Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy

Medicare Advantage Medical Policy #MA-011
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Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Blue Advantage does not cover investigational or experimental services, including any drug, device, procedure, or service provided under the investigational arm of a clinical trial or study unless mandated by the Centers for Medicare and Medicaid Services. Coverage is limited to routine services for Category A IDE studies and to devices and related services for Category B IDE studies when not supplied by the trial sponsor. Approved IDE studies are posted on www.cms.gov/medicare/coverage/evidence.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

STEREOTACTIC RADIOSURGERY (SRS)

Bone Metastases

Based on review of available data, the Health Plan may consider stereotactic radiosurgery (SRS) for treatment of bone metastases to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for stereotactic radiosurgery (SRS) for bone metastases may be considered **when ALL of the following criteria are met:**

- To treat a previously irradiated field; **AND**
- Re-treatment with 2D or 3D conformal external beam radiation therapy (EBRT) would result in significant risk of adjacent organ injury.

Note: When SRS/SBRT is being requested to treat a patient with oligometastatic disease with potentially curative intent, please refer to separate criteria in the Oligometastatic Extracranial Disease section of the Policy.

Cranial Lesions

Based on review of available data, the Health Plan may consider stereotactic radiosurgery (SRS) for treatment of cranial lesions to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for stereotactic radiosurgery (SRS) for cranial lesions may be considered **when ANY of the following criteria are met:**

- Intracranial lesions
  - o High-grade gliomas (grade 3-4) in individuals w**hen EITHER of the following conditions is met:**
    - Recurrent disease; **OR**
    - To treat a previously irradiated field.

    OR

  - o Low-grade gliomas (grade 1-2) in individuals w**hen EITHER of the following conditions is met:**
    - Initial treatment; **OR**
    - Recurrent disease; **OR**
    - To treat a previously irradiated field;

    OR

  - o Medulloblastoma, supratentorial primitive neuroectodermal tumors (PNET), ependymoma, central nervous system (CNS) lymphoma:
    - **ONLY** to treat a previously irradiated field;

    OR

  - o Metastatic brain lesions **when ANY of the following conditions are met:**
    - Primary treatment of 10 or fewer unresected brain metastases**; OR**
    - Postoperative treatment of 1-2 brain metastases; **OR**
    - To treat a previously irradiated field;

    Note: Treatment of multiple lesions with SRS on different days within the same course of therapy should bebilled as SBRT with a maximum of 5 units.

    OR

  - o Benign brain lesions:
    - To treat small volume intracranial arteriovenous malformations (AVM volume less than or equal to 10 cm^3 or diameter less than or equal to 3cm);

      OR

    - To treat trigeminal neuralgia when individual is not a surgical candidate or refuses surgery;

OR

- To treat jugular paraganglioma when individual is not a surgical candidate or refuses surgery;

OR

- Pituitary adenomas **when EITHER of the following conditions is met:**
  - When individual is symptomatic; **OR**
  - To treat a previously irradiated field.

OR

- Meningioma **when ANY of the following conditions are met:**
  - When lesion is unresectable or recurrent, or if there is residual disease following surgery; **OR**
  - To treat a previously irradiated field;

OR

- Other benign brain tumors including acoustic neuromas, craniopharyngiomas, pineal gland tumors, schwannomas;

OR

- Uveal melanoma **when ANY of the following conditions are met:**
  - For treatment of melanoma of the choroid; **OR**
  - To treat a previously irradiated field.

<u>Other Malignancies</u>

Based on review of available data, the Health Plan considers stereotactic radiosurgery (SRS) for treatment of renal cancer metastases to the brain and spine for lesions less than 5 cm in diameter treated in a single fraction to be **eligible for coverage.****

Based on review of available data, the Health Plan considers stereotactic radiosurgery (SRS) for treatment of chondrosarcoma to be **eligible for coverage.****

Based on review of available data, the Health Plan may consider stereotactic radiosurgery (SRS) for treatment of malignancies listed below **ONLY** to treat a previously irradiated field to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for stereotactic radiosurgery (SRS) **ONLY** to treat a previously irradiated field may be considered **for ANY of the following conditions:**

- Hodgkin or Non-Hodgkin lymphoma; **OR**
- Pediatric individuals (age 20 years or younger) with a radiosensitive tumor; **OR**
- Sarcoma; **OR**
- Thymoma and thymic carcinoma**.**

STEREOTACTIC BODY RADIATION THERAPY (SBRT)

Bone Metastasis

Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of bone metastases to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for stereotactic body radiation therapy (SBRT) for bone metastases may be considered **when ALL of the following criteria are met:**

- To treat a previously irradiated field; **AND**
- Re-treatment with 2D or 3D conformal external beam radiation therapy (EBRT) would result in significant risk of adjacent organ injury.

Note: When SRS/SBRT is being requested to treat a patient with oligometastatic disease with potentially curative intent, please refer to separate criteria in the Oligometastatic Extracranial Disease section of the Policy.

Breast Cancer

Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for breast cancer to be **eligible for coverage.****

Patient Selection Criterion
Coverage eligibility for stereotactic body radiation therapy (SBRT) for breast cancer when the following criterion is met:

- To treat a previously irradiated field.

Note: Five fraction accelerated partial breast irradiation (APBI) regimens should not be billed as SBRT as this is not an ablative dose and similar dose fractionation schedules can be safely delivered to the whole breast.

Central Nervous System (CNS) - Primary or Metastatic Spine Lesions

Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of spine lesions to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for stereotactic body radiation therapy (SBRT) for spine lesions may be considered **when EITHER of the following criteria is met:**

- When other treatment options are not available **(BOTH must be met)**
  - Not amenable to surgical resection **(at least ONE must apply)**
    - Related to prior surgery, tumor location, or surgical candidacy; **OR**
    - Surgery alone is not an option;
      AND
  - When lesions are not amenable to 3D conformal techniques (see below);

OR

- To treat a previously irradiated field.

Note:
When SRS/SBRT is being requested to treat a patient with oligometastatic disease with potentially curative intent, please refer to separate criteria in the Oligometastatic Extracranial Disease section of the Policy.

SBRT may be considered for spinal or vertebral metastases that are radioresistant (e.g., renal cell carcinoma, melanoma, sarcoma).

Cranial and Head and Neck Lesions
Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of intracranial metastatic brain lesions to be eligible for coverage.**

Patient Selection Criterion
Coverage eligibility for stereotactic body radiation therapy (SBRT) for intracranial metastatic brain lesions may be considered **when ANY of the following conditions are met:**

- Primary treatment of 4 or fewer unresected brain metastases**; OR**
- Postoperative treatment of 1-2 brain metastases; **OR**
- To treat a previously irradiated field.

Note:
Multi-fraction stereotactic radiation should be billed as SBRT.

Based on review of available data, the Health Plan may consider multifraction SRS/ stereotactic body radiation therapy (SBRT) for treatment of large volume intracranial arteriovenous malformations (AVM volume greater than 10 cm^3 or diameter greater than 3 cm) when individual is not a surgical candidate or refuses surgery to be **eligible for coverage.****

Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of jugular paraganglioma when individual is not a surgical candidate or refuses surgery to be **eligible for coverage.****

Liver Cancer - Hepatocellular Carcinoma or Liver Metastases

Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of liver cancer to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for stereotactic body radiation therapy (SBRT) for liver cancer may be considered **when ANY of the following criteria are met:**

- Hepatocellular carcinoma (HCC)
    - As palliative treatment for individuals with liver-related symptoms;

      OR

    - As treatment of new or recurrent HCC unsuitable for surgery, embolization, or transarterial chemoembolization (TACE), when these therapies have been done and have failed, or are contraindicated, **when BOTH of the following conditions are met:**
        - Less than or equal to 5 HCC lesions with a sum of less than 20 cm; **AND**
        - Patients with Child-Pugh category A or B, **OR** Barcelona Clinic Liver Cancer Stage A, B, or C disease;

      OR

    - As a bridge to liver transplant or when such treatment may allow a patient to be downstaged to become transplant eligible;

      OR

    - To treat a previously irradiated field;

      OR

- Liver metastases
    - As palliative treatment for individuals with liver-related symptoms;

      OR
    - To treat a previously irradiated field.

Lung Cancer- Non-Small Cell Lung Cancer (NSCLC), Small Cell Lung Cancer (SCLC), Lung Metastasis

Non-Small Cell Lung Cancer (NSCLC)
Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of non-small cell lung cancer (NSCLC) to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for stereotactic body radiation therapy (SBRT) for NSCLC lung cancer may be considered **when ANY of the following criteria are met:**

- As an alternative to surgical resection when **(ALL must apply)**
  - Treatment intent is cure; **AND**
    - There is no evidence of nodal or distant metastases based on conventional staging techniques (Stage IA, IB, or IIA with negative lymph nodes); **AND**
  - Single lesion measuring less than or equal to 5 cm; **AND**
  - Lesion is inoperable **for ANY of the following reasons:**
    - Tumor location; **OR**
    - Individual is not a surgical candidate or refuses surgery;

OR

- To treat a previously irradiated field;

Note: The maximum number of fractions that is medically necessary for SBRT is 5.

Small Cell Lung Cancer (SCLC)
Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of small cell lung cancer (SCLC) to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for stereotactic body radiation therapy (SBRT) for SCLC lung cancer may be considered **when ANY of the following criteria are met:**

- As an alternative to surgical resection when **(ALL must apply)**
  - Treatment intent is cure; **AND**
    - There is no evidence of nodal or distant metastases based on conventional staging techniques (Stage IA, IB, or IIA with negative lymph nodes); **AND**
  - Single lesion measuring less than or equal to 5 cm; **AND**
  - Lesion is inoperable **for ANY of the following reasons:**
    - Tumor location; **OR**
    - Individual is not a surgical candidate.

OR

- To treat a previously irradiated field;

Note: The maximum number of fractions that is medically necessary for SBRT is 5.

Metastatic Lesions in the Lung
Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of metastatic lesions in the lung to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for stereotactic body radiation therapy (SBRT) for metastatic lesions in the lung may be considered **when EITHER of the following criteria are met:**
- To treat oligometastatic disease (see separate section below); **OR**
- To treat a previously irradiated field.

Note: When SRS/SBRT is being requested to treat a patient with oligometastatic disease with potentially curative intent, please refer to separate criteria in the Oligometastatic Extracranial Disease section of the Policy.

Oligometastatic Extra-Cranial Disease
Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for extra-cranial oligometastatic disease to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for SBRT for extra-cranial oligometastatic disease may be considered **when ALL of the following conditions are met:**
- 1-3 metastatic lesions involving the lungs, liver, adrenal glands, or bone; **AND**
- Primary tumor is breast, colorectal, melanoma (cutaneous, uveal), non-small cell lung, pancreas, prostate, renal cell, or sarcoma; **AND**
- Primary tumor is controlled (or newly diagnosed prostate cancer with metachronous oligometastases); **AND**
- No prior history of metastatic disease.

Note: *For oligoprogressive disease, SBRT is approved for 1-3 lesions if there has been prior control with systemic therapy for over a year since last radiation treatment.*

Pancreatic Cancer
Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of pancreatic cancer to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for stereotactic body radiation therapy (SBRT) for pancreatic cancer may be considered **when EITHER of the following criteria are met:**

- To treat borderline resectable or unresectable, locally advanced or recurrent disease without evidence of distant metastasis; **OR**
- To treat a previously irradiated field.

Prostate Cancer

Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for treatment of prostate cancer to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for stereotactic body radiation therapy (SBRT) for prostate cancer may be considered **when ANY of the following conditions and criteria are met:**

- Low-risk of recurrence **(ALL must be present to qualify as low-risk)**
  - Stage T1 –T2a; **AND**
  - Gleason Score of 6; **AND**
  - Prostate-specific Antigen (PSA) less than 10 ng/mL; **AND**
  - No metastatic disease;

    AND

    - As primary treatment; **OR**
    - To treat a previously irradiated field;

Note: Active surveillance is a reasonable alternative to radiation treatment in individuals with low-risk prostate cancer;

OR

- Intermediate-risk of recurrence and no metastatic disease **(ANY ONE characteristic)**
  - Stage T2b to T2c; **OR**
  - Gleason score of 7; **OR**
  - PSA 10-20 ng/mL;

    AND

    - As primary treatment; **OR**
    - To treat a previously irradiated field;

OR

- High risk of recurrence and no metastatic disease **(ANY ONE characteristic)**
  - Stage T3a; **OR**

- Gleason score of 8-10; **OR**
- PSA greater than 20ng/mL;

AND

- Only to treat a previously irradiated field;

OR

- Post-prostatectomy
  - Only to treat a previously irradiated field;

OR

- Local recurrence after radiotherapy
  - To treat locally recurrent disease with no evidence of distant metastasis;

OR

- Primary prostate cancer with metachronous oligometastases
  - To treat primary prostate cancer with 1-3 oligometastases

Other Malignancies

Based on review of available data, the Health Plan considers stereotactic body radiation therapy (SBRT) for chondrosarcoma to be **eligible for coverage.****

Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for renal cancer to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for stereotactic body radiation therapy (SBRT) for renal cancer is appropriate **when ANY of the following criteria are met:**

- Primary treatment for T1 tumors (less than 7 cm); **OR**
- Ablative treatment for intact extracranial metastases, including spine; **OR**
- Fractionated stereotactic radiation therapy (SRT)/ SBRT is appropriate for larger metastases to the brain and spine (greater than 5 cm).

Based on review of available data, the Health Plan may consider stereotactic body radiation therapy (SBRT) for malignancies listed below **ONLY** to treat a previously irradiated field to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for stereotactic body radiation therapy (SBRT) **ONLY** to treat a previously irradiated field may be considered **for ANY of the following conditions:**

- Head and neck cancers, including thyroid cancer; **OR**
- Hodgkin and Non-Hodgkin lymphoma; **OR**
- Colorectal cancer (CRC) and anal cancer; **OR**
- Other gastrointestinal (GI) cancers, e.g. cholangiocarcinoma and other bile duct tumors, esophageal, gastric; **OR**
- Genitourinary cancers, e.g. bladder (including cystic urethral cancer), penile, testicular; **OR**
- Gynecologic (GYN) cancers, e.g. cervical, fallopian tube, ovarian, uterine neoplasms, vulvar/vaginal; **OR**
- Pediatric individuals (age 20 years or younger) with a radiosensitive tumor; **OR**
- Sarcoma; **OR**
- All other malignancies.

When Services Are Considered Not Medically Necessary

The use of stereotactic radiosurgery (SRS) or stereotactic body radiation therapy (SBRT) when patient selection criteria are not met is considered to be **not medically necessary.****

Policy Guidelines

Radiation Source
This medical policy addresses the use of stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) delivered by gamma-ray or high-energy photons generated by a linear accelerator (LINAC) unit. The use of charged-particle (proton or helium ion) radiotherapies is not addressed.

Fractionation
Fractionated SRS refers to SRS or SBRT performed more than once on a specific site.

SRS is most often single-fraction treatment; however, multiple fractions may be necessary when lesions are near critical structures.

SBRT is commonly delivered over 3 to 5 fractions.

Child-Pugh categories
Modified Child-Pugh classification of the severity of liver disease is based on the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time (PT) or INR, and the degree of encephalopathy. Classes correlate with one- and two-year patient survival: class A: 100 and 85%; class B: 80 and 60%; and class C: 45 and 35%.

Ascites: absent (1 point), slight (2 points), moderate (3 points)

Bilirubin: less than 2 mg/dL (1), 2 to 3 mg/dL (2), greater than 3 mg/dL (3)
Albumin: greater than 3.5 g/dL (1), 2.8-3.5 g/dL (2), less than 2.8 g/dL (3)
PT (seconds over control): less than 4 (1), 4 to 6 (2), greater than 6 (3); or INR: less than 1.7 (1), 1.7 to 2.3 (2), greater than 2.3 (3)
Encephalopathy: none (1), grade 1 to 2 (2), grade 3 to 4 (3)

Class A- score of 5-6 (well-compensated disease)
Class B- score 7-9 (significant functional compromise)
Class C – score 10-15 (decompensated disease)

Barcelona Clinic Liver Cancer (BCLC) stages
The BCLC Staging System is widely used to stage primary liver cancer. The system is used to predict the patient's chance of recovery and to plan treatment based on whether the cancer has spread within the liver or to other parts of the body, how well the liver is working, the general health and wellness of the patient, and the symptoms caused by the cancer.

BCLC stage	**ECOG PS**	**Liver function: Child-Pugh**	**Tumor stage**
Very early stage (0)	0	A	Single less than or equal to 2 cm
Early stage (A)	0	A-B	Single less than or equal to 3, nodules less than or equal to 3 cm
Intermediate stage (B)	0	A-B	Multinodular
Advanced stage (C)	1-2	A-B	Vascular invasion, extrahepatic spread
Terminal stage (D)	3-4	C	Any

Stage 0, A, and B, all criteria should be fulfilled.
Stage C and D at least one criterion should be fulfilled.
ECOGPS, Eastern Cooperative Oncology Group Performance Status.

ECOG Performance Status Scale

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

2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

Background/Overview

Bone Metastases

Initial Treatment

Metastasis to the bony skeleton is a common site of spread for many solid tumors including breast, prostate and lung cancers. Bone metastases can be seen with any cancer histology and affects more than 250,000 patients per year in the United States. It has been estimated that up to 80% of patients with solid cancers will develop painful bone metastases to the pelvis, spine or extremities during the course of their illness. Metastases to the bone can cause accelerated bone breakdown which may result in pain, pathologic fracture and nerve or spinal cord compression resulting in sensory loss or motor weakness. Laboratory abnormalities may include hypercalcemia and myelosuppression. Radiation therapy has long been used to palliate pain and other symptoms of bone metastases with excellent results.

Stereotactic body radiation therapy (SBRT) or stereotactic ablative body radiotherapy (SABR) is being studied in the treatment of bony metastatic disease. Proposed indications for this modality include standalone or postoperative treatment in patients with progressive or recurrent disease following conventional external beam radiotherapy (cEBRT) and in the treatment of tumors traditionally considered radioresistant to cEBRT such as sarcoma, melanoma and renal cell carcinoma. Several recent studies have not shown improvement in pain control compared to conventional radiation although the relief was more durable.

There have been 3 randomized controlled trials investigating the role of SBRT for painful spinal metastases. Two of these trials have shown significant improvement in pain control with SBRT over conventional radiation therapy. A recent report from the phase 2, randomized VERTICAL trial looked at quality of life, functional interference and psychosocial aspects with either 8 Gy single fraction conventional radiotherapy or single fraction SBRT to a total of 18 Gy. Twelve weeks after treatment completion, treatment with conventional radiation improved functional interference significantly more than SBRT (25.5 vs 14.1 points, $P = 0.04$). Similarly, psychosocial aspects scores also improved more with conventional radiation (12.2 vs 7.3, $P = 0.04$). A similar trial published by Canadian and Australian investigators compared 20 Gy of conventional radiation delivered in 5

fractions with SBRT given as 12 Gy times two. In comparing these regimens, the SBRT arm had significantly complete pain relief at 3 months compared to the lower dose fractionated conventional radiation (35% vs 14%, P less than 0.0002). The prospective randomized trial RTOG 0631 was the largest trial evaluating the role of SBRT for spinal bone metastases but was limited by a lower BED dosing regimen compared to other trials and did not use a spinal instability neoplastic score which may have contributed to its negative results. Given the trial limitations and the data from 2 other randomized controlled trials demonstrating significant improvements in pain outcomes with SBRT, ASTRO elected to conditionally recommend SBRT in this context in its guideline update last year.

Repeat Treatment
Following initial treatment with radiation therapy for bony metastasis, some patients will develop recurrent or progressive symptoms for which additional radiation therapy is indicated. Studies have shown repeat radiation therapy to be effective in reducing pain in approximately 48% of patients. Responders have been shown to have improved quality of life. When a given site is re-treated, the effect of prior irradiation on the surrounding normal tissues must be considered. This is especially important when treating vertebral lesions where to cumulative dose to the spinal cord must be minimized. The generally accepted maximum cumulative dose to the spinal cord is 50 Gy in 2 Gy fractions (or equivalent). If repeat radiation using 2D or 3D techniques would result in a cumulative dose to the spinal cord greater than 50 Gy in 2 Gy fractions then consideration should be given to intensity modulated radiation therapy (IMRT), SRS, or SBRT. If there is concern about further recurrence or radio-resistant histology, stereotactic treatment (either SBRT or SRS) may be preferred.

Central Nervous System (CNS) Cancers (Intracranial, Spinal, Ocular and Neurologic)
Brain metastasis is the most common CNS malignancy. Patients with brain metastasis have a poor prognosis, with a median survival of 2-3 months when treated with steroids alone. The addition of whole brain radiation therapy (WBRT) generally extends median survival to 3-6 months. Individual results vary significantly based on the number of metastatic lesions, the performance status of the patient and the extent of extracranial disease. In recent years, there has been a trend away from the use of WBRT in patients with limited disease who are candidates for surgery or radiosurgery in order to minimize the neurocognitive complications of WBRT. WBRT with standard 2D or 3D conformal radiation therapy is recommended for individuals with multiple brain metastases (greater than 4 treated in a given session), and should also be considered in individuals with brain metastases and any of the following: ECOG performance status greater than 2, presence of progressive and symptomatic visceral disease, or metastases significantly progressing after multiple treatment options. The RTOG has studied several different fractionation schedules for WBRT and prolonged fractionation schedules did not improve outcomes compared to 30 Gy in 10 fractions.

A 2019 evidence-based review by the Congress of Neurological Surgeons on the role of whole brain radiotherapy recommends a dose of 30 Gy in 10 fractions to improve progression-free survival in patients with more than four metastases.

To minimize the neurocognitive toxicity, local therapy in the form of surgery or stereotactic radiosurgery is recommended for patients with four or fewer accessible lesions. When WBRT is used, 6 months of memantine therapy should be offered to potentially delay, lessen or prevent the associated neurologic toxicity. Results from the phase III NRG CC001 trial have recently been reported. There were 518 patients randomized to either hippocampal avoidance (HA-WBRT) or whole brain radiation therapy (WBRT). Both groups were treated with memantine. The HA-WBRT treated patients were found to have a lower risk of cognitive failure compared to standard WBRT (HR 0.74, P = .02) attributable to preservation of executive function, learning, and memory. There were no differences in OS, intracranial PFS or toxicity.

Historically, surgical resection has been performed in patients with solitary metastasis in accessible locations. Postoperative WBRT has been shown to reduce the risk of recurrence in a randomized trial. For brain metastases greater than 4 cm in diameter or causing mass effect, surgery is preferred over SRS.

In 2022, a combined practice guideline on treatment of brain metastases was published by the American Society of Clinical Oncology (ASCO), the Society for Neuro-Oncology (SNO) and the American Society of Radiation Oncology (ASTRO). They recommend that SRS should be offered to patients with 4 or fewer metastatic lesions. They also recommend postoperative SRS for patients with 1 or 2 resected metastatic lesions. Patients with more lesions are recommended to receive whole brain irradiation unless they have poor KPS performance status of less than 50.

External beam radiation treatment is a common treatment for primary brain tumors as either definitive or adjuvant therapy after resection. For high grade gliomas, concurrent temozolomide chemotherapy is generally recommended as it has been shown to increase survival compared to radiotherapy alone. In 2016, ASTRO published an evidence-based clinical practice guideline on radiation therapy for glioblastoma. For patients with reasonable performance status up to age 70, a dose of 60 Gy in 30 fractions should be given. For elderly patients, hypofractionated treatment such as 40 Gy in 15 fractions gives similar results. IMRT may provide better coverage for primary brain lesions, with decreased exposure of normal brain tissue. IMRT is recommended when a lesion is in close proximity to a critical or sensitive structure and 3D conformal radiation would result in unsafe exposure to these structures. The use of IMRT for hippocampal sparing is under active investigation and should only be used in the context of a clinical trial. IMRT is considered medically necessary in any case of repeat irradiation of overlapping or bordering treatment fields.

SRS has an excellent safety profile for many clinical situations when targets are localized, and it has applications for both benign and malignant lesions. It also often represents an alternative to surgical intervention when patients are not optimal surgical candidates. SRS has been extensively studied in the treatment of limited brain metastases. Control rates of approximately 90% are reported. Although recurrence elsewhere in the brain is common, the addition of WBRT to SRS does not improve survival. This has led to the ASTRO Choosing Wisely recommendation not to routinely add WBRT to SRS for limited brain metastasis. SRS is not recommended for the treatment of CNS lymphoma.

Stereotactic boost for high grade gliomas has been studied in several randomized controlled clinical trials. RTOG 93-05 randomized patients with glioblastoma multiforme to upfront SRS followed by conventional radiotherapy and carmustine to the same treatment without SRS. With a median follow-up of 61 months, there was no difference in survival, pattern of failure or quality of life in the two groups. RTOG 0023 studied the use of a stereotactic conformal boost for supratentorial glioblastoma multiforme. In this study, four weekly stereotactic boost treatments were delivered to give a cumulative dose of 70-78 Gy to the postoperative enhancing tumor. There was no difference in survival compared to historical controls. Based on these studies, SRS or SBRT are considered investigational for the primary treatment of grade 3-4 gliomas.

For certain benign CNS abnormalities, SRS has been shown to be a safe and effective treatment. Soon after the development of the Gamma Knife®‡ by Leksell in the 1970s, it was studied for the treatment of AVM where is has been shown to have an 80% obliteration rate. Based on this proof of concept, SRS has subsequently been shown to be an effective alternative to surgery for a wide variety of benign lesions including ocular melanoma, retinoblastoma, schwannoma, craniopharyngioma, pineal lesions and pituitary adenoma. SRS for the treatment of trigeminal neuralgia is medically necessary in cases refractory to medical management. SRS for the treatment of epilepsy, Parkinson's disease and other movement disorders is listed as "insufficient evidence" in an evidence-based review by the American Academy of Neurology and therefore remains investigational at this time.

SRS is given as a single fraction. Cranial stereotactic treatment given in 2-5 fractions is billed as SBRT.

For metastatic lesions outside the brain, please refer to specific guidelines for the appropriate location (e.g., Lung Cancer for lung metastases).

Radiation therapy, especially stereotactic radiosurgery (SRS), is a non-invasive treatment option for arteriovenous malformations (AVMs), most commonly in the brain. It is particularly useful for small AVMs or those in locations where surgery would be high risk. SRS delivers highly focused beams of radiation directly to the AVM. The radiation damages the abnormal blood vessel walls, causing them to scar and thicken. Over 1 to 3 years, the scarred vessels close off, effectively obliterating the AVM. The treatment is usually performed in a single session, though larger AVMs may require multiple sessions (staged SRS). The outpatient procedure has minimal discomfort and a quick recovery.

For AVMs less than or equal to 3 cm, the 3-year obliteration rate is 70%-80%. For larger AVMs, success rates are lower (30%-70%) and may require staged treatments. SRS is also used to reduce AVM size before surgery to treat AVMs not suitable for surgical removal. Most patients experience few acute side effects, such as mild scalp irritation or localized hair loss. There is a small risk of delayed symptoms due to radiation, and the risk of bleeding remains until the AVM is fully closed.

Radiation therapy for trigeminal neuralgia (TN) typically involves stereotactic radiosurgery (SRS)—most commonly using the Gamma Knife—to deliver highly focused beams of radiation to the trigeminal nerve, specifically at its entry point into the brainstem. Radiation damages the nerve fibers, disrupting the transmission of pain signals to the brain, which often results in significant pain relief.

About 70%-80% of patients experience significant pain relief after treatment. Complete pain relief is achieved in about 40%-60% of patients, with many maintaining this relief for years. However, over time, some patients may experience recurrence. Most common side effect is mild facial numbness or tingling, occurring in up to 10%-30% of patients. Serious complications are rare. Although not as effective as microvascular decompression (MVD), it is advantageous for older patients or those with surgical contraindications, offering pain relief with fewer serious complications.

Colorectal and Anal Cancers

Anal Cancer

Cancer of the anal region are relatively rare, accounting for less than 3% of all digestive system cancers. They are almost always squamous cell carcinomas and are frequently associated with Human papilloma virus (HPV) infection. Because of the lymphatic drainage of this area, the inguinal lymph nodes are at risk and are commonly involved when lesions involve the area below the dentate line. Although these cancers have been treated with abdominoperineal resection in the past, the current standard of care is concomitant chemoradiotherapy with a fluoropyrimidine and either mitomycin or cisplatin. Doses of 45 Gy are given for early stage tumors. More advanced and node positive cancers are treated to doses of 54-59.4 Gy. IMRT techniques, which can reduce the toxicity associated with radiation, are preferred over 3D conformal techniques for the treatment of anal cancer and cancers of the anal canal. The radiation field includes the pelvis, the anus, the perineum, and the inguinal lymph nodes. Definitive treatment of anal cancers typically involves concurrent radiation and chemotherapy.

Palliative radiation with 3D conformal techniques is recommended for metastatic disease or to enhance local control of a symptomatic bulky primary.

Rectal Cancer

Colorectal cancer is much more common than anal cancer and is the second most common cause of cancer death. Rectal cancers, which occur below the peritoneal reflection, benefit from radiation therapy which has been shown to reduce local recurrence and improve survival. Radiation is generally given with 5-fluorouricil or capecitabine chemotherapy. Preoperative chemoradiation is preferable because it is better tolerated and improves the chance of sphincter sparing surgery in marginally resectable patients. Precision techniques like 3D conformal radiotherapy and IMRT have been shown to reduce the dose to bowel and minimize side effects. The radiation field should include the presacral nodes, internal iliac nodes, and external iliac nodes for T4 tumors. Typically, 45 Gy is

given to the initial field with an additional 5.4 – 9 Gy being given to a cone down boost field. Short-course preoperative radiotherapy to a dose of 25 Gy is another alternative.

Tanaka et al. recently reported the results of the RAPIDO trial, a phase III study comparing 3D-CRT versus IMRT(including VMAT). Patients were treated with short-course RT followed by systemic chemotherapy (TNT) or standard concurrent chemoradiation. No differences were found in early or late radiation-related toxicity. Of note, some lower grade toxicities were more frequent after IMRT, in particular fatigue during TNT.

Colon Cancer
Radiation is not a standard part of local treatment for colon cancer but is incorporated into treatment for selected patients. It is generally used in situations where there is an elevated risk of local recurrence due to local invasion of the surrounding tissues. 3D conformal radiation is the standard option, and IMRT is reserved for repeat irradiation of previously treated patients.

Stereotactic radiation techniques have been considered in highly selected cases of limited hepatic metastases; however, surgical resection is the standard of care. Please see the section on hepatobiliary cancers for more guidance on the treatment of liver metastases.

For review of metastatic sites, please refer to specific guidelines for the appropriate location. (e.g., CNS Cancers for brain metastases, Lung Cancer for lung metastases)

Gastrointestinal Cancers, Non-Colorectal (Cholangiocarcinoma, Esophageal, Gastric, Liver and Pancreatic)

Esophageal Cancer
Esophageal cancers can be histologically classified as squamous cell carcinoma or adenocarcinoma. Squamous cancers are more common in the cervical and mid-thoracic esophagus while adenocarcinomas are more common in the distal esophagus and gastroesophageal junction. The latter are more common in Western countries and are associated with gastroesophageal reflux and Barrett's esophagus. Radiation therapy is a common part of the multidisciplinary treatment of esophageal cancers. Radiation can be used pre-operatively, post-operatively, as primary therapy in conjunction with chemotherapy or as a palliative modality to improve swallowing. Long-term results of the CROSS randomized controlled trial of neoadjuvant chemoradiation followed by surgery showed improved survival compared to surgery alone. Radiation in that study was given with 3D-conformal techniques. Retrospective comparisons have not demonstrated improved survival but have shown a decrease in grade 3 toxicities such as hospitalization, feeding tube placement and greater than 20% weight loss. A 2016 population analysis of SEER-Medicare data found that the use of IMRT was found to be significantly associated with lower all-cause mortality, cardiac mortality, and other-cause mortality in patients with esophageal cancer. IMRT should only be used in curative cases.

Gastric Cancer
Gastric cancer is relatively uncommon in the United States but is a common cause of cancer and cancer mortality worldwide. It is associated with Helicobacter pylori infection, smoking and heavy drinking. Gastric cancer frequently presents at an advanced stage. Chemoradiation has an established role in the adjuvant treatment of resected tumors based on the results of intergroup study 0116. Patients in that randomized study who received chemoradiation had improved survival compared to patients treated with surgery alone. Use of 3D treatment planning is recommended. Treatment recommendations depend on the location of the bulk of the tumor, location and lymph node involvement. In addition to adjuvant post-operative treatment, radiation is used in a variety of clinical situations, including pre-operative treatment, in combination with chemotherapy, and as a palliative therapy. Significant supportive care is required during a full course of treatment. No prospective studies of IMRT in gastric cancer have been published. Several institutions have noted improved dose distribution and better organ sparing with IMRT for stomach cancer. No survival advantage with IMRT has been reported.

Hepatobiliary Cancer
HCC and cholangiocarcinomas of the gallbladder, intrahepatic and extrahepatic bile ducts are relatively rare but lethal cancers of the liver and bile ducts. HCC is commonly associated with cirrhosis due to hepatitis and other factors. Although there are no prospective data on the use of IMRT for the treatment of these cancers, the liver is very sensitive to radiation therapy, IMRT may have a limited role in the treatment of HCC and cholangiocarcinoma when 3D-conformal therapy would result in unacceptable toxicity due to exposure of the liver and other surrounding normal tissues. There is growing literature support for the use of SBRT as a local treatment option for hepatocellular cancer. This technology remains under active investigation in many clinical situations, and more data is needed to clarify the role of SBRT. Patients should first be evaluated for potential curative therapy, such as resection, radiofrequency ablation (RFA), transcatheter arterial chemoembolization (TACE) or transplantation. Several studies have recently reported improved local control and PFS with SBRT versus treatment with RFA.

The recently reported long term results of RTOG 1112, a multicenter phase 3 randomized clinical trial looking at patients with HCC randomized to either sorafenib or SBRT followed by sorafenib, showed that SBRT was associated with a clinically important but not statistically significant improved overall survival compared with sorafenib alone.

Selective Internal Radiation Therapy (SIRT) is also known as radio embolization. This technique targets the delivery of small beads or microspheres containing yttrium-90 to the tumor. It is used for palliation of liver tumors and is sometimes used as a bridge to liver transplantation.

Liver Metastases
The use of stereotactic techniques to treat liver metastases is the subject of clinical trials. Small trials have addressed this issue, but long-term survival and quality of life remain unclear.

Pancreatic Cancer
For the treatment of pancreatic cancer, radiation is recommended in the setting of unresectable or borderline resectable disease (neoadjuvant or definitive), adjuvant treatment after surgery, and palliation of symptoms. Outside of palliative care, radiation is traditionally administered concurrently with chemotherapy. There is no clear standard for neoadjuvant therapy, and multiple chemoradiotherapy options are available. 3D conformal radiation techniques are considered standard. A recent systematic review by Bittner compares outcomes and toxicity in patients treated with IMRT and 3D-conformal radiotherapy for pancreatic adenocarcinoma. There were no apparent differences in overall or progression free survival. Both nausea/vomiting and diarrhea were statistically lower with IMRT compared to 3D-conformal, although the differences were modest (7.8% vs. 13% and 2% vs. 11.6% respectively, p less than 0.001 for both). Long term grade 3 or greater GI toxicity was 5% with IMRT vs. 10.6% with 3D (p=0.017). Given the lack of improved outcomes, IMRT should only be used in curative cases where 3D-conformal planning would result in unacceptable doses to surrounding normal tissues. Care should be taken to adhere to recommended target coverage and dose specifications as radiation quality has been shown to impact survival in several studies.

Initial experience with single fraction SBRT for unresectable pancreatic cancer resulted in favorable local control rates but high rates of late gastrointestinal complications. Subsequent studies using fractionated SBRT have shown lower rates of late toxicity. A systematic review and meta- analysis comparing conventional radiation with SBRT confirms these findings. The SBRT treated patients had a 2-year overall survival of 26.9% compared to 13.7% with conventionally fractionated radiotherapy. Acute toxicitywas significantly lower for SBRT and late toxicity was equivalent. A recent prospective, multi-center, single-arm open- label phase 2 trial of SBRT delivered on a MRI-Linear accelerator (SMART) demonstrated 2-year OS from diagnosis and SMART of 53.6% and 40.5%, respectively, with very limited severe toxicity.

SBRT is considered medically necessary for the treatment of locally advanced, non-metastatic adenocarcinoma of the pancreas.

For review of other metastatic sites, please refer to specific guidelines for the appropriate location. (e.g., CNS for brain metastases, Lung for lung metastases)

<u>Genitourinary Cancers (Bladder, Penile, and Testicular)</u>
Bladder Cancer (including cystic urethral cancer)
Bladder cancers arise in the transitional urothelium which lines the urinary bladder. About two-thirds of these do not invade the muscle layer at the time of diagnosis and are treated with transurethral resection (TURBT) with or without instillation of an intravesicle adjuvant therapy such as Bacillus Calmette-Guérin (BCG), mitomycin or gemcitabine. Muscle invasive cancer requires more aggressive treatment. The standard of care is radical cystectomy. Postoperative radiotherapy is indicated for T3 or T4 tumors and when there is involvement of the pelvic lymphatics. Bladder preservation therapy with concurrent chemoradiotherapy is an alternative for highly motivated patients after maximal TURBT and results in 60-80% rates of functional bladder sparing. In the

palliative setting, radiation alone is an effective treatment for hematuria. Two radiotherapy fractionation schedules are used to treat locally advanced bladder cancer: 64 Gy in 32 fractions over 6·5 weeks and a hypofractionated schedule of 55 Gy in 20 fractions over 4 weeks. Long-term outcomes of these schedules in several cohort studies and case series suggest that response, survival, and toxicity are similar. A meta-analysis of the BC2001 and BCOPN trials showed that the hypofractionated schedule of 55 Gy in 20 fractions was non-inferior to 64 Gy in 32 fractions in both invasive locoregional control and toxicity. Hypofractionation was also superior regarding invasive locoregional control. While there has been increasing acceptance of hypofractionation as a standard of care, there remain questions regarding its safety in combination with immunotherapy. When high doses of radiotherapy are given, IMRT is often indicated to minimize the dose to pelvic organs at risk, especially the small bowel.

Penile Cancer
Penile cancer is rare and requires multidisciplinary management. Brachytherapy is the preferred approach in selected cases of early-stage penile cancers. Concurrent chemoradiotherapy as primary treatment, or after surgery is recommended for larger tumors and when there is nodal involvement. Radiation may also be used when surgical margins are positive.

Renal Cancer
Renal cell cancer is a relatively common primary tumor of the kidney. Surgical resection alone has historically been the recommended treatment for localized disease. However, recent randomized trials have supported definitive SBRT for T1 tumors (less than 7 cm) in non-optimal patients as an alternative to surgery.

Testicular Cancer
Following inguinal orchiectomy for early stage pure seminoma, there is an approximately 15% risk of recurrence in the para-aortic lymph nodes. External beam radiation significantly reduces this risk and is an option to surveillance or single agent chemotherapy in stage I disease. Radiation to the para-aortic and ipsilateral iliac nodes is an alternative to chemotherapy in individuals with stage IIA and IIB disease. IMRT is not recommended for treatment of pure testicular seminomas due to the low doses given and the increased risk of secondary malignancy in the kidney, liver, or bowel with IMRT. Radiation is not a standard component in the treatment of non-seminomatous testicular cancer.

For review of metastatic sites, please refer to specific guidelines for the appropriate location. (e.g. CNS for brain metastases, Lung for lung metastases)

Gynecologic Cancers (Cervical, Fallopian Tube, Ovarian, Uterine, and Vulvar/Vaginal)
Brachytherapy is considered standard of care in the treatment of many GYN malignancies, and both high dose rate (HDR) and low dose rate (LDR) brachytherapy treatments are used.

External beam radiation is used in many clinical situations to treat pelvic tissues and regional lymph nodes. With significant toxicity constraints, particularly GI and urologic toxicity, IMRT is often the recommended modality.

IMRT is not routinely recommended for palliative treatment of symptoms in the setting of advanced disease.

Cervical Cancer
In the United States, cervical cancer is relatively uncommon. About 80% of cases are squamous cell carcinoma. HPV infection is known to increase the risk of cervical cancer and this had led to development of a vaccine to prevent the disease. Early stage cervical cancer can be treated with either surgery or radiation. More advanced disease is treated with concurrent chemoradiotherapy followed by brachytherapy. If high risk features are found at the time of surgery, adjuvant postoperative radiotherapy is indicated. IMRT is helpful in minimizing radiation dosage to the critical structures in the pelvis, particularly the bowel. Compared to 3D conformal radiotherapy, IMRT has been shown to reduce the incidence of acute and chronic gastrointestinal side effects and also lower the risk of bowel obstruction.

External beam radiation techniques should not be considered alternatives to brachytherapy for an intact cervix.

Brachytherapy is commonly incorporated into the definitive management of cervical cancer. For treatment of the intact cervix, tandem and ovoid or tandem and ring applicators are most often used. For more advanced cases, interstitial implants may be required. Brachytherapy can be delivered with either LDR or HDR techniques. When LDR brachytherapy is used, two applications are typically performed. For HDR treatment, up to six fractions are appropriate. Brachytherapy can be used alone for very early stage cervical cancer. More commonly, brachytherapy is used as a boost following external beam radiotherapy. When tumors are not adequately dosed with brachytherapy, completion hysterectomy may be of benefit. Concurrent platinum based chemotherapy has been shown to improve survival compared to radiotherapy alone for early stage high risk disease as well as advanced stage disease. Chemoradiotherapy has been shown to be more effective than radiotherapy alone in the adjuvant setting in intermediate and high-risk patients but with increased toxicity.

Uterine Neoplasms
Endometrial cancers arise in the uterine lining and commonly present as post-menopausal bleeding. They are more common than cervical cancer with approximately 69,000 new cases estimated in 2025. The primary treatment for endometrial cancer is surgery. Primary radiation can be used in patients who are not surgical candidates. Adjuvant radiation therapy has been shown to decrease recurrences in women at risk. Risk factors for recurrence include age, depth of myometrial invasion, tumor grade and presence of lymphovascular invasion. Most recurrences are in the vaginal cuff. EBRT targets any gross disease present, the parametrial regions, upper vaginal and paravaginal tissues, as well as pelvic lymph nodes (lower common iliac, external iliac, internal iliac, presacral).

IMRT techniques reduce the radiation dose to nearby critical pelvic structures, such as small bowel. The use of IMRT was associated with a significant decrease in grade 3 late effects and other adverse events in both the PARCER and PORTEC-3 studies comparing IMRT to 3- dimensional conformal radiotherapy. External pelvic radiotherapy is the preferred treatment for stage IB grade 3 lesions and patients with involved nodes. A brachytherapy boost is appropriate for patients with endocervical or cervical stromal involvement. Whether external radiotherapy can be replaced by vaginal brachytherapy and chemotherapy for high risk stage I and stage II patients is currently being studied by the Gynecologic Oncology Group (GOG). Vaginal brachytherapy alone is preferred for most other stage I patients based on the results of the PORTEC-2 randomized trial, although EBRT may be reasonable for those at especially high risk of locoregional recurrence (LRR). As advocated in the 2014 Choosing Wisely campaign, stage IA patients with grade 1 or 2 disease and no other risk factors should be observed.

Regarding electronic brachytherapy, the American Brachytherapy Society states that "it is not recommended that electronic brachytherapy be utilized for accelerated partial breast irradiation, non-melanomatous skin cancers, or vaginal cuff brachytherapy outside prospective clinical trials at this time."

Uterine sarcomas are rare tumors arising in muscle or connective tissue. Postoperative radiation therapy is recommended for patients at high risk for pelvic recurrence after surgery. As with other GYN cancers, IMRT may be used to reduce the dose to the small bowel.

Ovarian Cancer
Radiation therapy is no longer a common component of initial treatment or consolidative therapy for primary epithelial ovarian cancer treatment. Standard of care includes surgical resection or debulking and systemic chemotherapy. Palliative radiation remains an option to manage symptoms in recurrent or metastatic disease.

For review of metastatic sites, please refer to specific guidelines for the appropriate location (e.g., CNS Cancers for brain metastases and Lung Cancer for lung metastases).

Head and Neck Cancers (including Thyroid Cancer)
Head and Neck Cancers are defined as cancers of the lip, oral cavity, oropharynx, hypopharynx, nasopharynx, glottic larynx, supraglottic larynx, ethmoid and maxillary sinus, nasal cavity, salivary glands (including Parotid), Mucosal Melanoma, and Head and Neck occult primary.

IMRT has demonstrated improvement for Head and Neck cancer irradiation by reducing long-term side effects in the oropharyngeal, paranasal sinus, and nasopharyngeal cancers by reducing the dose to salivary glands, temporal lobes, auditory and optic structures. The use of IMRT to other regions has similar benefits and may be administered at the discretion of the ordering physician. However, the use of IMRT for early stage (stages I, II) glottic cancer has not been well established. Definitive or consolidative radiation for head and neck lymphomas often includes similar anatomic targets the

other head and neck malignancies and IMRT may be considered medically necessary to spare salivary function and prevent permanent xerostomia.

Differentiated thyroid cancers are most often treated with surgical resection, with or without radioactive iodine (RAI). External beam radiation is used in a variety of clinical situations, including inadequate RAI uptake, unresectable or incompletely resected disease, LRR, and metastatic disease.

Anaplastic thyroid cancer represents a highly lethal malignancy, with no clearly effective treatment protocols. External beam radiation, with or without chemotherapy, may improve short-term survival, and can be used to palliate symptoms, particularly airway obstruction. IMRT techniques have been shown to reduce toxicity.

For review of metastatic sites, please refer to specific guidelines for the appropriate location (e.g., CNS for brain metastases, Lung for lung metastases).

Jugular Paraganglioma
Jugular paragangliomas (also called glomus jugulare tumors) are rare, typically benign, highly vascular tumors located at the skull base. Radiation therapy (RT), including conventional external beam radiation therapy (EBRT) and stereotactic radiosurgery (SRS), is a well-established, effective, and safe treatment option, especially for patients who are not ideal surgical candidates or wish to avoid the risks of surgery.

RT achieves excellent local tumor control rates, with 5- and 10-year local control rates ranging from 91%-100%. SRS and fractionated RT both provide similar tumor control, with SRS showing tumor control rates of about 94%-96% at 5 years. Symptom stabilization or improvement is common, and progression-free survival is high.

RT is associated with minimal morbidity and a much lower complication rate compared to surgery. Major complications and new cranial nerve deficits are rare, especially with modern techniques. Late toxicities, such as vascular events or radiation-induced secondary tumors, are very uncommon but have been reported in long-term follow-up. RT is often preferred for patients with significant surgical risk or medical comorbidities, tumors with high surgical morbidity risk, patients who decline surgery, or tumors not amenable to complete surgical resection.

Conventional fractionated EBRT: Typical dose is 45-50.4 Gy in 1.8 -2 Gy fractions. SRS: Usually delivered as a single large dose of 12-15 Gy, or in a few fractions (SBRT), depending on tumor size and proximity to critical structures.

Lung Cancer, Small Cell and Non-Small Cell
Radiation therapy has a potential role for the treatment of lung cancers in all stages of disease.

For NSCLC, radiation may be used as an adjunct to surgery. It may also serve as definitive therapy in unresectable disease. For unresectable stage II and III disease, concurrent chemoradiotherapy is considered standard of care, when tolerated. 3D conformal radiation typically provides optimal coverage of tumor volumes. IMRT may improve dose-volume constraints, but at the expense of increasing the volume of normal tissue exposed to low doses of radiation. If normal tissue tolerances would be exceeded with 3D conformal planning, IMRT is considered medically necessary.

The optimal dose and fractionation for both definitive and palliative treatment of NSCLC has been the subject of numerous clinical investigations. Based on several earlier phase I/II trials of dose escalation, RTOG 0617 compared standard-dose (60 Gy) with high-dose (74 Gy) conformal radiotherapy given concurrently with carboplatin and paclitaxel chemotherapy with and without the addition of cetuximab. There was no benefit from the use of cetuximab in either arm. Overall survival was better in the standard-dose arms (28.7 vs 20.3 mos, p less than 0.004). Standard-dose radiotherapy also resulted in better median progression free survival (11.8 vs 9.8 mos), lower risk of severe esophagitis (7% vs 21%, p less than 0.0001) and fewer treatment related deaths. ASTRO recently published an evidence-based clinical practice guideline which concluded that the ideal external beam dose fractionation for curative intent chemoradiotherapy for NSCLC is 60 Gy given in 2 Gy once daily fractions over 6 weeks. Dose escalation beyond 60 Gy was not recommended outside the setting of clinical trial. This guideline has also been endorsed by ASCO. When used without concurrent chemotherapy, the guideline recommends a minimum dose of 60 Gy.

In metastatic NSCLC where palliative treatment is being considered, the goal is to strike a balance between symptom relief, local control and treatment toxicity. ASTRO published a comprehensive evidence based guideline on palliative radiotherapy in lung cancer. The guideline concluded that higher-dose/fractionation regimens (30-Gy/10-fraction or higher) may benefit patients with good performance status. These higher dose regimens are associated with significant adverse effects such as esophagitis. Shorter course treatment is recommended for patients with poor performance status. Despite this recommendation, Koshy et al. found that almost half of stage IV lung cancer patients received inappropriately high doses of radiation (defined as more than 15 fractions). A recent update of the ASTRO guideline now supports concurrent chemoradiotherapy with a platinum doublet in stage III patients with ECOG performance status of 0-2 and a life expectancy of at least 3 months.

Stereotactic radiation may be used as definitive therapy in earlier stages of disease for patients who may not be candidates for invasive surgery. Even for operable patients, stereotactic radiation has been shown to be non- inferior to video-assisted thorascopic resections with mediastinal lymph node dissections (VATS L-MLND). Chang et al. reported a 3-year overall survival rate of 91% with SBRT which was the same OS rate reported with VATS L-MLND. Stereotactic radiation may be recommended for local palliation or prevention of symptoms such as hemoptysis, obstruction, or pain. There is an emerging role for SBRT to treat oligometastatic disease (3 or fewer metastatic lesions). Please refer to the Oligometastatic disease section for further discussion.

Radiation therapy is also used in all stages of small cell lung cancer, either as definitive treatment in combination with chemotherapy, or as palliative therapy. Concurrent chemotherapy is preferred to sequential chemotherapy with RT. Target volumes are best defined with pre-treatment positron emission tomography/computed tomography (PET/CT) obtained at the time of radiotherapy planning. Consolidative thoracic radiation may be beneficial to select patients with extensive stage disease who have significant responses to standard chemotherapy. Hyperfractionated radiation given twice dailyhas been shown to improve survival compared to conventionally fractionated treatment.

The utility of 2D radiation is likely limited to palliative treatment of metastatic disease.

The minimum standard used to treat intrapulmonary lesions is 3D conformal, with CT planning. PET/CT is noted to significantly improve targeting accuracy. Tumor motion should be accounted for.

The clinically appropriate use of more advanced modalities, such as IMRT and SBRT, are limited to specific clinical scenarios. It is the responsibility of the Radiation practice to create optimal treatment plans when evaluating modality choices for treatment.

For review of metastatic sites, please refer to specific guidelines for the appropriate location (e.g., CNS Cancers for brain metastases and Lung Cancer for lung metastases).

Lymphoma: Hodgkin and Non-Hodgkin

Hodgkin Lymphoma

Hodgkin lymphoma is a malignancy of the lymphatic system with distinct clinical and pathologic features which set it apart from Non-Hodgkin lymphoma. The disease commonly affects lymph nodes in the mediastinum but can affect nodes and other lymphatic organs throughout the body. Occasionally, the bone marrow and liver are also involved. Pathologically, Hodgkin lymphoma is characterized by the presence of characteristic lymphocytes called Reed-Sternberg cells.

There are four distinct subtypes of Hodgkin lymphoma. About 80% of cases are termed nodular sclerosis Hodgkin lymphoma. The other types include lymphocyte-predominant, mixed cellularity and lymphocyte-depleted Hodgkin lymphoma. Over the years, treatment has evolved from radiotherapy or chemotherapy alone to a risk adapted approach of chemotherapy and involved site radiotherapy. Treatment intensity is also guided by treatment response on PET scan performed after multiple cycles of chemotherapy.

For favorable stage I and II disease, 20-30 Gy of involved site radiotherapy is given after chemotherapy. For bulky disease at presentation, doses of 30-36 Gy are appropriate. Although these doses are generally below the dose tolerance of the surrounding normal tissues, there are situations where advanced planning techniques are likely to result in a meaningful decrease in late toxicity from radiotherapy. Koeck et al. published a planning comparison of 3D versus IMRT for patients with unfavorable mediastinal Hodgkin lymphoma and found reduced mean heart and spinal cord

doses with IMRT. Doses to the lungs and breasts were higher with 3D conformal radiation. The most pronounced benefits were seen in patients with lymph nodes anterior to the heart. Since IMRT has been shown to increase low dose exposure to the breasts and lungs, the potential benefit of cardiac sparing needs to be weighed against increased risks of breast and lung cancer, especially in female patients. The role of IMRT in the treatment of non-mediastinal Hodgkin lymphoma has not been studied and therefore IMRT in these cases is considered not medically necessary.

Non-Hodgkin Lymphoma (NHL)
Non-Hodgkin Lymphoma is a cancer arising in lymphocytes and includes all subtypes except Hodgkin Lymphoma (described below). The disease most commonly involved B-cells but can involve other types of lymphocytes. Historically, lymphomas have been grouped based on histology into low grade, intermediate grade and high grade. Advances in tumor phenotyping have allowed more sophisticated subtyping to guide treatment.

Specific treatment depends on the grade and extent of disease. Treatments may include chemotherapy, immunotherapy or other targeted therapy, radiation therapy and stem cell transplantation. Some asymptomatic follicular (low grade) lymphomas may not require active treatment. In other cases, involved site radiotherapy alone or in combination with systemic therapy is used. Doses range from 20-36 Gy. Stage I and II diffuse large B-cell lymphoma is typically treated with combined chemotherapy and radiotherapy. The dose to the involved site is guided by the response to 3-6 cycles of R-CHOP chemotherapy (regimen of cyclophosphamide, doxorubicin, vincristine, and prednisone). Doses of 30-36 Gy are given to consolidate complete responses while doses of 40-50 Gy are used to treat partial responses. Radiotherapy is also applied to bulky sites of involvement after chemotherapy in stage III and IV lymphoma. Lymphoma including mucosal associated (MALT) lymphomas, mantle cell lymphoma, Burkitt's lymphoma and others may involve radiotherapy with doses up to 45 Gy as part of the treatment. Total Body Irradiation (TBI) continues to be an important step prior to stem cell transplantation. The most common regimens will consist of 1-2 radiation treatments per day given over 3-4 days.

Because the doses of radiation needed for non-Hodgkin lymphoma are lower than doses used for most other types of cancer, the need for advanced planning techniques such as IMRT is limited. As with Hodgkin lymphoma, IMRT is appropriate for mediastinal disease and head and neck presentations due to the proximity of the target to sensitive normal structures. For other sites, there are limited data regarding IMRT and therefore it is considered not medically necessary.

Oligometastatic Extra-Cranial Disease
Metastasis can occur when one or more cancer cells develop the capacity to enter the bloodstream and establish secondary tumors in distant organs such as the brain, lungs, liver and bone. While widespread metastatic disease is generally considered incurable, there exists a subset of patients with limited metastatic involvement who can potentially be cured of their disease. This state has been termed "oligometastatic" and is most defined as having 3 or fewer metastatic lesions. In the past, aggressive metastasis-directed therapy largely consisted of surgical resection of lung and liver

lesions. Radiotherapy was generally reserved for palliation of symptoms. Advances in system therapy and the widespread availability of stereotactic body radiation therapy have renewed interest in ablative therapy for oligometastatic disease.

Much of the data on treatment of oligometastatic cancer consist of single institution retrospective reviews. Several series have shown long-term benefit from resection of limited liver metastases in patients with colorectal cancer. Five-year disease-free survival rates approach 30% in this setting. Similarly, radiofrequency ablation of limited hepatic metastases from colorectal cancer has been shown to improve survival. A phase II randomized EORTC trial studied the addition of radiofrequency ablation to standard systemic therapy in 119 patients without extrahepatic disease. Ruers et al. recently reported an 8-year overall survival rate of 36% for patients randomized to radiofrequency ablation of liver lesions compared to 9% for patients receiving systemic therapy alone.

Stereotactic body radiation therapy (SBRT), also termed stereotactic ablative radiation therapy (SABR), has also been studied in the treatment of oligometastatic cancer. Control rates with this ablative technology approach 90%. Several prospective phase II studies have examined the potential benefit of SABR in oligometastatic disease. Gomez et al. reported results of a multi-institutional phase II randomized study of local consolidative therapy (LCT) versus maintenance therapy or observation. Patients with non-small cell lung cancer and 1-3 metastatic lesions were eligible for randomization only if disease had not progressed on chemotherapy. The study was stopped early due to a significant improvement in progression-free survival with LCT (11.9 months) versus maintenance only (3.9 mos) yielding a hazard ratio of 0.35 (p less than 0.005). Iyengar et al. studied whether consolidative radiotherapy to the primary and up to 5 metastatic lesions would improve disease-free survival in NSCLC compared to maintenance chemotherapy alone. Twenty-nine patients were randomized. Disease-free survival in SABR-treated patients was 9.7 months compared to 3.5 months in the maintenance group (p less than 0.01).

In a single-arm phase II study of SABR in 147 patients with up to 5 metastatic lesions, Sutera et al. report a 5-year overall survival rate of 43%. In addition to lung cancer, they treated colorectal, head and neck, breast, and prostate cancers among others. Although they allowed up to 5 metastatic lesions, 96.5% of patients had 3 or fewer lesions. On multivariate analysis, patients with a Karnofsky Performance Status (KPS) of 80 or less was associated with worse survival.

The phase II STOMP trial randomized men with castration-sensitive, oligometastatic prostate cancer recurrence to either ablative metastasis-directed therapy (MDT) or surveillance. There were 62 patients studied using androgen deprivation therapy (ADT)-free survival as the primary endpoint. Up to 3 metastatic lesions were allowed in either nodal or non-nodal sites and MDT included either surgery or SABR. At a median follow up of 3 years, MDT resulted in a median ADT-free survival of 21 months versus 13 months with surveillance (HR 0.6, p=0.11). Quality of life was similar in both groups at baseline, 3 months, and one year.

Long-term results of the SABR-COMET (NCT01446744) trial were recently reported. This randomized trial compared overall survival in patients with a controlled primary cancer and up to 5 metastatic lesions treated with either SABR to all oligometastatic lesions or palliative standard of care (SOC). Eligible patients had ECOG PS 0-1 and an estimated life expectancy of at least 6 months. A total of 99 patients were treated using a 1:2 ratio of SOC versus SABR. The most common primary cancer types included breast, colorectal, lung, and prostate, and the most treated sites were lung, bone, liver, and adrenal gland. Although up to 5 oligometastatic lesions were allowed, 93% had 1-3 metastases. Five-year overall survival for the SABR-treated patients was 42.3% vs 17.7% in the palliative SOC patients (P =.006). Five-year progression-free survival was 17.3% with MDT Compared to zero in the palliative standard of care group (P=0.001). Compared with SOC, treatment with SBRT was not associated with decreased quality of life.

A phase 2 randomized trial (SAFRON II) compared single fraction SBRT to 28 Gy with fractionated SBRT of 48Gy in 4 fractions in 87 patients with 1-3 pulmonary oligometastases. There were no differences in local control, disease-free survival, or overall survival at 2 years. Toxicities and adverse events were not significantly different between the groups.

Recently the EXTEND Phase II Trial showed that the addition of metastasis-directed therapy (MDT) to systemic therapy for patients with oligometastatic pancreatic ductal adenocarcinoma improved PFS. At a median follow-up time of 17 months, the median PFS increased from 2.5 months to 10.3 months with the addition of MDT to systemic therapy (p=0.030).

Unlike other disease sites, NRG-BR002, a phase II/III trials of standard of care systemic therapy with or without SBRT and/or surgical resection failed to show benefit for newly oligometastatic breast cancer (NCT02364557). The trial was halted before moving to phase III.

For patients with newly diagnosed prostate cancer and metachronous oligometastases, two randomized phase II trials support the use of SBRT. The ARTO trial looked at abiraterone+/- SBRT for 157 patients with oligometastatic castrate-resistant prostate cancer. SBRT yielded a significant PFS improvement. At the 2025 ASCO GU Symposium, Niazi presented the results of the PCS-9 study, a randomized phase II/III trial looking at SBRT in addition to standard systemic therapy in oligometastatic castration resistant prostate cancer. The addition of SBRT to enzalutamide + ADT was associated with a 52% risk reduction in radiological progression or death.

Other tumor types, including Sarcoma, Thymoma and Thymic Carcinoma, Pediatric Tumors and other malignancies

Sarcomas

Soft tissue sarcomas are rare malignancies arising in connective tissue. Multimodality treatment with surgery, radiation and chemotherapy is common, especially in high grade sarcomas. Multiple studies have shown that radiation improves local control. Soft tissue sarcomas are often treated with preoperative therapy to a dose of 50 Gy. Placement of clips at the time of surgery aids with boost planning if needed. Alternatively, postoperative radiation therapy can be given. External beam

treatment typically consists of 50 Gy to a larger field encompassing the preoperative tumor volume plus a margin followed by a smaller boost field. Boost doses of 10-26 Gy are used, depending on the final surgical margins. Brachytherapy may also be used postoperatively, particularly in the setting of microscopic or gross residual disease after resection. Alternatively, intra-operative radiation may be considered as boost treatment at the time of surgery.

In terms of radiation planning, the use of MRI imaging and CT based planning are recommended. IMRT is sometimes utilized but is particularly helpful in the setting of pelvic or retroperitoneal sarcoma, to minimize toxicity in this high-risk anatomic region. IMRT for sarcomas in other regions remains an area of active investigation. A recent RTOG study of image guidance suggested that toxicity is lower when field size is reduced in conjunction with daily IGRT. Many of these patients were treated with IMRT Other retrospective comparisons of conventional radiation and IMRT have been published. A study by Folkert reported recurrence rates for 319 consecutive patients, about half of whom were treated with IMRT. There was an association between IMRT and improved local control. The authors note, however, that other confounding factors such as the use of MRI in treatment planning may explain the difference. The use of IMRT for soft tissue sarcomas is appropriate for pelvic, retroperitoneal and extremity soft tissue sarcoma.

Thymoma and Thymic Carcinoma
Thymomas are rare tumors arising in epithelial cells within the thymus. They can be benign or malignant. For lesions which are resectable, complete thymectomy and excision of tumor is recommended. Radiotherapy is added for stage III disease or in cases where the tumor is unresectable or incompletely resected. Doses of 45-50 Gy are used after resection with clear or close margins. A dose of 54 Gy is used for microscopically positive margins and doses of 60-70 Gy are given for gross disease. Chemotherapy is used in advanced or metastatic disease. CT-based treatment planning is recommended, as is respiratory motion management if available. Much like mediastinal Hodgkin lymphoma, IMRT is appropriate to spare heart and lung tissue.

Pediatric Tumor Types
IMRT is a method to spare normal tissue from radiation damage, and reduce the risk of toxicity, complications, and secondary malignancy in normal tissues that are still developing. IMRT has demonstrated excellent potential in sparing the organs at risk while achieving good local control. Therefore, IMRT is helpful in treating pediatric tumors that are sensitive to radiation therapy. Please see proton beam guidelines for further details regarding use of protons in pediatric tumors.

Other Tumor Types
IMRT and stereotactic radiation techniques are used in the setting of overlapping with a previously irradiated field, due to the risk of toxicity or complications.

For review of metastatic sites, please refer to specific guidelines for the appropriate location (e.g., CNS Cancers for brain metastases and Lung Cancer for lung metastases).

Prostate Cancer

Prostate cancer is the most common cancer seen in men. Early detection has resulted in a decrease in prostate cancer mortality over the past two decades.

Active surveillance options should be discussed with individuals with low-risk prostate cancers. Furthermore, individuals with low-risk or intermediate-risk prostate cancer and an anticipated survival of less than 10 years based on comorbidity are recommended to be followed with observation, as the risk of over-treatment may outweigh the clinical benefit.

External beam radiotherapy and surgery are the primary treatment modalities in patients who do not opt for surveillance. Improvement in radiation therapy delivery, including 3D-conformal radiation and IMRT, have allowed for the safe dose escalation which has improved cure rates in patients with localized disease. Pelvic nodal irradiation should be limited to individuals with intermediate-risk or high-risk disease.

There is a trend toward hypofractionation (fewer treatments to deliver the same biologic dose) which allows patients to be treated with less disruption of their daily lives. There have been several randomized clinical trials comparing conventionally fractionated external radiotherapy with hypofractionated regimens. RTOG 0415 was designed to evaluate the non-inferiority of hypofractionated treatment (70.8 Gy in 28 fractions) compared to conventional fractionation (73.8 Gy in 42 fractions). There were 1092 participants. At a median follow-up of 5.9 years, the estimated 5-year disease-free survival rate was 85.3% in the conventional radiotherapy arm and 86.3% in the hypofractionated radiotherapy arm. The hypofractionated arm was associated with a significant increase in late grade 2 and 3 gastrointestinal and genitourinary adverse events. Based on the DFS rates, hypofractionated radiotherapy was found to be non-inferior. In the HYPRO trial, patients with intermediate to high-risk prostate cancer were randomized to receive 78 Gy in 38 fractions or 64.6 Gy in 19 fractions. At 5-years, the relapse free survival rates for conventional fractionation versus hypofractionation were 77.1% and 80.5% respectively. Since the goal of the trial was to prove superiority of hypofractionation, the authors concluded that hypofractionation had not been proven superior to standard fractionation. Hypofractionation does appear non-inferior in this study. In the PROFIT trial, investigators randomly assigned patients with intermediate risk prostate cancer to receive 78 Gy in 39 fractions or 60 Gy in 20 fractions. With 6 years of follow up, biochemical disease free survival was the same in both groups. There were no differences in greater than or equal to grade 3 late GI or GU toxicities reported. Five-year results of the CHHip trial were recently published. This was an open-label, randomized study looking at both effectiveness and toxicities. A total of 3216 men were included. They compared 74 Gy in 37 fractions over a period of 7.4 weeks with hypofractionated radiotherapy at 60 Gy in 20 fractions over a period of 4 weeks or 57 Gy in 19 fractions over a period of 3.8 weeks. At the 5 year follow-up, biochemical or clinical failure-free rates were 88.3% in the conventional 74-Gy group, 90.6% in the hypofractionated 60-Gy group, and 85.9% in the hypofractionated 57-Gy group. While bladder and bowel symptoms peaked sooner in the hypofractionated groups (4-5 vs 7-8 weeks), at 18 weeks, rates were similar for all groups. Long-term adverse effects were similar among the treatment groups. The authors concluded that the

hypofractionated approach using 60 Gy in 20 fractions was non-inferior to standard fractionation using 74 Gy in 37 fractions.

In 2018, ASTRO, ASCO, and AUA published an evidence-based guideline on hypofractionated radiation therapy for localized prostate cancer. They defined moderate hypofractionation as daily fractions ranging from 240 cGy to 340 cGy and ultrahypofractionation as daily fractions greater than 500 cGy. The latter is given in up to 5 fractions of SBRT. In comparing moderately fractionated IMRT with conventionally fractionated treatment, the panel has recommended that hypofractionated therapy should be offered to men with low- risk or intermediate-risk prostate cancer who opt for active treatment. These recommendations were both considered strong, were based on high-quality evidence, and had 100% consensus. Moderate hypofractionation should also be offered for high-risk prostate cancer where pelvic nodes will not be treated based on 94% consensus. They recommended that men be counselled of a small increased risk of temporary GI toxicity with hypofractionated regimens but noted that late GI and GU toxicities were similar in hypofractionated and conventional treatments. The suggested fractionation patterns are either 6,000 cGy in 20 fractions or 7,000 cGy in 28 fractions.
Postoperative radiotherapy (EBRT/IMRT) can be delivered in either the adjuvant or salvage setting. Indications for adjuvant prostate bed radiotherapy include T3 primary, extracapsular disease, seminal vesicle involvement, Gleason 8 or 9 disease and positive margins. Salvage radiotherapy is indicated in patients at risk for local failure who have a rising prostate specific antigen (PSA) level. When adjuvant radiation therapy is indicated, it should be given within 1 year of radical prostatectomy, but after any post-operative issues have stabilized. OAR tolerances thus should be carefully considered and prioritized. Hypofractionated post-prostatectomy RT to the prostate fossa alone is supported by toxicity and outcome equipoise in post-hoc evaluation of the RADICALS-RT trial (52.5 Gy/20 fractions vs. 66 Gy/33 fractions) and in the 2-year report of the NRG GU003 trial (62.5 Gy/25 fractions vs. 66.6 Gy/37 fractions). However, these regimens have shorter follow-up than historically studied conventionally fractionated regimens and data for simultaneous integrated treatment of the pelvic lymph nodes is currently limited. ASTRO and AUA published an updated clinical practice guideline on the use of adjuvant and salvage radiotherapy after prostatectomy in 2019 to reflect new level 1 evidence demonstrating the addition of hormonal ablation to salvage treatment. In the SAKK 09/10 randomized clinical trial for salvage radiotherapy, dose-intensification of 70 Gy in 30 fractions was not found to be advantageous over 64 Gy in 32 fractions for patients with early biochemical progression of prostate cancer after radical prostatectomy.

SBRT is an established precision technology that delivers a high biologic dose of radiation over a short period of time. The hypofractionation associated with SBRT shortens the treatment time to five visits, compared to the 4 to 6 weeks typically required for IMRT. This shortened one week treatment time is appreciated by individuals. The key outcomes include both tumor control and toxicity, primarily focusing on acute and chronic rectal and genitourinary complications." PACE is an open-label, multicohort, randomized, controlled, phase 3 trial conducted at 35 hospitals in the UK, Ireland, and Canada. In PACE-B, men aged 18 years and older with a WHO performance status 0–2 and low-risk or intermediate-risk histologically- confirmed prostate adenocarcinoma (Gleason 4 + 3 excluded) were randomly allocated (1:1) by computerized central randomization with

permuted blocks (size four and six), stratified by center and risk group to control radiotherapy (CRT; 78 Gy in 39 fractions over 7·8 weeks or, following study modification, 62 Gy in 20 fractions over 4 weeks) or SBRT (36·25 Gy in five fractions over 1–2 weeks). Androgen deprivation was not permitted. In the PACE-B trial, 2-year RTOG toxicity rates were similar for five fraction SBRT and conventional schedules of radiotherapy. Prostate SBRT was found to be safe and associated with low rates of side-effects. Five-fraction SBRT was non-inferior to CRT with the same rate of biochemical or clinical failure in low-to-intermediate-risk localized prostate cancer.

In the MIRAGE phase 3 clinical trial, men who were receiving SBRT at a single center for clinically localized prostate cancer were randomized to either SBRT with CT guidance or SBRT with MRI guidance. Compared with CT-guidance, MRI-guided SBRT significantly reduced both moderate acute physician-scored toxic effects and decrements in patient-reported quality of life.

The 2018 ASTRO, ASCO, and AUA guideline on ultrahypofractionated radiotherapy for prostate cancer recommends offering SBRT to men with low-risk disease, considers SBRT an option in intermediate-risk disease, and does not recommend SBRT for high-risk disease outside of a clinical trial or registry.

Brachytherapy or prostate implant is another option to deliver highly conformal doses to the prostate. For a low dose rate (LDR) implant, permanent radioactive seeds are implanted evenly throughout the gland under ultrasound guidance. For a high dose rate (HDR) implant, catheters are placed into the gland which is later irradiated as the high activity seed stops in fixed dwell positions throughout the volume. Recently, the ASCO/Ontario Guideline on brachytherapy for prostate cancer was updated. For low risk patients, LDR brachytherapy is a proven option to surgery or external beam radiotherapy. For intermediate and high risk patients either LDR or HDR brachytherapy should be considered as boost options in appropriate patients. Studies have shown improved survival when brachytherapy is used in this setting compared to external treatment alone. Both I-125 and palladium-103 are reasonable isotopes for LDR brachytherapy. No recommendation could be made for or against the use of Cs-131.

Several recent publications have reported results of HDR brachytherapy in the treatment of low risk and low- intermediate risk prostate cancer. These studies have shown equivalent results to those seen with IMRT, SBRT, and LDR brachytherapy. Additionally, the Groupe Europė en de Curiethė rapie (GEC) and the European Society for Radiotherapy and Oncology (ESTRO) have published a joint prostate brachytherapy guideline. They note that they no longer consider the recommendations for LDR and HDR brachytherapy separately and therefore HDR monotherapy is now considered a standard treatment for low- and intermediate-risk disease.

For patients who are newly diagnosed with metachronous oligometastases, two randomized phase II trials support the use of SBRT. The ARTO trial looked at abiraterone+/- SBRT for 157 patients with oligometastatic castrate-resistant prostate cancer. SBRT yielded a significant PFS improvement. At the 2025 ASCO GU Symposium, Niazi presented the results of the PCS-9 study, a randomized phase II/III trial looking at SBRT in addition to standard systemic therapy in oligometastatic castration

resistant prostate cancer. The addition of SBRT to enzalutamide + ADT was associated with a 52% risk reduction in radiological progression or death.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Several devices that use cobalt 60 radiation (gamma-ray devices) for SRS have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The most commonly used gamma-ray device, approved in 1999, is the Gamma Knife®‡ (Elekta; product code IWB), which is a fixed device used only for intracranial lesions. Gamma-ray emitting devices that use cobalt 60 degradation are also regulated through the U.S. Nuclear Regulatory Commission.

A number of LINAC movable platforms that generate high-energy photons have been cleared for marketing by the FDA through the 510(k) process. Examples include the Novalis Tx®‡ (Novalis); the TrueBeam STx (Varian Medical Systems; approved 2012; FDA product code IYE); and the CyberKnife®‡ Robotic Radiosurgery System (Accuray; approved 1998; FDA product code MUJ). LINAC-based devices may be used for intracranial and extracranial lesions.

Centers for Medicare and Medicaid Services (CMS)

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

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Policy History

Original Effective Date: 03/19/2024
Current Effective Date: 05/01/2026

03/19/2024	Utilization Management Committee review/approval. New policy.
02/18/2025	Utilization Management Committee review/approval. Clarified that the maximum number of fractions for SBRT is 5 in both NSCLC and SCLC. Added coverage with criteria for stereotactic body radiation therapy (SBRT) for extra-cranial oligoprogressive disease.
01/01/2026	Coding update.
02/18/2026	Utilization Management Committee review/approval. Extensive revisions throughout the policy.

Next Scheduled Review Date: 02/2027

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2025 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	32701, 61796, 61797, 61798, 61799, 61800, 63620, 63621, 77371, 77372, 77373, 77432, 77435
HCPCS	G0339, G0340 Delete codes effective 01/01/2026: G6001, G6002, G6003, G6004, G6005, G6006, G6007, G6008, G6009, G6010, G6011, G6012, G6013, G6014, G6016, G6017
ICD-10 Diagnosis	All related diagnoses

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan's Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: All codes listed on the Medical Policy require prior authorization. This ensures appropriate utilization and alignment with current clinical guidelines.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Blue Advantage), Blue Advantage may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Blue Advantage health plan.

Medicare Advantage Members
Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-benehelp.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.

InterQual®
Interqual® is utilized as a source of medical evidence to support medical necessity and level of care decisions. InterQual® criteria are intended to be used in connection with the independent professional medical judgment of a qualified health care provider. InterQual® criteria are clinically based on best practice, clinical data, and medical literature. The criteria are updated continually and released annually. InterQual® criteria are a first-level screening tool to assist in determining if the proposed services are clinically indicated and provided in the appropriate level or whether further evaluation is required. The utilization review staff does the first-level screening. If the criteria are met, the case is approved; if the criteria are not met, the case is referred to the medical director.