometastatic (one to five metastases in three or fewer organs) or recurrent cancer, with a Zubrod PS of zero to one, and adequate laboratory parameters. Those with lymphoma, leukemia, multiple myeloma, and central nervous primaries were ineligible. Additionally, any individual with another primary cancer within the last three years, diffuse metastatic spread confined to one organ, pregnancy, sites not treatable with SABR, or severe active co-morbidities were excluded. Participants (n = 147) were seen in follow-up six weeks post SABR, then every three months for three years, and at six-month intervals thereafter. Feasibility of SABR in participants with oligometastatic disease was the primary endpoint. Secondary endpoints were five-year OS, five-year local PFS, QOL, and toxicity. The most common primary tumors included lung (21.8%, non-small cell: n = 29, small cell: n = three), colorectal adenocarcinoma (21.1%), and head and neck (10.9%, squamous cell carcinoma: n = 11). In a median follow-up of 41.3 months (interquartile range: 14.6-59.0), the median OS was 42.3 months (95% CI: 27.4-∞) with a five-year OS of 43%. Five-year local PFS and distant PFS were 74% and 17%, respectively. Acute grade 2+ and 3+ toxicity were 7.5% and 2.0%, respectively, and late grade 2+ and 3+ toxicity were both 1.4%. There was no significant change in QOL at completion and six weeks, three months, and nine months after treatment. At six months and 12 months, participants were found to have statistically significant improvement in patient-reported QOL. The authors concluded that SABR was a feasible and tolerable treatment with minimal acute and late grade 3 toxicity for those with oligometastatic cancer. Limitations included lack of randomization and a heterogenous participant population. The authors recommended future RCTs to support their results.

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, two to six) and the maintenance chemotherapy-alone arm had a median of two metastases (range, two to five). 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 versus 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 to PFS in those 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 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 RFA ±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 versus 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 five 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 Radium Society (ARS)

Amini et al. (2022) developed an ARS Appropriate Use Criteria to evaluate the role of consolidative local therapy for the management of oligometastatic or oligoprogressive NSCLC and provide evidence-based recommendations. The recommendations are as follows (not all-inclusive):

- The panel strongly recommends that consolidative radiotherapy is appropriate for patients with oligometastatic disease (three sites or less, counted after up-front systemic therapy) who have not progressed after two to three months, or two to three cycles, of chemotherapy, provided that all sites are amenable to radiation.
- The panel strongly recommends that consolidative RT is usually appropriate for patients with oligometastatic disease (three sites or less, counted after up-front systemic therapy) who received two to three months of PD-1/PD-L1-based immunotherapy or chemoimmunotherapy with no progression on repeat imaging where the sites are amenable to radiation.
- The panel recommends that consolidative RT in patients with four to five sites of oligometastatic disease (counted after up-front systemic therapy) be considered on a case-by-case basis, owing to the under-representation of these cases in published clinical trials.
- The panel does not currently recommend consolidative RT in patients with six or more sites of metastatic disease outside a clinical trial, rather endorsing systemic therapy alone.
- The panel recommends that RT be considered on a case-by-case basis for oligoprogressive patients harboring limited sites of disease progression while on systemic therapy, provided that other sites of metastatic disease remain controlled.
- In general, if available, the panel strongly recommends enrollment on a clinical trial in the setting of oligometastatic or oligoprogressive disease.

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 two 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.

Lievens et al. (2020) developed a consensus statement for ESTRO-ASTRO to define oligometastatic disease from the pererspective of a radiation oncologist. The authors concluded that based on the current literature, oligometastatic disease could be defined as one to five metastatic lesions, a controlled primary tumor being optional, and where all metastatic sites must be safely treatable. The authors recommended future prospective studies.

International Stereotactic Radiosurgery Society (ISRS)

Mayinger et al. (2023) developed an 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 and 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 OAR and without broad chest wall contact. Level of evidence: high; strength of recommendation: strong

National Comprehensive Cancer Network (NCCN)

NCCN guidelines for kidney cancer recommend considering SBRT for ablative treatment for intact extracranial metastases in individuals with oligometastases unless metastasectomy is planned or SBRT delivery is hindered by factors such as the anatomic location, proximity to OARs, or previous treatments. NCCN states that for prostate cancer, SBRT is recommended for those with limited metastatic disease (e.g., oligometastatic) when ablation is the goal (NCCN, 2025).

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, four to 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 included study heterogeneity and lack of RCTs.

Sheehan et al. (2012) conducted a multi-center case series analysis of 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 EBRT 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 GKRS 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 LINA 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 recommended future prospective studies with larger participant numbers treated with RS as a primary treatment modality and longer follow-up.

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 recommended 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 five fractions. The median OS after (initial) diagnosis was 39 months with an actuarial one-, three-, and five-year OS rates of 88%, 56%, and 30%, respectively. After treatment with SRS or FSRT, the median OS was nine months with an actuarial one-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 (rGBMs). 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 cm^3 and 3.80 cm^3, 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 ≥ 80 was independently associated with longer OS, while small tumor volume (< 15 cm^3) 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 versus 3.2 months), while three were identified for OS (median OS of 15.2 versus 10.5 versus 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, one to six), and median target volume and prescriptions were seven cm^3 (range, 0.3 to 39.0 cm^3) 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 versus 35% showing purely recurrent tumor. The necrosis/mixed group had lower mean isodose prescription compared with the tumor group (16.2 versus 17.8 Gy; $p = 0.003$) and larger mean treatment volume (10.0 versus 5.4 cm^3; $p = 0.009$). 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.

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, 2025).

Spinal Lesions (Primary and Metastatic)

The aim of the multicenter, randomized, phase III trial by Guckenberger et al. (2024) was to evaluate whether SBRT for painful vertebral metastases leads to higher rates of pain improvement compared to cEBRT (control) six months post-treatment. Inclusion criteria consisted of those 18years or older with a diagnosis of a solid tumor, maximum of two painful vertebral metastases, KPS of ≥ 60%, and life expectancy of greater than one year. Exclusion criteria included those with spinal instability, involvement of more than three cervical spine or four thoracic, lumbar, or sacral spine contiguous vertebra, more than two treatment sites, neurologic symptoms, previous RT at the site, or surgery of affected vertebra. Patient-reported pain improvement was the primary end point. Acute and late adverse events, OS, and QOL were

secondary end points. Sixty-three participants were randomized to receive SBRT (n = 33 with 36 metastases) or cEBRT (30 participants with 31 metastases). In the intention-to-treat analysis, the six-month proportion of participants who had metastases with pain reduction by two or more points was significantly higher in the SBRT group versus the control group (69.4% versus 41.9%, respectively; two-sided p = .02). Changes in opioid medication intake relative to baseline were nonsignificant between the groups. No differences were observed in vertebral compression fracture or adverse event rates between the groups. The authors concluded that the dose-intensified SBRT was more effective at improving the pain score than cEBRT at six months without increasing toxicity. Limitations included the small sample size and low compliance of the number of participants in reporting QOL.

Guninski et al. (2024) conducted a systematic review and meta-analysis in preparation for an ESTRO guideline for the treatment of spinal metastases with SBRT. Sixty-nine studies, 7236 metastases in 5736 individuals, were included in the review. SBRT for spine metastases showed high efficacy, with a pooled overall pain response rate of 83% (95% CI 68%-94%), pooled complete pain response of 36% (95% CI: 20%-53%), and one-year local control rate of 94% (95% CI: 86%-99%), although with high levels of heterogeneity among studies (I 2 = 93%, I 2 = 86%, and 86%, respectively). Furthermore, SBRT was safe, with a pooled vertebral fracture rate of 9% (95% CI: 4%-16%), pooled radiation induced myelopathy rate of 0% (95% CI 0 – 2%), and pooled pain flare rate of 6% (95% CI: 3%-17%), although with mixed levels of heterogeneity among the studies (I 2 = 92%, I 2 = 0%, and 95%, respectively). Only 1.7% of vertebral fractures required surgical stabilization. The authors concluded SBRT for the spine is characterized by its effective and safe treatment outcomes, offering long-lasting relief from pain and control over disease progression which is especially beneficial for patients with oligometastatic conditions. Ryu et al. 2023, and Sprave et al. 2018, are included in this review.

In a phase III RCT, Ryu et al. (2023) investigated whether SRS enhanced patient-reported pain relief compared to cEBRT for individuals with one to three vertebral metastases. (According to the authors, the results from the phase II study, Ryu et al. 2014, demonstrated that SRS was both feasible and safe for treating vertebral metastases within a multi-institutional cooperative group setting.) A total of 339 participants, 114 in the SRS group and 70 in the cEBRT group, were included in this study. Those eligible for inclusion were at least 18 years old, with a Zubrod score of zero to two, and had one to three treatment-naïve vertebral metastases. Tumors with vertebral compression fractures with more than 50% height loss and /or bony retropulsion were excluded. Patient-reported pain response defined as a three-point or more improvement on the Numerical Rating Pain Scale (NRPS) without the use of pain medication or worsening pain at the secondary site was the primary endpoint. Treatment-related toxic effects, QOL, and long-term effects on vertebral bone and spinal cord were the secondary endpoints. The baseline mean (SD) pain score at the index vertebra was 6.06 (2.61) in the SRS group and 5.88 (2.41) in the cEBRT group. The primary end point of pain response at three months favored cEBRT (41.3% for SRS versus 60.5% for cEBRT; difference, −19 percentage points; 95% CI, −32.9 to −5.5; one-sided p = .99; two-sided p = .01). Zubrod score was the significant factor influencing pain response. There were no differences in the proportion of acute or late adverse effects. Vertebral compression fracture at 24 months was 19.5% with SRS and 21.6% with cEBRT (p = .59). No spinal cord complications were reported at 24 months. The authors concluded that the study did not demonstrate the superiority of SRS in terms of patient-reported pain response at three months. No clinical or radiographic spinal cord toxic effects were observed two years after SRS, which the authors highlight as a valuable prospective report on long-term spinal cord tolerance following SRS. Additionally, these findings prospectively show that one-year and two-year survival rates of individuals with spine metastases treated with SRS are promising, emphasizing the importance of continuing to identify the optimal SRS radiation dose and fractionation for those with vertebral metastases. The authors suggested that further research is warranted to explore the use of SRS for oligometastases, where long-term cancer control is crucial. Limitations included lack of blinding and low patient compliance regarding pain reporting.

Conti et al. (2022) performed a systematic review and meta-analysis of RS for individuals with benign spinal hemangiomas. Peer-reviewed studies or case series of individuals with spinal vertebral hemangiomas treated with RS or SBRT were included. Twenty-three individuals with 24 spinal vertebral hemangiomas assessed in three studies. The follow-up time was 7.3-84 months. The vast majority of lesions were located at dorsal level (n = 18; 75%). In 20 (83.3%) patients, pain was the initial clinical presentation. Complete, partial, and stable responses after radiation were reported in 45.7% (p < 0.001), 23.6% (p = 0.02), and 37.2% (p = 0.7) of cases. The overall response was reported in 94.1% (p = 0.7). No progressive disease was reported. Pain relief was achieved in 87.5% of patients (p = 0.2). Damage to surrounding tissue caused by irradiation was reported in 22.3% (p = 0.02) cases in one study, in which higher doses of radiation were delivered. According to the authors, RS was safe and effective for spinal hemangiomas. Limitations included the small sample size.

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). The 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 zero to two, 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 versus 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 RT 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, QOL, and patient values and goals. Per the guidelines:

- 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 one fraction, 1600 cGy in two fractions, 2000 cGy in five 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 one fraction (nonspine) and 2400 cGy in two fractions (spine) are recommended. Implementation remark: Other established SBRT dose and fractionation regimens (e.g., three to five fractions) with similar BEDs may be an option based on patient tumor and normal tissue factors, and physician experience. Strength of recommendation: strong; quality of evidence: moderate.
- For patients with symptomatic bone metastases with ECOG PS zero to two, 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.
- For patients with spine bone metastases that would benefit from reirradiation to the same site, treatment with SBRT is conditionally recommended. Strength of recommendation: conditional; quality of evidence: expert opinion.

National Comprehensive Cancer Network (NCCN)

Per NCCN guidelines regarding RT 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. In certain cases, SRS/SBRT may be suitable for treating primary spinal cord tumors such as hemangioblastoma, with care to respect normal tissue constraints of the spinal cord and surrounding structures. (NCCN, 2025).

National Institute for Health and Care Excellence (NICE)

NICE developed a guideline for spinal metastases that states to consider SBRT for those who have painful spinal metastases and no metastatic spinal cord compression with a good overall prognosis or oligometastases (up to three discrete metastases) with spinal involvement (NICE, 2023).

Uveal Melanoma

Du and Luo (2025) conducted a systematic review to evaluate the effectiveness of CyberKnife radiotherapy for local tumor control, complications, selectivity, secondary enucleations, and OS in individuals with uveal melanoma. Inclusion criteria consisted of single-arm studies, RCT, case or cohort studies of adults with uveal melanoma treated with CyberKnife radiotherapy, and at least one perioperative measure. Ten studies met the inclusion criteria for a total of 2370 individuals (2372 uveal melanomas). Meta-analysis showed 811 of 912 patients (0.89, 95% CI: 0.86, 0.92) maintained local control for three years, and 1448 of 1724 individuals (0.84, 95% CI: 0.81, 0.88) preserved the eye in three years. During follow-up, 91% (0.91, 95% CI: 0.85, 0.97) individuals survived and 351 of 1720 individuals (0.23, 95% CI: 0.09, 0.37) involving 1722 eyes had tumor recurrence. In addition, 1376 individuals (0.79, 95% CI: 0.77, 0.82) preserved the eyeball in five years. Following treatment, approximately 20% of individuals had radiation retinopathy (95% CI: 0.13, 0.28), 19% developed glaucoma (95% CI: 0.11, 0.28), and 22% experienced retinal detachment (95% CI: 0.07, 0.36). The authors concluded that CyberKnife radiotherapy was an effective, noninvasive method for enhancing tumor control and preserving the eye in medium and large UMs. Limitations included the retrospective nature of the studies and most of the studies were single-arm with no parallel comparisons.

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 GKS. 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; I2 = 16%) from 19 studies had local control, and 378 of 478 individuals (0·81, 0·70-0·90; I2 = 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 recommended future research focusing on generating level one 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 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 age was 54 years (range, 18 to 82 years) and 104 (58%) were male. The median tumor diameter and thickness was 10 mm (range, two 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, two to 79 months). Complete and partial response was observed in eight and 104 eyes, respectively. The rate of five-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 recommended 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.

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, 2025).

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 May 21, 2025)

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Policy History/Revision Information

Date	Summary of Changes
02/01/2026	**Coverage Rationale** • Added notation to indicate this policy applies to individuals 19 years of age and older; stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT) are covered without further review for individuals younger than 19 years of age • Revised list of proven and medically necessary indications for stereotactic radiation therapy, including SRS and SBRT: o Added: ▪ Bone metastasis (non-spine) when all the following criteria are met: – Symptomatic – Up to five fractions” ▪ Neurologic conditions (epilepsy, Parkinson’s disease, essential tremor) that are refractory to medical treatment and/or invasive surgical interventions ▪ Spinal lesions when one of the following criteria are met: – Palliative treatment of symptomatic spinal bone metastasis when all the following criteria are met: • Using five fractions or less • Individual has no spinal cord compression or cauda equina compression – Primary spinal lesions that cannot be treated with surgical resection or 3D conformal techniques o Revised coverage criteria for:

Date	Summary of Changes
	Definitive Treatment ▪ Added criterion requiring: – Intrahepatic bile duct cancer (cholangiocarcinoma) for unresectable tumors – Small cell lung cancer when all the following criteria are met: • Stage I or node negative stage IIA • Lesion is medically inoperable, or the individual is a non-optimal surgical candidate ▪ Replaced criterion requiring: – "Non-small cell lung cancer when the individual is medically inoperable or *refuses to have* surgery after *thoracic surgery evaluation*" with "non-small cell lung cancer when the individual is medically inoperable or *has made a decision not to pursue* surgery after *an appropriate consultation*" – "Prostate cancer without evidence of distant metastases" with "prostate cancer without evidence of distant metastases; *for Oligometastatic Disease, refer to the criteria [listed in the policy]*" ***Extracranial Oligometastatic Disease*** ▪ Replaced criterion requiring: – "*Performance status* KPS score ≥ 70% or ECOG performance status of 0-2" with "KPS score greater than or equal to 70% or ECOG performance status of zero to two" – "Individual has a total of up to *three* 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 three lesions*" with "individual has a total of up to *five* metastatic lesions" • Removed language indicating 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 **Medical Records Documentation Used for Reviews** • Added language to indicate: ○ Benefit coverage for health services is determined by the federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service ○ Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the service requested ○ The patient's medical record must contain documentation that fully supports the medical necessity for the requested services ○ This documentation includes but is not limited to relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures ○ Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available upon request **Definitions** • Updated definition of: ○ Definitive Treatment ○ Oligometastatic Disease (OMD) **Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version CS180OH.D

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

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