Stereotactic Body Radiation Therapy and Stereotactic Radiosurgery

Policy Number: 2026T0611L
Effective Date: October 1, 2026

Instructions for Use

Table of Contents **Page**

Application 1
Coverage Rationale 1
Medical Records Documentation Used for Reviews 3
Definitions 3
Applicable Codes 3
Description of Services 4
Clinical Evidence 4
U.S. Food and Drug Administration 45
References 45
Policy History/Revision Information 53
Instructions for Use 54

Related Commercial/Individual Exchange Policies

- Intensity-Modulated Radiation Therapy
- Proton Beam Radiation Therapy
- Radiation Therapy: Fractionation, Image-Guidance, and Special Services

Community Plan Policy

- Stereotactic Body Radiation Therapy and Stereotactic Radiosurgery

Application

UnitedHealthcare Commercial

This Medical Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Policy applies to Individual Exchange benefit plans.

Coverage Rationale

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

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

- Acoustic neuroma (vestibular schwannoma)
- Bone metastasis (nonspine) when **all** the following criteria are met:
  - Symptomatic
  - Up to five fractions
- Brain metastasis when **one** of the following criteria is met:
  - Newly diagnosed brain metastasis and **all** the following criteria are met:
    - Individual has a good performance status [Karnofsky Performance Status (KPS) score of ≥ 70% or Eastern Cooperative Oncology Group (ECOG) performance status of 0-2]
    - Absence of diffuse brain metastases
    - Absence of diffuse leptomeningeal metastases
    - Individual does not have a diagnosis of lymphoma or germ cell tumor
    - Has up to 10 lesions or cumulative tumor volume of less than 15 cm^3
    - All lesions must be treated in a single treatment for SRS or in two to five fractions for SBRT (also known as fractionated stereotactic radiation therapy)
  - Individual is undergoing repeat stereotactic radiation therapy when **all** the following criteria are met:

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

        - Individual has a good performance status (KPS score of ≥ 70% or ECOG performance status of 0-2)
        - Absence of diffuse leptomeningeal metastases
        - Extracranial disease is well controlled, or there are accessible and effective systemic treatment options available
        - Life expectancy is greater than 6 months
        - All lesions must be treated in a single treatment for SRS or in two to five fractions for SBRT (also known as fractionated stereotactic radiation therapy)
    - Re-treatment after previous whole-brain radiation therapy
- 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 ≤ 5 cm
        - Individual is medically inoperable or has decided not to pursue surgery after an appropriate consultation
    - Pancreatic adenocarcinoma without evidence of distant metastasis
    - Prostate cancer without evidence of distant metastases (refer to the criteria below for Oligometastatic Disease)
    - Renal cancer when **all** the following criteria are met:
        - Stage I
        - Individual is a nonoptimal 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 nonoptimal surgical candidate
- Extracranial Oligometastatic Disease when **all** the following criteria are met:
    - Primary tumor type is any of the following:
        - Colorectal cancer
        - Melanoma
        - Non-small cell lung cancer
        - Prostate cancer
        - Renal cancer
        - Sarcoma
    - Controlled primary tumor (defined as at least 3 months since the original tumor was treated definitively, with no progression at primary site)
    - KPS score of ≥ 70% or ECOG performance status of 0 to 2
    - Life expectancy is at least 6 months
    - Has a total of up to five metastatic lesions
    - Each lesion is ≤ 5 cm in size
    - No evidence of malignant pleural effusion or 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
- Hemangiomas of the brain
- Intracranial arteriovenous malformations
- Meningioma
- Neurological conditions (e.g., epilepsy, Parkinson disease, essential tremor) that are refractory to medical treatment and/or invasive surgical interventions
- Pineal gland tumors
- Pituitary adenoma
- Recurrent gliomas
- Spinal lesions when **one** of the following criteria is 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 three-dimensional conformal techniques
- To treat a previously irradiated field

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

- Trigeminal neuralgia refractory to medical therapy
- Uveal melanoma

Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the member specific benefit plan document 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; refer to the guidelines titled Medical Records Documentation Used for Reviews.

Definitions

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

Oligometastatic Disease: The Oligometastatic Disease state was first defined by Hellman and Weichselbaum in 1995 and refers to a stage of disease in which 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 a 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 the member specific benefit plan document 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)

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

CPT Code	Description
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

CPT® is a registered trademark of the American Medical Association

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, also known as stereotactic ablative radiotherapy, is a method that is used to deliver external beam radiation therapy 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 nonsurgical 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 that involve intracranial structures, as well as select extracranial lesions. Although SRS ordinarily refers to a 1-day treatment, physicians may suggest multiple stereotactic delivered treatments for tumors that are larger than 1 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 that is 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 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, 2023)

Clinical Evidence

Acoustic Neuroma (Vestibular Schwannoma)

Hajikarimloo et al. (2024) performed a systematic review and meta-analysis to evaluate the efficacy and outcomes of repeat stereotactic radiosurgery (SRS) in the management of recurrent or progressive vestibular schwannoma (VS) after failure of the first SRS treatment. Overall, 11 studies (260 individuals) were included in the review. The median time interval between initial and repeat SRSs ranged from 43 to 62 months. The analysis revealed a pooled tumor control of 91% (95% CI, 86%-94%). Regarding the radiological response, the pooled regression rate was 59% (95% CI, 52%-65%), while the pooled progression rate was 9% (95% CI, 6%-14%). Regarding the clinical outcomes, the pooled serviceable hearing preservation rate was 36% (95% CI, 22%-53%), while worsened fifth cranial nerve and seventh cranial nerve rates were 12% (95% CI, 7%-19%) and 8% (95% CI, 5%-12%), respectively. In addition, the pooled adverse radiation effect (ARE) rate was 6% (95% CI, 3%-11%). According to the authors, their findings indicate that performing repeat SRS after the initial SRS fails in VS led to positive outcomes such as effective tumor control and serviceable hearing preservation, with relatively low rates of cranial nerve worsening and AREs. Limitations include the retrospective nature of all included studies and the presence of other therapeutic interventions before the initial SRS that may influence the outcomes following SRS.

Balossier et al. (2023) conducted a systematic review and meta-analysis that centered on long-term hearing preservation after treatment with SRS. The inclusion criteria consisted of peer-reviewed clinical studies or case series of VS treated with a single dose of SRS that reported hearing outcomes, had a median or mean audiometric follow-up of at least 5 years, and were published between January 1990 and October 2020. The primary outcome that was evaluated was hearing preservation; the secondary outcomes that were assessed were cranial nerve outcomes and tumor control. Overall, 23 studies were included. Hearing preservation was found in 59.4% of cases (median follow-up, 6.7 years; 1,409 individuals). Young age, good hearing status, early treatment after diagnosis, small tumor volume, low marginal irradiation

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

dose, and maximal dose to the cochlea were the main favorable prognostic factors. Tumor control was achieved in 96.1%. Facial nerve deficit and trigeminal neuropathy were found in 1.3% and 3.2% of individuals, respectively, and were both significantly higher in linear accelerator (LINAC) series than Gamma Knife (GK) series ($p < 0.05$). The authors concluded that hearing preservation can be achieved for at least 6 years in almost 60% of individuals who are undergoing SRS for VS. Limitations include the small sample size of some included studies and variation in tumor progression and tumor control definitions across studies. (Boari et al., 2014, previously cited in this policy, is included in this review.)

Tosi et al. (2021) performed a systematic review and meta-analysis to assess outcomes of irradiation for large VS. The rate of tumor control, serviceable hearing, need for salvage surgery, trigeminal nerve and facial nerve impairment, presence of vertigo/dizziness, and hydrocephalus that required shunting were the primary end points. Three categories of studies were identified: (1) single-dose SRS (13 studies; 483 individuals), (2) combination of microsurgery and SRS (seven studies; 182 individuals), and (3) fractionated SRS (three studies; 82 individuals). Tumor control was achieved in 89%, 94%, and 91% of individuals, respectively. Odds ratios (ORs) of post-over pretreatment serviceable hearing were 0.42, 0.47, and 0.60; for facial nerve impairment, these ORs were 1.08, 3.45, and 0.87, respectively. The authors noted that given the high likelihood of local structure compromise, tendency to continue growing in size, and difficulties associated with both microsurgery and SRS, large VS poses a therapeutic challenge. The authors concluded that SRS, either as a single dose, in conjunction with microsurgery, or fractionated, provides good tumor control, with acceptable cranial nerve morbidity, and is a valid treatment alternative. Additionally, the authors recommended further structured studies. Limitations include the lack of randomized controlled trials (RCTs) included in the study and limited study sizes. Additionally, data were reported in a heterogeneous manner.

Clinical Practice Guidelines

Congress of Neurological Surgeons (CNS)

Germano et al. (2018) developed evidence-based guidelines for the CNS regarding the use of radiosurgery (RS) and radiation therapy in patients with VS. The systematic literature review included 137 articles that met the inclusion criteria and were published from January 1, 1990, to December 31, 2014. Only class III evidence studies were available to develop the guidelines. The following recommendations were made (not all inclusive):

- As there is no difference in radiographic control using different doses, it is recommended that for single-fraction SRS doses, < 13 Gy should be used to facilitate hearing preservation and minimize new onset or worsening of preexisting cranial nerve deficits.
- When there has been progression of a tumor after SRS, SRS can be safely and effectively performed as a re-treatment.
- RS is a treatment option for patients with neurofibromatosis type 2 whose VSs are enlarging and/or causing hearing loss.
- Patients should be informed that there is a minimal risk of malignant transformation of VS after SRS.

Germano et al. (2026) updated the 2018 evidence-based guidelines for the CNS to include four new level III recommendations:

- In adult patients with sporadic intracanalicular or < 2-cm VS, SRS should not be recommended as superior to observation alone for hearing preservation.
- In adult patients with sporadic VS treated with SRS, cochlear dose constraint should be considered, as it provides better hearing preservation than no constraint. In the same population, single-fraction SRS should be recommended rather than hypofractionated SRS (more than one and fewer than five fractions), as it results in decreased cranial nerve dysfunction.
- Adult patients with sporadic VS who are undergoing SRS should be informed that SRS does not result in an increased number of secondary malignancies compared with the rate that is expected in the overall population.

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. Overall, 12 series met the inclusion criteria, reporting on treatment outcomes in 677 individuals. The 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 the last follow-up. Cochlear functional preservation immediately after microsurgery was 58.8%, decreasing to 57.4% at the 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 the following:

- Nerve-sparing intracapsular microsurgical resection with facial nerve preservation. Strength of recommendation:

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

strong; level of evidence: III.
- Up-front SRS should be considered as opposed to observation due to the potential to optimize long-term local control and should occur within 3 to 6 months following subtotal resection. Strength of recommendation: conditional; level of evidence: III.
- Radiation therapy alone can be used as up-front treatment in patients with medical comorbidities that preclude up-front surgery. Strength of recommendation: strong; level of evidence: III.
- First postoperative magnetic resonance imaging (MRI) should be performed within 3 to 6 months to determine residual disease and an evaluation for postoperative SRS. Strength of recommendation: strong; level of evidence: III.

Bone Metastasis (Nonspine)

Singh et al. (2024) conducted a systematic review and meta-analysis that evaluated stereotactic body radiation therapy (SBRT) for nonspinal bone metastases. Eligible studies included individuals with nonspinal bone metastases who were treated with SBRT that delivered at least 5 Gy per fraction in one to five fractions and reported one or more primary outcomes, with at least 10 individuals or lesions per study. The primary outcomes were 1-year local control, acute and late grade 3 to 5 toxicities, and 3-month pain response, with local control defined radiographically and pain response defined as subjective improvement or complete resolution of pain. The pooled analysis comprised 528 individuals, with 597 nonspinal bone lesions from one prospective and eight retrospective observational studies, a median age of 64 years, and a median follow-up of 11.7 months. SBRT demonstrated an estimated 1-year local control rate of 94.6% (95% CI, 87.0%-99.0%). At 3 months, the combined complete and partial pain response rate was 87.7% (95% CI, 55.1%-100.0%). The treatment exhibited a low incidence of toxicity, with a combined acute and late grade 3 to 5 toxicity rate of 0.5% (95% CI, 0%-5.0%) and a pathologic fracture rate of 3.1% (95% CI, 0.2%-9.1%). The estimated 1-year overall survival (OS) rate, which was a secondary end point, was 71.0% (95% CI, 51.7%-87.0%). The authors concluded that SBRT achieves high rates of local control and effective symptom palliation, with minimal treatment-related toxicity; however, additional prospective studies are needed to further characterize long-term outcomes in those with nonspinal bone metastases. Key limitations include the predominantly retrospective study designs and absence of control groups. Additionally, short follow-up (approximately 1 year) in a heterogeneous metastatic population may have led to underestimation of late toxicities and fracture risk, as well as potential overestimation of local control.

Nguyen et al. (2019) conducted a phase 2 RCT that compared pain relief from high-dose single-fraction SBRT with that from conventional multifraction radiotherapy (MFRT) in participants with mostly nonspine bone metastases. The primary end point was pain response. The secondary end points were quality of life (QOL) and symptom burden, narcotic use post treatment, toxic effects, local control of irradiated metastases, and OS. The inclusion criteria included those who were aged 18 years or older, had a diagnosis of cancer and painful bone metastases, and had more than a 3-month life expectancy. Concurrent treatment of three radiation fields or less was allowed. Prior radiation to the site, untreated spinal cord compression, pathological fracture at the site, and previous radioactive isotope therapy within 30 days of randomization were the study exclusions. Overall, 160 participants were randomized to receive either SBRT or MFRT. In this phase 2 portion of a phase 2/3 noninferiority trial in 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 plus partial response) at 2 weeks [34 of 55 (62%) vs 19 of 52 (36%); p = 0.01], 3 months [32 of 44 (73%) vs 17 of 35 (49%); p = 0.04], and 9 months [17 of 22 (77%) vs 12 of 26 (46%); p = 0.04]. 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 the 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 vs 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 who were evaluated, SBRT showed higher rates of pain response (both complete and partial) than MFRT and should be considered for individuals with a relatively long expected survival. Additionally, the authors recommended larger phase 3 studies. Limitations include the inclusion of metastases from various types of primary cancer; additionally, the attrition rate rose with increasing follow-up time due to the nature of having metastatic cancer.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's guideline on palliative radiation therapy for symptomatic bone metastases (Alcorn et al., 2024) provides recommendations using consensus-building methodology based on a systematic review by the Agency for Healthcare Research and Quality (Skelly et al., 2023). The authors note that developing the most favorable radiation therapy regimen requires an assessment that includes prognosis, any previous radiation therapy doses, normal tissue risks, QOL, and patient values and goals. The guidelines suggest the following:

- For patients with symptomatic spine bone metastases, including those that are causing compression of the spinal cord or cauda equina, radiation therapy is recommended to improve ambulatory status, improve sphincter function,

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

and reduce pain. An implementation remark states that before initiating radiation therapy, evaluation for spine stability and surgery is necessary. Strength of recommendation: strong; quality of evidence: high.

- For patients with symptomatic bone metastases who are treated with SBRT, 1,200 to 1,600 cGy in one fraction (nonspine) and 2,400 cGy in two fractions (spine) are recommended. An implementation remark states that 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 who have an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 to 2, are not receiving surgical intervention, and do not have neurological symptoms, SBRT is conditionally recommended over conventional palliative radiation therapy. An implementation remark states that 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 who would benefit from reirradiation to the same site, single-fraction (800 cGy in one fraction) or multifraction conventional palliative radiation therapy (2,000 cGy in five fractions or 2,400 cGy in six fractions) is recommended. Strength of recommendation: strong; quality of evidence: moderate.

NCCN

Per NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), SRS or SBRT may be considered for metastatic bone disease, especially for oligometastases. (NCCN, 2026)

Brain Metastasis

Aizer et al. (2026) conducted a phase 3, open-label, randomized clinical trial at four U.S. centers that was coordinated by Brigham and Women's Hospital/Dana-Farber Cancer Institute. Eligible adults were aged 18 to 80 years, had five to 20 brain metastases, had a Karnofsky Performance Status (KPS) of 70 to 100, and had no prior brain-directed radiation. Overall, 196 participants were randomized 1:1 to stereotactic radiation or hippocampal-avoidance whole-brain radiation with memantine, analyzed by randomized group assignment regardless of treatment received. The primary end point was the within-participant mean change in MD Anderson Symptom Inventory for Brain Tumor composite score from baseline to 6 months, weighted by the number of postbaseline assessments, with a clinically meaningful difference defined as 0.98. Overall, 83 participants (42%) completed the 6-month assessment, and stereotactic radiation improved the composite score [mean change, -0.32 vs 0.74; mean difference (MD), -1.06; 95% CI, -1.54 to -0.58; $p < 0.001$]. The prespecified secondary end points included OS, neurological death, new brain metastases, local recurrence, progressive intracranial disease, radiation necrosis, leptomeningeal disease, steroid use, seizures, salvage therapies, functional independence, KPS, neurocognitive function, and per-metastasis outcomes. The authors concluded that in participants with five to 20 brain metastases, stereotactic radiation was supported over hippocampal-avoidance whole-brain radiation to improve symptom burden and interference with daily functioning, which are key components of QOL. Key limitations include the absence of blinding and reliance on a subjective primary outcome. There are limitations related to study design, as randomization was not stratified by treating center, which may have introduced unmeasured imbalances. High mortality limited long-term data collection, reducing precision and potentially biasing results toward survivors.

Li et al. (2026) conducted a systematic review and meta-analysis that compared SRS and whole-brain radiotherapy (WBRT) for brain metastases in small cell lung cancer (SCLC). Ten retrospective cohort studies that involved 41,240 patients (2,887 SRS and 38,353 WBRT) from America, China, Canada, and international cohorts were included. Eligible studies compared SRS and WBRT without restrictions on WBRT dose or regimen, and data extraction covered study characteristics, treatment regimens, and outcomes such as OS and prognostic factors. A meta-analysis was performed using R software, with heterogeneity assessed by the Q test and I^2 statistic, applying a fixed-effect model when the p value was ≥ 0.05 and I^2 was ≤ 50%, and a random-effects model when the p value was < 0.05 or I^2 was > 50%. For survival outcomes, effect sizes were expressed as HRs with corresponding 95% CI. The primary outcome, OS, was significantly better with SRS than WBRT (pooled HR, 0.74; 95% CI, 0.71-0.78; $p < 0.0001$), and sensitivity analyses confirmed result stability, with no significant publication bias. The prespecified secondary end points included prognostic factors such as ECOG PS, gender, chemotherapy, immunotherapy, age, number of brain metastases, and extracranial metastases. The authors concluded that SRS was associated with improved OS compared with WBRT in individuals with SCLC brain metastases, with the survival benefit most evident in younger individuals who had good performance status, limited intracranial lesions, and well-controlled systemic disease, and that differences in baseline prognostic characteristics may partly explain the observed survival association. Although the meta-analysis followed established methodological standards, several limitations remain. Key limitations include the retrospective design of all included studies, meaning that the findings are exploratory and not directly comparable to RCT evidence. Some studies did not adequately control for confounding factors such as performance status, number of brain metastases, extracranial disease burden, and systemic therapy exposure. Differences in radiotherapy parameters and systemic therapy practices across

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

studies, as well as overlapping National Cancer Database study periods, may have influenced the assessment of efficacy and survival outcomes.

Gaebe et al. (2023) conducted a systematic review and meta-analysis of controlled trials and cohort studies that compared SRS with WBRT to evaluate survival outcomes and assess treatment outcomes following SRS in those with intracranial metastatic disease (IMD) secondary to SCLC. The inclusion criteria included adults who had SCLC and a diagnosis of IMD and were treated with SRS. Studies were considered eligible if they were published in English and reported on either first-line SRS or salvage SRS; single-arm SRS studies were included retrospectively but prior to data extraction. Studies that did not report on individuals who received SRS for IMD secondary to SCLC were excluded. OS was the primary end point. Overall, 31 studies were included in the review, and seven were included in the meta-analysis. OS following SRS was longer than that following WBRT, with or without SRS boost (HR, 0.85; 95% CI, 0.75-0.97; seven studies; n = 18,130 individuals), or WBRT alone (0.77; 0.72-0.83; seven studies; n = 16,961 individuals) but not WBRT plus SRS boost (1.17; 0.78-1.75; four studies; n = 1,167 individuals). With single-arm studies, the pooled median OS with SRS was 8.99 months (95% CI, 7.86-10.16 months; 14 studies; n = 1,682 individuals). Between-study heterogeneity was considerable when pooled among all comparative studies (I^2 = 71.9%). The authors concluded that survival outcomes are comparable in individuals with SCLC and IMD who are treated with SRS vs WBRT. Further prospective RCTs to evaluate the impact of IMD burden and differences in intracranial control between WBRT and SRS were recommended by the authors. Limitations include the retrospective nature of the studies included in the review; additionally, most studies did not include those with previous prophylactic cranial irradiation (PCI). Rusthoven et al. (2020), summarized below, is included in this study.

Vlachos et al. (2023) conducted a systematic review and meta-analysis to evaluate whether those with postoperative SRS had comparable results in local and distant recurrence, leptomeningeal disease, and OS compared with individuals with a solitary, previously resected brain metastasis (BM). Two RCTs and two retrospective studies were included in the review. Overall, 128 individuals received postoperative WBRT, while 120 individuals were treated with postoperative SRS. There was no difference between SRS and WBRT in the risk of local recurrence [risk ratio (RR), 0.92; CI, 0.51-1.66; p = 0.78; I^2 = 0%] and leptomeningeal disease (RR, 1.21; CI, 0.49-2.98; p = 0.67; I^2 = 18%) or OS (HR, 1.06; CI, 0.61-1.85; p = 0.83; I^2 = 63%). SRS appeared to increase the risk of distant brain failure (DBF; RR, 2.03; CI, 0.94-4.40; p = 0.07; I^2 = 61%). Neurocognitive function and QOL in the SRS group were equal or superior to those in the WBRT group. The authors concluded that SRS may increase the risk of DBF compared with WBRT. However, in terms of local control, risk of leptomeningeal disease, and OS, SRS appears as effective as WBRT, and SRS spared the individuals of the WBRT-associated cognitive deterioration. Limitations include the various types of primary tumor sites, failure to report the type of surgical resection, and relatively good preoperative performance status in all individuals.

Rusthoven et al. (2020) conducted a cohort study in 710 individuals with SCLC BMs who were treated with SRS, without prior PCI or WBRT, to compare SRS outcomes with those in individuals treated with first-line WBRT. OS, time to central nervous system (CNS) progression, and progression-free survival (PFS) after SRS were the primary end points. The median OS was 8.5 months, median time to CNS progression was 8.1 months, and median CNS PFS was 5 months. When stratified by the number of BMs treated, the median OS was 11.0 months (95% CI, 8.9-13.4 months) for one lesion, 8.7 months (95% CI, 7.7-10.4 months) for two to four lesions, 8 months (95% CI, 6.4-9.6 months) for five to 10 lesions, and 5.5 months (95% CI, 4.3-7.6 months) for 11 or more lesions. Competing risk estimates were 7.0% (95% CI, 4.9%-9.2%) for local failures at 12 months and 41.6% (95% CI, 37.6%-45.7%) for distant CNS failures at 12 months. Leptomeningeal progression [46 of 425 individuals (10.8%) with available data] and neurological mortality [80 of 647 individuals (12.4%) with available data] were uncommon. On propensity score–matched (PSM) analyses that compared SRS with WBRT, WBRT was associated with improved time to CNS progression (HR, 0.38; 95% CI, 0.26-0.55; p < 0.001), without an improvement in OS [median, 6.5 months (95% CI, 5.5-8.0 months) with SRS vs 5.2 months (95% CI, 4.4-6.7 months) with WBRT; p = 0.003] or CNS PFS (median, 4 months with SRS vs 3.8 months with WBRT; p = 0.79). Multivariable analyses that compared SRS and WBRT, including subset analyses that controlled for extracranial metastases and extracranial disease control status, demonstrated similar results. The authors concluded that treatment with SRS for SCLC had encouraging outcomes overall, especially in those with a single BM. Limitations include the retrospective design, with potential confounding and lack of control beyond the first CNS progression. This study is included in the Gaebe et al. (2023) systematic review and meta-analysis.

Fogarty et al. (2019) conducted a multicenter, international, phase 3, randomized trial (NCT01503827) to compare WBRT with observation after local treatment of one to three melanoma BMs (MBMs). The primary end point was distant intracranial failure within 12 months of randomization. The a priori neurocognitive function end point was Hopkins Verbal Learning Test-Revised (HVLT-R) delayed recall at 4 months. The secondary end points included local failure, OS, and global QOL. Analyses were conducted on an intention-to-treat basis, with a nominal two-sided significance level of 5%. Drug therapy was allowed. Effective drugs became available during the trial, and their impact was analyzed. A total of 215 participants consented to participate in the study, and of them, eight withdrew or had no data collected. Overall, 100

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

participants were randomized to the WBRT arm and 107 participants to the observation arm. The mean age was 62 years; 67% were males; 61% had a single MBM, with a mean size of 2 cm; and 67% had extracranial disease at randomization. Neurocognitive function was completed by participants who spoke English: 50 participants who were randomized to WBRT and 70 participants to observation at baseline, with a decline to 26 and 35 participants, respectively, at 4 months. Within 12 months, 54 participants (50.5%) in the observation arm had distant intracranial failure compared with 42 participants (42.0%) in the WBRT arm (OR, 0.71; 95% CI, 0.41-1.23; p = 0.222). There was no difference in local failure (p = 0.100) or OS (p = 0.861). At 12 months, 53% of participants in the observation arm and 59% of participants in the WBRT arm were alive. There was no difference in the mean intervention effect on global QOL (p = 0.083) between the two arms. Participants who received T-cell checkpoint inhibitors and/or mitogen-activated protein kinase (MAPK) pathway inhibitors and WBRT before or within 12 months of randomization had a distant intracranial failure rate of 29% compared with 44% of participants in the observation arm with no systemic therapy; however, this difference was not significant (p = 0.228). The observation arm had greater relative improvement from baseline in HVLT-R at every time point. At 4 months, the observation arm had a 20.9% improvement from baseline in HVLT-R delayed recall compared with a 2.7% decline in the WBRT arm; the overall adjusted average intervention effect was 23.6% (95% CI, 9.0%-38.2%; p = 0.0018). There was no difference in time to cognitive failure or in proportions with global cognitive impairment between the arms. The authors concluded that this RCT shows that WBRT does not improve outcomes in MBMs and that this trial justifies the recent move away from WBRT.

Yamamoto et al. (2019) conducted a retrospective cohort analysis in patients with BM who underwent multiple SRS procedures to validate whether BM velocity (BMV), a prognostic grading system, is generally applicable. The BMV score is the cumulative number of new BMs that developed after the first SRS divided by time (years) since the initial SRS. Patients were categorized into three classes based on their BMV scores (e.g., ≤ 3, 4-13, and ≥ 14). Overall, 833 patients who underwent a second SRS procedure for newly detected BMs were included in the analysis. Of them, 250 underwent a third procedure, and 88 had a fourth SRS procedure. The median survival times after the second SRS were 12.9 months (95% CI, 10.2-17.1 months) in the BMV group, with a score of ≤ 3; 7.5 months (95% CI, 6.5-9.0 months) in the group scoring 4 to 13; and 5.1 months (95% CI, 4.0-5.6 months) in the group scoring ≥ 14 (p = 0.0001). The corresponding median survival times after the third SRS were 13.2 months (95% CI, 9.1-21.6 months), 8.0 months (95% CI, 6.2-11.2 months), and 5.7 months (95% CI, 4.8-7.8 months; p = 0.0001). Respective median survival times after the fourth SRS were 13.2 months (95% CI, 9.1-21.6 months), 8.0 months (95% CI, 6.2-11.2 months), and 5.7 months (95% CI, 4.8-7.8 months; p < 0.0001). The mean BMV score in patients with SCLC, which was 24.8, was significantly higher than that in patients with non-small cell lung cancer (NSCLC), with a mean score of 17.7 (p = 0.032). The authors concluded that the results of this analysis support the validity of BMV for predicting survival not only after the second SRS but also after the third and fourth SRS. The study is limited by its retrospective design, with heterogeneous clinical factors and significant selection/follow-up biases.

Farris et al. (2017) conducted a single-center, retrospective, cohort analysis to characterize BMV as a prognostic metric for patient outcomes with BMs, determine the factors that predict higher BMV, and determine whether BMV is associated with other important clinical outcomes such as OS and likelihood of neurological death. The BMV score is the cumulative number of new BMs that developed after the first SRS divided by time (years) since the initial SRS. Patients were categorized into three classes based on their BMV scores (e.g., ≤ 3, 4-13, and ≥ 14). Histology, number of metastases at the time of first SRS, and systemic disease status were assessed for effect on BMV. Following initial SRS treatment, patients were followed up with MRI of the brain and a clinical examination at 4 to 8 weeks after the procedure and thereafter every 3 months. The number of new metastases on every follow-up MRI scan was recorded to generate the BMV. A new metastasis was determined on follow-up MRI to be completely outside of the prior radiosurgical treatment volume, as defined by the prescription isodose line. Of 737 patients who were treated with up-front SRS without WBRT, 286 (38.8%) had at least one DBF event. The median follow-up was estimated at 66.5 months (95% CI, 50.9-85.7 months), and median OS from the time of first SRS in all patients with BMV data was 16.3 months (95% CI, 14.6-18.6 months). A lower BMV predicted for improved OS following initial DBF (p < 0.0001). Median OS in the low, intermediate, and high BMV groups was 12.4 months (95% CI, 10.4-16.9 months), 8.2 months (95% CI, 5.0-9.7 months), and 4.3 months (95% CI, 2.6-6.7 months), respectively. A multivariate analysis showed that BMV remained the dominant predictor of OS, with an HR of 2.75 in the high BMV group (95% CI, 1.94-3.89; p < 0.0001) and an HR of 1.65 in the intermediate BMV group (95% CI, 1.18-2.30; p < 0.004). A lower BMV was associated with decreased rates of salvage WBRT (p = 0.02) and neurological death (p = 0.008). The factors predictive of a higher BMV included at least two initial BMs (p = 0.004) and melanoma histology (p = 0.008). The authors concluded that BMV is a novel metric that is associated with OS, neurological death, and need for salvage WBRT after initial DBF following up-front SRS alone. The limitations include the retrospective nature of the study and potential for selection bias.

Yamamoto et al. (2017) published a follow-up study to the JLGK0901 study (Yamamoto et al., 2014) to confirm the long-term safety of SRS in participants with five to 10 BMs. Yamamoto et al. (2014) was a multicenter, nonrandomized, observational study to examine whether SRS without WBRT, as the initial treatment in participants with five to 10 BMs,

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

was noninferior to that in participants with two to four BMs in terms of OS. The study enrolled 1,194 participants, and the median OS after SRS was 13.9 months (95% CI, 12.0-15.6 months) in 455 participants with one tumor, 10.8 months (9.4-12.4 months) in 531 participants with two to four tumors, and 10.8 months (9.1-12.7 months) in 208 participants with five to 10 tumors. OS did not differ between the participants with two to four tumors and those with five to 10. SRS-induced adverse events occurred in 101 participants (8%); nine participants (2%) with one tumor had one or more grade 3 to 4 events compared with 13 participants (2%) with two to four tumors and six participants (3%) with five to 10 tumors. The proportion of participants who had one or more treatment-related adverse events of any grade did not differ significantly between the two groups of participants with multiple tumors. Four participants died, mainly from complications related to SRS (two with one tumor and one each in the other two groups). The authors concluded that SRS without WBRT in participants with five to 10 BMs is noninferior to that in participants with two to four BMs; additionally, the minimal invasiveness of SRS and fewer side effects compared with WBRT may make SRS a suitable alternative for individuals with up to 10 BMs. The follow-up study (Yamamoto et al., 2017) reappraised, after an additional 2 years of follow-up, whether GK SRS alone for five to 10 BMs is safe in the long term compared with that for two to four BMs and even for one BM; WBRT results were also reported. The focus of this study was Mini-Mental State Examination (MMSE) results and complications. The 1,194 eligible participants were categorized into the following groups: group A (one tumor; n = 455); group B (two to four tumors; n = 531); and group C (five to 10 tumors; n = 208). Cumulative rates of MMSE score maintenance (MMSE score decrease of < 3 from baseline) were determined with a competing risk analysis in groups A, B, and C: 93%, 91%, and 92%, respectively, at the 12th month after SRS; 91%, 89%, and 91% at the 24th month; 89%, 88%, and 89% at the 36th month; and 87%, 86%, and 89% at the 48th month (HR in group A vs group B, 0.719, 95% CI, 0.437-1.172, p = 0.18; HR in group B vs group C, 1.280, 95% CI, 0.696-2.508, p = 0.43). During observations that ranged from 0.3 to 67.5 months (median, 12.0 months; IQR, 5.8-26.5 months), as of December 2014, 145 participants (12.1%) had SRS-induced complications. The cumulative complication incidences by competing risk analysis in groups A, B, and C were 7%, 8%, and 6%, respectively, at the 12th month after SRS; 10%, 11%, and 11% at the 24th month; 11%, 11%, and 12% at the 36th month; and 12%, 12%, and 13% at the 48th month (HR in group A vs group B, 0.850, 95% CI, 0.592-1.220, p = 0.38; HR in group B vs group C, 1.052, 95% CI, 0.666-1.662, p = 0.83). Leukoencephalopathy occurred in 12 of the 1,074 participants (1.1%) with follow-up MRI and was detected after salvage WBRT in 11 of these 12 participants. In those 11 participants, leukoencephalopathy was detected by MRI 5.2 to 21.2 months (median, 11.0 months; IQR, 7.0-14.4 months) after WBRT. The authors concluded that neither MMSE score maintenance nor post-SRS complication incidence differed among groups A, B, and C and that this longer-term follow-up study further supports the noninferiority of SRS alone in individuals with five to 10 BMs vs two to four BMs. Limitations include potential participant selection, observation bias, and limited statistical power in subgroup analyses due to small sample sizes.

Brown et al. (2016) conducted a multicenter randomized trial to determine whether there is less cognitive deterioration at 3 months after SRS alone vs SRS plus WBRT. Adult participants (18 years of age or older) with one to three BMs, all smaller than 3.0 cm in diameter, were eligible for the trial. Participants who were randomly assigned to SRS alone received 24 Gy in a single fraction if lesions were less than 2.0 cm or 20 Gy if lesions were 2 to 2.9 cm in maximum diameter. Participants who were randomly assigned to SRS plus WBRT received 22 Gy in a single fraction if lesions were less than 2.0 cm or 18 Gy if lesions were 2 to 2.9 cm in maximum diameter. Participants who were randomly assigned to SRS plus WBRT received 30 Gy in 12 fractions of 2.5 Gy WBRT delivered 5 days per week. WBRT began within 14 days of SRS. The primary end point was cognitive deterioration (decline of > 1 SD from baseline on at least one cognitive test at 3 months) in participants who completed the baseline and 3-month assessments. The secondary end points included time to intracranial failure, QOL, functional independence, long-term cognitive status, and OS. A total of 213 participants participated in the study (SRS alone, n = 111; SRS plus WBRT, n = 102), with a mean age of 60.6 years (SD, 10.5 years); 103 (48%) were women. There was less cognitive deterioration at 3 months after SRS alone [40 of 63 participants (63.5%)] than when combined with WBRT [44 of 48 participants (91.7%); difference, -28.2%; 90% CI, -41.9% to -14.4%; p < 0.001]. QOL was higher at 3 months with SRS alone, including overall QOL (mean change from baseline, -0.1 vs -12.0 points; MD, 11.9; 95% CI, 4.8-19.0 points; p = 0.001). Time to intracranial failure was significantly shorter with SRS alone than SRS plus WBRT (HR, 3.6; 95% CI, 2.2-5.9; p < 0.001). There was no significant difference in functional independence at 3 months between the treatment groups. Median OS was 10.4 months with SRS alone and 7.4 months with SRS plus WBRT (HR, 1.02; 95% CI, 0.75-1.38; p = 0.92). In long-term survivors, the incidence of cognitive deterioration was less after SRS alone at 3 months [five of 11 (45.5%) vs 16 of 17 (94.1%); difference, -48.7%; 95% CI, -87.6% to -9.7%; p = 0.007] and at 12 months [six of 10 (60%) vs 17 of 18 (94.4%); difference, -34.4%; 95% CI, -74.4% to 5.5%; p = 0.04]. The authors concluded that (1) among participants with one to three BMs, the use of SRS alone compared with SRS combined with WBRT resulted in less cognitive deterioration at 3 months and that (2) in the absence of a difference in OS, these findings suggest that in individuals with one to three BMs who are amenable to RS, SRS alone may be a preferred strategy. The limitations include overrepresentation of lung cancer, limiting applicability to other primary tumors, and substantial participant attrition, largely due to death from systemic disease. Additional limitations include the lack of blinding and a short 3-month primary end point, which may capture only transient declines in cognitive function and QOL following WBRT.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Minniti et al. (2016) conducted a case series analysis to evaluate the efficacy and toxicity of repeated SRS in individuals with recurrent/progressive BMs. A total of 43 individuals (21 men and 22 women), with 47 lesions, received a second course of SRS that was given in three daily fractions of 7 to 8 Gy. With a follow-up study of 19 months, the 1- and 2-year survival rates with repeated SRS were 37% and 20%, respectively, and the 1- and 2-year local control rates were 70% and 60%. Actuarial local control was significantly better for breast and lung metastases than for melanoma metastases; 1-year local control rates were 38% for melanoma, 78% for breast carcinoma, and 73% for NSCLC metastases (p = 0.01). The cause of death was progressive systemic disease in 25 individuals and progressive brain disease in 11 individuals. Stable extracranial disease (p = 0.01) and KPS (p = 0.03) were predictive of longer survival. Radiological changes that were suggestive of brain radionecrosis were observed in nine of 47 lesions (19%), with an actuarial risk of 34% at 12 months. Neurological deficits [Radiation Therapy Oncology Group (RTOG) grade 2 or 3] that were associated with brain necrosis occurred in 14% of individuals. The authors concluded that a second course of SRS given in three daily fractions is a feasible treatment for selected individuals with recurrent/progressive BMs and that additional studies that explore the efficacy and safety of different dose-fractionation schedules, especially in individuals with melanoma or large metastases, are needed. Key limitations include the retrospective, single-center design; lack of a comparator arm; and heterogeneity in individuals' characteristics.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

The 2022 ASTRO clinical practice guidelines provide evidence-based recommendations for the treatment of BMs. The ASTRO recommendations are as follows (not all inclusive):

- Indications for SRS alone for intact BMs:
  - SRS is recommended for patients with an ECOG PS of 0 to 2 and up to four intact brain BMs. Strength of recommendation: strong; quality of evidence: high.
  - SRS is conditionally recommended for patients with an ECOG PS of 0 to 2 and five to 10 intact BMs. Strength of recommendation: conditional; quality of evidence: low.
  - Single-fraction SRS with a dose of 2,000 to 2,400 cGy is recommended for patients with intact BMs that measure < 2 cm in diameter; if multifraction SRS is given, options include 2,700 cGy in three fractions or 3,000 cGy in five fractions. Strength of recommendation: strong; quality of evidence: moderate.
- Indications for observation, postoperative SRS, WBRT, or preoperative SRS:
  - Radiation therapy with SRS or WBRT is recommended to improve intracranial disease control in those with resected BMs. Strength of recommendation: strong; quality of evidence: high.
  - SRS is recommended over WBRT to preserve neurocognitive function and patient-reported QOL in those with resected BMs and limited additional BMs. Strength of recommendation: strong; quality of evidence: moderate.

ASTRO suggests that there is an ongoing need for inclusive clinical trials that assess different modalities and have end points such as survival, cognitive outcomes, and QOL. (Gondi et al., 2022)

American Society of Clinical Oncology (ASCO)

ASCO determined that the recommendations from the ASTRO *Radiation Therapy for Brain Metastases Clinical Practice Guidelines* are clear, thorough, and based on the most relevant scientific evidence. ASCO endorsed the guidelines above. (Schiff et al., 2022)

Congress of Neurological Surgeons (CNS)

Graber et al. (2019) developed an evidence-based guideline for the CNS to address the management of adults with new or recurrent BMs from solid tumors. Part 4 of 9 of the guideline provides recommendations for the use of SRS in this patient population. Huntoon et al. (2025) updated the guideline on managing metastatic brain tumors, focusing on the role of emerging therapies in adult patients. The guideline continues to recommend the following (not all inclusive):

- For newly diagnosed metastatic brain tumors, SRS is preferred over surgery for single BMs when surgery risks neurological harm and radiation can be safely delivered.
- After open surgical resection of a solitary BM, SRS should be delivered to decrease local recurrence rates.
- SRS should be given to reduce tumor growth in patients with one BM or in those with two to four small tumors (total volume under 7 mL) instead of whole-brain radiation.
- SRS alone is recommended to improve median OS in patients with more than four metastases that have a cumulative volume of < 7 mL.

NCCN

Per the NCCN Guidelines® for CNS cancers, SRS is generally preferred over WBRT for limited BMs. Compared with postoperative WBRT, SRS to the surgical cavity improves local control over observation, offers similar OS, and offers

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

superior overall cognitive preservation. For larger cavities, multifraction SRS may be preferred. In the context of reirradiating BMs, SRS alone is generally preferred when there is evidence of tumor progression following prior WBRT. New metastatic lesions that have not previously been treated with SRS can typically be managed safely in future SRS courses. Tumor treating fields plus SRS is recommended for those with NSCLC who do not have targetable genetic mutations. For lesions that have already undergone SRS, repeat SRS may be considered as a treatment option. However, this carries a heightened risk of radiation-induced effects. When recurrence is too diffuse or widespread to be effectively addressed with focal therapies like SRS, WBRT may be reconsidered as a broader treatment strategy. (NCCN, 2026)

The NCCN Guidelines for SCLC state that patients with a small number of BMs may be treated with SRS, and for those who develop BMs after PCI, SRS is preferred, if feasible. (NCCN, 2026)

Chordoma and Chondrosarcoma

Maroufi et al. (2024) conducted a systematic review and meta-analysis that aimed to evaluate the safety and effectiveness of SRS in the management of skull base chordomas. The inclusion criteria included primary or recurrent skull base chordomas that were treated with SRS as primary, adjunctive, or salvage treatment, and outcomes/complications that were associated with SRS were reported. The 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 that did not mention SRS timing, and nonoriginal studies and case reports. Overall, 33 retrospective cohorts and series (n = 714 individuals) that were published from 1991 to 2023 were included in the review. Individuals, who were predominantly male (57.37%) and had a mean age of 46.54 years, had a conventional chordoma subtype (74.77%) and primary lesions (77.91%), mainly in the clivus (98.04%). The mean lesion volume was 13.49 cm^3, and 96.68% of individuals had undergone prior surgical attempts. GK RS (88.76%) was the predominant SRS method. Radiologically, 27.19% of individuals experienced tumor regression, while 55.02% had 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. RS 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 who were treated with SRS achieved local tumor control and that the safety and efficacy of SRS in the treatment of skull base chordomas are supported. Limitations include the retrospective nature of many included studies and limited long-term data.

Kano et al. (2015) conducted a multicenter retrospective evaluation to analyze the outcome of SRS in patients with chondrosarcoma who underwent this treatment as part of multimodality management. Overall, 46 patients who underwent SRS for skull base chondrosarcomas were identified at seven participating centers of the North American Gamma Knife Consortium. Overall, 36 patients had previously undergone tumor resections, and five had been treated with fractionated radiation therapy. 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 patients had died. The actuarial OS after SRS was 89% at 3 years, 86% at 5 years, and 76% at 10 years. Local tumor progression occurred in 10 patients. The rate of PFS after SRS was 88% at 3 years, 85% at 5 years, and 70% at 10 years. Prior radiation therapy was significantly associated with shorter PFS. Eight patients required salvage resection, and three patients (7%) developed AREs. Cranial nerve deficits improved in 22 of the 39 patients (56%) who had deficits before SRS. Clinical improvement after SRS was noted in patients 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%), or hearing loss (10%). Limitations include the retrospective nature of the study and length of follow-up of less than 12 months in some patients. The authors concluded that (1) SRS provided a reasonable benefit-to-risk profile in those with residual or newly diagnosed small skull base chondrosarcomas and that (2) maximal safe resection should be the primary initial management. The authors additionally noted that SRS is a potent treatment option for small to medium-sized chondrosarcomas and is associated with improvement of cranial nerve function in selected cases, especially in individuals who present with diplopia that is related to abducens nerve palsy. Limitations include the retrospective study design, with potential selection bias, heterogeneity in treatment protocols, and relatively limited long-term follow-up.

Hasegawa et al. (2007) conducted a case series analysis to evaluate outcomes in individuals with skull base chordomas and chondrosarcomas who were treated with SRS and to determine which tumors are appropriate for SRS as adjuvant therapy following maximum tumor resection. Overall, 37 individuals (48 lesions) were treated using GK 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 5- and 10-year survival rates after GKS were 80% and 53%, respectively. The actuarial 5- 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

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

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 who experienced worsened facial numbness despite successful tumor control. The authors concluded that as an adjuvant treatment after resection, GKS is a reasonable option for selected individuals who harbor 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. Limitations include the retrospective nature of the study and small sample size.

Clinical Practice Guidelines

NCCN

The NCCN Guidelines regarding chordoma state that specialized techniques such as SRS should be considered as clinically indicated 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, 2026)

Craniopharyngioma

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

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

Niranjan et al. (2010) conducted a single-center case series analysis to evaluate the outcomes of GK RS 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 male and 24 female individuals, with a median age of 23.5 years (range, 4-77 years). The median tumor volume was 1.0 cm^3 (range, 0.07-8.0 cm^3). The median prescription dose that was delivered to the tumor margin was 13.0 Gy (range, 9-20 Gy). The median maximal dose was 26.0 Gy (range, 20-50 Gy). The mean follow-up time was 62.2 months (range, 12-232 months). The OS rate after SRS was 97.1% at 5 years. The 3- and 5-year PFS rates (solid tumor control) were both 91.6%. The overall local control rate (for both solid tumor and cyst control) was 91%, 81%, and 68% at 1, 3, and 5 years, respectively. No individuals with normal pituitary function developed hypopituitarism after SRS. Two individuals developed homonymous hemianopsia due 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

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

management of residual or recurrent craniopharyngiomas and that complete radiosurgical coverage of the tumor was associated with better tumor control. Limitations include the retrospective nature of the study and small sample size.

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

Xi et al. (2025) conducted a randomized, open-label, controlled trial that evaluated the safety and efficacy of radiofrequency ablation (RFA) compared with those of SBRT in the treatment of recurrent hepatocellular carcinoma (HCC) with small solitary nodules (≤ 5 cm). The inclusion criteria consisted of participants (aged 18-75 years) with recurrent, small HCC without extrahepatic metastasis or vascular invasion at recurrence; a KPS score of 90 or more; and liver function of Child-Pugh class A. Concomitant severe dysfunction of other systems and contraindications for SBRT or RFA were the primary exclusion criteria. Local PFS (LPFS) was the main end point. The secondary end points were PFS, OS, local control rate, and safety. Overall, 83 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 RFA (HR, 0.45; 95% CI, 0.24-0.87; p = 5.014). The 2-year LPFS rates were 92.7% (95% CI, 87.3%-98.5%) with SBRT and 75.8% (95% CI, 67.2%-85.7%) with RFA. The median PFS time in the SBRT and RFA groups was 37.6 months (95% CI, 26.0-49.2 months) and 27.6 months (95% CI, 20.3-34.8 months), respectively (HR, 0.76; 95% CI, 0.50-1.15; p = 5.190). Nine participants in the SBRT group and 10 in the RFA group died during the follow-up. The 2-year OS rates were 97.6% (95% CI, 94.3%-100.0%) in the SBRT group and 93.9% (95% CI, 88.9%-99.2%) in the RFA group (HR, 0.91; 95% CI, 0.37-2.22; 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 participants with small, single, recurrent HCC, SBRT provided better LPFS than RFA, especially in HCC of ≤ 2 cm. Additionally, PFS, OS, and safety were similar between the two treatments. Limitations include 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. The inclusion criteria consisted of studies in English that had at least 10 individuals with inoperable, nonmetastatic, primary, or recurrent intrahepatic cholangiocarcinoma. Studies regarding SBRT were included, even if SBRT preceded or was followed by systemic treatments or other local therapies. Studies on adjuvant SBRT after radical surgery were excluded. OS was the primary end point, and local control, PFS, and treatment-related toxicity were the secondary end points. Six studies (n = 145 individuals) met the inclusion criteria. SBRT was frequently used as a salvage treatment since 28.6% to 66.7% of individuals received previous systemic or local treatments. The median SBRT dose was 45 Gy, which was delivered in three to five fractions. The median follow-up was 16 months, and the 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 radioembolization (TARE). The 1-year local control rate was 85% in one study, and 1-year PFS rates were 50% and 68% in two studies. Toxicity was generally not reported in detail or was reported and included 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 noninvasive therapy, and should be considered for selected individuals with intrahepatic cholangiocarcinoma. Limitations include the limited evidence available regarding the effectiveness of SBRT in intrahepatic cholangiocarcinoma; small sample sizes; and retrospective design of most of the studies.

Jang et al. (2020) conducted a multicenter, phase 2, single-arm, open-label trial to evaluate the safety and efficacy of SBRT in participants 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 2 months after SBRT. The primary end point was treatment-related severe toxicity at 1 year after SBRT. The secondary end points were the 2-year local control, PFS, and OS rates. Overall, 74 participants were enrolled, and 65 eligible participants were analyzed. The median follow-up was 41 months (range, 4-69 months). One participant experienced radiation-induced liver disease with acute grade ≥ 3 toxicity 1 month after SBRT. In addition, one participant had a grade 3 esophageal ulcer with stenosis 5 months after SBRT. The actuarial rate of treatment-related severe toxicity at 1 year was 3%. The pre-SBRT and post-SBRT EGD findings were not significantly different among the 57 evaluable participants who underwent EGD. The 2-year and 3-year local control rates were 97% and 95%, respectively. The PFS and OS rates were 48% and 84% at 2 years, respectively, and 36% and 76% at 3 years. The authors concluded that SBRT in individuals with HCC is well tolerated and an effective treatment modality. Limitations include the lack of a prospective quality-assurance program and the small sample size.

Wang et al. (2020) conducted a systematic review and meta-analysis that was aimed at comparing the safety and efficacy of RFA with SBRT for HCC. Seven studies were identified from January 1990 to May 2020, with a total of 7,928 individuals, and were included in the review. The results showed that SBRT was not inferior to RFA based on the pooled

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

HRs for OS; however, the pooled HR for the local control rate showed the superiority of SBRT. A subgroup analysis showed that the pooled HR for the local control rate favored SBRT in individuals with tumors sized > 2 cm, but no significant difference was observed in individuals with tumors sized 2 cm. In addition, no significant differences in the incidence of late severe complications were observed between the SBRT and RFA groups. The authors concluded that SBRT had an OS equal to that with RFA, was well tolerated, and may be used as an alternative to RFA. Additionally, SBRT was superior to RFA in terms of local control of HCC, especially in those with tumors > 2 cm. Limitations include the retrospective nature of the studies in the review; additionally, the population in each study was different, which may result in heterogeneity. (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 predetermined criteria, was performed using the PubMed, MEDLINE, Embase, and Cochrane Library databases. The primary end points were OS and local control, and the secondary end point was grade ≥ 3 complications. Overall, 32 studies, comprising 33 cohorts and consisting of 1,950 individuals, were included in the meta-analysis. The majority (85%) of the studies used a retrospective design. Pooled 1-, 2-, and 3-year OS rates were 72.6% (95% CI, 65.7%-78.6%), 57.8% (50.9%-64.4%), and 48.3% (40.3%-56.5%), respectively. Pooled 1-, 2-, and 3-year local control rates were 85.7% (95% CI, 80.1%-90.0%), 83.6% (77.4%-88.3%), and 83.9% (77.6%-88.6%), respectively. The overall median tumor size was 3.3 cm (range, 1.6-8.6 cm). Median radiation doses, calculated in equivalent dose in 2 Gy per fraction, ranged from 48 to 114.8 Gy (median, 83.3 Gy). A subgroup comparison of tumor size showed significant differences for 1- and 2-year OS rates and 1-, 2-, and 3-year local control rates. In addition, radiation dose showed no difference for OS and a marginal difference for 1-year local control rate. Pooled rates of hepatic and gastrointestinal grade ≥ 3 complications were 4.7% (95% CI, 3.4%-6.5%) and 3.9% (2.6%-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 3 years. They reported that both OS and local control were affected by tumor size, and radiation dose marginally affected local control; while severe complications were rare, liver function should be considered to prevent serious hepatic toxicity. The limitations include reliance on observational studies that had heterogeneous populations of individuals and study designs, which limits the overall strength of evidence compared with randomized trials. Additionally, potential selection bias exists because SBRT is typically reserved for individuals who are not candidates for other treatment options.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

The ASTRO guideline for primary liver cancers provides evidence-based recommendations for the treatment of HCC and intrahepatic cholangiocarcinoma with external beam radiation therapy (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 is 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 intrahepatic cholangiocarcinoma, induction chemotherapy, followed by consolidation with EBRT, alone or in combination with chemotherapy, is recommended. An implementation remark states that 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 intrahepatic cholangiocarcinoma treatment. (Apisarnthanarax et al., 2022)

European Society for Medical Oncology (ESMO)

Vogel et al. (2025) developed guidelines for the diagnosis, treatment, and follow-up of HCC for ESMO. The recommendations are developed by a multidisciplinary, international panel of experts and reflect both current scientific evidence and their collective clinical judgment. The recommendations include the following (not all inclusive):

- In early-stage HCC, SBRT, proton therapy, and image-guided high-dose-rate brachytherapy can be considered as alternatives to thermal ablation for tumors that are not well suited for or are recurrent following thermal ablation. Level

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

of evidence: II; grade of recommendation: B.
- When a prolonged waiting time (> 3 months) is anticipated, patients can be offered local high-dose-rate brachytherapy, SBRT, transarterial chemoembolization, TARE, or thermal ablation as a bridge to orthotopic liver transplant (III, B). TARE is recommended over transarterial chemoembolization for small tumors in patients who are waiting for orthotopic liver transplant. Level of evidence: II; grade of recommendation: A.

International Stereotactic Radiosurgery Society (ISRS)

Bae et al. (2024) developed a guideline for the ISRS based on a systematic review and meta-analysis in liver-confined HCC to address appropriate patient management. The review included 17 observational studies between 2003 and 2019, with a total of 1,889 patients who underwent treatment for HCC with nine or fewer SBRT fractions. The recommendations are as follows (not all inclusive):

- Patients with HCC of < 3 cm can be considered for SBRT, with favorable local control and survival outcomes. SBRT to HCC of ≥ 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.

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 radiation therapy is recommended when SBRT is used to improve accuracy and reduce toxicity. (NCCN, 2026)

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 five 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, 2026)

Definitive Treatment of Non-Small Cell Lung Cancer

Adar et al. (2026) conducted a systematic review and meta-analysis that compared sublobar resection, SBRT, and image-guided thermal ablation for early-stage NSCLC. Eligible studies included those with individuals who had pathologically confirmed T1-T2b, N0, M0 disease and a tumor size of less than 5 cm and evaluated surgical vs nonsurgical modalities. Comparative analyses were restricted to PSM studies that reported HRs for overall and cancer-specific survival, while single-arm pooled analyses used reconstructed individual patient data. The meta-analysis applied an inverse-variance random-effects model with Hartung-Knapp adjustment, and heterogeneity was assessed using τ^2 and I^2. Seven PSM studies that compared SBRT and sublobar resection showed that sublobar resection improved OS (HR, 1.51; 95% CI, 1.18-1.93), while cancer-specific survival was similar between groups (HR, 1.08; 95% CI, 0.48-2.45). Across 16 single-arm studies, pooled 3-year OS was highest with sublobar resection (80%) compared with SBRT (64%) and image-guided thermal ablation (64%). Three-year cancer-specific survival was also highest with sublobar resection (88%), followed by SBRT (84%) and image-guided thermal ablation (76%). The authors concluded that sublobar resection offers better OS than SBRT and image-guided thermal ablation, although cancer-specific survival is similar across treatments, with SBRT and image-guided thermal ablation remaining appropriate alternatives for nonsurgical candidates and treatment decisions being best made through a multidisciplinary, individualized approach. Limitations include residual confounding due to unmeasured differences between surgical and nonsurgical individuals despite PSM, a limited number of studies (particularly PSM analyses) that compared image-guided thermal ablation with surgery, and heterogeneity in outcome definitions and individual risk classification, which restricts the robustness and scope of the meta-analysis.

Zhang et al. (2022) conducted a systematic review and meta-analysis in individuals with inoperable, early-stage NSCLC to compare local control, OS, and toxicities between SBRT and RFA. Articles that were published in English in peer-reviewed journals, included individuals with stage I NSCLC who were not candidates for surgery, and reported on clinical outcomes were eligible for the review. The following articles were excluded: 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 a fraction number of more than eight and fraction dose of ≤ 8 Gy; and studies that involved other treatments. Overall, 87 SBRT studies (12,811 individuals) and 18 RFA studies (1,535 individuals) met the eligibility criteria. With SBRT, the local control rates (with 95% CI) at 1, 2, 3, and 5 years were 98% (97%-98%), 95% (95%-96%), 92% (91%-93%), and 92% (91%-93%), respectively, which were significantly higher than those with RFA [75% (69%-82%), 31% (22%-39%), 67% (58%-76%), and 41% (30%-52%)] ($p < 0.01$). There were no significant differences in short-term OS between SBRT and RFA [1-year OS rate: 87% (86%-88%) vs 89% (88%-91%), $p = 0.07$; 2-year OS rate: 71% (69%-72%) vs 69% (64%-74%), $p = 0.42$]. Regarding long-term OS, the 3- and 5-year OS rates with SBRT were 58% (56%-59%) and 39%

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

(37%-40%), respectively, which were significantly ($p < 0.01$) superior to those with RFA [48% (45%-51%) and 21% (19%-23%)]. The most common complication of SBRT was radiation pneumonitis (grade ≥ 2), affecting 9.1% of individuals who were treated with SBRT, while pneumothorax was the most common complication of RFA, affecting 27.2% of individuals who were treated with RFA. The authors concluded that SBRT demonstrated superior local control and long-term OS rates compared with RFA, while short-term OS rates remained similar. The authors suggested that large-scale RCTs are needed to further compare the efficacy of SBRT and RFA. Limitations include the heterogeneity of the studies; additionally, the included studies were published between 2000 and 2020, and SBRT and RFA may have evolved during that time frame.

Ball et al. (2019) performed a phase 3 open-label RCT [TROG 09.02 (CHISEL)] that compared stereotactic ablative body radiotherapy (SABR) and standard fractionated radiotherapy in participants with stage I NSCLC who were either inoperable or who had refused surgery, with the aim of evaluating 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). The inclusion criteria consisted of those who were aged 18 years or older, had an ECOG PS of 0 or 1, and had a peripherally located tumor. The exclusion criteria included previous chemotherapy or radiotherapy and multiple primary tumors that required radiotherapy. Five participants (7.6%) 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 the data cutoff (July 31, 2017), the median follow-up for local treatment failure was 2.1 years (IQR, 1.2-3.6 years) in participants who were randomly assigned to standard radiotherapy and 2.6 years (IQR, 1.6-3.6 years) in participants who were assigned to SABR. Overall, 20 of 101 participants (20%) had experienced progression locally: nine of 66 participants (14%) in the SABR group and 11 of 35 participants (31%) in the standard radiotherapy group. 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; $p = 0.0077$). The median time to local treatment failure was not reached in either group. In participants who were 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) that were related to treatment compared with two grade 3 events (chest pain) in the standard treatment group. The authors concluded that compared with standard radiotherapy, SABR had superior local control, without an increase in major toxicity, in those with inoperable, peripherally located, stage I NSCLC. Limitations include the inclusion of a large proportion of participants who had previous cancer and a small sample size. In 2023, Bucknell et al. conducted an analysis of the TROG 09.02 (CHISEL) phase 3 trial to compare pulmonary function tests and the 6 Minute Walk Test after SBRT compared with conventional three-dimensional conformal radiation therapy at 3 and 12 months after treatment. The authors concluded that there was no difference in reduced respiratory function between the two groups despite the higher BEDs delivered to the tumor in SBRT. Limitations include a small sample size and inclusion of a large population of participants with previous cancer.

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 3 trials that compared SABR with surgery in participants with stage I NSCLC. The primary outcome for this pooled analysis was OS according to treatment group (SABR vs surgery), and the secondary outcomes included recurrence-free survival and grade 3 or worse acute or chronic toxicity. Overall, 58 participants were enrolled, with 31 participants randomized to SABR and 27 participants to surgery. The median follow-up was 40.2 months (IQR, 23.0-47.3 months) in the SABR group and 35.4 months (18.9-40.7 months) in the surgery group. Six participants in the surgery group died compared with one participant in the SABR group. The estimated OS at 3 years was 95% (95% CI, 85%-100%) in the SABR group compared with 79% (64%-97%) in the surgery group (HR, 0.14; 95% CI, 0.017-1.190; log-rank $p = 0.037$). Recurrence-free survival at 3 years was 86% (95% CI, 74%-100%) in the SABR group and 80% (65%-97%) in the surgery group (HR, 0.69; 95% CI, 0.21-2.29; 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 participants (10%) 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 who were given SABR had grade 4 events or treatment-related death. In the surgery group, one participant (4%) died of surgical complications, and 12 participants (44%) had grade 3 to 4 treatment-related adverse events. Grade 3 events that occurred 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 (1) the results of this pooled analysis of STARS and ROSEL data suggest that SABR can be considered a treatment option in operable individuals who need a lobectomy and that (2) the equipoise that is suggested by the results justifies efforts for additional RCTs. Limitations include the small sample size and early closures of both clinical trials due to poor accrual.

Timmerman et al. (2010) conducted a multicenter, phase 2, single-arm trial (RTOG 0236) to evaluate the 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 that were less than 5.0 cm in diameter and medical conditions that precluded surgical treatment were included in the analysis. The prescription dose was 18 Gy

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

per fraction in three fractions (54 Gy total) delivered in 1.5 to 2 weeks. The primary end point was primary tumor control, with OS, disease-free survival (DFS), adverse events, involved lobe, and regional and disseminated recurrence as secondary end points. The study aimed to improve the 2-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, which was seen in a previously published study (Timmerman et al., 2006). A total of 59 participants accrued, of whom 55 were evaluable (44 T1 and 11 T2 tumors), with a median follow-up of 34.4 months (range, 4.8-49.9 months). Only one participant had a primary tumor failure; the estimated 3-year primary tumor control rate was 97.6% (95% CI, 84.3%-99.7%). Three participants had recurrence in the involved lobe; the 3-year primary tumor and involved lobe (local) control rate was 90.6% (95% CI, 76.0%-96.5%). Two participants experienced regional failure; the local-regional control rate was 87.2% (95% CI, 71.0%-94.7%). Eleven participants experienced disseminated recurrence; the 3-year rate of disseminated failure was 22.1% (95% CI, 12.3%-37.8%). The rates of DFS and OS at 3 years were 48.3% (95% CI, 34.4%-60.8%) and 55.8% (95% CI, 41.6%-67.9%), respectively. The median OS was 48.1 months (95% CI, 29.6 months to not reached). Protocol-specified, treatment-related, grade 3 adverse events were reported in seven participants (12.7%; 95% CI, 9.6%-15.8%); grade 4 events were reported in two participants (3.6%; 95% CI, 2.7%-4.5%). No grade 5 adverse events were reported. The authors concluded that participants with inoperable NSCLC who received SBRT had a survival rate of 55.8% at 3 years and high rates of local tumor control compared with historical data. Limitations include a small sample size and single-arm design.

Fakiris et al. (2009) conducted a single-center, phase 2, single-arm trial to report 50-month follow-up results from a phase 1 dose-escalation trial in participants with medically inoperable, stage I NSCLC (Timmerman et al., 2003, and McGarry et al., 2005). A total of 70 medically inoperable participants 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 to 66 Gy prescribed to the 80% isodose volume in three fractions. The median follow-up was 50.2 months (range, 1.4-64.8 months). Kaplan-Meier local control at 3 years was 88.1%. Regional (nodal) and distant recurrence occurred in six (8.6%) and nine (12.9%) participants, respectively. Median survival was 32.4 months, and the 3-year OS was 42.7% (95% CI, 31.1%-54.3%). Cancer-specific survival at 3 years was 81.7% (95% CI, 70.0%-93.4%). In participants with T1 tumors, median survival was 38.7 months (95% CI, 25.3-50.2 months), and with T2 tumors, median survival was 24.5 months (95% CI, 18.5-37.4 months) (p = 0.194). Tumor volume (≤ 5 cc, 5-10 cc, 10-20 cc, or > 20 cc) did not significantly impact survival; median survival was 36.9 months (95% CI, 18.1-42.9 months), 34.0 months (95% CI, 16.9-57.1 months), 32.8 months (95% CI, 21.3-57.8 months), and 21.4 months (95% CI, 17.8-41.6 months), respectively (p = 0.712). There was no significant difference in survival between participants with peripheral vs central tumors (median survival, 33.2 vs 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 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. Limitations include a small study population and no comparison group.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's 2018 guideline titled *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 in 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 3 years are not well established. (Schneider et al., 2018)

National Institute for Health and Care Excellence (NICE)

NICE developed a guideline for the diagnosis and management of lung cancer that states that for those with stage I to 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)

NCCN

The NCCN Guidelines for NSCLC state that for stage I and selected node-negative stage IIA, SBRT has achieved good primary tumor control rates and OS that are higher than those with conventionally fractionated radiotherapy (CFRT). The NCCN recommends definitive SBRT for patients with stage I or II NSCLC who are medically inoperable, and SBRT may be a reasonable alternative to surgery for patients who have potentially operable disease and are high risk, are ≥ 75 years of age, or refuse surgery after appropriate consultation. (NCCN, 2026)

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Definitive Treatment of Pancreatic Adenocarcinoma Without Evidence of Distant Metastasis

Montesi et al. (2026) conducted a systematic review and meta-analysis that compared SBRT and CFRT in those with locally advanced pancreatic cancer (LAPC). Both prospective and retrospective studies that were published between January 2015 and July 2025 were eligible, and five retrospective studies that comprised 768 individuals were included. The analysis followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and used random-effects models to pool HRs for OS and PFS and RRs for severe acute toxicity, with bias assessed by the ROBINS-I (Risk of Bias in Non-Randomized Studies of Interventions) tool. OS was defined as the time from diagnosis or treatment initiation to death or censoring, and PFS was defined as time to disease progression, death, or censoring. No significant differences were found in OS (HR, 0.74; 95% CI, 0.46-1.20; p = 0.22) or PFS (HR, 1.89; 95% CI, 0.91-3.95; p = 0.09) between SBRT and CFRT, while SBRT showed a significantly lower risk of severe acute toxicity (RR, 0.24; 95% CI, 0.11-0.52; p < 0.001). The authors concluded that SBRT achieved survival outcomes comparable to those with CFRT, with a significantly lower incidence of severe acute toxicity in LAPC; this supports its clinical use as a consolidative approach following induction chemotherapy. Key limitations include the retrospective design of most studies and substantial heterogeneity across clinical and methodological factors, which restrict the strength and consistency of the current evidence.

Zeng et al. (2026) conducted a systematic review and meta-analysis for the ISRS that evaluated prospective trials of SBRT for nonmetastatic LAPC. Inclusion criteria included prospective studies that involved those who had nonmetastatic LAPC with in-situ disease and were treated using multifraction photon SBRT up to six fractions, with delivery of more than 5 Gy per fraction and reporting of at least one end point of local control, PFS, OS, or toxicities. Overall, 23 studies that comprised 901 individuals were analyzed, with a weighted median age of 66 years; 51% were male, and most received systemic therapy before SBRT. The primary outcomes were local control and toxicities. The pooled 12-month and 24-month local control rates were 82% (95% CI, 76%-86%) and 70% (95% CI, 58%-79%), respectively, while the pooled risk of grade 3 to 4 toxicities was 2% (95% CI, 1%-6%) and of grade 5 toxicities was 0.2% (95% CI, 0%-3%); these were predominantly gastrointestinal bleeding. The prespecified secondary end points were PFS and OS at 12 and 24 months. The authors concluded that SBRT is a safe and efficacious treatment option for LAPC, provides durable locoregional control, with low toxicity rates, and serves as an important component in long-term management, with advancements in image guidance and improvement in the therapeutic ratio with adaptive radiotherapy planning. Key limitations include the lack of multicenter RCTs; heterogeneity in dose prescription, fractionation, and treatment delivery; and potential publication bias despite the inclusion of only prospective studies. Herman et al. (2015), previously cited in this policy, was included in this review.

Tchelebi et al. (2020) conducted a systematic review and meta-analysis that aimed to compare the efficacy and safety of SBRT with those of CFRT with concurrent chemotherapy for the treatment of LAPC. Overall, 21 studies were included in the analysis, including 11 CFRT and nine SBRT studies, for a total of 1,147 individuals. The primary outcome was efficacy, which was defined as 2-year OS. One-year OS and incidence of acute or late grade 3 or 4 toxicity were the secondary outcomes. For SBRT, the median dose was 30 Gy, and the most common regimen was 30 Gy per 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 2-year OS was 26.9% (95% CI, 20.6%-33.6%) for SBRT vs 13.7% (95% CI, 8.9%-19.3%) for CFRT and was statistically significant in favor of SBRT. The random-effects estimate for 1-year OS was 53.7% (95% CI, 39.3%-67.9%) for SBRT vs 49.3% (95% CI, 39.3%-59.4%) for CFRT and was not statistically significant. The random-effects estimate for acute grade 3 or 4 toxicity was 5.6% (95% CI, 0.0%-20.0%) for SBRT vs 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 or 4 toxicity was 9.0% for SBRT (95% CI, 3.3%-17.1%) vs 10.1% (95% CI, 1.8%-23.8%) for CFRT, which was not statistically significant. The authors concluded that in individuals with LAPC, SBRT may provide a modest improvement in 2-year OS, with reduced rates of acute grade 3 or 4 toxicity and no change in 1-year OS or late toxicity. The authors recommended future quality studies to evaluate SBRT in these individuals. Limitations include the phase 1 or 2 studies and retrospective nature of the SBRT studies; the CFRT studies were all phase 2 or phase 3.

Zhong et al. (2017) conducted a retrospective review that compared SBRT with CFRT therapy in LAPC using the National Cancer Database. Patients with cT2-4/N0-1/M0 adenocarcinoma of the pancreas, diagnosed from 2004 to 2013, were included in the review. Radiation therapy that was delivered at ≥ 4 Gy per fraction was considered SBRT, and radiation therapy that was delivered at ≤ 2 Gy was deemed CFRT. OS was the primary outcome. The total number of patients included in the review was 8,450: 7,819 received CFRT, and 631 received SBRT. Receipt of SBRT was associated with superior OS in the multivariate analysis (HR, 0.84; 95% CI, 0.75-0.93; p < 0.001). With propensity score matching, 988 patients in all were matched, with 494 patients in each cohort. In the propensity-matched cohorts, median OS (13.9 vs 11.6 months) and the 2-year OS rate (21.7% vs 16.5%) were significantly higher with SBRT vs CFRT. The authors concluded that SBRT was superior in OS compared with CFRT and that an additional benefit of SBRT was the shorter

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

duration of treatment. Additionally, the authors recommended future randomized trials to evaluate these results. Limitations include the retrospective nature of the study and lack of control for the specific type of chemotherapy in propensity matching.

Mellon et al. (2015) conducted a single-center case series analysis to evaluate outcomes and toxicity of induction chemotherapy and SBRT for borderline resectable pancreatic cancer (BRPC) and LAPC. The center's internal database was queried to identify all individuals who received at least one dose of induction chemotherapy and SBRT for the treatment of BRPC or LAPC. After staging, medically fit individuals underwent chemotherapy for 2 to 3 months, with the regimen at the discretion of the treating medical oncologist. Then, individuals received SBRT that was delivered in five consecutive daily fractions, with median total radiation doses of 30 Gy to the tumor and 40 Gy dose painted to tumor-vessel interfaces. That was followed by restaging imaging for possible resection. The outcomes included OS, event-free survival, and locoregional control rates. Overall, 159 individuals, 110 with BRPC and 49 with LAPC, with a median follow-up of 14.0 months, were included in the analysis. The resection and margin-negative (R0) rate in individuals with BRPC who completed neoadjuvant therapy was 51% and 96%, respectively. Estimated median OS was 19.2 months in individuals with BRPC and 15.0 months in individuals with LAPC ($p = 0.402$). Median OS was 34.2 months in individuals with surgical resection vs 14.0 months in individuals without ($p < (0.001)$. Five of 21 individuals (24%) with LAPC who received oxaliplatin, irinotecan, fluorouracil, and leucovorin (FOLFIRINOX) chemotherapy underwent R0 resection. Among individuals with LAPC, FOLFIRINOX recipients underwent R0 resection more often than other chemotherapy recipients (five of 21 vs zero of 28; $p = 0.011$). There was a trend for improved survival in individuals with LAPC who underwent resection ($p = 0.09$). In those who were not undergoing resection, 1-year locoregional control was 78%. The 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. Limitations include the retrospective, single-institution design; lack of a control group; and short median follow-up time.

Chuong et al. (2013) conducted a single-center, retrospective case series analysis to evaluate outcomes in patients with nonmetastatic pancreatic cancer who were treated with induction chemotherapy followed by SBRT. SBRT was delivered over five consecutive fractions using a dose-painting technique, including 7 to 10 Gy per fraction to the region of vessel abutment or encasement and 5 to 6 Gy per fraction to the remainder of the tumor. Restaging scans were performed at 4 weeks, and patients with resectable cancer were considered for resection. The primary end points were OS and PFS. Overall, 73 patients 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. Overall, 32 patients (56.1%) with BRPC underwent surgery, with 31 (96.9%) undergoing an R0 resection. Median OS, 1-year OS, median PFS, and 1-year PFS in patients with BRPC vs LAPC were 16.4 months vs 15 months, 72.2% vs 68.1%, 9.7 vs 9.8 months, and 42.8% vs 41%, respectively (all $p > 0.10$). Patients with BRPC who underwent R0 resection had improved median OS (19.3 vs 12.3 months; $p = 0.03$), 1-year OS (84.2% vs 58.3%; $p = 0.03$), and 1-year PFS (56.5% vs 25.0%; $p < 0.0001$), respectively, compared with all nonsurgical patients. The 1-year local control in nonsurgical patients 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 individuals with unresectable cancer and that these data support the expanded implementation of SBRT for pancreatic cancer. Limitations include the retrospective, single-institution design and small sample size.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

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

- Following surgical resection of pancreatic cancer, adjuvant SBRT is only recommended in a clinical trial or multi-institutional registry. Strength of recommendation: strong; quality of evidence: very low.
- For patients with BRPC and select LAPC that is 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 LAPC that is not appropriate for downstaging to eventual surgery, a definitive therapy regimen of systemic chemotherapy, followed by either CFRT with chemotherapy, dose-escalated chemoradiation, or multifraction SBRT without chemotherapy, is conditionally recommended. Strength of recommendation: conditional; quality of evidence: low.

NCCN

The NCCN Guidelines for pancreatic adenocarcinoma state that as first-line therapy, SBRT may be used in select patients with locally advanced disease without systematic metastases or those who are not candidates for combination therapy. As

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

subsequent therapy, SBRT may be used if not previously given and if the primary site is the sole site of progression. A single-fraction SBRT approach may be used as palliative treatment for relief of celiac axis–related pain. (NCCN, 2026)

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 with those of other treatments for localized prostate cancer. All studies consistently found minimal differences between treatments, except that prostatectomy individuals experienced significantly higher rates of erectile dysfunction than SBRT individuals.

van As et al. (2024) conducted a phase 3 RCT (PACE-B) that assessed noninferiority of five-fraction SBRT compared with that of conventionally or moderately hypofractionated radiotherapy for biochemical or clinical failure. Participants (n = 874) were randomized into two groups (control radiotherapy, 441; SBRT, 433) in 38 centers. The inclusion criteria included those aged 18 years or older who had prostate adenocarcinoma, a World Health Organization (WHO) performance status of 0 to 2, and a life expectancy of ≥ 5 years. Participants had T1 or T2 disease and were at low or intermediate risk. Those with Gleason grade 4 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 (ADT) was not permitted. The median age was 69.8 years, and the median prostate-specific antigen level was 8.0 ng/mL. The NCCN risk groups were 9.3% low and 90.7% intermediate. After a median follow-up of 74.0 months, the 5-year biochemical/clinical failure–free rate (95% CI) was 94.6% (91.9%-96.4%) with control radiotherapy vs 95.8% (93.3%-97.4%) with SBRT. SBRT was noninferior to control radiotherapy, with an unadjusted HR of 0.73 (90% CI, 0.48-1.12; p value for noninferiority = 0.004). To 5 years, the cumulative rate of late RTOG grade 2 or worse genitourinary (GU) toxicity was 18.3% (95% CI, 14.8%-22.5%) with control radiotherapy vs 26.9% (95% CI, 22.8%-31.5%) with SBRT (p < 0.001). The rate of gastrointestinal toxicity was 10.2% (95% CI, 7.7%-13.5%) with control radiotherapy vs 10.7% (95% CI, 8.1%-14.2%) with SBRT (p = 0.94). The authors concluded that in those with low-/intermediate-risk localized prostate cancer, SBRT (five fractions) is noninferior to control radiotherapy for biochemical/clinical failure and is an effective treatment option that offered similar efficacy, with greater convenience, in the participants.

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 that were published between January 1990 and January 2018. The primary end points included 5-year overall biochemical recurrence–free survival (bRFS), physician-reported acute and late grade ≥ 3 toxicity for both GU and gastrointestinal domains, and patient-reported QOL using the EPIC (Expanded Prostate Cancer Index Composite). Secondary analyses included a meta-regression of the impact of covariables on bRFS and late toxicity. Overall, 38 studies were included in the analysis, comprising 6,116 individuals. In total, 22 studies were clinical trials, of which one was a phase 1 trial that included 45 individuals; four were phase 1/2 trials that included 245 individuals, 17 were phase 2 or 3 trials that included 2,174 individuals, and 16 were prospective observational studies that included 3,652 individuals. The median follow-up period was 39 months (range, 12-115 months). Overall, 92%, 78%, and 38% of studies included low-, intermediate-, and high-risk individuals, respectively. Overall, 5- and 7-year bRFS rates were 95.3% (95% CI, 91.3%-97.5%) and 93.7% (95% CI, 91.4%-95.5%), respectively. The estimated late grade ≥ 3 GU and gastrointestinal toxicity rates were 2.0% (95% CI, 1.4%-2.8%) and 1.1% (95% CI, 0.6%-2.0%), respectively. By 2 years post SBRT, EPIC urinary and bowel domain scores returned to baseline. An 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 that supports its use as a standard treatment option, with favorable tumor control, patient-reported QOL, and levels of toxicity. This analysis is limited by its study-level meta-analysis design and restriction to uniformly reported time points, as well as incomplete reporting of risk stratification and ADT use.

Widmark et al. (2019) conducted a multicenter, phase 3, randomized, open-label, noninferiority trial to show that ultrahypofractionation is noninferior to conventional fractionation regarding failure-free survival, without any significant differences in late normal tissue complications. Participants were men who were up to 75 years of age with histologically verified, intermediate- to high-risk prostate cancer and a WHO performance status of between 0 and 2. Participants were randomly assigned to ultrahypofractionation (42.7 Gy in seven fractions, 3 days per week for 2.5 weeks) or conventional fractionated radiotherapy (78.0 Gy in 39 fractions, 5 days per week for 8 weeks). No ADT was allowed. The primary end point was time to biochemical or clinical failure. The prespecified noninferiority margin was 4% at 5 years, corresponding to a critical HR limit of 1.338. Physician-recorded toxicity was measured according to the RTOG morbidity scale, and participant-reported outcome measurements were obtained with the Prostate Cancer Symptom Scale questionnaire. Overall, 1,200 participants were randomly assigned to conventional fractionation (n = 602) or ultrahypofractionation (n = 598), of whom 1,180 (591 conventional fractionation and 589 ultrahypofractionation) constituted the per-protocol population. Overall, 89% of participants (n = 1,054) were intermediate risk, and 11% (n = 126) were high risk. The median follow-up time was 5 years (IQR, 3.1-7.0 years). The estimated failure-free survival at 5 years was 84% (95% CI, 80%-

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

87%) in both treatment groups, with an adjusted HR of 1.002 (95% CI, 0.758-1.325; p = 0.99). There was weak evidence of an increased frequency of physician-reported acute RTOG grade 2 or worse urinary toxicity in the ultrahypofractionation group at the end of radiotherapy [158 of 569 participants (28%) vs 132 of 578 participants (23%); 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 ultrahypofractionation group compared with the conventional fractionation group at the 1-year follow-up [32 of 528 participants (6%) vs 13 of 529 participants (2%); p = 0.0037]. There were no differences between groups in frequencies at 5 years in RTOG grade 2 or worse urinary toxicity and bowel toxicity. Participant-reported outcomes revealed significantly higher levels of acute urinary and bowel symptoms in the ultrahypofractionation group compared with the conventional fractionation group, but no significant increases in late symptoms were found, except for increased urinary symptoms at the 1-year follow-up, which is consistent with the physician-evaluated toxicity. The authors concluded that ultrahypofractionated radiotherapy is noninferior to CFRT for intermediate- to high-risk prostate cancer as it relates to failure-free survival; therefore, their results support the use of ultrahypofractionation for radiotherapy of prostate cancer. The limitations include the relatively short 5-year follow-up, which limits assessment of long-term outcomes and late effects. They also include the small proportion of high-risk participants and the use of a nonstandard, region-specific Prostate Cancer Symptom Scale questionnaire, which may reduce generalizability and comparability with other studies.

Clinical Practice Guidelines

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

Eastham et al. (2022) developed the AUA/ASTRO guideline for localized prostate cancer that strongly recommends the use of dose escalation when EBRT is the primary treatment for patients with prostate cancer. Additionally, clinicians should use 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. (2026) published an amendment to the 2022 guideline that did not alter the previously established recommendations noted above. The amendment includes the following statements regarding radiation management:

- When combined ADT and radiation is used, ADT may be initiated neoadjuvantly or concurrently (conditional recommendation).
- When treating a subgroup of high-risk localized patients (at least two of the following: prostate-specific antigen ≥ 40 ng/dL, Gleason ≥ 8, or ≥ cT3) or locally advanced prostate cancer (cN1) with radiation therapy, clinicians should combine ADT with abiraterone acetate and prednisone for 24 months (strong recommendation).

NCCN

The 2026 NCCN Guidelines for prostate cancer state that SBRT is acceptable for the 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 disease progression (e.g., oligoprogression) or limited residual disease in the setting of otherwise effective systemic therapy.
- Lesion occurs in or immediately adjacent to a previously irradiated treatment field.
- At physician discretion to achieve more sustained pain control than typically seen with standard with typical palliative regimens.

Definitive Treatment of Renal Cancer

Glicksman et al. (2026) conducted a prospective, single-center, phase 2, single-arm clinical trial that evaluated kidney-directed SBRT in adults with solid kidney lesions [primary renal cell carcinoma (RCC) or metastatic deposits] who were medically inoperable or declined surgery. Eligible participants were > 18 years old, had an ECOG performance status of 0 to 3, and had a renal lesion that was amenable to SBRT, with key exclusions that included highly nephrotoxic systemic therapy within 60 days, end-stage renal failure [estimated glomerular filtration (eGFR) < 15 mL/min or dialysis], certain familial syndromes, and prior overlapping abdominal radiation. Overall, 30 participants, with 32 renal tumors, were enrolled (median age, 76 years; 87% primary kidney cancer; 93% chronic kidney disease stage ≥ 2), and the median radiation dose was 35 Gy in five fractions. The primary end point was nephron toxicity, which was measured as change in eGFR over 2 years; 18 of 30 participants were evaluable for eGFR at 2 years, and noninferiority was not established because the mean eGFR change from baseline to 2 years was -8.7 mL/min/1.73 m^2 (95% one-sided CI, -14.06 to 0.00 mL/min/1.73 m^2; p = 0.71). The prespecified secondary end points were serum creatinine level kinetics, changes in ipsilateral and contralateral renal function scan, change in systolic and diastolic blood pressure, change in urine albumin/creatinine ratio, local control, distant control (excluding those with preexisting distant metastatic disease), OS, acute and late toxicity (Common Terminology Criteria for Adverse Events v5), and health-related QOL. The authors

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

concluded that SBRT for renal tumors (primary or metastatic) causes only modest declines in eGFR that are comparable to those with other standard treatments and that it is an effective option for inoperable individuals at 2 years. Additionally, SBRT provides high local control, has low grade ≥ 2 toxicity, and preserves QOL. The authors noted that randomized trials are needed to further assess its efficacy and overall impact. There are limitations, including the single-arm design, which makes it challenging to compare results with those of other treatment modalities; single-center setting despite being a tertiary cancer center that receives outside referrals and has multidisciplinary kidney cancer experience; and follow-up of approximately 2 years, which limits assessment of longer-term renal function and oncological outcomes.

Siva et al. (2024a) conducted the FASTRACK II international, nonrandomized clinical trial to evaluate the efficacy of SABR as a treatment alternative for participants with primary renal cell cancer who were not suitable for surgery and had limited curative options. The phase 2 study took place in seven centers in Australia and one center in the Netherlands. Overall, 70 participants who were 18 years of age or older, had primary renal cell cancer (single lesion) that was confirmed by biopsy, had an ECOG PS of 0 to 2, declined surgery or were medically inoperable, or were at a high risk of complications from surgery were included in the study. A multidisciplinary decision that treatment was warranted was also required. The exclusion criteria included tumors that were larger than 10 cm, tumors abutting the bowel, previous high-dose radiation therapy to an overlapping area, previous systemic treatment for renal cell cancer, and an eGFR of less than 30 mL/min per 1.73 m^2. The primary end point was local control. Before enrollment, 49 of 70 participants (70%) had documented serial growth on initial surveillance imaging. Overall, 49 of 70 participants (70%) were male, and 21 (30%) were female. The median tumor size was 4 to 6 cm (IQR, 3.7-5.5 cm). All participants who were enrolled had T1-T2a and N0-N1 disease. In total, 23 participants received single-fraction SABR of 26 Gy, and 47 received 42 Gy in three fractions. The median follow-up was 43 months (IQR, 38-60 months). Local control at 12 months from treatment commencement was 100% ($p < 0.0001$). Seven participants (10%) 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 participants (4%)]; abdominal, flank, or tumor pain [four (6%)]; colonic obstruction [two (93%)]; and diarrhea [one (1%)]. No treatment-related or cancer-related deaths occurred. The authors concluded that SABR can be considered a proven modality for inoperable participants with larger renal cell cancer tumors or those with tumors in a location that is not amenable to thermal ablation. The authors recommended future randomized trials. Study limitations include the lack of randomization, small sample size, and lack of a control group.

Suleja et al. (2024) conducted a systematic review and meta-analysis to evaluate the current evidence for the treatment of individuals with localized RCC using SBRT. Studies that assessed safety and clinical effectiveness in individuals with localized RCC using SBRT in single-arm trials or those that compared SBRT 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. Overall, 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 individuals, and their estimated rate was 0.03 (95% CI, 0.01-0.11; n = 291). One- and 2-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 1- and 2-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, results in 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 are needed, and surgical treatment remains the standard of care in operable individuals. Limitations include short-term follow-ups and a lack of RCTs. Siva et al. (2024a) is included in this systematic review and meta-analysis.

Siva et al. (2022) conducted an individual patient data meta-analysis that included 190 adults with primary RCC who were treated with SABR across 12 institutions in five countries. Eligible individuals were aged 18 years or older, had nonmetastatic disease, had at least 2 years of follow-up, and had no prior local therapy or abdominal radiotherapy. SABR was delivered as single-fraction (n = 81) or multifraction (n = 109) regimens, with a median follow-up of 5 years. The primary end point was investigator-assessed local failure per Response Evaluation Criteria in Solid Tumors version 1.1. At 5 years, the cumulative incidence of local failure was 5.5% (95% CI, 2.8%-9.5%), with single-fraction SABR showing fewer local failures than multifraction SABR (Gray p = 0.020; HR, 6.10; 95% CI, 1.02-36.66; p = 0.048). No grade 3 or higher toxic effects or treatment-related deaths occurred, and seven individuals (4%) required dialysis after SABR. The prespecified secondary end points included treatment-related toxic effects, patterns of failure, survival, and renal function outcomes. According to the authors, SABR was effective and safe in the long term in those with primary RCC, with single-fraction SABR associated with fewer local failures than multifraction SABR. The mature outcome and safety data support renal SABR as a viable treatment option for individuals who are inoperable or at high surgical risk, including those with smaller renal masses in whom outcomes appear comparable to those with other local therapies. Key limitations include the retrospective collection of toxicity data that may have led to underreporting and lack of pathological confirmation in all

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

individuals. Additional limitations include the heterogeneity across institutions and treatment techniques and inclusion of larger renal masses than those typically treated with thermal ablation.

Clinical Practice Guidelines

International Stereotactic Radiosurgery Society (ISRS)

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

- Optimal dose regimens for SBRT in patients with primary RCC include 26 Gy in one fraction if the tumor is ≤ 4 to 5 cm, 42 to 48 Gy in three fractions if the tumor is > 4 to 5 cm, or potentially 40 Gy in five fractions if the dose constraints for organs at risk (OARs) 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 that are concerning for disease progression. Strength of recommendation: strong.
- For patients with a solitary kidney, SBRT is an approach that is associated with both excellent local control and acceptable renal function preservation (except in patients with stage 4 or 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.
- The optimal posttreatment follow-up schedule after SBRT for primary RCC includes cross-axial imaging of the abdomen, including both kidneys and adrenals every 6 months, and surveillance scans, including chest imaging at a minimum. Strength of recommendation: moderate.

NCCN

The NCCN Guidelines for primary kidney cancer state that definitive therapy with SBRT can be considered for those who are not surgical candidates and have T1-T2a tumors (≤ 10 cm), although evidence is limited for tumors that are larger than 7 cm. For tumors that are located near the bowel, a five-fraction SBRT approach is recommended, with strict bowel dose constraints, prioritizing bowel safety over full target coverage. Nephrectomy (radical or partial) is recommended when feasible and clinically indicated, including as primary treatment for resectable stage IV (T4, M0) disease. For patients who are not optimal surgical candidates, SBRT may be considered for stage II (category 2B) and stage III RCC (category 3). (NCCN, 2027)

Definitive Treatment of Small Cell Lung Cancer

Safavi et al. (2021) conducted a systematic review and meta-analysis to evaluate and summarize oncological and toxicity outcomes in those with inoperable T1-2N0M0 SCLC. The inclusion criteria consisted of peer-reviewed journal articles that assessed eight or fewer fractions of SABR for T1-2N0M0 SCLC. Excluded from the analysis were reviews, editorials, commentaries, guidelines, prefaces, case series with fewer than five individuals, and studies that were published in languages other than English. Overall, 11 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% of individuals (75%-100%). The median follow-up and tumor size were 19.5 months (11.9-32 months) and 24 mm (19-29 mm), 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 1 year and 95.7% (95% CI, 74.2%-100.0%) at 2 years. OS was 86.3% (95% CI, 74.4%-94.9%) at 1 year and 63.7% (95% CI, 45.7%-79.9%) at 2 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 (Common Terminology Criteria for Adverse Events) 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. The authors suggested conducting future prospective studies to assess the use of SABR in individuals with higher risks of toxicity with surgery or combined chemoradiation. Limitations include the retrospective nature of the included studies and small sample sizes.

Verma et al. (2019) compared SBRT with CFRT in individuals (n = 2,107) with inoperable stage I SCLC. The National Cancer Database was searched (2004-2014) for histologically confirmed, T1-2N0M0 SCLC. The inclusion criteria included those with newly diagnosed, T1-2N0M0 SCLC who received chemotherapy. Those who had surgery, were not receiving EBRT, and/or lacked survival/follow-up information or received chemotherapy that started less than 3 months before or less than 2 months after radiation therapy were excluded. Of 2,107 individuals, 7.1% underwent SABR/chemotherapy, and 92.9% received CFRT/chemotherapy. The median (IQR) dose of SABR was 50 Gy (48-54 Gy) in four (three to five) fractions and of CFRT was 55.8 Gy (45-60 Gy) in 30 (30-33) fractions. Individuals who were receiving SABR/chemotherapy were more often older, had T1 disease, were treated at academic/integrated network facilities, and were managed in more recent years ($p < 0.05$ for all). Respective median survival figures were 29.2 vs 31.2 months ($p =$

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

0.77), which persisted following propensity matching (25.4 vs 34.3 months; p = 0.85). On multivariable analysis, radiotherapeutic technique was not associated with OS (p = 0.95). According to the authors, in 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 that these retrospective data should be strongly considered when advocating for SABR/chemotherapy as the preferred treatment option in this group of individuals. Limitations include the retrospective nature of the study and small SABR cohort.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

Simone II et al. (2020) developed an ASTRO guideline for radiation therapy of SCLC, which strongly recommends definitive thoracic radiation therapy 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.

NCCN

The NCCN Guidelines for SCLC indicate that the principals of SBRT for SCLC are similar to those for NSCLC. Patients with stage I to 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. The NCCN states that for those with SCLC and a small number of BMs, SRS may be appropriate; SRS is preferred for patients who develop BMs after PCI. (NCCN, 2026)

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. OS, PFS, and local recurrence rate were assessed and compared between both groups. Overall, 141 studies on metastasectomy (n = 29,932) and 16 studies on SBRT (n = 1,381) were included in the final analysis. The pooled 5-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 5-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 local recurrence rate 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 GRADE (Grading of Recommendations Assessment, Development, and Evaluation) 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 performed because the outcome measures were too similar across studies, and the known prognostic factors were not evenly balanced between the two groups. The authors recommended future RCTs that compare surgery and SBRT in this population of individuals. Limitations include the nonrandomized comparison of the two local treatment strategies.

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 in individuals with oligometastatic prostate cancer compared with those in individuals with no metastasis-directed therapy. The primary outcomes were OS and grade ≥ 3 toxicity. Systemic therapy–free survival, QOL, grade 5 toxicity, local control, and PFS were secondary outcomes. Seven phase 2 RCTs, with 559 individuals, were included in the review. Four trials included multiple types of primary cancer. The outcome definitions were heterogeneous, except for OS and toxicity. For OS, only one study reported events in both arms. A 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 concern or high. The quality of evidence was low or moderate. The authors concluded that phase 2 trials have demonstrated promising enhancements in PFS for various oligometastatic prostate cancer states, without significant toxicity; however, OS comparisons remain inconclusive. The authors suggested that future phase 3 trials are needed and should include larger sample sizes, blinding, and improved adherence to assigned interventions. Limitations of the study include the small sample sizes and varying groups of individuals and treatment approaches.

Harrow et al. (2022) states that the SABR-COMET (Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastases Tumors) trial was amended in 2016 to extend follow-up to 10 years; this report contains oncological outcomes beyond 5 years. Overall, 99 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 vs SABR to all metastases plus standard of care. The primary end point was OS, and the secondary end points were PFS, toxicity, QOL, and time to new metastases. Eight-year OS was 27.2% in the SABR arm vs 13.6% in the control arm. Eight-year PFS estimates were 21.3% vs 0.0%, respectively. Rates of grade ≥ 2 acute or late toxic effects were 30.3% vs 9.1%, with no new grade 3 to 5 toxic effects. FACT-G (Functional Assessment of Cancer Therapy – General) QOL scores declined

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

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 that SABR had significant improvements in OS and PFS. Additionally, there were no new safety signals detected with extended follow-up. The authors recommended future larger studies. Limitations include several participants who were either lost to follow-up or died before the last report, and, additionally, the trial included multiple histologies, which limits conclusions that can be made about specific histologies.

Marvaso et al. (2021) conducted a systematic review and meta-analysis to better define the role of SBRT in individuals with oligorecurrent prostate cancer. All prospective studies that included individuals with prostate cancer and nodal and/or bone oligometastases and one to five lesions were considered eligible. Six studies that were published between 2013 and 2020 were included in the review. Data from 445 individuals, of whom 396 received SBRT (67 in randomized studies and 329 in observational studies), were incorporated. Five studies considered LPFS and reported values close to 100%; one study reported a value of 80% in the observational arm. Benefit in terms of biochemical PFS due to 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 end points of interest. Most events were classified as either grade 1 or grade 2, and the only grade ≥ 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 that compared SBRT with an active treatment. (Ost et al., 2018, 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. SABR-COMET was a multicenter, randomized, phase 2, 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 et al., 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 on the tumor location and indication, and prescribed doses ranged from 8 Gy in one fraction to 30 Gy in 10 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 to 60 Gy in three to eight fractions, depending on target size and location. Participants were seen every 3 months after randomization for the first 2 years and every 6 months thereafter. Overall, 99 participants were enrolled at 10 centers; 33 were randomly assigned to the control group, and 66 were assigned 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). Overall, 93% of the participants (92 of 99) had one to three metastases. In the initial report (Palma et al., 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, 46-58 months). The primary outcome event, death (all cause), occurred in 24 of 33 participants (73%) in the control group and 35 of 66 participants (53%) in the SABR group. The median OS was 28 months (95% CI, 19-33 months) in the control group vs 41 months (26 months to not reached) in the SABR group (HR, 0.57; 95% CI, 0.30-1.10; p = 0.090). The 5-year OS rate was 17.7% in the control group (95% CI, 6%-34%) vs 42.3% in the SABR group (95% CI, 28%-56%; p = 0.006). The 5-year PFS rate was not reached in the control group (3.2%; 95% CI, 0%-14% at 4 years with last participant censored) and 17.3% in the SABR group (95% CI, 8%-30%; p = 0.001). There were no new grade 2 to 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 had a 22-month improvement in median OS compared with participants who received a standard-of-care approach alone, which corresponds to an absolute survival benefit of 25% at 5 years. Furthermore, they reported that there were no new safety concerns detected during the extended follow-up period. Limitations include the inclusion of multiple histologies, phase 2 design, and small sample size.

Gomez et al. (2019) reported extended outcomes from a previously published multicenter phase 2 RCT. The original study (Gomez et al., 2016) evaluated PFS after aggressive local consolidative therapy (LCT) vs maintenance therapy or observation (MT/O) in participants with stage IV NSCLC and three or fewer metastases remaining after frontline systemic therapy. That trial was closed early after it demonstrated an 8-month benefit in PFS in participants who received LCT compared with participants who received MT/O; the median PFS was 11.9 months in the LCT arm (90% CI, 5.72-20.90 months) vs 3.9 months in the MT/O arm (p = 0.005). The extended outcomes included PFS, OS, toxicity, and the appearance of new lesions. Overall, 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, 28.3-61.4 months), and the PFS benefit was durable [median, 14.2 months (95% CI, 7.4-23.1 months) with LCT vs 4.4 months (95% CI, 2.2-8.3 months) with MT/O; p = 0.022]. There was an OS benefit in the LCT arm [median, 41.2 months (95% CI, 18.9 months to not reached) vs 17.0 months (95% CI, 10.1-39.8 months) with MT/O; p = 0.017]. No additional grade 3 or greater toxicities were observed. Survival after

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

progression was longer in the LCT arm (37.6 months with LCT vs 9.4 months with MT/O; p = 0.034). Of the 20 participants who experienced progression in the MT/O arm, nine received LCT to all lesions after progression, and the median OS was 17 months (95% CI, 7.8 months to not reached). The authors concluded that in participants with oligometastatic NSCLC who did not experience progression after frontline systemic therapy, LCT prolonged PFS and OS compared with MT/O. Limitations include the small sample size. (This study is included in the ISRS guideline below.)

Sutera et al. (2019) conducted a phase 2 multicenter trial to assess outcomes, toxicity, and QOL in participants with oligometastatic cancer who were prospectively treated with SABR. Participants were 18 years of age or older, had oligometastatic (one to five metastases in three or fewer organs) or recurrent cancer, had a Zubrod PS of 0 to 2, and had adequate laboratory parameters. Those with lymphoma, leukemia, multiple myeloma, or central nervous primaries were ineligible. Additionally, any participant with another primary cancer within the last 3 years, diffuse metastatic spread that was confined to one organ, pregnancy, sites not treatable with SABR, or severe active comorbidities were excluded. Participants (n = 147) were seen in follow-up 6 weeks post SABR, then every 3 months for 3 years, and at 6-month intervals thereafter. The feasibility of SABR in participants with oligometastatic disease was the primary end point. The secondary end points were 5-year OS, 5-year LPFS, QOL, and toxicity. The most common primary tumors included lung (21.8%; non-small cell: n = 29; small cell: n = 3), colorectal adenocarcinoma (21.1%), and head and neck (10.9%; squamous cell carcinoma: n = 11). In a median follow-up of 41.3 months (IQR, 14.6-59.0 months), the median OS was 42.3 months (95% CI, 27.4 months to ∞), with a 5-year OS of 43%. Five-year LPFS and distant PFS were 74% and 17%, respectively. Acute grade ≥ 2 and ≥ 3 toxicity was 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 6 weeks, 3 months, and 9 months after treatment. At 6 months and 12 months, participants were found to have statistically significant improvement in participant-reported QOL. The authors concluded that SABR was a feasible and tolerable treatment, with minimal acute and late grade 3 toxicity, in those with oligometastatic cancer. The authors recommended future RCTs to support their results. Limitations include the lack of randomization and a heterogeneous participant population.

Iyengar et al. (2018) conducted a single-center, phase 2, randomized trial to determine if noninvasive SABR prior to maintenance chemotherapy in participants with nonprogressive, limited, metastatic NSCLC after induction therapy led to significant improvements in PFS. Participants were eligible if they were aged 18 years or older, had a KPS score of 70 or better, and had biopsy-proven metastatic NSCLC (primary plus up to five metastatic sites with no more than three sites in the liver or lung); additionally, 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; the secondary end points included toxic effects, local and distant tumor control, patterns of failure, and OS. Overall, 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 years (range, 51.0-79.0 years), were allocated to the maintenance chemotherapy alone arm. The SABR plus maintenance chemotherapy arm had a median of three metastases (range, 2-6), and the maintenance chemotherapy alone arm had a median of two metastases (range, 2-5). The trial was stopped early after an interim analysis found a significant improvement in PFS in the SABR plus maintenance chemotherapy arm of 9.7 months vs 3.5 months in the maintenance chemotherapy alone arm (p = 0.01). Toxic effects were similar in both arms. There were no in-field failures, with fewer overall recurrences in the SABR arm, while those participants who were 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 in participants who had limited metastatic disease appears similar to PFS in those with a greater metastatic burden; this further supports the potential benefits of local therapy in limited metastatic settings. Limitations include the single-center, phase 2 design and small sample size. (This study is included in the ISRS guideline below.)

Ruers et al. (2017) published updated outcomes from a previously conducted multicenter, phase 2, randomized trial. The original study investigated the possible benefits of RFA in participants with nonresectable colorectal liver metastases. A total of 119 participants with unresectable colorectal liver metastases (< 10 metastases and no extrahepatic disease) participated in the study. Overall, 59 participants were randomized to systemic treatment alone, and 60 participants were randomized to systemic treatment plus aggressive local treatment by RFA with or without resection. The authors reported that the primary end point (30-month OS > 38%) was met (Ruers et al., 2012). In this updated report, the authors reported long-term OS results. At a median follow-up of 9.7 years, 92 of 119 participants (77.3%) 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, 0.38-0.88; p = 0.01). Three-, 5-, and 8-year OS were 56.9% (95% CI, 43.3%-68.5%), 43.1% (95% CI, 30.3%-55.3%), and 35.9% (95% CI, 23.8%-48.2%), respectively, in the combined modality arm and 55.2% (95% CI, 41.6%-66.9%), 30.3% (95% CI,

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

19.0%-42.4%), and 8.9% (95% CI, 3.3%-18.1%), respectively, in the systemic treatment arm. Median OS was 45.6 months (95% CI, 30.3-67.8 months) in the combined modality arm vs 40.5 months (95% CI, 27.5-47.7 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. Limitations include a small sample size.

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 computed tomography to detect asymptomatic metastatic disease earlier). Searches were conducted using MEDLINE (Ovid), Embase, the Cochrane Library and Web of Science, Scopus, CINAHL (Cumulative Index to Nursing and Allied Health Literature) (EBSCO), PubMed publisher, Google Scholar, LILACS (Latin American and Caribbean Health Sciences Literature), 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 10 months (IQR, 5-24 months). In 10 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 that was made more intensive by introducing new methods or increasing the frequency of existing follow-up protocols vs less invasive monitoring. No detectable difference in OS was associated with more intensive monitoring protocols (HR, 0.98; 95% CI, 0.87-1.11). 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. Limitations include that publication bias may have affected the observed outcomes, as unpublished data, abstracts, and presentations were not included.

Clinical Practice Guidelines

American Radium Society (ARS)

Amini et al. (2022) developed 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 experienced progression after 2 to 3 months or two to three cycles of chemotherapy, provided that all sites are amenable to radiation.
- The panel strongly recommends that consolidative radiation therapy is usually appropriate for patients with oligometastatic disease (three sites or less, counted after up-front systemic therapy) who received 2 to 3 months of programmed cell death 1 protein/programmed cell death 1 ligand 1–based immunotherapy or chemoimmunotherapy, with no progression on repeat imaging where the sites are amenable to radiation.
- The panel recommends that consolidative radiation therapy in patients with four to five sites of oligometastatic disease (counted after up-front systemic therapy) be considered on a case-by-case basis due to the underrepresentation of these cases in published clinical trials.
- The panel does not currently recommend consolidative radiation therapy in patients with six or more sites of metastatic disease outside a clinical trial and rather endorses systemic therapy alone.
- The panel recommends that radiation therapy be considered on a case-by-case basis in patients with oligoprogressive disease who harbor 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 in 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 is as follows:

- For oligometastatic NSCLC, definitive local therapy is recommended only for patients who have up to five distant metastases that are diagnosed with appropriate imaging. An implementation remark states that despite some prospective trials that included patients with up to five extracranial metastases, most patients who were enrolled had one to two treated oligometastatic lesions, which should be factored into decision-making. Strength of recommendation: strong; quality of evidence: moderate.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

- For patients with oligometastatic NSCLC, highly conformal radiation therapy 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 radiation therapy (preferred), hypofractionated radiation therapy, 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 radiation therapy should use doses and fractionations that achieve durable local control. Strength of recommendation: strong; quality of evidence: high.
- Implementation remarks:
  - Durable local control, defined as minimum 85% local control at 2 years.
  - Higher BED10 (typically > 75 Gy) with SBRT alone is associated with optimal local control.
  - Lower BED10 (50- to 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 perspective of a radiation oncologist. The authors concluded that based on the current literature, oligometastatic disease could be defined as one to five metastatic lesions, with a controlled primary tumor being optional and all metastatic sites being 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 oligometastases. Overall, 35 studies (27 retrospective, five prospective, and three randomized trials) were included in the review that reported on the treatment of > 3,600 patients and > 4,650 metastases. The authors concluded that SBRT is an effective local treatment modality, with high local control rates and low risk of radiation-induced toxicities. Overall, 21 practice recommendations that covered the areas of staging and patient selection, SBRT treatment, and follow-up were developed and summarized below:

- For patients who are diagnosed with pulmonary oligometastatic disease and have 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 who are diagnosed with pulmonary oligometastatic disease and have an indication for definitive local therapy after discussion in a multidisciplinary tumor board, the optimal patient-individual local treatment modality SBRT vs pulmonary metastasectomy should be discussed in a multidisciplinary setting and should consider the patient's preference. Level of evidence: moderate; strength of recommendation: strong.
- For patients who are 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 who are 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 who are 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 who are 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 OARs, and without broad chest wall contact. Level of evidence: high; strength of recommendation: strong.

NCCN

The NCCN Guidelines for kidney cancer recommend considering SBRT for ablative treatment for intact extracranial metastases in patients with oligometastases, unless metastasectomy is planned or SBRT delivery is hindered by factors such as the anatomical location, proximity to OARs, or previous treatments. (NCCN, 2026)

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

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

a total of 460 individuals. Average rates of tinnitus, hearing loss, and lower cranial nerve deficit as presenting symptoms were 56%, 56%, and 42%, respectively. The overall clinical status improvement rate after treatment was 47%. Rates of tinnitus, hearing loss, and lower cranial nerve improvement after treatment were 54%, 28%, and 22%, respectively. The mean follow-up time across studies was 47 months (range, 4-268 months). The aggregate tumor control rate at the time of follow-up was 95%. The authors concluded that the tumor control rate of 95% and 47% symptomatic improvement suggests that SRS may be a viable alternative to resection and a suitable treatment for GJTs. The authors recommended future studies to further evaluate the role of SRS in the management of GJTs. Limitations include the study heterogeneity and lack of RCTs.

Sheehan et al. (2012) conducted a multicenter case series analysis to examine the outcomes in individuals with glomus tumors who underwent RS. Overall, 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. Overall, 40% 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, 5-220 months). Overall tumor control was achieved in 93% of individuals at the last follow-up; actuarial tumor control was 88% at 5 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 who had new or progressive cranial nerve deficits were also likely to have 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 GK RS 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. Limitations include the retrospective nature of the study and small sample size.

Guss et al. (2011) performed a systematic review and meta-analysis regarding the 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 to be eligible for inclusion if they were original research studies that reported the results of RS for GJTs. Overall, 19 studies, with a total of 335 individuals, were included in the meta-analysis. Data on 335 individuals with glomus jugulare were extracted and included 278 individuals who had received GK and 57 who had received LINAC or CyberKnife. The results across all studies found that 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 GK, LINAC, and CyberKnife technologies all exhibited high rates of tumor and clinical control. The authors concluded that because of its high effectiveness, RS should be considered for the primary management of GJTs. The authors recommended future prospective studies that have larger numbers of participants who are treated with RS as a primary treatment modality and have longer follow-up. Limitations noted include the small sample size in the studies and various treatments received (GK, LINAC, or CyberKnife).

Hemangiomas of the Brain

Mishra et al. (2023) conducted an individual patient data–based meta-analysis and systematic review that evaluated the effect and complications of SRS for cavernous sinus hemangiomas (CSHs) compared with those of surgical excision. Overall, 21 case series, including 199 individuals (69.3% female; mean age, 48.4 ±14.9 years) met the inclusion criteria. In total, 50 individuals (25%) had undergone surgery before SRS, whereas 149 individuals (75%) received stand-alone SRS. Most (93.5%) received GK RS as the mode of SRS, with a mean marginal dose of 14.6 ±2.9 Gy and mean follow-up of 35.8 ±31.6 months. The primary outcome was tumor volume reduction. Clinical improvement after SRS was strongly associated with the degree of tumor shrinkage, occurring in 91.4% of individuals (106 of 116) with remarkable shrinkage, 81.5% (25 of 27) with minimal reduction, and 69.2% (nine of 13) with stable tumors. The sixth cranial nerve was most commonly affected (36.7%), with 89% showing functional improvement after treatment with SRS. The authors concluded that SRS is a safe and effective treatment for CSHs, achieved over 50% tumor volume reduction in most individuals, and had superior outcomes compared with surgery, with primary SRS providing better tumor control and clinical improvement than adjuvant SRS. There are limitations, including that the quality of the meta-analysis is constrained by the quality of the included studies and by the predominance of retrospective chart reviews rather than prospective designs. Additional limitations arise from minor variations in SRS technique across centers, which may introduce heterogeneity, and from the study's resemblance to a single large case series that could limit generalizability.

Lee et al. (2017) conducted a multicenter case series analysis to review the outcome in individuals who had CSHs and were treated with SRS. Overall, 31 individuals were included in the analysis. Eleven individuals had initial microsurgery before SRS, and the other 20 individuals (64.5%) underwent GK RS as the primary management for their CSH. The median age at the time of RS was 47 years, and 77.4% of individuals had cranial nerve dysfunction before SRS. Individuals received a median tumor margin dose of 12.6 Gy (range, 12-19 Gy) at a median isodose of 55%. Tumor

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

regression was confirmed by imaging in all 31 individuals, and all individuals had a greater than 50% reduction in tumor volume at 6 months post SRS. None of the individuals had delayed tumor growth, new cranial neuropathy, visual function deterioration, AREs, or hypopituitarism after SRS. Overall, 24 individuals had presented with cranial nerve disorders before SRS, and six (25%) of them had gradual improvement. Four of the six individuals (66.7%) with orbital symptoms had symptomatic relief at the last follow-up. The authors concluded that SRS was effective in reducing the volume of CSH and attaining long-term tumor control in all individuals at a median of 40 months. The authors also concluded that their experience suggests that SRS is a reasonable primary and adjuvant treatment modality for individuals who are diagnosed with CSH. Limitations include the small sample size and retrospective nature of the study.

Clinical Practice Guidelines

International Stereotactic Radiosurgery Society (ISRS)

Akdemir et al. (2025) developed ISRS guidelines based on a PRISMA-guided systematic review and meta-analysis of 16 studies (324 patients) that evaluated SRS or fractionated SRS (five or fewer fractions) for CSHs. The recommendations are as follows (not all inclusive):

- The presence of minimal characteristic findings in MR imaging of CSH (homogeneous hyperintensity on T2-weighted sequences and intense enhancement) should be confirmed when performing SRS/fractionated SRS in the definitive setting. Strength of recommendation: conditional; quality of evidence: moderate.
- Adult patients with CSH regardless of symptom status can be treated in a definitive or adjuvant setting with SRS/fractionated SRS. Strength of recommendation: conditional; quality of evidence: low.
- SRS/fractionated SRS should be considered as a first-line treatment for select patients with CSH. Strength of recommendation: conditional; quality of evidence: low.
- A prescription dose of 12 to 16 Gy in a single fraction, with a recommendation on the lower end of the spectrum at 12 Gy in one fraction for relatively small tumors or 21 Gy in three fractions for larger tumors, can be used, similar to other benign tumors, depending on the tumor volume and proximity to nearby OARs. Strength of recommendation: conditional; quality of evidence: low.

Tos et al. (2024) developed guidelines based on a systematic review and meta-analysis regarding SRS for intracranial cavernous malformations (ICMs). The meta-analysis included 32 studies (n = 2,672 individuals) and concluded that SRS was effective for ICM treatment, significantly reduced rates of hemorrhage, and improved seizure outcomes. The guideline recommendations are as follows (not all inclusive):

- For patients with a surgically inaccessible or eloquently situated ICM with previous symptomatic hemorrhage, SRS is recommended, with the intent of reducing the risk of subsequent hemorrhage. Low quality of evidence: conditional.
- For patients with ICM that causes epilepsy, with poor medication control, SRS is recommended, with the intent of improving seizure control. Low quality of evidence: conditional.
- SRS is not typically recommended for asymptomatic ICM. Low quality of evidence: moderate.

Intracranial Arteriovenous Malformations

Maroufi et al. (2024) conducted a systematic review and meta-analysis of the available literature to assess the safety and efficacy of repeat SRS for arteriovenous malformations (AVMs). Overall, 16 retrospective cohort studies were included in the review and included 1,168 individuals who received repeat SRS from 1976 to 2022 due to incomplete obliteration. The inclusion criteria consisted of studies in individuals who had recurrent or residual AVM following SRS (single session), were undergoing repeat SRS, and had the obliteration rate reported after repeat SRS. The meta-analysis, with a mean follow-up of 45.57 months, revealed repeat SRS as a viable option for AVMs, which achieved a 60.82% obliteration rate, with a mean time to obliteration of 33.18 months. Meta-regression identified AVM volume and Spetzler-Martin (SM) grade as factors that influence obliteration, with smaller volume and lower SM grades associated with higher rates. Complications included radiation-induced changes (10.33%), post-RS hemorrhage (5.26%), neurological deficits (2.56%), and cyst formation (0.67%). Heterogeneity in complications is primarily attributed to male proportion and SM grade, while factors influencing post-RS hemorrhage remain unclear. The type of RS, whether GK RS or LINAC, does not significantly impact outcomes. The authors concluded that for AVMs that failed initial SRS, repeat SRS, when used in appropriate subgroups of individuals, is a safe and effective treatment and has an acceptable risk-to-benefit profile. Limitations include the retrospective nature of the studies in the review.

Ding et al. (2017) conducted an international multicenter study that analyzed and collected data from individuals with SM grade III AVMs who were treated with SRS at eight institutions. The cohort inclusion criteria comprised individuals with SM grade III AVMs and a minimum follow-up length of 12 months. AVM obliteration, absence of post-SRS hemorrhage, and absence of permanently symptomatic radiation-induced changes were defined as an optimal outcome. The SM grade III AVM cohort comprised 891 individuals, with a mean age of 34 years at the time of SRS. The mean nidus volume, radiosurgical margin dose, and follow-up length were 4.5 cm^3, 20 Gy, and 89 months, respectively. The actuarial obliteration rates at 5 and 10 years were 63% and 78%, respectively. The annual post-RS hemorrhage rate was 1.2%.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Symptomatic and permanent radiation-induced changes were observed in 11% and 4% of the individuals, respectively. Optimal outcome was achieved in 56% of the individuals and was significantly more frequent in cases of unruptured AVMs (OR, 2.3; p < 0.001). The lack of a previous hemorrhage (p = 0.037), absence of previous AVM embolization (p = 0.002), smaller nidus volume (p = 0.014), absence of AVM-associated arterial aneurysms (p = 0.023), and higher margin dose (p < 0.001) were statistically significant independent predictors of optimal outcome in a multivariate analysis. The authors found that SRS had an acceptable risk-to-benefit profile and noted better outcomes in small, unruptured SM grade III AVMs than in large or ruptured SM grade III nidi. The authors recommended future prospective trials. Limitations include the biases of a retrospective study and lack of comparison with other AVM interventions.

Kano et al. (2012b) published a series of studies to evaluate the outcomes in individuals with AVMs who were treated with SRS. The authors performed GKS in a total of 996 individuals with AVMs and conducted subgroup analyses based on AVM classification, anatomical location, and clinical scenario. Those subgroups included individuals with (1) SM grade I and II AVMs (Kano et al., 2012a); (2) repeat RS for AVMs; (3) basal ganglia and thalamus AVMs; (4) brainstem (medulla, pons, and midbrain) AVMs; and (5) multistaged volumetric management of large AVMs. To describe the outcomes and risks of repeat SRS for incompletely obliterated cerebral AVMs, a subgroup of 105 individuals was analyzed. In this subgroup, the median time after initial SRS was 40.9 months (range, 27.5-139 months). The median AVM target volume was 6.4 cm^3 (range, 0.2-26.3 cm^3) at initial SRS but was reduced to 2.3 cm^3 (range, 0.1-18.2 cm^3) at the time of the second procedure. The median margin dose at both initial SRS and repeat SRS was 18 Gy. The actuarial rate of total obliteration by angiography or MRI after repeat SRS was 35%, 68%, 77%, and 80% at 3, 4, 5, and 10 years, respectively. The median time to complete angiographic or MRI obliteration after repeat SRS was 39 months. Factors that were associated with a higher rate of AVM obliteration were smaller residual AVM target volume (p = 0.038) and a volume reduction of 50% or more after the initial procedure (p = 0.014). Seven individuals (7%) had a hemorrhage in the interval between initial SRS and repeat SRS. A total of 17 individuals (16%) had hemorrhage after repeat SRS, and six individuals died. The cumulative actuarial rates of new AVM hemorrhage after repeat SRS were 1.9%, 8.1%, 10.1%, 10.1%, and 22.4% at 1, 2, 3, 5, and 10 years, respectively, which translate to annual hemorrhage rates of 4.05% and 1.79% of individuals developing new post–repeat SRS hemorrhages per year for years 0 to 2 and 2 to 10 following repeat SRS. Factors associated with a higher risk of hemorrhage after repeat SRS were a greater number of prior hemorrhages (p = 0.008), larger AVM target volume at initial SRS (p = 0.010), larger target volume at repeat SRS (p = 0.002), initial AVM volume reduction of less than 50% (p = 0.019), and a higher Pollock-Flickinger score (p = 0.010). Symptomatic AREs developed in five individuals (4.8%) after initial SRS and in 10 individuals (9.5%) after repeat SRS. Prior embolization (p = 0.022) and a higher SM grade (p = 0.004) were significantly associated with higher rates of AREs after repeat SRS. Delayed cyst formation occurred in five individuals (4.8%) at a median of 108 months after repeat SRS (range, 47-184 months). The authors concluded that repeat SRS for incompletely obliterated AVMs increased the eventual obliteration rate. They also concluded that the best results for individuals with incompletely obliterated AVMs were seen in those with a smaller residual nidus volume and no prior hemorrhages.

Kano et al. (2012c) described the long-term outcomes and risks of SRS for AVMs of the basal ganglia and thalamus; a subgroup of 56 individuals with basal ganglia and 77 with thalamus AVMs was analyzed. In this series, 113 of 133 individuals (85%) had a prior hemorrhage. The median target volume was 2.7 cm^3 (range, 0.1-20.7 cm^3), and the median margin dose was 20 Gy (range, 15-25 Gy). Obliteration of the AVM eventually was documented on MRI in 78 individuals and on angiography in 63 individuals in a median follow-up period of 61 months (range, 2-265 months). The actuarial rates documenting total obliteration after RS were 57%, 70%, 72%, and 72% at 3, 4, 5, and 10 years, respectively. Factors associated with a higher rate of AVM obliteration included AVMs that were in the basal ganglia and had a smaller target volume, smaller maximum diameter, and higher margin dose. Overall, 15 of 133 individuals (11%) had a hemorrhage during the latency period, and seven individuals died. The rates of post-SRS AVM hemorrhage were 4.5%, 6.2%, 9.0%, 11.2%, and 15.4% at 1, 2, 3, 5, and 10 years, respectively. The overall annual hemorrhage rate was 4.7%. When five individuals, who had seven hemorrhages that occurred earlier than 6 months after SRS, were removed from this analysis, the annual hemorrhage rate decreased to 2.7%. Larger-volume AVMs had a higher risk of hemorrhage after SRS. Permanent neurological deficits due to AREs developed in six individuals (4.5%), and in one individual, a delayed cyst developed 56 months after SRS. No individual died of AREs. Factors associated with a higher risk of symptomatic AREs were larger target volume, larger maximum diameter, lower margin dose, and a higher Pollock-Flickinger score. The authors concluded that SRS is a gradually effective and relatively safe management option for deep-seated AVMs in the basal ganglia and thalamus and that individuals remain at risk during the latency interval between SRS and obliteration. In addition, they concluded that the best candidates for SRS are individuals with smaller-volume AVMs that are located in the basal ganglia.

Kano et al. (2012d) described the long-term outcomes and risks of SRS for AVMs of the medulla, pons, and midbrain; a subgroup of 56 individuals was analyzed. In this series, 51 individuals (76%) had a prior hemorrhage. The median target volume was 1.4 cm^3 (range, 0.1-13.4 cm^3). The median margin dose was 20 Gy (range, 14-25.6 Gy). Obliteration of the AVMs was documented in 35 individuals at a median follow-up of 73 months (range, 6-269 months). The actuarial rates of

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

documentation of total obliteration were 41%, 70%, 70%, and 76% at 3, 4, 5, and 10 years, respectively. Higher rates of AVM obliteration were associated only with a higher margin dose. Four individuals (6%) had a hemorrhage during the latency period, and two individuals died. The rates of AVM hemorrhage after SRS were 3.0%, 3.0%, and 5.8% at 1, 5, and 10 years, respectively. The overall annual hemorrhage rate was 1.9%. Permanent neurological deficits due to AREs developed in seven individuals (10%) after SRS, and a delayed cyst developed in two individuals (3%). One individual died with symptoms of AREs and unrecognized hydrocephalus. Higher 12-Gy volumes and higher SM grades were associated with a higher risk of symptomatic AREs. Ten of 22 individuals who had ocular dysfunction before SRS had improvement, nine were unchanged, and three were worse due to AREs. Eight of 14 individuals who had hemiparesis before SRS improved, five were unchanged, and one was worse. The authors concluded that although hemorrhage after obliteration did not occur in their series, individuals remained at risk during the latency interval until obliteration occurred. Overall, 38% of the individuals who had neurological deficits due to prior hemorrhage improved. In addition, they concluded that higher dose delivery, in association with conformal and highly selective SRS, is required for safe and effective RS.

Kano et al. (2012e) described the long-term outcomes and risks of AVM management using two or more stages of SRS for symptomatic large-volume lesions that were unsuitable for surgery; a subgroup of 47 individuals was analyzed. In this series, 18 individuals (38%) had a prior hemorrhage, and 21 individuals (45%) underwent prior embolization. The median interval between the first-stage SRS and the second-stage SRS was 4.9 months (range, 2.8-13.8 months). The median target volume was 11.5 cm^3 (range, 4.0-26 cm^3) in the first-stage SRS and 9.5 cm^3 in the second-stage SRS. The median margin dose was 16 Gy (range, 13-18 Gy) for both stages. In 17 individuals, AVM obliteration was confirmed after two to four SRS procedures at a median follow-up of 87 months (range, 0.4-209 months). Five individuals had near-total obliteration (volume reduction > 75% but residual AVM). The actuarial rates of total obliteration after two-stage SRS were 7%, 20%, 28%, and 36% at 3, 4, 5, and 10 years, respectively. The 5-year total obliteration rate after the initial staged volumetric SRS, with a margin dose of 17 Gy or more, was 62% (p = 0.001). Overall, 16 individuals underwent additional SRS at a median interval of 61 months (range, 33-113 months) after the initial two-stage SRS. The overall rates of total obliteration after staged and repeat SRS were 18%, 45%, and 56% at 5, 7, and 10 years, respectively. Ten individuals sustained hemorrhage after staged SRS, and five of these individuals died. Three of 16 individuals who underwent repeat SRS sustained hemorrhage after the procedure and died. Based on Kaplan-Meier analysis (excluding the second hemorrhage in the individual who had two hemorrhages), the cumulative rates of AVM hemorrhage after SRS were 4.3%, 8.6%, 13.5%, and 36.0% at 1, 2, 5, and 10 years, respectively. This corresponded to annual hemorrhage risks of 4.3%, 2.3%, and 5.6% for years 0 to 1, 1 to 5, and 5 to 10 after SRS. Multiple hemorrhages before SRS correlated with a significantly higher risk of hemorrhage after SRS. Symptomatic AREs were detected in 13% of individuals, but no individual died as a result of an ARE. Delayed cyst formation did not occur in any individual after SRS. The authors concluded that prospective, volume-staged SRS in individuals with large AVMs who are unsuitable for surgery has potential benefit but often requires more than two procedures to complete the obliteration process. The authors also concluded that to have a reasonable chance of benefit, the minimum margin dose should be 17 Gy or greater, depending on the AVM location, and that prospective, volume-staged SRS followed by embolization (to reduce flow, obliterate fistulas, and occlude associated aneurysms) may improve obliteration results and further reduce the risk of hemorrhage after SRS. Key limitations include the retrospective nature of the studies and single-center design.

Clinical Practice Guidelines

International Stereotactic Radiosurgery Society (ISRS)

Graffeo et al. (2025) developed ISRS guidelines for the management of patients with SM grade III to V AVMs using SRS. The recommendations are as follows (not all inclusive):

- SRS is a safe, effective treatment for grade III to V AVM. Level of evidence: 2b.
- SRS should be considered among the frontline management strategies for grade III to V AVM, alongside observation and microsurgery. Level of evidence: 2b.
- SRS may be preferred as the primary therapy for those with grade III AVM that is deemed less favorable for resection (e.g., IIIb/IIIc). Level of evidence: 2b.
- SRS may be preferred as the primary therapy in grade IV to V AVM, absent a configuration of features deemed optimal for resection. Level of evidence: 2b.

Graffeo et al. (2020) conducted a systematic review and meta-analysis aimed to establish SRS practice guidelines for grade I to II AVMs. The inclusion criteria included publications that reported post-SRS outcomes in ≥ 10 grade I to II AVMs, with a follow-up of ≥ 24 months. Obliteration and hemorrhage were primary end points; the secondary outcomes were SM parameters, dosimetric variables, and excellent outcomes, which were defined as total obliteration without new post-SRS deficit. Eight studies were chosen for inclusion, representing 1,102 AVMs, of which 836 (76%) were grade II. Obliteration was achieved in 884 (80%) at a median of 37 months; 66 hemorrhages (6%) occurred during a median follow-up of 68 months. Total obliteration without hemorrhage was achieved in 78%. Of 836 grade II AVMs, SM parameters were

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

reported in 680; 377 were eloquent brain, and 178 had deep venous drainage, which totaled 555 of 680 (82%) high-risk, SRS-treated, grade II AVMs. The authors concluded that SRS appears to be a safe, effective treatment for grade I to II AVMs and may be considered as a frontline treatment, especially for lesions in deep or eloquent locations. The authors noted limitations, including a small sample size and high risk of bias.

Meningioma

Habibi et al. (2025) performed a systematic review and meta-analysis to evaluate the use of GK RS in the management of individuals with neurofibromatosis 2 (NF2)–associated meningiomas. Four studies (n = 101 individuals) met the inclusion criteria, which consisted of individuals with NF2-associated meningiomas and clinical outcomes after SRS; English publications with human individuals; and original research articles. OS rates remained high (100%) up to 3 years post treatment, with slight declines at 5 years of 98% (95% CI, 0.95-1.01) and 10 years of 68% (95% CI, 0.48-0.87). PFS rates were similarly favorable, with 95% (95% CI, 89%-101%) at 3 years, 93% (95% CI, 86%-99%) at 5 years, and 81% (95% CI, 51%-111%) at 10 years. The pooled radiation necrosis rate was 5% (95% CI, 3%-7%), while the overall radiation toxicity rate was 16% (95% CI, 11%-21%). Local tumor control rates were high at 6 months, and at 12 months, they were 100% (95% CI, 1.00-1.00). The authors concluded that GK RS is a highly effective treatment option, with a favorable safety profile. The authors recommended future larger studies that focus on long-term effects. Limitations include the lack of RCTs and small study sizes.

Sheehan et al. (2014) conducted a multicenter case series analysis to evaluate outcomes in individuals with meningiomas who were treated with GK RS. At 10 centers, all individuals with sellar and/or parasellar meningiomas who were treated with GK RS were included in the analysis. Individuals were required to have a minimum of 6 months of imaging and clinical follow-up after GK RS. Factors that were predictive of new neurological deficits following GK RS were assessed via univariate and multivariate analyses. Kaplan-Meier analysis and Cox multivariate regression analysis were used to assess factors that were predictive of tumor progression. Overall, 763 individuals were assessed clinically and with neuroimaging at routine intervals following GK RS. There were 567 female individuals (74.3%) and 196 male individuals (25.7%), with a median age of 56 years (range, 8-90 years). In total, 355 individuals (50.7%) had undergone at least one resection before GK RS, and 3.8% had undergone prior radiation therapy. The median follow-up after GK RS was 66.7 months (range, 6-216 months). At the last follow-up, tumor volumes remained stable or decreased in 90.2% of individuals. Actuarial PFS rates at 3, 5, 8, and 10 years were 98%, 95%, 88%, and 82%, respectively. More than one prior surgery, prior radiation therapy, or a tumor margin dose of < 13 Gy significantly increased the likelihood of tumor progression after GK RS. At the last clinical follow-up, 86.2% of individuals experienced no change or improvement in their neurological condition, whereas 13.8% of individuals experienced symptom progression. New or worsening cranial nerve deficits were seen in 9.6% of individuals, with cranial nerve V being the most adversely affected nerve. Functional improvements in cranial nerves, especially in cranial nerves V and VI, were observed in 34% of individuals with preexisting deficits. New or worsened endocrinopathies were seen in 1.6% of individuals; hypothyroidism was the most frequent deficiency. An unfavorable outcome with tumor growth and accompanying neurological decline was statistically more likely in individuals with larger tumor volumes (p = 0.022) and more than one prior surgery (p = 0.021). The authors concluded that GK RS provides a high rate of tumor control in individuals with parasellar or sellar meningiomas, and tumor control is accompanied by neurological preservation or improvement in most individuals. Limitations include the retrospective nature of the study. (This study is included in the ISRS systematic review and meta-analysis below.)

Pollock et al. (2012) conducted a retrospective case series analysis to evaluate patients who had single-fraction SRS for benign intracranial meningiomas to determine factors associated with tumor control and neurological complications. Overall, 416 patients (304 women; 112 men) who had single-fraction SRS for imaging defined (n = 252) or confirmed WHO grade I (n = 164) meningiomas were included in the analysis. Excluded were patients with radiation-induced tumors, multiple meningiomas, NF2, and previous or concurrent radiotherapy. The majority of the tumors [n = 337 (81%)] involved the cranial base or tentorium. The median tumor volume was 7.3 cm^3; the median tumor margin dose was 16 Gy. The median follow-up was 60 months. The disease-specific survival rates were 97% at 5 years and 94% at 10 years. The 5- and 10-year local tumor control rates were 96% and 89%, respectively. Male sex (HR, 2.5; p = 0.03), previous surgery (HR, 6.9; p = 0.002), and tumor location in the parasagittal/falx/convexity regions (HR, 2.8; p = 0.02) were negative risk factors for local tumor control. In 45 patients (11%), permanent radiation-related complications developed at a median of 9 months after SRS. The 1- and 5-year radiation-related complication rates were 6% and 11%, respectively. Risk factors for permanent radiation-related complication rate were increasing tumor volume (HR, 1.05; p = 0.008) and tumors in the parasagittal/falx/convexity regions (HR, 3.0; p = 0.005). The authors concluded that single-fraction SRS at the studied dose range provided a high rate of tumor control in patients with benign intracranial meningiomas, and patients with small-volume, nonoperated cranial base or tentorial meningiomas had the best outcomes after single-fraction SRS. Limitations include the retrospective nature of the study. (This study is included in the ISRS systematic review and meta-analysis below.)

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Santacroce et al. (2012) conducted a multicenter, retrospective case series analysis to evaluate the long-term efficacy and safety of RS for meningiomas. Overall, 4,565 consecutive patients, with 5,300 benign meningiomas, were included in the analysis. All were treated with GK RS at least 5 years before assessment for this study. Clinical and imaging data were retrieved from each center and uniformly entered into a database. The median tumor volume was 4.8 cm^3, and the median dose to the tumor margin was 14 Gy. All tumors with imaging follow-up of < 24 months were excluded. Detailed results from 3,768 meningiomas (71%) were analyzed. The median imaging follow-up was 63 months. The volume of treated tumors decreased in 2,187 lesions (58%), remained unchanged in 1,300 lesions (34.5%), and increased in 281 lesions (7.5%), demonstrating a control rate of 92.5%. Only 84 enlarging tumors (2.2%) required further treatment. Five- and 10-year PFS rates were 95.2% and 88.6%, respectively. Tumor control was higher in imaging-defined tumors vs grade I meningiomas ($p < 0.001$); female vs male patients ($p < 0.001$); sporadic vs multiple meningiomas ($p < 0.001$); and skull base vs convexity tumors ($p < 0.001$). The permanent morbidity rate was 6.6% at the last follow-up. The authors concluded that RS is a safe and effective method for treating benign meningiomas, even in the medium to long term. Limitations include the retrospective nature of the study.

Clinical Practice Guidelines

International Stereotactic Radiosurgery Society (ISRS)

Marchetti et al. (2022) conducted a systematic review and meta-analysis on SBRT and intracranial noncavernous sinus benign meningiomas and developed an evidence-based guideline on behalf of the ISRS. Studies from January 1964 to April 2018 were evaluated, with a total of 27 studies included in the review. All but one were retrospective studies. The primary outcomes examined were rates of local control, PFS, and OS. Prognostic factors and analyses of symptom control and radiation-induced toxicity were the secondary objectives. The 10-year local control rate ranged from 71% to 100%. The 10-year PFS rate ranged from 55% to 97%. The prescription dose ranged typically between 12 and 15 Gy and was delivered in a single fraction. The toxicity rate was generally low. The authors concluded that SRS can be considered a primary treatment in many cases of intracranial noncavernous sinus benign meningiomas based on the strong consensus of class III evidence and favorable outcomes (recommendation level: II). The authors recommended future larger, multi-institutional studies that include longer observation periods. Limitations include the retrospective nature of the majority of studies in the review. Kondziolka et al. (2008), previously cited in this policy, was included in this review.

NCCN

The NCCN Guidelines state that studies show that SRS is associated with excellent tumor control and good survival outcomes in the treatment of meningiomas, especially in grade 1 tumors. For those with grade 2 meningiomas, such as those with recurrent disease following prior radiation and with smaller, suitable lesions, SRS may be considered. If the lesion is located near critical structures, hypofractionated SRT (HSRT) may be an alternative option. (NCCN, 2026)

Neurological Conditions (e.g., Epilepsy, Parkinson Disease, Essential Tremor)

de Haan et al. (2026) conducted a PRISMA-guided systematic review that evaluated the effect of SRT on tremors in those with Parkinson disease, including six retrospective case series published after 1995, with a total of 193 individuals who were aged 41 to 88 years; 61% were male, and the disease duration ranged from 0.5 to 30 years. All studies applied single-fraction SRT doses between 85 and 165 Gy, which were most commonly 130 to 140 Gy. The primary outcome was change in tremor, assessed by clinical observation and validated rating scales [Fahn-Tolosa-Marin (FTM) or Unified Parkinson's Disease Rating Scale]. The prespecified secondary end points included adverse events, mortality, and QOL. The ventral intermediate nucleus was the most commonly targeted structure, which was identified in half of the included studies. Tremor improvement ranged from 71% to 100%, with severity reductions of 38% to 67% and complete tremor resolution reported in up to 70% individuals in some studies. Medication use decreased in 6% to 75% of cases. Reporting on QOL and recurrence was variable, although recurrence rates ranged from 3% to 24%. Adverse events were uncommon and occurred in approximately 7% of individuals. The authors concluded that SRT is a promising noninvasive treatment for medically refractory Parkinson disease tremor and provides substantial tremor reduction and low toxicity; this supports its potential effectiveness and safety in those with disabling tremors that are not suitable for deep brain stimulation (DBS). Key limitations include the small number of eligible studies, exclusion of articles that conflated different neurological conditions, and small sample sizes that may have introduced reporting and publication bias.

Dong et al. (2025) performed a systematic review and meta-analysis that compared five surgical methods, open and minimally invasive, that were used for the treatment of individuals with drug-resistant epilepsy. The 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, radiofrequency thermocoagulation (RFT), or GK RS and had availability of mean, SD, 95% CI, or median IQR for seizure free. Studies were excluded if they included individuals who were under 18 years of age; had a follow-up of less than 1 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 the inclusion criteria, for a total of 5,958 individuals. The analysis results indicate that ATL

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

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, laser interstitial thermal therapy, RFT, and GK RS were 62%, 70%, 58%, 47%, and 57%, respectively. Only three studies addressed GK RS; therefore, a subgroup analysis based on follow-up time was not performed. The authors concluded that among the surgical treatments that were included in this review, ATL and SAH were the best in both overall and long-term follow-up. However, the authors noted that when professionals are choosing a specific treatment, specific situations such as type and location of epileptic seizures should be considered; additionally, a treatment plan should be developed that maximizes effectiveness and reduces risks. The authors recommended future high-quality, long-term follow-up studies. Limitations include the limited number of RCTs and lack of unified outcome measures across different studies, which reduced the ability to analyze adverse effect data, QOL, and cognitive function.

Bilski et al. (2024) conducted a systematic review to evaluate four treatment modalities that were received by individuals with essential tremors (ETs) who did not achieve a treatment response to medical management. The methods that were compared were DBS, SRS, radiofrequency thalamotomy, and focused ultrasound thalamotomy. The inclusion criteria consisted of prospective and retrospective clinical trials that had published results in the English language. Overall, 22 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, which reached 80%; achievement of manual task improvement; lessening of the tremor; and an increase in the QOL in the majority of the operated individuals. After SRS, a considerable number of individuals had 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 include the small sample sizes in the included studies.

Goncalves et al. (2024) conducted a systematic review and single-arm meta-analysis that aimed to evaluate the efficacy, safety, and long-term impact of SRS, including GK RS, in ET, focusing on tremor control and related adverse effects. The inclusion criteria consisted of randomized and nonrandomized studies in four or more individuals who had ET and underwent GK RS. Reviews, case reports, letters, comments, and studies that were not performed only in those with ET were excluded. The main outcomes that were assessed included the proportion of successful treatments, instances of technical failure, and frequency of postoperative complications. Treatment was deemed successful if the individual experienced either complete or near-complete resolution of tremors or had a positive response or noticeable improvement. The study evaluated secondary outcomes, including the MD scores in specific components of the 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%. Postprocedure complications were observed in 9.7% of individuals. A meta-analysis of five studies revealed a statistically significant reduction in tremor from the FTM scale after treatment with GK RS (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 GK RS (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 GK RS (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 GK RS (MD, -1.6; 95% CI, -1.9 to -1.3; $p < 0.01$; $I^2 = 11\%$). The authors concluded that GK RS for ET had a high overall success rate and low failure rate and was a safe and effective treatment for managing this population of individuals. Limitations include the nature of the retrospective studies included in the review, small sample sizes, and lack of tremor data after 6 and 12 months.

Barbaro et al. (2018) conducted an RCT that compared SRS with ATL for the treatment of participants with pharmacoresistant, unilateral mesial temporal lobe epilepsy. The inclusion criteria included adults who were aged 18 years or older; were eligible for open surgery; had at least three focal-onset seizures in 3 months, with impairment of consciousness occurring during anticonvulsant administration; and had no neurological or visual deficits. Pregnancy, supratentorial MRI abnormalities, diabetes mellitus, use of vigabatrin, psychiatric diagnoses that could hinder accurate seizure assessment, significant comorbidities, poor adherence, or current drug abuse were the exclusion criteria. The primary outcomes that were assessed were seizure remission, verbal memory, and QOL at the 36-month follow-up. Overall, 58 participants (31 in SRS; 27 in ATL) were treated. Overall, 16 SRS (52%) and 21 ATL participants (78%) achieved seizure remission. Mean verbal memory changes from baseline in 21 English-speaking, dominant-hemisphere participants did not differ between groups; consistent worsening occurred in 36% of SRS and 57% of ATL participants. QOL improved with seizure remission. Adverse events were anticipated cerebral edema and related symptoms in some SRS participants and cerebritis, subdural hematoma, and others in ATL participants. The authors concluded that ATL offered an advantage over SRS in terms of the proportion of participants who achieved seizure remission. Both SRS and ATL demonstrated effectiveness and safety as treatment options for mesial temporal lobe epilepsy. SRS serves as a viable alternative for individuals who have contraindications or are reluctant to undergo open surgery. Limitations include small sample sizes.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Eekers et al. (2018) performed a systematic review to determine the efficacy and treatment-related side effects of SRS in individuals with drug-resistant focal epilepsy. Overall, 16 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 individuals (on average, 58%; range, 25%-95%) reporting no or rare seizures [defined as RAEC (radiotherapy-adapted Engel class) I and II]. In total, 20% of the individuals (34 individuals) needed subsequent surgery due to radionecrosis, cyst 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 in those with drug-resistant, focal, non-neoplastic epilepsy, radiotherapy is a possible treatment option, with a favorable effect on seizure outcome. Limitations include a low level of evidence and 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. Overall, 55 articles were included in the review; no level 1 evidence was available. The review consisted of two level 2 prospective trials that were 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 extratemporal epilepsy, only level 4 data were 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 in specific individuals compared with traditional microsurgery. Additionally, SRS offers a more favorable risk-benefit ratio for treating small hypothalamic hamartomas than surgical methods. Limitations include the retrospective nature of the majority of articles included in the review. A formal ISRS guideline was unable to be developed due to the lack of nonrandomized 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. Overall, 34 studies, three prospective, one retrospective comparative, and 30 retrospective, were included in the review. The one retrospective comparative study that evaluated 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 include the small sample sizes and 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 in whom medical therapy has failed and who are not candidates for invasive surgery.
- SRS should be considered, even for patients with tremor in whom medical therapy has failed, even if they are candidates for invasive surgery since SRS appears to have a lower level of complications.
- GK RS has been performed with a single 4-mm collimator, single-fraction maximum dose of 130 to 150 Gy, with the lesion made in the ventral intermediate nucleus located using advanced imaging modalities and stereotactic atlases.

Pineal Gland Tumors

Gagliardi et al. (2023) performed a systematic review to assess the efficacy and safety in individuals who underwent GK RS for pineal region tumors. Overall, 14 studies were considered eligible for inclusion. A total of 76 individuals reached the final analysis; 56.5% (n = 43) received a histological diagnosis. Confirmed lesions included WHO grade I pineocytoma (60.5%), WHO grade II pineocytoma (14%), WHO grade IV pineoblastoma (7%), WHO grade II/III pineal tumor with intermediate differentiation (4.7%), WHO grade II/III papillary tumor of pineal region (4.7%), germ cell tumor (2.3%), WHO grade I neurocytoma (2.3%), WHO grade II astrocytoma (2.3%), and WHO grade III astrocytoma (2.3%). Presumptive diagnoses were achieved in the remaining 43.5% of cases (n = 33) and comprised pineocytoma (9%), germ cell tumor (6%), low-grade glioma (6%), high-grade glioma (3%), and meningioma (3%); diagnoses were undefined in 73%. The mean age at the time of GK RS was 38.7 years, and the mean lesional volume was 4.2 ±4 cc. All individuals received GK RS, with a mean marginal dose of 14.7 ±2.1 Gy (50% isodose). At a median 36-month follow-up, local control was achieved in 80.3% of cases. Thirteen individuals experienced progression after a median time of 14 months. The overall mortality was 13.2%. The median OS was not reached for all included lesions, except high-grade gliomas (8 months). The 3-year OS was 100% for low-grade glioma and pineal tumors with intermediate differentiation; 91% for low-grade pineal lesions; 66% for high-grade pineal lesions; 60% for germ cell tumors; 50% for high-grade glioma; and 82% for undetermined tumors. The 3-year PFS was 100% for low-grade glioma and pineal intermediate tumors; 86% for low-grade pineal; 66% for high-grade pineal; 33.3% for germ cell tumors; and 0% for high-grade glioma. Median PFS was 5 months for high-grade glioma and 34 months for germ cell tumors. The radionecrosis rate was 6%, and cystic degeneration was

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

observed in 2%. Ataxia as a presenting symptom strongly predicted mortality (OR, 104; p = 0.02), while germ cell tumors and high-grade glioma histology well predicted disease progression (OR, 13; p = 0.04). The authors concluded that in individuals with pineal tumors, primary treatment with GK RS is safe and effective. The authors suggested that future studies are needed to validate results. Limitations include the retrospective design, lack of control group, and small number of lesions that were included in the study due to the rarity of the disease. Hasegawa et al. (2002), previously cited in this policy, is included in this review.

Iorio-Morin et al. (2017) conducted a multicenter case series analysis in individuals with SRS-treated pineal region tumors to provide reliable histology-stratified outcomes. For individuals with at least 6 months of follow-up, baseline data recorded at the time of the first GK procedure were collected, including the indication and treatment parameters. Follow-up data were obtained from the medical records. Local control was assessed on the last available MRI before any subsequent treatment of failure and defined as tumor disappearance, tumor regression (volume reduction m > 10%), tumor stability (change in volume, < 10%), or tumor progression (volume increase, > 10%). Overall, 70 individuals were treated, with a median follow-up of 47 months. Diagnoses were pineocytoma (37%), pineoblastoma (19%), pineal parenchymal tumor of intermediate differentiation (10%), papillary tumor of the pineal region (9%), germinoma (7%), teratoma (3%), embryonal carcinoma (1%), and unknown (14%). The median prescription dose was 15 Gy at the 50% isodose line. Actuarial local control and survival rates were 81% and 76% at 20 years for pineocytoma, 50% and 56% at 5 years for pineal parenchymal tumor of intermediate differentiation, 27% and 48% at 5 years for pineoblastoma, 33% and 100% at 5 years for papillary tumor of the pineal region, 80% and 80% at 20 years for germinoma, and 61% and 67% at 5 years for tumors of unknown histology. New focal neurological deficit, Parinaud syndrome, and hydrocephalus occurred in 9%, 7%, and 3% of cases, respectively. The authors concluded that SRS is a safe modality for the management of pineal region tumors. Its specific role is highly dependent on tumor histology, and as such, all efforts should be made to obtain a reliable histological diagnosis. Limitations include the small sample size and retrospective nature of the study.

Kano et al. (2009) conducted a single-center case series analysis in individuals with pineal parenchymal tumors who underwent RS. The analysis included a total of 20 individuals; 13 individuals had pineocytoma, five individuals had pineoblastoma, and two individuals had mixed pineal parenchymal tumors. The median RS prescription dose to the tumor margin was 15.0 Gy (range, 12-20 Gy). At an average of 54.1 months (range, 7.7-149.2 months), six individuals died, and 14 individuals were alive. The OS after RS was 95.0%, 68.6%, and 51.4% at 1, 5, and 10 years, respectively. Individuals with pineocytomas had a 1-, 3-, and 5-year OS of 100%, 92.3%, and 92.3%, respectively. In 19 individuals who were evaluated with imaging, five (26%) had complete regression, nine (47%) had partial regression, two (11%) had stable tumors, and two (11%) had local in-field progression. The PFS after SRS for all types of pineal parenchymal tumors was 100%, 89.2%, and 89.2% at 1, 3, and 5 years after RS, respectively. The authors concluded that SRS is an effective and safe alternative to the surgical resection of pineocytomas and as part of multimodal therapy for more aggressive pineal parenchymal tumors. Limitations include the single-center design and small sample size.

Pituitary Adenoma

De Nigris Vasconcellos et al. (2024) conducted a single-arm systematic review and meta-analysis to evaluate the safety and efficacy in tumor control for recurrent/residual nonfunctioning pituitary adenomas (NFPAs) following treatment with SRS. Studies that were published up to February 2024, both retrospective and prospective, were deemed eligible if they assessed the use of SRS for recurrent or residual NFPAs and provided data on procedural outcomes and complications. The exclusion criteria included case reports, studies without abstracts or full texts, those that were not published in English, and studies that grouped NFPAs with other pituitary adenomas, without specific counts of individuals or treatment timeline. Overall, 24 studies, with a total of 3,781 individuals, were included; all those in the analysis had at least one prior surgical resection prior to SRS. The mean follow-up duration was 60 months. Tumor control was achieved in approximately 92.3% of individuals. The risk of developing hypopituitarism post SRS was 13.62%, while the risk for panhypopituitarism was 2.55%. New visual field deficits occurred in 3.94% of individuals. Cranial nerve deficits were rare, with event rates below 1% for cranial nerves III, V, and VI. The authors concluded that SRS demonstrates high efficacy in the management of recurrent or residual NFPAs. However, there is a significant risk of hypopituitarism post treatment that will need periodic monitoring, as well as possible visual field deficits. Limitations include the retrospective nature of all included studies and lack of a direct comparison group. Starke et al. (2012), previously cited in this policy, was included in this systematic review and meta-analysis.

Kotecha et al. (2020) performed a systematic review and meta-analysis on outcomes and toxicities following SRS in individuals (n = 2,671) with NFPAs. Overall, 35 retrospective studies in ≥ 10 individuals with NFPAs, treated between 1971 and 2017 with either single-fraction SRS or HSRT, were included. SRS was used in 27 studies (median dose, 15 Gy; range, 5-35 Gy), and HSRT was used in eight studies (median total dose, 21 Gy; range, 12-25 Gy; delivered in three to five fractions). The 5-year random-effects local control estimate after SRS was 94% (95% CI, 93.0%-96.0%) and 97.0% (95% CI, 93.0%-98.0%) after HSRT. The 10-year local control random-effects estimate after SRS was 83.0% (95% CI, 77.0%-88.0%). Hypopituitarism was the most common treatment-related toxicity that was observed post SRS, with a

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

random-effects estimate of 21.0% (95% CI, 15.0%-27.0%); visual dysfunction or other cranial nerve injuries were uncommon (range, 0%-7%). The authors determined that SRS is a safe and effective treatment for individuals with NFPAs and that single-fraction SRS is associated with long-term (10-year) disease control. The authors noted that HRST can be used in select individuals with NFPAs, with encouraging short-term results reported; however, mature outcomes are needed before definitive recommendations can be made. (Lee et al., 2014b, and Sheehan et al., 2013, previously cited in this policy, were included in this systematic review and meta-analysis.)

Wan et al. (2009) conducted a single-center case series analysis to evaluate outcomes in individuals with secretory pituitary adenomas who were treated with GK RS. Overall, 347 individuals, with at least 60 months of follow-up data, were included in the analysis. In 47 of those individuals, some form of prior treatment such as transsphenoidal resection or craniotomy and resection had been conducted. The others were deemed ineligible for microsurgery because of body health or private choice, and GK RS served as the primary treatment modality. Endocrinologic, ophthalmologic, and neuroradiological responses were evaluated. The mean follow-up period was 67.3 months (range, 60-90 months). Late radioreaction was noted in one individual and consisted of consistent headaches. Of the 68 individuals with adrenocorticotropic hormone–secreting adenomas, 89.7% had tumor volume decrease or remain unchanged, and 27.9% experienced normalization of the hormone level. Of the 176 individuals with prolactinomas, 23.3% had normalization of the hormone level, and 90.3% had tumor volume decrease or remain unchanged. Of the 103 individuals with growth hormone–secreting adenomas, 95.1% experienced tumor volume decrease or remain unchanged, and 36.9% had normalization of hormone level. The authors concluded that GK RS is safe and effective in treating secretory pituitary adenomas and may serve as a primary treatment method in some or as a salvage treatment in others; however, treatment must be tailored to meet the individual's symptoms, tumor location, tumor morphometry, and overall health. The authors also recommended that longer follow-up is required for a more complete assessment of late radioreaction and treatment efficacy. Limitations include the single-center design and retrospective nature of the study.

Clinical Practice Guidelines

Congress of Neurological Surgeons (CNS)

Green et al. (2025) developed evidence-based guidelines for the CNS that address the role of SRS for individuals with functioning pituitary adenomas. The systematic review analyzed 21 studies and yielded class III evidence that supports the following recommendations:

- SRS, hypofractionated SRS, fractionated (more than five fractions) radiotherapy, and conventional radiation therapy provide excellent radiographic control, with variable hormonal reduction and endocrine remission rates. With SRS and fractionated radiotherapy, hormonal reduction may continue for up to 10 years after treatment.
- Clinicians may continue to administer endocrine-suppressive medical treatment before SRS, as this may not affect radiographic control.

Recurrent Gliomas

De Maria et al. (2021) performed a systematic review and meta-analysis to establish the safety and efficacy of CyberKnife treatment for recurrent WHO grade III or 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. OS from initial diagnosis and CyberKnife treatment was 22.6 months and 8.6 months. The median time to progression and median PFS were 6.7 months and 7.1 months. Median OS with CyberKnife treatment was 8.4 months for WHO grade IV gliomas compared with 11 months for WHO grade III gliomas. Median OS with CyberKnife treatment was 4.4 months in individuals who underwent CyberKnife treatment alone compared with 9.5 months in individuals who underwent CyberKnife treatment plus chemotherapy. No correlation was observed between the median time to recurrence and median OS with 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. In 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 that includes larger, prospective studies. Limitations of the meta-analysis include its reliance on a small number of single-center case series and the small sample sizes of the included 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. Overall, 25 individuals who were aged 23 to 74 years were reirradiated 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 actuarial 1-, 3-, and 5-year OS rates of 88%, 56%, and 30%, respectively. After treatment with SRS or FSRT, median OS was 9 months, with an actuarial 1-year OS rate of 29%. After 6 months, local control, which was assessed for 28 tumors, was 57%, while local control after 1 year was 39%. Three individuals experienced local failure.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

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 reirradiation following recurrent glioblastoma (rGBM) and that treatment volume may predict local control in the salvage setting. Limitations include the retrospective nature of the study and small sample size.

Sharma et al. (2018) conducted a single-center, retrospective case series analysis to evaluate the role of SRS in patients with rGBMs. Patients' 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 end points, respectively. A total of 53 patients with rGBM underwent salvage SRS that targeted 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, 12-24 Gy), and the homogeneity index was 1.90 (range, 1.11-2.02). The median OS after salvage SRS was estimated to be 11.0 months (95% CI, 7.1-12.2 months), and the median PFS after salvage SRS was 4.4 months (95% CI, 3.7-5.0 months). A KPS score of ≥ 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, respectively) and PFS (p = 0.01 and 0.002). Based on these factors, two prognostic groups were identified for PFS (5.4 vs 3.2 months), while three were identified for OS (median OS, 15.2 vs 10.5 vs 5.2 months). The authors concluded that good performance, smaller tumor volumes, and treatment at higher homogeneity indices were associated with longer OS and/or PFS despite multiple prior treatments for rGBM and that for individuals with rGBM and those clinical characteristics, SRS is a reasonable salvage treatment option. Limitations include the single-center, retrospective nature of the study and small sample size.

Imber et al. (2017) conducted a single-center, retrospective case series analysis to identify proper indications, efficacy, and anticipated complications of SRS for rGBM. Patients 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 was used to identify potential predictor covariate cut points, and Kaplan-Meier and proportional hazards modeling was used to identify factors associated with post-SRS and postdiagnosis survival. A total of 174 patients with glioblastoma (median age, 54.1 years) underwent SRS at a median of 8.7 months after initial diagnosis. Overall, 75% had one treatment target (range, 1-6), and the median target volume and prescriptions were 7 cm^3 (range, 0.3-39.0 cm^3) and 16.0 Gy (range, 10-22 Gy), respectively. Median OS was 10.6 months after SRS and 19.1 months after diagnosis. Kaplan-Meier and multivariable modeling revealed that a younger age at SRS, higher prescription dose, and longer interval between original surgery and SRS are significantly associated with improved post-SRS survival. In total, 46 patients (26%) underwent salvage craniotomy after SRS, with 63% having radionecrosis or mixed tumor/necrosis vs 35% having a purely recurrent tumor. The necrosis/mixed group had lower mean isodose prescription than the tumor group (16.2 vs 17.8 Gy; p = 0.003) and larger mean treatment volume (10.0 vs 5.4 cm^3; p = 0.009). The authors concluded that GK RS may benefit a subset of individuals with focal recurrence, particularly those who are younger and have smaller recurrences. The authors also stated that higher prescription doses are associated with improved post-SRS survival and do not seem to have a greater risk of symptomatic treatment effect. Limitations include the single-center, retrospective nature of the study and small sample size.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

Yeboa et al. (2025) developed clinical practice guidelines for the treatment of WHO grade IV adult-type diffuse glioma with radiation therapy. The guidelines state the following:

- For patients with recurrent WHO grade IV diffuse glioma and a KPS of ≥ 70, an in-field radiation therapy interval of ≥ 6 months, and/or focal tumor maximum diameter of ≤ 6 cm, reirradiation is conditionally recommended following a multidisciplinary, patient-centered discussion. Implementation remark: Patient enrollment in clinical trials or multi-institutional registries is encouraged. Strength of recommendation: conditional; quality of evidence: moderate.
- For patients with recurrent WHO grade IV diffuse glioma who elect reirradiation, the following treatment options are conditionally recommended: conventionally fractionated radiation therapy, hypofractionated radiation therapy, SRS, fractionated stereotactic radiation therapy, or brachytherapy. Strength of recommendation: conditional; quality of evidence: moderate.

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, as it facilitates precise dose delivery to target tissue while minimizing exposure to adjacent critical structures and reduces overlap with previously irradiated fields. (NCCN, 2026)

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Spinal Lesions (Primary and Metastatic)

Bindels et al. (2024) conducted a systematic review and meta-analysis that compared SBRT with conventional EBRT (cEBRT) for relieving metastatic bone pain. Eligible studies were comparative trials that assessed pain response in those with painful bone metastases from solid tumors that were treated with cEBRT or SBRT, excluding those with prior radiotherapy or surgery at the target site. Overall, 18 studies that involved 1,685 individuals were included in the systematic review. Of these, eight RCTs, comprising 1,090 individuals, were included in the meta-analysis, with 980 individuals (90%) completing their allocated treatment. The primary outcome was overall and complete pain response, which was measured at 1, 3, and 6 months after treatment. The secondary outcomes included complete pain response, local tumor control, PFS, toxic effects, pathological fractures, QOL, and OS. Intention-to-treat analyses showed no difference in overall pain response between SBRT and cEBRT at 1 month (RR, 1.14; 95% CI, 0.99-1.30), 3 months (RR, 1.19; 95% CI, 0.96-1.47), or 6 months (RR, 1.22; 95% CI, 0.96-1.54), while SBRT achieved higher complete pain response at 1 month (RR, 1.43; 95% CI, 1.02-2.01), 3 months (RR, 1.80; 95% CI, 1.16-2.78), and 6 months (RR, 2.47; 95% CI, 1.24-4.91) following treatment. The authors concluded that those with painful bone metastases had comparable overall pain relief with SBRT and cEBRT; however, SBRT resulted in higher rates of complete pain resolution, which indicates that certain subgroups may derive greater benefit from SBRT. The findings are limited by substantial heterogeneity in SBRT and cEBRT dose regimens across the included RCTs, which may affect comparability of pain outcomes. Additionally, incomplete reporting of pain response at all time points and pooling of spinal and nonspinal lesions may obscure setting-specific treatment effects. Ryu et al. (2023), Sahgal et al. (2021), and Sprave et al. (2018), previously cited in this policy, are included in this systematic review and meta-analysis.

Guckenberger et al. (2024) conducted a multicenter, randomized, phase 3 trial to evaluate whether SBRT for painful vertebral metastases leads to higher rates of pain improvement than cEBRT (control) 6 months post treatment. The inclusion criteria consisted of those who were aged 18 years or older and had a diagnosis of a solid tumor; a maximum of two painful vertebral metastases; a KPS of ≥ 60%; and a life expectancy of greater than 1 year. The 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; neurological symptoms; previous radiation therapy at the site; or surgery of affected vertebra. Participant-reported pain improvement was the primary end point. Acute and late adverse events, OS, and QOL were secondary end points. Overall, 63 participants were randomized to receive SBRT (33 participants with 36 metastases) or cEBRT (30 participants with 31 metastases). In the intention-to-treat analysis, the 6-month proportion of participants who had metastases with pain reduction by two or more points was significantly higher in the SBRT group vs the control group (69.4% vs 41.9%, respectively; two-sided p = 0.02). 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 6 months, without increasing toxicity. Limitations include the small sample size and low number of participants who reported 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. Overall, 69 studies, with 7,236 metastases in 5,736 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 1-year local control rate of 94% (95% CI, 86%-99%); however, high levels of heterogeneity were noted 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%); however, levels of heterogeneity were mixed among the studies (I^2 = 92%, I^2 = 0%, and 95%, respectively). Only 1.7% of vertebral fractures required surgical stabilization. The authors concluded that SBRT for the spine is characterized by its effective and safe treatment outcomes and offers long-lasting relief from pain and control over disease progression, which are especially beneficial in individuals with oligometastatic conditions. The limitations include incomplete reporting and missing data, along with heterogeneous study populations that encompassed varied histologies and both oligo- and polymetastatic disease. Additionally, the extended study period (2005-2023) was a limitation, during which evolving stereotactic techniques and experience likely influenced outcomes and tolerability. Ryu et al. (2023) and Sprave et al. (2018) are included in this review.

Conti et al. (2022) performed a systematic review and meta-analysis of RS in individuals with benign spinal hemangiomas. Peer-reviewed studies or case series in individuals with spinal vertebral hemangiomas who were treated with RS or SBRT were included. Overall, 23 individuals, with 24 spinal vertebral hemangiomas, were assessed in three studies. The follow-up time was 7.3 to 84 months. The vast majority of lesions were located at the dorsal level [n = 18 (75%)]. In 20 individuals (83.3%), 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% of cases (p = 0.7). The overall response was reported in 94.1% (p = 0.7). No progressive disease was reported. Pain relief was achieved in 87.5% of individuals (p = 0.2). Damage to surrounding tissue that was caused by irradiation was reported in 22.3% of cases (p = 0.02) in one study,

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

in which higher doses of radiation were delivered. According to the authors, RS was safe and effective for spinal hemangiomas. Limitations include the small sample size.

Clinical Practice Guidelines

American Society for Radiation Oncology (ASTRO)

ASTRO's guideline on palliative radiation therapy for symptomatic bone metastases (Alcorn et al., 2024) provides recommendations using consensus-building methodology based on a systematic review by the Agency for Healthcare Research and Quality (Skelly et al., 2023). The authors note that developing the most favorable radiation therapy regimen requires an assessment that includes prognosis, any previous radiation therapy doses, normal tissue risks, QOL, and patient values and goals. The guidelines state the following:

- For patients with symptomatic spine bone metastases, including those that are causing compression of the spinal cord or cauda equina, radiation therapy is recommended to improve ambulatory status, sphincter function, and reduce pain. An implementation remark states that before initiating radiation therapy, evaluation for spine stability and surgery is necessary. Strength of recommendation: strong; quality of evidence: high.
- In patients with spine bone metastases that are causing compression of the spinal cord or cauda equina who are not eligible for initial surgical decompression and are treated with conventional palliative radiation therapy, 800 cGy in one fraction, 1,600 cGy in two fractions, 2,000 cGy in five fractions, or 3,000 cGy in 10 fractions is recommended. Strength of recommendation: strong; quality of evidence: high.
- For patients with symptomatic bone metastases who are treated with SBRT, 1,200 to 1,600 cGy in one fraction (nonspine) and 2,400 cGy in two fractions (spine) are recommended. An implementation remark states that 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, as well as physician experience. Strength of recommendation: strong; quality of evidence: moderate.
- For patients with symptomatic bone metastases and an ECOG PS of 0 to 2 who are receiving no surgical intervention and do not have neurological symptoms, SBRT is conditionally recommended over conventional palliative radiation therapy. An implementation remark states that 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 who would benefit from reirradiation to the same site, treatment with SBRT is conditionally recommended. Strength of recommendation: conditional; quality of evidence: expert opinion.

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; no metastatic spinal cord compression, with a good overall prognosis; or oligometastases (up to three discrete metastases) with spinal involvement. (NICE, 2023)

NCCN

Per NCCN Guidelines regarding radiation therapy for metastatic spinal tumors, stereotactic approaches such as SRS and SBRT may be preferred in those in whom ablation of the tumor is a goal of treatment, life expectancy is 3 months or more, or the tumors are radioresistant (e.g., renal cell, melanoma, sarcoma, hepatocellular, some colorectal cases, 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, 2026)

To Treat a Previously Irradiated Field

The ASTRO model policy for SRS (2022) notes that SRS is considered appropriate for patients with recurrent disease in a previously irradiated cranial field when highly precise, stereotactic delivery is necessary to safely re-treat the target. In this setting, prior radiation limits the tolerance of surrounding normal brain and critical structures, making conventional approaches less suitable.

The ASTRO model policy for SBRT (2020) notes that SBRT may be used for tumors that are located within or near previously irradiated areas when clearly supported by documentation. It is appropriate for patients whose overall health and performance status support aggressive local treatment, either to achieve complete control of limited (oligometastatic) disease or to meaningfully reduce total tumor burden for a defined clinical benefit. Additionally, SBRT is suitable for recurrent or palliative cases in which other radiation approaches cannot be delivered as safely or effectively due to prior radiation exposure, particularly when high precision is required to protect nearby normal tissues from further injury.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Trigeminal Neuralgia Refractory to Medical Therapy

Hajikarimloo et al. (2025) performed a systematic review and meta-analysis that aimed to assess the safety and efficacy of SRS in individuals with tumor-related trigeminal neuralgia (TRTN). The inclusion criteria consisted of studies in which the outcomes of and adverse events with SRS in TRTN were reported; publications that reported complete pain free, adequate pain relief, and AREs; and clinical trials, cohort studies, case reports, or retrospective studies that included at least five individuals. Overall, 19 studies met the inclusion criteria, with a total of 454 individuals. Meningioma [67.7% (304 of 449)] was the most common tumor, followed by VS [18.3% (82 of 449)] and trigeminal schwannoma [8.2% (37 of 449)]. The meta-analysis demonstrated that SRS is associated with a pooled complete pain-free rate of 38% (95% CI, 27%-50%), adequate pain relief rate of 73% (95% CI, 63%-83%), and ARE rate of 14% (95% CI, 7%-22%). In those in whom the underlying etiology was petroclival meningiomas, SRS resulted in a pooled complete pain-free rate of 30% (95% CI, 5%-64%), adequate complete pain relief rate of 64% (95% CI, 33%-90%), and ARE rate of 13% (95% CI, 0%-48%). The authors concluded that in individuals with TRTN, SRS provides beneficial pain-related outcomes, with low AREs, and that both tumor-only and dual-targeted approaches produce comparable results. Limitations include the retrospective nature of most studies and differences in follow-up durations.

Khaboushan et al. (2025) conducted a systematic review and meta-analysis that compared SRS and rhizotomy for trigeminal neuralgia. Eligible studies were those that included individuals who were diagnosed with trigeminal neuralgia, compared SRS with rhizotomy techniques, and reported outcomes related to pain relief or complications. Overall, 15 studies that were published between 2005 and 2023, with a total of 1,251 individuals (577 SRS; 674 rhizotomy), were analyzed using a random-effects model; pain-free outcome was defined as Barrow Neurological Institute (BNI) I and pain relief as BNI I to IIIb. Rhizotomy provided superior initial pain-free outcomes (RR, 0.66; 95% CI, 0.49-0.91; $p < 0.01$), while no significant difference was found in pain-free rates at the last follow-up (RR, 0.99; 95% CI, 0.80-1.22; $p = 0.89$) or overall pain relief (RR, 1.14; 95% CI, 0.90-1.44; $p = 0.29$). SRS significantly reduced recurrence (RR, 0.70; 95% CI, 0.51-0.96; $p < 0.05$), re-treatment need (RR, 0.67; 95% CI, 0.46-0.96; $p < 0.05$), and facial numbness (RR, 0.61; 95% CI, 0.37-0.99; $p < 0.05$), with no significant difference in overall complications (RR, 0.70; 95% CI, 0.34-1.43; $p = 0.33$). The authors concluded that SRS and rhizotomy are both effective for trigeminal neuralgia, with rhizotomy offering faster pain relief and SRS providing longer-lasting benefits and fewer complications, particularly in individuals with multiple sclerosis, and that treatment decisions should be individualized based on urgency of relief, long-term effectiveness, side effects, and multiple sclerosis status. Key limitations include the retrospective, single-institution design that may have introduced selection bias and relatively short follow-up period, which could have underestimated recurrence rates.

Peciu-Florianu et al. (2021) conducted a systematic review and meta-analysis that focused on trigeminal neuralgia treated with SRS for meningiomas and VS and investigated rates of improvement of trigeminal neuralgia symptoms. Articles published between January 1990 and December 2019 (n = 330) were screened and assessed for eligibility. Ultimately, 20 studies were included in the qualitative synthesis, and 13 were included in the quantitative synthesis. Pain relief after SRS was reported as BNI Pain Intensity Scale scores of BNI I in 50.5% (range, 36%-65.1%) of individuals and BNI I to IIIb in 83.8% (range, 77.8%-89.8%) of individuals. There was no significant difference in series discussing outcomes for tumor targeting vs tumor and nerve targeting. Recurrences were described in 34.7% (range, 21.7%-47.6%; tumor targeting). Maintenance of BNI I was reported in 36.4% (range, 20.1%-52.7%) and of BNI I to IIIb in 41.2% (range, 29.8%-52.7%; tumor-targeting series). When both the nerve and tumor were targeted, only one series reported 86.7% with BNI I to IIIb at the last follow-up. Complications were encountered in 12.6% (range, 6.3%-18.8%; tumor-targeting series) of individuals; however, they were much higher, as high as 26.7%, in the only study that reported them after targeting both the nerve and tumor. Facial numbness was the most common complication. The authors concluded that SRS for trigeminal neuralgia that is secondary to benign tumors is associated with a favorable clinical course but is less favorable than idiopathic trigeminal neuralgia. Among reports and targeted approaches, there was heterogeneity. Targeting both the tumor and nerve seemed to achieve better long-term results; however, the rate of complications was much higher, and the number of individuals treated was limited. The authors recommended future clinical studies that focus on standard reporting of clinical outcomes and randomization of targeting methods. Limitations include the retrospective nature of the included studies. Additionally, some reports included other pathologies besides meningiomas and VS.

Tuleasca et al. (2018) conducted a systematic review to provide an objective summary of the published literature that was specific to the treatment of classical trigeminal neuralgia with RS and to develop consensus guideline recommendations for the use of RS, as endorsed by the ISRS. A search was conducted using the Embase, PubMed, and MEDLINE databases for articles published between 1951 to 2015 and identified a total of 585 studies. Overall, 65 studies were included in the review, and those included 45 GKS studies (5,687 individuals), 11 LINAC RS studies (511 individuals), and nine CyberKnife RS studies (263 individuals). All but one of the studies were retrospective. The mean maximal doses were 71.1 to 90.1 Gy (prescribed at the 100% isodose line) for GKS, 83.3 Gy for LINAC, and 64.3 to 80.5 Gy for CyberKnife RS (the latter two were prescribed at the 80% or 90% isodose lines, respectively). The ranges of maximal doses were as follows: 60 to 97 Gy for GKS, 50 to 90 Gy for LINAC, and 66 to 90 Gy for CyberKnife RS. Actuarial initial freedom from pain without medication ranged from 28.6% to 100% (mean, 53.1%; median, 52.1%) with GKS, from 17.3%

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

to 76% (mean, 49.3%; median, 43.2%) with LINAC, and from 40% to 72% (mean, 56.3%; median, 58%) with CyberKnife RS. Specific to hypesthesia, the crude rates (all BNI Pain Intensity Scale scores included) ranged from 0% to 68.8% (mean, 21.7%; median, 19%) with GKS, from 11.4% to 49.7% (mean, 27.6%; median, 28.5%) with LINAC, and from 11.8% to 51.2% (mean, 29.1%; median, 18.7%) with CyberKnife RS. Other complications included dysesthesias, paresthesias, dry eye, deafferentation pain, and keratitis. Hypesthesia and paresthesia occurred as complications only when the anterior retrogasserian portion of the trigeminal nerve was targeted, whereas the other listed complications occurred when the root entry zone was targeted. Recurrence rates ranged from 0% to 52.2% (mean, 24.6%; median, 23%) with GKS, from 19% to 63% (mean, 32.2%; median, 29%) with LINAC, and from 15.8% to 33% (mean, 25.8%; median, 27.2%) with CyberKnife RS. Two GKS series reported that 30% and 45.3% of individuals were pain free, without medication, at 10 years. The authors concluded that although the literature is limited in its level of evidence, at present, one can conclude that RS is a safe and effective therapy for drug-resistant trigeminal neuralgia. Based on this information, consensus statements have been made. Limitations include the retrospective nature of almost all included studies and high heterogeneity across studies.

Clinical Practice Guidelines

National Institute for Health and Care Excellence (NICE)

A NICE guideline (2022) on SRS and trigeminal neuralgia states that safety and efficacy are adequate to support using this procedure, provided that standard arrangements are in place for clinical governance, consent, and audit. A multidisciplinary team that is experienced in the management of trigeminal neuralgia should be used for patient selection, and the procedure should only be performed in specialized centers.

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. The inclusion criteria consisted of single-arm studies, RCTs, and case or cohort studies in adults with uveal melanoma who were treated with CyberKnife radiotherapy and at least one perioperative measure. Ten studies met the inclusion criteria, with a total of 2,370 individuals (2,372 uveal melanomas). A meta-analysis showed that 811 of 912 individuals (0.89; 95% CI, 0.86-0.92) maintained local control for 3 years, and 1,448 of 1,724 individuals (0.84; 95% CI, 0.81-0.88) preserved the eye in 3 years. During follow-up, 91% (0.91; 95% CI, 0.85-0.97) of individuals survived, and 351 of 1,720 individuals (0.23; 95% CI, 0.09-0.37), involving 1,722 eyes, had tumor recurrence. In addition, 1,376 individuals (0.79; 95% CI, 0.77-0.82) preserved the eyeball in 5 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 uveal melanomas. Limitations include the retrospective nature of the studies; additionally, most of the studies were single arm, with no parallel comparisons.

Parker et al. (2020) conducted a systematic review and meta-analysis that evaluated the clinical outcomes in individuals with uveal melanomas or intraocular metastases that were treated with GKS. The primary outcomes that were analyzed were local tumor control and tumor regression. Overall, 52 studies were eligible for systematic review; 1,010 individuals had uveal melanoma, and three had intraocular metastasis. The authors found that 840 of 898 individuals (0.96; 95% CI, 0.94-0.97; I^2 = 16%) from 19 studies had local control, and 378 of 478 individuals (0.81; 0.70-0.90; I^2 = 83%) from 16 studies experienced tumor regression. The authors concluded that GK RS 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 that focuses on generating RCTs with level 1 evidence of the efficacy of GK RS in treating ocular tumors, measures overall complication rates of GK RS, provides consistent reporting of visual acuity measurements after GK RS, and evaluates low-dose regimens to reduce radiation-induced side effects and subsequent vision loss. Limitations include the retrospective nature of the majority of the studies and lack of RCTs. (Fakiris et al., 2007, previously cited in this policy, is included in this review.)

Yazici et al. (2017) conducted a multicenter, retrospective case series analysis to evaluate treatment outcomes in patients with uveal melanoma who were treated with SRS or FSRT. Treatment was administered with CyberKnife. The primary end points were local recurrence–free survival (LRFS) and enucleation-free survival. The secondary end points included OS, DFS, distant metastasis–free survival, 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 was defined as a > 50% decrease in the tumor volume. Overall, 181 patients (182 uveal melanomas) who underwent SRS/FSRT were included in the analysis. The median age was 54 years (range, 18-82 years), and 104 (58%) were male. The median tumor diameter and thickness was 10 mm (range, 2-12 mm) and 8.0 mm (range, 1.5-18 mm), respectively. According to Collaborative Ocular Melanoma Study criteria, the tumor size was small in

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

1%, medium in 49.5%, and large in 49.5% of the patients. In total, 71 tumors received < 45 Gy, and 111 received ≥ 45 Gy. The median follow-up time was 24 months (range, 2-79 months). Complete and partial response was observed in 8 and 104 eyes, respectively. The rate of 5-year OS was 98%, DFS was 57%, LRFS was 73%, distant metastasis–free survival was 69%, and enucleation-free survival was 73%. There was a significant correlation between tumor size and DFS, SRS/FSRT dose, and enucleation-free survival; both were prognostic for LRFS. Enucleation was performed in 41 eyes due to progression in 26 and complications in 11. The authors concluded that with 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. Additional studies that include longer follow-up should be conducted. Limitations include the retrospective nature of the study and small sample size.

Clinical Practice Guidelines

European Society for Medical Oncology (ESMO)/Expert Care for Rare Adult Solid Cancers (EURACAN)

Piperno-Neumann et al. (2026) developed an ESMO/EURACAN guideline that addresses the diagnosis, treatment, and follow-up of uveal melanoma. The guideline notes that several radiotherapy approaches are used to treat uveal melanoma, each with specific roles. SRS, including hypofractionated forms, is generally reserved for cases in which brachytherapy or proton beam radiotherapy are not available. It is typically used for tumors that are thicker than 2 to 3 mm, with a basal diameter of 15 mm or less. The guideline states that evidence is limited, but available data suggest strong local control, with 5-year rates of approximately 89% to 90%. While SRS is effective, it is associated with a higher risk of complications, such as vitreous hemorrhage, than other radiotherapy options.

NCCN

The NCCN Guidelines for uveal melanoma state that 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. SABR for oligometastases should be delivered to the appropriate target volume using precise SBRT techniques with image guidance. (NCCN, 2026)

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 stereotactic body radiation therapy and stereotactic radiosurgery. 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 26, 2026)

References

Adar S, Ádám A, Balogh T, et al. Sublobar resection, stereotactic body radiotherapy, and thermal ablation for early-stage non-small cell lung cancer: a systematic review and meta-analysis. Lung Cancer. 2026 May;217:109467.

Aizer AA, Shin KY, Catalano PJ, et al. Treatment for brain metastases with stereotactic radiation vs hippocampal-avoidance whole brain radiation: a randomized clinical trial. JAMA. 2026 Apr;335(13):1127-1136.

Akdemir EY, Zhang Y, Yomo S, et al. Radiosurgical management of cavernous sinus hemangioma: systematic review, meta-analysis, and International Stereotactic Radiosurgery Society practice guideline. Int J Radiat Oncol Biol Phys. 2026 Apr;124(5):1208-1218.

Alcorn S, Cortés ÁA, Bradfield L, et al. External beam radiation therapy for palliation of symptomatic bone metastases: an ASTRO clinical practice guideline. Pract Radiat Oncol. 2024 Sep-Oct;14(5):377-397.

American College of Radiology (ACR) website. Stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT). Reviewed May 1, 2023. Available at: https://www.radiologyinfo.org/en/info/stereotactic. Accessed May 26, 2026.

American Society for Radiation Oncology (ASTRO) website. ASTRO Radiation Oncology Coding Resource 2024. Available at: https://www.astro.org/Daily-Practice/Coding/Coding-Resource. Accessed May 26, 2026.

American Society for Radiation Oncology (ASTRO) website. ASTRO stereotactic body radiation (SBRT) model policy. June 2020. Available at: https://www.astro.org/ASTRO/media/ASTRO/Daily%20Practice/PDFs/ASTROSBRTModelPolicy.pdf. Accessed May 26, 2026.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

American Society for Radiation Oncology (ASTRO) website. ASTRO stereotactic radiosurgery (SRS) model policy. June 2022. Available at: https://www.astro.org/ASTRO/media/ASTRO/Daily%20Practice/PDFs/ASTRO-SRS_ModelPolicy.pdf. Accessed July 14, 2026.

Amini A, Verma V, Simone CB 2nd, et al. American Radium Society appropriate use criteria for radiation therapy in oligometastatic or oligoprogressive non-small cell lung cancer. Int J Radiat Oncol Biol Phys. 2022 Feb;112(2):361-375.

Apisarnthanarax S, Barry A, Cao M, et al. External beam radiation therapy for primary liver cancers: an ASTRO clinical practice guideline. Pract Radiat Oncol. 2022 Jan-Feb;12(1):28-51.

Bae SH, Chun SJ, Chung JH, et al. Stereotactic body radiation therapy for hepatocellular carcinoma: meta-analysis and International Stereotactic Radiosurgery Society practice guidelines. Int J Radiat Oncol Biol Phys. 2024 Feb;118(2):337-351.

Ball D, Mai GT, Vinod S, et al.; TROG 09.02 CHISEL Investigators. Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial. Lancet Oncol. 2019 Apr;20(4):494-503.

Balossier A, Tuleasca C, Delsanti C, et al. Long-term hearing outcome after radiosurgery for vestibular schwannoma: a systematic review and meta-analysis. Neurosurgery. 2023 Jun;92(6):1130-1141.

Barbaro NM, Quigg M, Ward MM, et al. Radiosurgery versus open surgery for mesial temporal lobe epilepsy: the randomized, controlled ROSE trial. Epilepsia. 2018 Jun;59(6):1198-1207.

Bilski M, Szklener K, Szklener S, et al. Stereotactic radiosurgery in the treatment of essential tremor - a systematic review. Front Neurol. 2024 Apr;15:1370091.

Bindels BJJ, Mercier C, Gal R. Stereotactic body and conventional radiotherapy for painful bone metastases: a systematic review and meta-analysis. JAMA Netw Open. 2024 Feb;7(2):e2355409.

Bisello S, Camilletti AC, Bertini F, et al. Stereotactic radiotherapy in intrahepatic cholangiocarcinoma: a systematic review. Mol Clin Oncol. 2021 Aug;15(2):152.

Boari N, Bailo M, Gagliardi F, et al. Gamma Knife radiosurgery for vestibular schwannoma: clinical results at long-term follow-up in a series of 379 patients. J Neurosurg. 2014 Dec;121 Suppl:123-142.

Brown PD, Jaeckle K, Ballman KV, et al. Effect of radiosurgery alone vs radiosurgery with whole brain radiation therapy on cognitive function in patients with 1 to 3 brain metastases: a randomized clinical trial [published correction appears in JAMA. 2018 Aug;320(5):510]. JAMA. 2016 Jul;316(4):401-409.

Bucknell NW, Kron T, Herschtal A, et al.; CHISEL Coauthors. Comparison of changes in pulmonary function after stereotactic body radiation therapy versus conventional 3-dimensional conformal radiation therapy for stage I and IIa non-small cell lung cancer: an analysis of the TROG 09.02 (CHISEL) phase 3 trial. Int J Radiat Oncol Biol Phys. 2023 Oct;117(2):378-386.

Chang JY, Senan S, Paul MA, et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomized trials [published correction appears in Lancet Oncol. 2015 Sep;16(9):e427]. Lancet Oncol. 2015 May;16(6):630-637.

Chao ST, Dad LK, Dawson LA, et al. ACR-ASTRO practice parameter for the performance of stereotactic body radiation therapy. Am J Clin Oncol. 2020 Aug;43(8):545-552.

Chuong MD, Springett GM, Freilich JM, et al. Stereotactic body radiation therapy for locally advanced and borderline resectable pancreatic cancer is effective and well tolerated. Int J Radiat Oncol Biol Phys. 2013 Jul;86:516-522.

Conti A, Starnoni D, Barges-Coll J, et al. Radiosurgery for benign vertebral body hemangiomas of the spine: a systematic review and meta-analysis. World Neurosurg. 2022 Aug;164:97-105.

de Haan LMM, Demmink MCL, Zegers CML, et al. Stereotactic radiotherapy on Parkinson's disease induced tremors - a systematic review. Radiother Oncol. 2026 Jan;214:111281.

De Maria L, Terzi di Bergamo L, Conti A, et al. CyberKnife for recurrent malignant gliomas: a systematic review and meta-analysis. Front Oncol. 2021 Mar;11:652646.

De Nigris Vasconcellos F, Vilela MAD, Garcia Torrico F, et al. Stereotactic radiosurgery for recurrent/residual nonfunctioning pituitary adenoma: a single-arm systematic review and meta-analysis. Acta Neurochir (Wien). 2024 Oct;166(1):392.

Ding D, Starke RM, Kano H, et al. Stereotactic radiosurgery for Spetzler-Martin grade III arteriovenous malformations: an international multicenter study. J Neurosurg. 2017 Mar;126(3):859-871.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Dong H, Shi J, Wei P, et al. Comparative efficacy of surgical strategies for drug-resistant epilepsy: a systematic review and meta-Analysis. World Neurosurg. 2025 Mar;195:123729.

Du K and Luo W. Efficacy and safety of robotic Cyberknife radiotherapy in uveal melanoma: a systematic review and meta-analysis. Eye (Lond). 2025 Feb;39(3):548-555.

Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically localized prostate cancer: AUA/ASTRO guideline. Part III: principles of radiation and future directions. J Urol. 2022 Jul;208(1):26-33.

Eastham JA, Barocas DA, Chu CE, et al. Clinically localized prostate cancer: AUA/ASTRO guideline amendment (2026). J Urol. 2026 Jul;216(1):2-11.

ECRI. Stereotactic body radiation therapy for localized prostate cancer. Plymouth meeting (PA): ECRI; 2024 Dec. (Evidence Analysis).

Eekers DBP, Pijnappel EN, Schijns OEMG, et al. Evidence on the efficacy of primary radiosurgery or stereotactic radiotherapy for drug-resistant non-neoplastic focal epilepsy in adults: a systematic review. Seizure. 2018 Feb;55:83-92.

Fakiris AJ, Lo SS, Henderson MA, et al. Gamma Knife-based stereotactic radiosurgery for uveal melanoma. Stereotact Funct Neurosurg. 2007;85(2-3):106-112.

Fakiris AJ, McGarry RC, Yiannoutsos CT, et al. Stereotactic body radiation therapy for early-stage non-small-cell lung carcinoma: four-year results of a prospective phase II study. Int J Radiat Oncol Biol Phys. 2009 Nov;75(3):677-682.

Farris M, McTyre ER, Cramer CK, et al. Brain metastasis velocity: a novel prognostic metric predictive of overall survival and freedom from whole-brain radiation therapy after distant brain failure following upfront radiosurgery alone. Int J Radiat Oncol Biol Phys. 2017 May;98(1):131-141.

Fogarty G, Dolven-Jacobsen K, Morton RL, et al. Phase 3 international trial of adjuvant whole brain radiotherapy (WBRT) or observation (Obs) following local treatment of 1-3 melanoma brain metastases (MBMs). J Clin Oncol. 2019 May;37(suppl 15):9500.

Gaebe K, Li AY, Park A, et al. Stereotactic radiosurgery versus whole brain radiotherapy in patients with intracranial metastatic disease and small-cell lung cancer: a systematic review and meta-analysis. Lancet Oncol. 2022 Jul;23(7):931-939.

Gagliardi F, De Domenico P, Garbin E, et al. Primary Gamma Knife radiosurgery for pineal region tumors: a systematic review and pooled analysis of available literature with histological stratification. J Pineal Res. 2023 Dec;75(4):e12910.

Germano IM, Green S, Lehrer EJ, et al. Congress of Neurological Surgeons systematic review and evidence-based guideline on the role of radiosurgery (stereotactic radiosurgery) and radiation therapy in the management of patients with vestibular schwannomas: updates. Neurosurgery. 2026 Feb;98(2):293-297.

Germano IM, Sheehan J, Parish J, et al. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the role of radiosurgery and radiation therapy in the management of patients with vestibular schwannomas. Neurosurgery. 2018 Feb;82(2):E49-E51.

Gigliotti MJ, Hasan S, Karlovits SM, et al. Re-irradiation with stereotactic radiosurgery/radiotherapy for recurrent high-grade gliomas: improved survival in the modern era. Stereotact Funct Neurosurg. 2018;96(5):289-295.

Glicksman RM, Winter J, McPartlin A, et al. Stereotactic body radiation therapy for renal tumors: a prospective phase 2 clinical trial. Int J Radiat Oncol Biol Phys. 2026 May;125(1):154-163.

Gomez DR, Blumenschein GR Jr, Lee JJ, et al. Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicenter, randomized, controlled, phase 2 study. Lancet Oncol. 2016 Dec;17(12):1672-1682.

Gomez DR, Tang C, Zhang J, et al. Local consolidative therapy vs. maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer: long-term results of a multi-institutional, phase II, randomized study. J Clin Oncol. 2019 Jun;37(18):1558-1565.

Gonçalves OR, Lima HF, Borges CES, et al. Efficacy and safety of stereotactic radiosurgery with Gamma Knife machine in patients with essential tremor: a systematic review and single-arm meta-analysis. Neurosurg Rev. 2024 Nov;47(1):862.

Gondi V, Bauman G, Bradfield L, et al. Radiation therapy for brain metastases: an ASTRO clinical practice guideline. Pract Radiat Oncol. 2022 Jul-Aug;12(4):265-282.

Gooijer SA, Gazendam ASM, Torensma B, et al. Metastasectomy versus stereotactic body radiotherapy for patients with oligometastatic colorectal lung metastases: a systematic review. Eur J Surg Oncol. 2025 Apr;51(8):110056.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Graber JJ, Cobbs CS, Olson JJ. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the use of stereotactic radiosurgery in the treatment of adults with metastatic brain tumors. Neurosurgery. 2019 Mar;84(3):E168-E170.

Graffeo CS, Kotecha R, Sahgal A, et al. Stereotactic radiosurgery for intermediate (III) or high (IV-V) Spetzler-Martin grade arteriovenous malformations: International Stereotactic Radiosurgery Society practice guideline. Neurosurgery. 2025 Feb;96(2):298-307.

Graffeo CS, Sahgal A, De Salles A, et al. Stereotactic radiosurgery for Spetzler-Martin grade I and II arteriovenous malformations: International Society of Stereotactic Radiosurgery (ISRS) practice guideline. Neurosurgery. 2020 Sep;87(3):442-452.

Green S, Lehrer EJ, Cifarelli CP, et al. Congress of Neurological Surgeons systematic review and evidence-based guidelines for the role of radiosurgery for patients with functioning pituitary adenomas. Neurosurgery. 2025 Aug;97(3S):S36-S43.

Guckenberger M, Billiet C, Schnell D, et al. Dose-intensified stereotactic body radiotherapy for painful vertebral metastases: a randomized phase 3 trial. Cancer. 2024 Aug;130(15):2713-2722.

Guninski RS, Cuccia F, Alongi F, et al. Efficacy and safety of SBRT for spine metastases: a systematic review and meta-analysis for preparation of an ESTRO practice guideline. Radiother Oncol. 2024 Jan;190:109969.

Guss ZD, Batra S, Limb CJ, et al. Radiosurgery of glomus jugulare tumors: a meta-analysis. Int J Radiat Oncol Biol Phys. 2011 Nov;81(4):e497-e502.

Habibi MA, Mirjani MS, Ahmadvand MH, et al. Gamma Knife stereotactic radiosurgery for neurofibromatosis 2 (NF2)-associated meningiomas; a systematic review and meta-analysis. Acta Neurochir (Wien). 2025 Feb;167(1):35.

Hajikarimloo B, Habibi MA, Sabbagh Alvani M, et al. Repeat stereotactic radiosurgery in vestibular schwannoma patients: a systematic review and meta-analysis. J Clin Neurosci. 2024 Dec;130:110905.

Hajikarimloo B, Mohammadzadeh I, Tos SM, et al. Stereotactic radiosurgery for tumor-related trigeminal neuralgia: a systematic review and meta-analysis. BMC Neurol. 2025 May;25(1):195.

Harrow S, Palma DA, Olson R, et al. Stereotactic radiation for the comprehensive treatment of oligometastases (SABR-COMET): extended long-term outcomes. Int J Radiat Oncol Biol Phys. 2022 Nov;114(4):611-616.

Hasegawa T, Ishii D, Kida Y, et al. Gamma Knife surgery for skull base chordomas and chondrosarcomas. J Neurosurg. 2007 Oct;107(4):752-757.

Hasegawa T, Kondziolka D, Hadjipanayis CG, et al. The role of radiosurgery for the treatment of pineal parenchymal tumors. Neurosurgery. 2002 Oct;51(4):880-889.

Hellman S and Weichselbaum RR. Oligometastases. J Clin Oncol. 1995 Jan;13(1):8-10.

Herman JM, Chang DT, Goodman KA, et al. Phase 2 multi-institutional trial evaluating gemcitabine and stereotactic body radiotherapy for patients with locally advanced unresectable pancreatic adenocarcinoma. Cancer. 2015 Apr;121:1128-1137.

Huntoon K, Elder JB, Finger G, et al. Congress of Neurological Surgeons systematic review and evidence-based guidelines update for the role of emerging therapies in the management of patients with metastatic brain tumors. Neurosurgery. 2025 Jun;96(6):1172-1177.

Imber BS, Kanungo I, Braunstein S, et al. indications and efficacy of Gamma Knife stereotactic radiosurgery for recurrent glioblastoma: 2 decades of institutional experience. Neurosurgery. 2017 Jan;80(1):129-139.

Iorio-Morin C, Kano H, Huang M, et al. Histology-stratified tumor control and patient survival after stereotactic radiosurgery for pineal region tumors: a report from the international Gamma Knife research foundation. World Neurosurg. 2017 Nov;107:974-982.

Iyengar P, All S, Berry MF, et al. Treatment of oligometastatic non-small cell lung cancer: an ASTRO/ESTRO clinical practice guideline. Pract Radiat Oncol. 2023 Sep-Oct;13(5):393-412.

Iyengar P, Wardak Z, Gerber DE, et al. Consolidative radiotherapy for limited metastatic non-small-cell lung cancer: a phase 2 randomized clinical trial. JAMA Oncol. 2018 Jan;4(1):e173501.

Jackson WC, Silva J, Hartman HE, et al. Stereotactic body radiation therapy for localized prostate cancer: a systematic review and meta-analysis of over 6,000 patients treated on prospective studies. Int J Radiat Oncol Biol Phys. 2019 Jul;104(4):778-789.

Jang WI, Bae SH, Kim MS, et al. A phase 2 multicenter study of stereotactic body radiotherapy for hepatocellular carcinoma: safety and efficacy. Cancer. 2020 Jan;126(2):363-372.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Kano H, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, part 3: outcome predictors and risks after repeat radiosurgery. J Neurosurg. 2012b Jan;116(1):21-32.

Kano H, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, part 4: management of basal ganglia and thalamus arteriovenous malformations. J Neurosurg. 2012c Jan;116(1):33-43.

Kano H, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, part 5: management of brainstem arteriovenous malformations. J Neurosurg. 2012d Jan;116(1):44-53.

Kano H, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, part 6: multistaged volumetric management of large arteriovenous malformations. J Neurosurg. 2012e Jan;116(1):54-65.

Kano H, Lunsford LD, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, part 1: management of Spetzler-Martin Grade I and II arteriovenous malformations. J Neurosurg. 2012a Jan;116(1):11-20.

Kano H, Niranjan A, Kondziolka D, et al. Role of stereotactic radiosurgery in the management of pineal parenchymal tumors. Prog Neurol Surg. 2009;23:44-58.

Kano H, Sheehan J, Sneed PK, et al. Skull base chondrosarcoma radiosurgery: report of the North American Gamma Knife Consortium. J Neurosurg. 2015 Nov;123(5):1268-1275.

Khaboushan AS, Maroufi SF, Jarrah N, et al. Comparison of stereotactic radiosurgery and rhizotomy for trigeminal neuralgia: a systematic review and meta-analysis. Neurosurg Rev. 2025 Aug;48(1):613.

Kondziolka D, Mathieu D, Lunsford LD, et al. Radiosurgery as definitive management of intracranial meningiomas. Neurosurgery. 2008 Jan;62(1):53-60.

Kotecha R, Sahgal A, Rubens M, et al. Stereotactic radiosurgery for non-functioning pituitary adenomas: meta-analysis and International Stereotactic Radiosurgery Society practice opinion. Neuro Oncol. 2020 Mar;22(3):318-332.

Landsteiner A, Sowerby C, Ullman K, et al. Hypofractionation radiation therapy for definitive treatment of selected cancers: a systematic review. Washington (DC): Department of Veterans Affairs (US); 2023 May.

Lee CC, Kano H, Yang HC, et al. Initial Gamma Knife radiosurgery for nonfunctioning pituitary adenomas. J Neurosurg. 2014b Mar;120(3):647-654.

Lee CC, Sheehan JP, Kano H, et al. Gamma Knife radiosurgery for hemangioma of the cavernous sinus. J Neurosurg. 2017 May;126(5):1498-1505.

Lee CC, Yang HC, Chen CJ, et al. Gamma Knife surgery for craniopharyngioma: report on a 20-year experience. J Neurosurg. 2014a Dec;121 Suppl:167-178.

Li J, Tai Y, Pan B, et al. Efficacy and prognostic factors of stereotactic radiosurgery versus whole-brain radiotherapy for brain metastases in small cell lung cancer: a systematic review and meta-analysis. BMC Cancer. 2026 Mar;26(1):529.

Lievens Y, Guckenberger M, Gomez D, et al. Defining oligometastatic disease from a radiation oncology perspective: an ESTRO-ASTRO consensus document. Radiother Oncol. 2020 Jul;148:157-166.

Marchetti M, Sahgal A, De Salles AAF, et al. Stereotactic radiosurgery for intracranial noncavernous sinus benign meningioma: International Stereotactic Radiosurgery Society systematic review, meta-analysis and practice guideline. Neurosurgery. 2020 Oct;87(5):879-890.

Maroufi SF, Fallahi MS, Sabahi M, et al. Stereotactic radiosurgery in the management of skull base chordomas: a comprehensive systematic review and meta-analysis. Neurosurg Focus. 2024 May;56(5):E10.

Martínez-Moreno NE, Sahgal A, De Salles A, et al. Stereotactic radiosurgery for tremor: systematic review. J Neurosurg. 2018 Feb;130(2):589-600.

Marvaso G, Volpe S, Pepa M, et al. Oligorecurrent prostate cancer and stereotactic body radiotherapy: where are we now? A systematic review and meta-analysis of prospective studies. Eur Urol Open Sci. 2021 Mar;27:19-28.

Mayinger M, Kotecha R, Sahgal A, et al. Stereotactic body radiotherapy for lung oligo-metastases: systematic review and International Stereotactic Radiosurgery Society practice guidelines. Lung Cancer. 2023 Jun;182:107284.

McGarry RC, Papiez L, Williams M, et. al. Stereotactic body radiation therapy of early–stage non-small-cell lung carcinoma: phase I study. Int J Radiat Oncol Biol Phys. 2005 Nov;63(4):1010-1015.

McGonigal A, Sahgal A, De Salles A, et al. Radiosurgery for epilepsy: systematic review and International Stereotactic Radiosurgery Society (ISRS) practice guideline. Epilepsy Res. 2017 Nov;137:123-131.

Mellon EA, Hoffe SE, Springett GM, et al. Long-term outcomes of induction chemotherapy and neoadjuvant stereotactic body radiotherapy for borderline resectable and locally advanced pancreatic adenocarcinoma. Acta Oncol. 2015 Jul;54(7): 979-985.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Minniti G, Scaringi C, Paolini S, et al. Repeated stereotactic radiosurgery for patients with progressive brain metastases. J Neurooncol. 2016 Jan;126(1):91-97.

Mishra S, Kumar AG, Garg K, et al. Role of stereotactic radiosurgery for cavernous sinus hemangiomas - an individual patient data-based meta-analysis. Neurol India. 2023 Mar-Apr;71(Supplement):S21-S30.

Mokhles S, Macbeth F, Farewell V, et al. Meta-analysis of colorectal cancer follow-up after potentially curative resection. Br J Surg. 2016 Sep;103(10):1259-1268.

Montesi G, Miszczyk M, Niespolo RM, et al. Conventionally fractionated radiotherapy (CFRT) versus stereotactic body radiotherapy (SBRT) for locally advanced pancreatic cancer: a systematic review and meta-analysis of comparative studies. Cancers (Basel). 2026 Mar;18(6):971.

Mountain CF. The International System for Staging Lung Cancer. Semin Surg Oncol. 2000 Mar;18(2):106-115.

Naruke T, Tsuchiua R, Kondo H, et al. Prognosis and survival after resection for bronchogenic carcinoma based on the 1997 TNM-staging classification: the Japanese experience. Ann Thorac Surg. 2001 Jun;71(6):1759-1764.

National Cancer Institute. NCI Dictionary of Cancer Terms. Curative therapy. Available at: www.cancer.gov/publications/dictionaries/cancer-terms/def/curative-therapy. Accessed May 26, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Biliary tract cancer. V1.2026. March 10, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Bone cancer. V2.2026. December 19, 2025.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Central nervous system cancers. V1.2026. April 24, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Hepatocellular carcinoma. V1.2026. March 10, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Kidney cancer. V1.2027. July 1, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Melanoma: uveal. V2.2026. March 18, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. V5.2026. March 13, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Pancreatic adenocarcinoma. V2.2026. April 22, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Prostate cancer. V5.2026. January 23, 2026.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Small cell lung cancer. V2.2026. September 16, 2025.

National Comprehensive Cancer Network (NCCN). Guidelines for Patients. Non-small cell lung cancer – early and locally advanced. 2026.

National Comprehensive Cancer Network (NCCN). Radiation Therapy Compendium.

National Institute for Health and Care Excellence (NICE). HTG608. Stereotactic radiosurgery for trigeminal neuralgia. February 2022.

National Institute for Health and Care Excellence (NICE). NG122. Lung cancer: diagnosis and management. March 2019. Updated March 2024.

National Institute for Health and Care Excellence (NICE). NG234. Spinal metastases and metastatic spinal cord compression. September 2023.

Nguyen QN, Chun SG, Chow E, et al. Single-fraction stereotactic vs conventional multifraction radiotherapy for pain relief in patients with predominantly nonspine bone metastases: a randomized phase 2 trial. JAMA Oncol. 2019 Jun;5(6):872-878.

Niranjan A, Kano H, Mathieu D, et al. Radiosurgery for craniopharyngioma. Int J Radiat Oncol Biol Phys. 2010 Sep;78(1):64-71.

Ong V, Bourcier AJ, Florence TJ, et al. Stereotactic radiosurgery for glomus jugulare tumors: systematic review and meta-analysis. World Neurosurg. 2022 Jun;162:e49-e57.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Ost P, Reynders D, Decaestecker K, et al. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. J Clin Oncol. 2018 Feb;36(5):446-453.

Palavani LB, Silva GM, Borges PGLB, et al. Fractionated stereotactic radiotherapy in craniopharyngiomas: a systematic review and single arm meta-analysis. J Neurooncol. 2024 May;167(3):373-385.

Palma DA, Haasbeek CJ, Rodrigues GB, et al. Stereotactic ablative radiotherapy for comprehensive treatment of oligometastatic tumors (SABR-COMET): study protocol for a randomized phase II trial. BMC Cancer. 2012 Jul;12:305.

Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy for the comprehensive treatment of oligometastatic cancers: long-term results of the SABR-COMET phase II randomized trial. J Clin Oncol. 2020 Sep;38(25):2830-2838.

Palma DA, Olson R, Harrow S, et al. Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomized, phase 2, open-label trial. Lancet. 2019 May;393(10185):2051-2058.

Palta M, Godfrey D, Goodman KA, et al. Radiation therapy for pancreatic cancer: executive summary of an ASTRO clinical practice guideline. Pract Radiat Oncol. 2019 Sep-Oct;9(5):322-332.

Parker T, Rigney G, Kallos J, et al. Gamma Knife radiosurgery for uveal melanomas and metastases: a systematic review and meta-analysis. Lancet Oncol. 2020 Nov;21(11):1526-1536.

Peciu-Florianu I, Régis J, Levivier M, et al. Trigeminal neuralgia secondary to meningiomas and vestibular schwannoma Is improved after stereotactic radiosurgery: a systematic review and meta-analysis. Stereotact Funct Neurosurg. 2021;99(1):6-16.

Persson AE, Hallqvist A, Bjørn Larsen L, et al. Stereotactic body radiotherapy as metastasis-directed therapy in oligometastatic prostate cancer: a systematic review and meta-analysis of randomized controlled trials. Radiat Oncol. 2024 Dec;19(1):173.

Piperno-Neumann S, Angi M, Ascierto PA, et al.; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Uveal melanoma: ESMO-EURACAN clinical practice guideline for diagnosis, treatment and follow-up. ESMO Open. 2026 Apr;11(4):106888.

Pollock BE, Stafford SL, Link MJ, et al. Single-fraction radiosurgery of benign intracranial meningiomas. Neurosurgery. 2012 Sep;71(3):604-613.

Rim CH, Kim HJ, Seong J. Clinical feasibility and efficacy of stereotactic body radiotherapy for hepatocellular carcinoma: a systematic review and meta-analysis of observational studies. Radiother Oncol. 2019 Feb;131:135-144.

Ruers T, Punt C, Van Coevorden F, et al. Radiofrequency ablation combined with systemic treatment versus systemic treatment alone in patients with non-resectable colorectal liver metastases: a randomized EORTC Intergroup phase II study (EORTC 40004). Ann Oncol. 2012 Oct;23(10):2619-2626.

Ruers T, Van Coevorden F, Punt CJ, et al. Local treatment of unresectable colorectal liver metastases: results of a randomized phase II trial. J Natl Cancer Inst. 2017 Sep;109(9):djx015.

Rusthoven CG, Yamamoto M, Bernhardt D, et al. Evaluation of first-line radiosurgery vs whole-brain radiotherapy for small cell lung cancer brain metastases: the FIRE-SCLC cohort study. JAMA Oncol. 2020 Jul;6(7):1028-1037.

Ryu S, Deshmukh S, Timmerman RD, et al. Stereotactic radiosurgery vs conventional radiotherapy for localized vertebral metastases of the spine: phase 3 results of NRG oncology/RTOG 0631 randomized clinical trial. JAMA Oncol. 2023 Jun;9(6):800-807.

Safavi AH, Mak DY, Boldt RG, et al. Stereotactic ablative radiotherapy in T1-2N0M0 small cell lung cancer: a systematic review and meta-analysis. Lung Cancer. 2021 Oct;160:179-186.

Sahgal A, Myrehaug SD, Siva S, et al.; Trial Investigators. Stereotactic body radiotherapy versus conventional external beam radiotherapy in patients with painful spinal metastases: an open-label, multicentre, randomised, controlled, phase 2/3 trial. Lancet Oncol. 2021 Jul;22(7):1023-1033.

Santacroce A, Walier M, Régis J, et al. Long-term tumor control of benign intracranial meningiomas after radiosurgery in a series of 4565 patients. Neurosurgery. 2012 Jan;70(1):32-39.

Schiff D, Messersmith H, Brastianos PK, et al. Radiation therapy for brain metastases: ASCO guideline endorsement of ASTRO guideline. J Clin Oncol. 2022 Jul;40(20):2271-2276.

Schneider BJ, Daly ME, Kennedy EB, et al. Stereotactic body radiotherapy for early-stage non-small-cell lung cancer: American Society of Clinical Oncology endorsement of the American Society for Radiation Oncology evidence-based guideline. J Clin Oncol. 2018 Mar;36(7):710-719.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Sharma M, Schroeder JL, Elson P, et al. Outcomes and prognostic stratification of patients with recurrent glioblastoma treated with salvage stereotactic radiosurgery. J Neurosurg. 2018 Oct;131(2):489-499.

Sheehan JP, Starke RM, Kano H, et al. Gamma Knife radiosurgery for sellar and parasellar meningiomas: a multicenter study. J Neurosurg. 2014 Jun;120(6):1268-1277.

Sheehan JP, Starke RM, Mathieu D, et al. Gamma Knife radiosurgery for the management of nonfunctioning pituitary adenomas: a multicenter study. J Neurosurg. 2013 Aug;119(2):446-456.

Sheehan JP, Tanaka S, Link MJ, et al. Gamma Knife surgery for the management of glomus tumors: a multicenter study. J Neurosurg. 2012 Aug;117(2):246-254.

Shirakusa T and Kobayashi K. Lung cancer in Japan: analysis of lung cancer registry for resected cases in 1994. Jpn J Lung Cancer. 2002;42:555-562.

Simone CB 2nd, Bogart JA, Cabrera AR, et al. Radiation therapy for small cell lung cancer: an ASTRO clinical practice guideline. Pract Radiat Oncol. 2020 May-Jun;10(3):158-173.

Singh R, Valluri A, Lehrer EJ, et al. Clinical outcomes after stereotactic body radiation therapy for nonspinal bone metastases: a systematic review and meta-analysis. Int J Radiat Oncol Biol Phys. 2024 Jul;119(4):1099-1109.

Siva S, Ali M, Correa RJM, et al. 5-year outcomes after stereotactic ablative body radiotherapy for primary renal cell carcinoma: an individual patient data meta-analysis from IROCK (the International Radiosurgery Consortium of the Kidney). Lancet Oncol. 2022 Dec;23(12):1508-1516.

Siva S, Bressel M, Sidhom M, et al.; FASTRACK II Investigator Group. Stereotactic ablative body radiotherapy for primary kidney cancer (TROG 15.03 FASTRACK II): a non-randomised phase 2 trial. Lancet Oncol. 2024a Mar;25(3):308-316.

Siva S, Louie AV, Kotecha R, et al. Stereotactic body radiotherapy for primary renal cell carcinoma: a systematic review and practice guideline from the International Society of Stereotactic Radiosurgery (ISRS). Lancet Oncol. 2024b Jan;25(1):e18-e28.

Skelly AC, Chang E, Bordley J, et al. Radiation therapy for metastatic bone disease: effectiveness and harms [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2023 Aug. Report no.: 23-EHC026.

Sprave T, Verma V, Förster R, et al. Randomized phase II trial evaluating pain response in patients with spinal metastases following stereotactic body radiotherapy versus three-dimensional conformal radiotherapy. Radiother Oncol. 2018 Aug;128(2):274-282.

Starke RM, Williams BJ, Jane JA Jr, et al. Gamma Knife surgery for patients with nonfunctioning pituitary macroadenomas: predictors of tumor control, neurological deficits, and hypopituitarism. J Neurosurg. 2012 Jul;117(1):129-135.

Suleja A, Bilski M, Laukhtina E, et al. Stereotactic body radiotherapy (SBRT) for the treatment of primary localized renal cell carcinoma: a systematic review and meta-analysis. Cancers (Basel). 2024 Sep;16(19):3276.

Sutera P, Clump DA, Kalash R, et al. Initial results of a multicenter phase 2 trial of stereotactic ablative radiation therapy for oligometastatic cancer. Int J Radiat Oncol Biol Phys. 2019 Jan;103(1):116-122.

Tchelebi LT, Lehrer EJ, Trifiletti DM, et al. Conventionally fractionated radiation therapy versus stereotactic body radiation therapy for locally advanced pancreatic cancer (CRiSP): an international systematic review and meta-analysis. Cancer. 2020 May;126(10):2120-2131.

Timmerman R, McGarry R, Yiannoutsos C, et al. Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer. J Clin Oncol. 2006 Oct;24(30):4833-4839.

Timmerman R, Papiez L, McGarry R, et. al. Extracranial stereotactic radioablation: results of a phase I study in medically inoperable stage I non-small cell lung cancer. Chest. 2003 Nov;124(5):1946-1955.

Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early-stage lung cancer. JAMA. 2010 Mar;303(11):1070-1076.

Tos SM, Shaaban A, Mantziaris G, et al. Stereotactic radiosurgery for intracranial cavernous malformations: International Stereotactic Radiosurgery Society, systematic review, meta-analysis, and practice guidelines. World Neurosurg. 2024 Dec;192:e366-e401.

Tosi U, Lavieri MET, An A, et al. Outcomes of stereotactic radiosurgery for large vestibular schwannomas: a systematic review and meta-analysis. Neurooncol Pract. 2021 Feb;8(4):405-416.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Tuleasca C, Kotecha R, Sahgal A, et al. Large vestibular schwannoma treated using a cranial nerve sparing approach with planned subtotal microsurgical resection and stereotactic radiosurgery: meta-analysis and International Stereotactic Radiosurgery Society (ISRS) practice guidelines. J Neurooncol. 2025 Jun;173(2):245-262.

Tuleasca C, Régis J, Sahgal A, et al. Stereotactic radiosurgery for trigeminal neuralgia: a systematic review. J Neurosurg. 2018 Apr;130(3):733-757.

van As N, Griffin C, Tree A, et al. Phase 3 trial of stereotactic body radiotherapy in localized prostate cancer. n Engl J Med. 2024 Oct;391(15):1413-1425.

Verma V, Hasan S, Wegner RE, et al. Stereotactic ablative radiation therapy versus conventionally fractionated radiation therapy for stage I small cell lung cancer. Radiother Oncol. 2019 Feb;131:145-149.

Vlachos N, Lampros MG, Filis P, et al. Stereotactic radiosurgery versus whole-brain radiotherapy after resection of solitary brain metastasis: a systematic review and meta-analysis. World Neurosurg X. 2023 Feb;18:100170.

Vogel A, Chan SL, Dawson LA, et al.; ESMO Guidelines Committee. Electronic address: clinicalguidelines@esmo.org. Hepatocellular carcinoma: ESMO clinical practice guideline for diagnosis, treatment and follow-up. Ann Oncol. 2025 May;36(5):491-506.

Wahl DR, Stenmark MH, Tao Y, et al. Outcomes after stereotactic body radiotherapy or radiofrequency ablation for hepatocellular carcinoma. J Clin Oncol. 2016 Feb;34(5):452-459.

Wan H, Chihiro O, Yuan S. MASEP Gamma Knife radiosurgery for secretory pituitary adenomas: experience in 347 consecutive cases. J Exp Clin Cancer Res. 2009 Mar;28(1):36.

Wang L, Ke Q, Huang Q, et al. Stereotactic body radiotherapy versus radiofrequency ablation for hepatocellular carcinoma: a systematic review and meta-analysis. Int J Hyperthermia. 2020;37(1):1313-1321.

Widmark A, Gunnlaugsson A, Beckman L, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomized, non-inferiority, phase 3 trial. Lancet. 2019 Aug;394(10196):385-395.

Xi M, Yang Z, Hu L, et al. Radiofrequency ablation versus stereotactic body radiotherapy for recurrent small hepatocellular carcinoma: a randomized, open-label, controlled trial. J Clin Oncol. 2025 Mar;43(9):1073-1082.

Yamamoto M, Aiyama H, Koiso T, et al. Validity of a recently proposed prognostic grading index, brain metastasis velocity, for patients with brain metastasis undergoing multiple radiosurgical procedures. Int J Radiat Oncol Biol Phys. 2019 Mar;103(3):631-637.

Yamamoto M, Serizawa T, Higuchi Y, et al. A multi-institutional prospective observational study of stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901 study update): irradiation-related complications and long-term maintenance of mini-mental state examination scores. Int J Radiat Oncol Biol Phys. 2017 Sep;99(1):31-40.

Yamamoto M, Serizawa T, Shuto T, et al. Stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901): a multi-institutional prospective observational study. Lancet Oncol. 2014 Apr;15(4):387-395.

Yazici G, Kiratli H, Ozyigit G, et al. Stereotactic radiosurgery and fractionated stereotactic radiation therapy for the treatment of uveal melanoma. Int J Radiat Oncol Biol Phys. 2017 May;98(1):152-158.

Yeboa DN, Braunstein SE, Cabrera A, et al. Radiation therapy for WHO grade 4 adult-type diffuse glioma: an ASTRO clinical practice guideline. Pract Radiat Oncol. 2025 Sep-Oct;15(5):451-471.

Zeng KL, Louie AV, Kotecha R, et al. Stereotactic body radiotherapy for locally advanced pancreatic adenocarcinoma: a systematic review and meta-analysis of prospective trials. Pract Radiat Oncol. 2026 May 6:S1879-8500(26)00140-2.

Zhang R, Kang J, Ren S, et al. Comparison of stereotactic body radiotherapy and radiofrequency ablation for early-stage non-small cell lung cancer: a systematic review and meta-analysis. Ann Transl Med. 2022 Jan;10(2):104.

Zhong J, Patel K, Switchenko J, et al. Outcomes for patients with locally advanced pancreatic adenocarcinoma treated with stereotactic body radiation therapy versus conventionally fractionated radiation. Cancer. 2017 Sep;123(18):3486-3493.

Policy History/Revision Information

Date	Summary of Changes
10/01/2026	**Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version 2026T0611K

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its policies and guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Proprietary Information of UnitedHealthcare. Copyright 2026 United HealthCare Services, Inc.