Molina Clinical Policy
Radiation Therapy for Oncologic Indications: MEDICARE
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STATEMENT

General Information

- *It is an expectation that all patients receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.*
- *Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines and state/national recommendations. This guideline is not a prescription for treatment. All individual treatment decisions are the responsibility of the treating physician.*
- *The guideline criteria in the following sections were developed utilizing evidence-based and peer-reviewed resources from medical publications and societal organization guidelines as well as from widely accepted standard of care, best practice recommendations. This guideline considers treatment endorsed by professional organizations (ie, the American Society for Radiation Oncology and the National Comprehensive Cancer Network). It approves many treatment regimens that fall within that guidance, but it is also modified by significant factors such as toxicity and the level of available medical evidence.*

Purpose

The purpose of this guideline is to provide general information applicable to the review and appropriateness of Radiation Therapy services. Although a service, supply or procedure may be medically necessary, it may be subject to limitations and/or exclusions under a member's benefit plan. Although a service, supply or procedure may be discussed in the guideline, it may be subject to limitations and/or exclusions under a member's benefit plan. If a service, supply, or procedure is not covered and the member proceeds to obtain the service, supply or procedure, the member may be responsible for the cost. This guideline does not apply to inpatient treatment such as inpatient two-dimensional (2D), three-dimensional conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), brachytherapy, hyperthermia, stereotactic radiosurgery/stereotactic body radiation therapy (SRS/SBRT), selective internal radiation therapy (SIRT), and intraoperative radiation therapy (IORT) treatments. It only applies to simulation and treatment that is delivered to a patient as an outpatient.

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BREAST CANCER FEMALE/MALE (1)

Post-Lumpectomy and Lymph Node Negative

Indications for IMRT or 3D-CRT to the Whole Breast for pTis-T3N0, cM0 Stage 0-IIB (1)

Fractionation

- Hypofractionation
  - Treatment to the whole breast in up to 16 fractions of **IMRT or 3D-CRT** followed by an optional boost in up to 5 fractions for patients with no metastatic disease
- Ultra-hypofractionation
  - Treatment to the whole breast in 5 fractions with an optional simultaneous integrated boost of **IMRT or 3D-CRT** may be considered in selected pT1-3, pN0-1 patients following breast conservation surgery for patients with no metastatic disease based on the UK Fast-Forward trial

Fractionation Irradiation

- Conventional Fractionation
  - Treatment to the whole breast in up to 28 fractions of **IMRT or 3D-CRT** followed by an optional boost in up to 8 fractions boost for patients with no metastatic disease is allowed for **ANY** of the following:
    - Regional nodal irradiation requiring a separate supraclavicular, axillary, and/or internal mammary node field
    - Collagen vascular disease
    - Breast augmentation
    - Previous radiation therapy to the breast or chest wall

Indications for Partial Breast Irradiation (PBI) with IMRT, 3D-CRT, or Brachytherapy (1,2)

When **ALL** the following criteria are met:

- Age ≥ 40 years
- Low to intermediate grade (grade 1-2) disease
- Unifocal Invasive Ductal Carcinoma, ≤ 2 cm in size
- Estrogen receptor-positive disease
- Negative surgical margins

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- No lymphovascular invasion
- Node negative disease (pN0)
- Low-risk ductal carcinoma in situ, ≤ 2 cm in size, negative margins
- Patients with early-stage (non-metastatic) disease

OR when any **ONE** of the following criteria are met:

- High grade (grade 3) disease
- Invasive ductal carcinoma with estrogen receptor-negative histology
- Size > 2 to ≤ 3 cm (pT2, pN0, cM0, Stage IIA)

PBI Fractionation for IMRT or 3D-CRT

- 15 fractions **OR** 5 fractions

PBI Fractionation for Brachytherapy (including balloon/interstitial)

- Up to 10 fractions

NOTE: The following techniques are not recommended for routine use in the treatment of breast cancer [3]

- Electronic brachytherapy (see **Unique Treatment Modalities – IntraOperative Radiation Therapy**)
- Non-invasive breast brachytherapy (AccuBoost®)

Post-Lumpectomy and Lymph Node Positive

Indications for IMRT or 3D-CRT to the Whole Breast and Regional Lymph Nodes

Fractionation

- Conventional Fractionation [1]
  - Treatment to the whole breast and regional lymph nodes in up to 28 fractions of **IMRT or 3D-CRT or IMRT** followed by an optional boost in up to 5 fractions boost for patients with no metastatic disease

NOTE: Breast Cancer- See Local Hyperthermia and IORT

Local Hyperthermia with Radiation Therapy

Indications

Up to 10 local hyperthermia treatments are considered medically necessary when used in connection with radiation therapy for **ANY** of the following indications [113]:

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- Primary or metastatic cutaneous or subcutaneous superficial malignancies **OR**
- A chest wall recurrence of breast cancer [119] **OR**
- Recurrent cervical lymph node metastases from head and neck cancer [120]

Intraoperative Radiation Therapy (IORT

Post-Mastectomy

Indications for IMRT or 3D-CRT to the Chest Wall [1]

Fractionation

- Conventional Fractionation
  - Treatment to chest wall and regional lymph nodes in up to 28 fractions of **IMRT** or **3D-CRT** followed by an optional chest wall scar boost in up to 8 fractions for patients with no metastatic disease
- Hypofractionation
  - Treatment to chest wall and regional lymph nodes in up to 16 fractions of **IMRT** or **3D-CRT** followed by an optional chest wall scar boost in up to 8 fractions for patients with no metastatic disease

CENTRAL NERVOUS SYSTEM (CNS) TUMORS

Adult Medulloblastoma

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation [4]
  - Treatment with Craniospinal Irradiation (CSI) followed by a boost to the primary tumor site (tumor bed or posterior fossa)
  - CSI is delivered over 13-20 fractions, depending on risk stratification
  - This is followed by a boost to the primary site, with a total treatment course completed in up to 31 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Arteriovenous Malformations (AVM)

Indications for SRS or SBRT [5,6]

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Fractionation

- Treatment in 1 fraction of **SRS**
- Treatment in 2-5 fractions of **SBRT**

Benign Brain Lesions

Acoustic Neuroma (Vestibular Schwannoma)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation [7]
  - Treatment in up to 28 fractions

Indications for SRS or SBRT [7]

Fractionation

- Treatment in 1 fraction of **SRS**
- Treatment in 2-5 fractions of SBRT

Craniopharyngioma

Indications for IMRT or 3D-CRT [8,9]

Fractionation

- Conventional Fractionation
  - Treatment in up to 30 fractions using **IMRT or 3D-CRT**

Indications for SRS and SBRT [9,10]

Fractionation

- Treatment in 1 fraction of **SRS**
- Treatment in 2-5 fractions of **SBRT**

Brachytherapy [11]

Treatment using intracavitary **brachytherapy** via the installation of a radioisotope directly into cystic tumor components using an isotope (eg, Yttrium-90 (Y90) and Phosphorus-32 (P32))

Meningioma (Grade 1)

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Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation [4]
  - For residual, recurrent, or unresectable disease, treatment in up to 30 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for SRS or SBRT

Fractionation

- Treatment in 1 fraction of **SRS**
- Treatment in 2-5 fractions of **SBRT**

Meningioma (Grade 2)

Indications for IMRT or 3D-CRT [4]

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease for adjuvant treatment following resection or for residual/recurrent disease

Indications for SRS or SBRT [4]

Fractionation

- Treatment in 1 fraction of **SRS** for well-circumscribed lesions
- Treatment in 2-5 fractions of **SBRT** for lesions near critical structures or when **SRS** is **not** appropriate

Meningioma (Grade 3)

Indications for IMRT or 3D-CRT [4]

Fractionation

- Conventional Fractionation
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease for postoperative and/or unresectable disease

Pituitary Adenoma

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Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation [12]
  - Treatment in up to 30 fractions using **IMRT or 3D-CRT** for residual, recurrent, or unresectable disease

Indications for SRS or SBRT [13]

Fractionation

- Treatment in 1 fraction of **SRS**
- Treatment in 2-5 fractions of **SBRT**

Primary Brain and Spinal Cord Cancers [4]

Low Grade Adult Glioma (World Health Organization [WHO] Grade 1 [Pilocytic Astrocytoma, Subependymal Giant Cell Astrocytoma, Ganglioglioma, and Dysembryoplastic Neuroepithelial Tumor] & WHO Grade 2 [Pleomorphic Xanthoastrocytoma, Oligodendroglioma, and Oligoastrocytoma]) [14]

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 30 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease for patients who have high-risk features (eg, subtotal resection, age ≥ 40 years of age, tumor size ≥ 4-6 cm, tumor crossing midline, neurologic symptoms)
  - May be appropriate for low-risk patients following gross total resection

High Grade Adult Glioma (WHO Grade 3 [Anaplastic Astrocytoma, Anaplastic Oligodendroglioma, and Anaplastic Oligoastrocytoma] & WHO Grade 4 [GBM]) [14]

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation for patients with a Karnofsky Performance Status (KPS) ≥ 60 (KPS 60 means patients require occasional assistance but are able to care for most of their personal needs)

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- Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

- Hypofractionation for patients with a KPS < 60 [4]
  - Treatment in up to 15 fractions using **IMRT or 3D-CRT**

Indications for Brachytherapy [15,16]

- A single treatment of GammaTile (Cs-131) brachytherapy in patients only with recurrent high-grade glioma

Adult Intracranial and Spinal Ependymoma (Brain and/or Spine)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation [4]
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Primary CNS Lymphoma

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation [4]
  - Treatment with Whole Brain Radiation Therapy (WBRT) and a boost (if necessary) in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
  - WBRT may be used as consolidation therapy following systemic treatment or in select patients

Primary Spinal Cord Tumors

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation [4]
  - Treatment in up to 30 fractions using **IMRT or 3D-CRT**
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for tumors below the conus medullaris

Prophylactic Cranial Irradiation (PCI)

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Indications for IMRT or 3D-CRT [17]

ONLY when **ALL** the following apply:

- Diagnosis is small cell lung cancer
- The patient had a good response to initial therapy
- ECOG performance status ≤ 2

Fractionation

- Radiation therapy delivered as **WBRT**
- Treatment in up to 10 fractions

Trigeminal Neuralgia [18]

Indications for SRS

When **ONE** or more of the following apply:

- Failure of first-line medical therapy (eg, anticonvulsants)
- Patient is not a candidate for open survival intervention (eg, microvascular decompression)
- Patient cannot tolerate general anesthesia or invasive procedures due to comorbidities

Fractionation

- Treatment in 1 fraction of **SRS**

GASTROINTESTINAL CANCERS

Anal Cancer [19]

cT1-T2, cN0 with No Residual Primary Tumor after 25 Fractions of IMRT or 3D-CRT

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 25 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Carcinoid (Neuroendocrine) Tumors [20]

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for locoregional disease involving sites such as the esophagus, stomach, pancreas or rectum in a definitive or adjuvant (postoperative) setting
- Hypofractionation
  - Treatment in up to 20 fractions using **IMRT or 3D-CRT** for locoregional, oligometastatic, or oligoprogressive disease [21]

Indications for SBRT

Fractionation

- Treatment in up to 5 fractions of **SBRT** for locoregional, oligometastatic, or oligoprogressive disease

Indications for Lutetium-177-Dotatate [22]

- Lutetium-177-dotatate (Lu-177-dotate) is a radiolabeled somatostatin analog indicated for the treatment of pediatric patients aged 12-18 years and adult patients with somatostatin receptor-positive gastroenteropancreatic carcinoids (neuroendocrine tumors), including foregut, midgut, and hindgut carcinoids. Lu-177-dotatate is typically administered intravenously for up to 4 treatments.

Cholangiocarcinoma/Gallbladder Cancer [23,24]

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Hypofractionation
  - Treatment in up to 15 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for SBRT

Fractionation

- Treatment in up to 5 fractions of **SBRT** for patients with no metastatic disease

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NOTE: Cholangiocarcinoma - See **Selective** Internal Radiation Therapy (SIRT

Colon Cancer (25)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 30 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease, **ONLY** in patients meeting **ONE** of the following criteria:
    - T4 disease (tumor adherent to an adjacent structure after surgery)
    - Inoperable cancer

NOTE: Colon Cancer - See **IORT**

Esophageal Cancer (Cervical) (26,27)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease (28)

Esophageal Cancer (Thoracic) (27)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Gastric Cancer (29)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

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Hepatocellular Cancer (30)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Hypofractionation
  - Treatment in up to 15 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

NOTE: Hepatocellular carcinoma – See **Selective** Internal Radiation Therapy (SIRT

Indications for SBRT

Fractionation

- Treatment in up to 5 fractions of **SBRT** for patients with no metastatic disease

Pancreatic Cancer (31)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 31 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Hypofractionation
  - Treatment in up to 15 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
  - Treatment in up to 25 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for SBRT

Fractionation

- Treatment in up to 5 fractions of **SBRT** for patients with no metastatic disease

Rectal Cancer (31)

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Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 30 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

NOTE: Rectal Cancer – See **IORT**

GENITOURINARY CANCERS

Bladder Cancer (31)

cT2-4, cN0-3, Stage II-IVA (Organ Preservation/Nonsurgical)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment of the whole bladder (and optional boost to partial bladder along with elective treatment to the lymph nodes) in up to 37 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Hypofractionation
  - Treatment in up to 20 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Postoperative Treatment

Indications for IMRT or 3D-CRT

Following a radical cystectomy with suspected microscopic disease, positive lymph nodes, or positive margins.

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Kidney Cancer (32)

cT1, cN0, cM0, Stage I (Inoperable)

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Indications for SBRT or IMRT

Fractionation

- Hypofractionation
  - Treatment in up to 5 fractions using **SBRT or IMRT** for patients with no metastatic disease

Penile Cancer (33)

Any T, Any N, cM0, Stage I-IV (Organ Preservation/Nonsurgical)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for Brachytherapy (33)

Fractionation

- In cT1-2, cN0, cM0, stage I-IIA patients following a circumcision, monotherapy treatment using an interstitial implant in patients with no metastatic disease

Postoperative Treatment (33)

Indications for IMRT or 3D-CRT

Following a penectomy with any **ONE** of the following:

- Suspected microscopic disease
- Positive lymph nodes
- Positive margins
- Gross residual disease

Fractionation

- Conventional Fractionation
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for Brachytherapy (33)

Fractionation

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- Monotherapy treatment using an interstitial implant in cT1-2, cN0, cM0, stage I-IIA patients with no metastatic disease, following a circumcision
- Treatment using an interstitial implant in patients with a positive primary site margin and no metastatic disease, following a penectomy

Prostate Cancer

Low Risk [34,35]

Definition

Low Risk Prostate Cancer is defined as clinical Primary Tumor Stage [T] T1c-T2a, PSA < 10 ng/ml, and Grade Group 1 (Gleason score 3+3=6).

Indications for IMRT or 3D-CRT [34,35]

Fractionation

- Hypofractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Conventional Fractionation
  - For patients who are exempt from hypofractionation due to any **ONE** of the following criteria:
    - Prostate ≥ 80 grams [36]
    - History of inflammatory bowel disease (IBD) [37]
    - International Prostate Symptom Score (IPSS) ≥ 12 [38]
    - History of a prior transurethral resection of the prostate (TURP) [39]
  - Treatment
    - Treatment in up to 45 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for SBRT [35]

Fractionation

- Treatment in up to 5 fractions of **SBRT** for patients with no metastatic disease

Indications for Brachytherapy [35]

Fractionation

- Treatment with LDR or HDR brachytherapy as monotherapy for patients with no

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metastatic disease

- LDR (low dose-rate) brachytherapy options include:
  - 1 fraction of Cesium-131
  - 1 fraction of Palladium-103
  - 1 fraction of Iodine-125
- HDR (high dose-rate) brachytherapy options include:
  - 2 fractions given over 2 days using Iridium-192
  - 4 fractions given over 2 days (twice daily) using Iridium-192

Favorable/Unfavorable Intermediate Risk *(34,35)*

Definition

Favorable Intermediate Risk Prostate Cancer is defined as no high-risk or very high-risk group features, and no more than one of the following intermediate risk factors:

- Grade Group 1 (Gleason score 3+3=6) or 2 (Gleason score 3+4=7; risk factor)
- < 50% (eg, < 6 of 12) of the prostate biopsy cores contain cancer

Unfavorable Intermediate Risk Prostate Cancer is defined as no high-risk or very high-risk group features, and one or more of the following intermediate risk factors:

- Grade Group 3 (Gleason score 4+3=7)
- 2-3 intermediate risk factors, including:
  - Prostate-specific antigen (PSA) 10-20 ng/mL
  - Clinical primary tumor stage T2b-c
  - Grade Group 3 (Gleason score 4+3=7)
  - ≥ 50% of the prostate biopsy cores contain cancer (eg, ≥ 6 of 12)

Indications for IMRT or 3D-CRT

Fractionation

- Hypofractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Conventional Fractionation
  - For patients who are exempt from hypofractionation due to any **ONE** of the following criteria:

- Prostate ≥ 80 grams [36]
- History of IBD [37]
- IPSS ≥ 12 [38]
- History of a prior TURP [39]

- Treatment
  - Treatment in up to 45 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
  - Treatment in up to 35 fractions (with a simultaneous integrated micro-boost to the magnetic resonance imaging [MRI]-dominant nodules) using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for SBRT

Fractionation

- Treatment in up to 5 fractions of **SBRT** for patients with no metastatic disease

Indications for Brachytherapy

Fractionation

- Treatment with LDR or HDR brachytherapy as monotherapy for patients with no metastatic disease
  - LDR brachytherapy options include:
    - 1 fraction of Cesium-131
    - 1 fraction of Palladium-103
    - 1 fraction of Iodine-125
  - HDR brachytherapy options include:
    - 2 fractions given over 2 days using Iridium-192
    - 4 fractions given over 2 days (twice daily) using Iridium-192
- Treatment with LDR or HDR brachytherapy and a sequential SBRT boost for unfavorable intermediate risk patients with no metastatic disease

High/Very High-Risk *[34,35]*

Definition

High Risk Prostate Cancer has no very-high-risk features and at least one of the following high-risk features:

- Clinical Primary Tumor Stage T3-T4

- PSA > 20 ng/mL
- Grade Group 4 (Gleason score 8) or 5 (Gleason score 9-10)

Very High-Risk Prostate Cancer has at least one of the following very high-risk features:

- Clinical Primary Tumor Stage T3-T4
- PSA > 40 ng/mL
- Grade Group 4 (Gleason score 8) or 5 (Gleason score 9-10)

Indications for IMRT or 3D-CRT

Fractionation

- Hypofractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Conventional Fractionation
  - For patients who are exempt from hypofractionation due to any **ONE** of the following criteria:
    - The pelvic lymph node chains are included in the treatment plan [40]
    - Prostate ≥ 80 grams [36]
    - History of IBD [37]
    - IPSS ≥ 12 [38]
    - History of a TURP [39]
  - Treatment
    - Treatment in up to 45 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
    - Treatment in up to 35 fractions (with a simultaneous integrated micro-boost to the MRI-dominant nodules) using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for SBRT

Fractionation

- Treatment in up to 5 fractions of **SBRT** as monotherapy or as a sequential boost after LDR or HDR brachytherapy

Indications for Brachytherapy

Fractionation

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- With no metastatic disease
  - **IMRT or 3D-CRT** in up to 28 fractions + **LDR brachytherapy boost**. Brachytherapy boost options include:
    - 1 fraction of Cesium-131
    - 1 fraction of Palladium-103
    - 1 fraction of Iodine-125
  - **IMRT or 3D-CRT** in up to 28 fractions + **HDR brachytherapy boost**. Brachytherapy boost options include:
    - 1 fraction of Iridium-192
    - 2 fractions of Iridium-192

  NOTE: Requests for LDR brachytherapy monotherapy involving 1 fraction of Cesium-131, Iodine-125, or Palladium-103, or HDR brachytherapy involving 2 fractions of Iridium-192, for high-risk prostate cancer will be reviewed on a case-by-case basis.

Low-Volume Metastases *(35)*

Definition

Low-volume metastatic disease refers to prostate cancer that, based on conventional imaging, meets **ALL** the following criteria (per CHAARTED and STAMPEDE trial) [41,42]:

- 1-3 bone metastases (cM1b), **OR** ≥ 4 bone metastases all of which are confined to the spine and pelvis
- No visceral metastases

NOTE: Conventional imaging (CT/MRI with bone scan) remains the standard for metastatic volume classification because the pivotal trials mentioned above used these modalities. This definition does not rely on prostate-specific membrane antigen (PSMA) positron emission tomography (PET) imaging.

In contrast, high-volume metastases are defined as either of the following:

- ≥ 4 bone metastases with ≥ 1 bone metastasis beyond the spine and pelvis
- Visceral metastases (eg, lung or liver involvement)

Indications for IMRT or 3D-CRT

Fractionation

Hypofractionation

- Treatment in up to 28 fractions to the primary tumor using **IMRT or 3D-CRT**

Indications for SBRT

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Fractionation

- Treatment in up to 5 fractions to the prostate using **SBRT**

For metastasis-directed therapy (MDT), see **Treatment of Oligometastatic Disease** and **Treatment of Oligoprogressive Disease**.

Metastatic (Any T, Any N, cM1, Stage IVB) Castration-Resistant (mCRPC)

Radiopharmaceutical Therapy

Lutetium-177-PSMA-617 [35]

Lu-177-PSMA-617 is indicated for the treatment of adults with PSMA–positive mCRPC. Up to 6 fractions of Lu-177-PSMA-617 is considered medically necessary.

Radium-223 Dichloride [35]

Radium-223 dichloride is indicated for the treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases, and no known visceral metastatic disease or bulky nodal disease (> 3 cm). Up to 6 fractions of radium-223 dichloride is considered medically necessary.

Samarium-153 Lexidronam [43]

Samarium-153 lexidronam is indicated for relief of pain in patients with confirmed osteoblastic metastatic bone lesions that enhance on radionuclide bone scan. Up to 6 fractions of samarium-153 lexidronam is considered medically necessary.

Post-Prostatectomy (Adjuvant/Salvage) Radiation Therapy [35]

Definition

Post-Prostatectomy Radiation Therapy Suitable Patients are patients with no metastatic disease who require **Adjuvant Radiation** due to concerning pathologic features following a radical prostatectomy **OR Salvage Radiation** due to persistently rising/detectable PSA after a radical prostatectomy.

- Patients who require **Adjuvant Radiation** after a radical prostatectomy include those with any **ONE** of the following:
  - Extracapsular extension (pT3a disease)
  - Seminal vesicle invasion (pT3b)
  - Positive surgical margin(s)
  - Gleason score 8-10 (on either a biopsy or found at the time of surgery)
- Patients who require **Salvage Radiation** after a radical prostatectomy include those with

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either of the following:

- A PSA that was undetectable after surgery and later became detectable again and increased on 2 additional measurements
- A PSA that remained persistently detectable after surgery

Indications for Post-Prostatectomy IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT**
- Hypofractionation
  - Treatment in up to 25 fractions using **IMRT or 3D-CRT** to the prostate fossa alone

Prophylactic Breast Irradiation (For Patients Receiving Androgen Deprivation Therapy (ADT))

Indications for 2D-Conventional Radiation Therapy (2D-CRT) or 3D-CRT (44)

- Treatment in up to 5 fractions using **2D-CRT** (eg, electron beam therapy) **or 3D-CRT** for prophylactic breast irradiation in men receiving ADT, to prevent gynecomastia

Regional Disease (Any cT, cN1, cM0, Stage IVA) (35)

Definition

Regional disease refers to prostate cancer that has spread to regional lymph nodes with no nonregional lymph node (cM1a) and distant metastases (cM1b-1c) based on conventional imaging (ie, CT scan, MRI scan, or bone scan). This definition does not rely on PSMA PET imaging.

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 45 fractions using **IMRT or 3D-CRT** for patients with no distant metastatic disease (M0)
- Hypofractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT**

Testicular Cancer (45)

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NOTE: The mean dose of radiation to sensitive organs may be lower when using 3D-CRT compared to IMRT.

Pure Seminoma (Stage IA/IB)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 17 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Pure Seminoma (Stage IIA/IIB)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 17 fractions for patients using **IMRT or 3D-CRT** with 1-2 cm disease and up to 20 fractions for patients with 2-3 cm disease

Urethral Cancer (31)

cT2-T4, Any cN, cM0, Stage II-IV (Organ Preservation/Nonsurgical)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Postoperative Treatment

Indications for IMRT or 3D-CRT

Following a urethrectomy with suspected microscopic disease, positive lymph nodes, or positive margins.

Fractionation

- Conventional Fractionation
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT** for patients with no

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metastatic disease

Recurrent Disease

Indications for IMRT or 3D-CRT

For areas of gross recurrent disease.

Fractionation

- Conventional Fractionation
  - Treatment in up to 41 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

GYNECOLOGICAL CANCERS

General

NOTE: Treatment with additional fractions of **IMRT or 3D-CRT** may be approved (following manual review by a physician reviewer) in select cases including:

- **Parametrial/Pelvic Sidewall Boost** for patients with bulky parametrial/pelvic sidewall disease.
- **Lymph Node Boost** for patients with grossly positive nodal disease.
- **Gross Residual Disease Boost** for patients with gross residual disease postoperatively.

Cervical Cancer (46–48)

Postoperative (Post-hysterectomy)

Indications for IMRT or 3D-CRT and a Brachytherapy Boost

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease followed by a **brachytherapy boost** in cases of close or positive margin at the vaginal cuff with either:
    - An **HDR vaginal cuff boost** in up to 5 insertions
    - An **LDR vaginal cuff boost** in up to 2 insertions

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Intact Cervix (Nonsurgical)

Indications for IMRT or 3D-CRT and a Brachytherapy Boost

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease followed by a **brachytherapy boost** with either:
    - An **HDR boost** in up to 5 insertions
    - An **LDR boost** in up to 2 insertions

NOTE: Cervical Cancer - See **IORT**

Endometrial Cancer (48,49)

Postoperative (Post-hysterectomy) *(50,51)*

Indications for Brachytherapy Alone

Fractionation

- **HDR vaginal cuff brachytherapy** in up to 5 insertions
- **LDR vaginal cuff brachytherapy** in up to 2 insertions

Indications for IMRT or 3D-CRT and a Brachytherapy Boost

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease followed by a **brachytherapy boost** with either:
    - An **HDR vaginal cuff boost** in up to 5 insertions
    - An **LDR vaginal cuff boost** in up to 2 insertions

Nonsurgical (Inoperable)

Indications for IMRT/3D-CRT with a Brachytherapy Boost OR Brachytherapy Alone

Treatment of medically inoperable uterine cancer is determined by the risk of extrauterine spread.

Fractionation

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- IMRT or 3D-CRT with a Brachytherapy Boost
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease followed by a **brachytherapy boost** with either:
    - An **HDR boost** in up to 5 insertions
    - An **LDR boost** in up to 2 insertions
- Brachytherapy Alone
  - **HDR Brachytherapy** in up to 6 insertions
  - **LDR Brachytherapy** in up to 2 insertions

NOTE: Endometrial Cancer - See **IORT**

Vaginal Cancer (48,52)

Very Early Nonsurgical (Inoperable)

Indications for Brachytherapy Alone

Treatment of very early-stage vaginal cancers (< 5 mm) for patients with no metastatic disease

Fractionation

- Intra-cavitary HDR **brachytherapy** alone in up to 8 fractions
- Intra-cavitary LDR **brachytherapy** alone in up to 4 fractions

Nonsurgical (Inoperable)

Indications for IMRT/3RD-CRT and a Brachytherapy Boost

Treatment of vaginal cancers ≥ 5 mm for patients with no metastatic disease

Fractionation

- Conventional Fractionation
  - Treatment in up 28 fractions with **IMRT/3D-CRT** followed by:
    - **HDR brachytherapy** in up to 10 fractions
    - **LDR brachytherapy** in up to 4 fractions

Vulvar Cancer (53)

Squamous Cell Carcinoma and Adenocarcinoma

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NOTE: Brachytherapy may be approved (following manual review by a physician reviewer) when used as a boost to treat anatomically amenable primary tumors.

Nonsurgical (Inoperable)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT** for unresectable patients with gross primary vulva disease or unresectable lymph node disease with no metastatic disease

Postoperative

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with negative margins and clinically and/or radiographically uninvolved inguinofemoral nodes with no metastatic disease
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with close or positive margins with no metastatic disease
  - Treatment in up to 39 fractions using **IMRT or 3D-CRT** for patients with gross residual or unresectable disease

Melanoma

NOTE: Brachytherapy may be approved (following manual review by a physician reviewer) when used as a boost to treat anatomically amenable primary tumors.

Nonsurgical (Inoperable)

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for gross primary vulva or unresectable lymph node disease in patients with no metastatic disease

Postoperative

Indications for IMRT or 3D-CRT

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Fractionation

- Conventional Fractionation
  - Treatment in up to 30 fractions using **IMRT or 3D-CRT** for elective nodal basins or extracapsular extension in patients with no metastatic disease
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for positive margins or extracapsular extension in patients with no metastatic disease

HEAD AND NECK CANCERS

Ethmoid and Maxillary Sinus Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Postoperative Treatment

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Glottic Larynx Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - cTis-T1, cN0, cM0, Stage 0-I
    - Treatment in up to 33 fractions of **IMRT or 3D-CRT**
  - cT2-T4, cN0-N1, cM0, Stage II-IVA

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- Treatment in up to 35 fractions of **IMRT or 3D-CRT**

Postoperative Treatment

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Hypopharynx Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Postoperative Treatment

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Maxillary Sinus Tumors (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with or without metastatic disease

Postoperative Treatment

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Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Nasopharynx Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with or without metastatic disease (55)

Oral Cavity Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with cT1-4b, cN1-3, cM0, Stage I-IVB disease with no distant metastases (not any cT, any cN, cM1, Stage IVC)

    NOTE: For cT1–T2, cN0, cM0, Stage I-II simple lip lesions, see **Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC) of the Skin**.

Indications for Brachytherapy

Treatment using **brachytherapy** as monotherapy or in combination with **IMRT or 3D-CRT** for patients with no metastatic disease:

Fractionation

- LDR interstitial **brachytherapy**
  - In a single fraction as an LDR boost in combination with **IMRT or 3D-CRT** in up to 25 fractions **OR**

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- In a single fraction as LDR monotherapy

OR

- HDR interstitial **brachytherapy**
  - In 7 fractions as an HDR boost in combination with **IMRT or 3D-CRT** in up to 25 fractions **OR**
  - In 10 fractions as HDR monotherapy

Postoperative Treatment

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Oropharynx Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Postoperative Treatment

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Salivary Gland Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

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- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Postoperative Treatment

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Supraglottic Larynx Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Postoperative Treatment

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Unknown Primary Head and Neck Cancer (54)

Organ Preservation/Nonsurgical

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

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Postoperative Treatment

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

NOTE: Head and Neck cancer – See **Local** Hyperthermia

LUNG CANCER

Malignant Pleural Mesothelioma (Postoperative)

Indications for IMRT or 3D-CRT *(56)*

Fractionation

- Conventional Fractionation
  - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Non-Small Cell Lung Cancer (NSCLC) (57)

Early Stage (cT1a-T1c (≤ 3 cm), cN0, cM0, Stage I – cT2b (> 4 and ≤ 5 cm), cN0, cM0 or cT1, cN1, cM0, Stage IIA) NSCLC (Nonsurgical)

Indications for SBRT (58)

Fractionation

- Hypofractionation
  - Treatment in up to 5 fractions using **SBRT** for patients with no metastatic disease

Indications for IMRT or 3D-CRT

Fractionation

- Hypofractionation
  - Treatment in up to 15 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease (59)
- Conventional Fractionation

- Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

cT1-3, N0-1, cM0, Stage IIB-cT4, cN0, cM0, cT3-4, cN1, cM0 or any cT, cN2-3, cM0, Stage III NSCLC (Nonsurgical)

Indications for SBRT (58)

Fractionation

- Hypofractionation
  - Treatment in up to 5 fractions using SBRT for patients with cT3, cN0, cM0, Stage IIB cancers

Indications for IMRT or 3D-CRT (57,60)

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Hypofractionation (61)
  - Treatment in up to 15 fractions using **IMRT or 3D-CDT** for patients with no metastatic disease

High-Risk, pN2 NSCLC (Postoperative) (57)

NOTE*:* High-risk, pN2 disease includes extracapsular extension, multi-station nodal involvement, inadequate lymph node dissection/sampling, and/or refusal or intolerance of adjuvant systemic therapy

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Small Cell Lung Cancer (SCLC) (62)

Limited Stage (any cT, any cN, cM0, Stage I-III) SCLC (Nonsurgical)

NOTE: Treatment principles of SBRT for SCLC are like those for NSCLC

Indications for SBRT (for cT1-T2a, cNo, cM0, Stage I, cT2b, cN0, cM0, Stage IIA or cT3, cN0, cM0 Stage IIB) [57]

Fractionation

- Hypofractionation
  - Treatment in up to 5 fractions using **SBRT** for patients with tumors ≤ 5 cm

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- Hyperfractionation
  - Treatment in up to 30 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease [63]
- Hypofractionation
  - Treatment in up to 26 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease [63,64]

Limited Stage SCLC (Postoperative)

NOTE: Treatment principles for SCLC are like those for NSCLC

Indications for IMRT or 3D-CRT [57]

For postoperative patients with N1 or N2 disease.

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

NOTE: For Prophylactic Cranial Irradiation (PCI), see **PCI section of CNS tumors**.

Extensive Stage (any cT, any cN, cM1, Stage IV) SCLC

Indications for IMRT or 3D-CRT

For selected patients with complete response or good response to systemic therapy.

Fractionation

- Conventional Fractionation

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- Treatment in up to 35 fractions using **IMRT or 3D-CRT**

NOTE: For Prophylactic Cranial Irradiation (PCI), see **PCI section of CNS tumors**. (65)

LYMPHOMA

Hodgkin's Lymphoma – Involved Site Radiation Therapy Alone (66)

Indications for IMRT or 3D-CRT

Treatment using **IMRT or 3D-CRT** alone is considered medically necessary for all regions of the body.

Fractionation

- Definitive Radiation Therapy (1.5-2.0 Gy/fraction)
  - Treatment in up to 24 fractions.

    NOTE: The treatment of Hodgkin Lymphoma with radiotherapy alone is uncommon except for patients with Nodular Lymphocyte Predominant Hodgkin Lymphoma (NLPHL).
- Palliative Radiation Therapy (2.0-8.0 Gy/fraction)
  - Treatment in up to 15 fractions

Hodgkin's Lymphoma – Involved Site Radiation Therapy Combined with Chemotherapy (66)

Indications for IMRT or 3D-CRT

Treatment using **IMRT or 3D-CRT** with chemotherapy is considered medically necessary for all regions of the body.

Fractionation

- Definitive Radiation Therapy (1.5-2.0 Gy/fraction)
  - Treatment in up to 20 fractions for patients with **non-bulky disease (stage I–II),**
  - Treatment in up to 20 fractions for patients with **non-bulky disease (stage IB & IIB)**,
  - Treatment in up to 20 fractions for patients with **bulky disease (all stages),**
  - Treatment in up to 27 fractions for patients with a **partial response/refractory disease (Deauville 4–5)**,
- Palliative Radiation Therapy (2.0-8.0 Gy/fraction)

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- Treatment in up to 15 fractions

Non-Hodgkin's Lymphoma (B-cell, Non-Cutaneous) (67)

Indications for IMRT or 3D-CRT

Treatment using **IMRT or 3D-CRT** is considered medically necessary for **all regions of the body**.

Fractionation

- Definitive Radiation Therapy (1.5-2.0 Gy/fraction)
  - Treatment in up to 20 fractions for patients with stage I-II classic **Follicular Lymphoma (FL),**
  - Treatment in up to 16 fractions for patients with stage I-II non-cutaneous (either extranodal or nodal) or cutaneous **Marginal Zone Lymphoma (MZL)**,
  - Treatment in up to 24 fractions for patients for patients with stage I or stage II, nonbulky **Mantle Cell Lymphoma (MCL)**
  - Treatment in up to 33 fractions for patients with **Diffuse Large B-Cell Lymphoma (DLBCL)** with no metastatic disease
  - Treatment in up to 33 fractions for patients with **High-Grade B-cell Lymphoma (HGBL)** with no metastatic disease
  - Treatment in up to 33 fractions for patients with **Primary Mediastinal B-cell Lymphoma (PMBL)** with no metastatic disease
- Palliative Radiation Therapy (2.0-8.0 Gy/fraction)
  - Treatment in up to 15 fractions

Non-Hodgkin's Lymphoma (T-cell, Non-Cutaneous) (68)

Indications for IMRT or 3D-CRT

Treatment using **IMRT or 3D-CRT** is considered medically necessary for treating **all regions of the body**. **Fractionation**

- Definitive Radiation Therapy (1.5-2.0 Gy/fraction)
  - Treatment in up to 37 fractions for patients with **Peripheral T-Cell Lymphoma (PTCL), including Extranodal Nasal/NK T-Cell Lymphoma (ENKL;** previously known as **Lethal Midline Granuloma)** with no metastatic disease
  - Treatment in up to 24 fractions for patients with **Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) and Post-Transplant Lymphoproliferative Disorders (PTLD)** with no metastatic disease

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- Palliative Radiation Therapy (2.0-8.0 Gy/fraction)
  - Treatment in up to 18 fractions

Cutaneous Lymphomas (B/T-cell) [69]

Indications for Electrons, Low Energy X-rays, and 2/3-D CRT

Treatment using **electrons** or **low energy X-rays (eg, 50-300 kV)** is considered medically necessary for Cutaneous Lymphomas. For certain body surfaces, treatment with higher energy photon fields **(2D or 3D-CRT)** may be required.

Fractionation

- Definitive Radiation Therapy (1.5-2.0 Gy/fraction)
  - Treatment in up to 20 fractions for patients with **Mycosis Fungoides (MF) and Sezary Syndrome (SS)** with no metastatic disease
  - Treatment in up to 16 fractions for patients with **Primary Cutaneous Anaplastic Large Cell Lymphoma (PC-ALCL)** with no metastatic disease
  - Treatment in up to 16 fractions for patients with **Primary Cutaneous Follicle Center Lymphoma (PCFCL) and Primary Cutaneous Marginal Zone Lymphoma (PCMZL)** with no metastatic disease
  - Treatment in up to 37 fractions for patients with **Primary Cutaneous NK/T-Cell Lymphoma (PCNKTCL)** with no metastatic disease [70]
  - Treatment in up to 24 fractions for patients requiring **Total Skin Electron Beam Therapy (TSEBT)** for patients with no metastatic disease
  - Treatment in up to 27 fractions for patients with **Subcutaneous Panniculitis-like T-Cell Lymphoma (SPTCL)** with no metastatic disease
- Palliative Radiation Therapy (2.0-8.0 Gy/fraction)
  - Treatment in up to 15 fractions

PALLIATION OF METASTATIC CANCER

Non-Oligo Metastatic Disease

Indications for IMRT or 3D-CRT

Fractionation

- Palliative Fractionation

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- Treatment in up to 15 fractions of **IMRT or 3D-CRT** for palliative treatment to an **organ or soft tissue metastasis** (71,72)
- Treatment in up to 10 fractions of **IMRT or 3D-CRT** for palliative treatment to a non-spinal **bone** metastasis (73)
- Twice a day fractions (BID) for 2 consecutive days (4 fractions total; ie, a quad shot for one cycle with up to 3 cycles altogether) of **IMRT or 3D-CRT** for palliative treatment of metastatic **Head and Neck cancers** (71,72,74)

NOTE: Liver Metastases – see **Selective** Internal Radiation Therapy (SIRT

Spinal Bone Metastases

Indications for SBRT

There are painful spinal bone metastases

Fractionation

- Treatment in up to 5 fractions using **SBRT**

Indications for IMRT or 3D-CRT

Fractionation (73)

- Treatment in up to 15 fractions of **IMRT or 3D-CRT** for palliative treatment **to a spinal bone metastasis**

Brain Metastases

Indications for SBRT (4)

Fractionation for Non-surgical and Postoperative patients

- Treatment in 1 fraction using **SRS**
- Treatment in 2 to 5 fractions using **SBRT**

Indications for Whole Brain IMRT or 3D-CRT (4,62)

NOTE: Hippocampal avoidance (HA) WBRT using **IMRT** technique is preferred when possible.

Fractionation

- Whole brain treatment in up to 10 fractions using **IMRT or 3D-CRT**

Treatment of Oligometastatic Disease (75)

Indications for SBRT

Oligometastatic Disease (OMD) is limited metastatic disease in a patient with a total of ≤ 5 metastases present at the time of the initial cancer diagnosis or within 3 months of the initial treatment.

Fractionation

- Hypofractionation
  - Treatment in up to 5 fractions using **SBRT**

NOTE: Sufficient radiology documentation explaining the extent of the metastatic disease should be provided with a PET/CT scan report **OR** with CT and/or MRI scan reports. These scans must be performed no more than 3 months prior to the Treatment Start Date (TSD).

Treatment of Oligoprogressive Disease (75)

Indications for SBRT

Oligoprogressive Disease (OPD) is defined as the development of limited metastatic tumor progression, generally, but not always limited to, 1-5 progressing metastases anywhere in the body (non-brain) when:

- New limited metastases (or limited progression of prior metastases) have developed after an initially successful course of systemic therapy was given to a patient with metastatic disease **AND**
- The primary tumor and metastases are controlled with no progression

Fractionation

- Hypofractionation
  - Treatment in up to 5 fractions using **SBRT**

NOTE: Sufficient radiology documentation explaining the extent of the metastatic disease should be provided with a PET/CT scan report **OR** with CT and/or MRI scan reports. These scans must be recent and performed no more than 3 months prior to the TSD.

MYELOMA

Multiple Myeloma (76)

Definition

Multiple Myeloma (MM) is a plasma cell cancer that involves abnormal plasma cells in multiple locations.

Indications for IMRT or 3D-CRT

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Fractionation

- Palliative Fractionation:
  - Treatment in up to 15 fractions using **IMRT or 3D-CRT**

Solitary Plasmacytoma (76)

Definition

Solitary Plasmacytoma (SP) is a rare plasma cell cancer that involves abnormal plasma cells in one bone(solitary bone plasmacytoma) or in soft tissues with no skeletal component (extramedullary plasmacytoma) without any evidence of systemic involvement.

Indications for IMRT or 3D-CRT

Fractionation

- Conventional Fractionation:
  - Treatment in up to 25 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

NON-CANCEROUS CONDITIONS

Several non-cancerous conditions were previously discussed in several prior sections of this guideline. These include:

- Acoustic Neuroma (Vestibular Schwannoma)
- Arteriovenous Malformations
- Craniopharyngioma
- Desmoid Tumor (Aggressive Fibromatosis)
- Gynecomastia
- Pituitary Adenoma
- Trigeminal Neuralgia

For all other non-cancerous indications, refer to ***MCP 492 Radiation Therapy for Non-Oncologic Indications***

PALLIATION OF A PRIMARY TUMOR

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Indications for 3D-CRT or IMRT

Fractionation

- Palliative Fractionation
  - Treatment in up to 15 fractions of **IMRT or 3D-CRT** (to slow progression of the local disease or to palliate symptoms) for palliative treatment of a **primary tumor** (71,72)
  - For palliative treatment given in twice a day fractions (BID) for 2 consecutive days (4 fractions total; ie, a quad shot, for one cycle with up to 3 cycles altogether) of **IMRT or 3D-CRT** (74)

PEDIATRIC MALIGNANCIES

All treatments (i.e., 2D/3D-CRT, IMRT, SBRT, SRS, IORT, and Brachytherapy) will be approved for pediatric cancer patients with a radiosensitive tumor. A pediatric cancer patient is defined as ≤ 18 years old or ≤ 21 years old with cancers that display the same histology as common pediatric cancers.

Please refer to NCCN Clinical Practice Guidelines in Oncology for cancer specific information.

RE-IRRADIATION (103)

Re-irradiation is defined as the use of additional radiation treatment to treat an area of the body that has already received prior radiation to that same area.

The term "re-irradiation" does not apply to situations where a patient has received radiation treatment to one area of the body (eg, the lung) and now requires radiation to a separate area of the body (eg, the brain).

Treatments such as IMRT, IORT, Brachytherapy, SRS, SBRT, and Proton Beam Radiation Therapy are considered medically necessary for re-irradiation to decrease toxicity when normal tissue constraints cannot be met with 2D-CRT or 3D-CRT. The radiation dose and the number of fractions prescribed for each patient receiving re-irradiation will be based on the patient's prior treatment history. The dose and number of fractions will be left to the discretion of the treating physician and, when possible, be based on peer-reviewed literature.

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SARCOMA

Desmoid Tumors (Aggressive Fibromatosis)

Indications for IMRT or 3D-CRT *(104)*

Fractionation

- Conventional Fractionation
  - Treatment in up to 31 fractions using **IMRT or 3D-CRT**

Kaposi Sarcoma

Indications for 2D-CRT (including Electron Beam Therapy, Superficial Radiation Therapy, or Orthovoltage Radiational Therapy), 3D-CRT External Beam Radiation Therapy, or IMRT *(105)*

Fractionation

- Treatment in up to 20 fractions using **2D-CRT** (including Electron Beam Therapy, Superficial Radiation Therapy, or Orthovoltage Radiation Therapy)**, 3D-CRT external beam radiation therapy, or IMRT**

Retroperitoneal/Abdominal Sarcoma (Preoperative)

Indications for IMRT or 3D-CRT *(104)*

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Retroperitoneal Sarcoma - See section on **IORT**

Soft Tissue Sarcoma: Extremity/Body Wall/Head and Neck

Pre-Operative

Indications for IMRT and 3D-CRT **(104,106)**

Fractionation

- Conventional Fractionation
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

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NOTE: Treatment with additional fractions as a boost of **IMRT or 3D-CRT** may be approved (following manual review by a physician reviewer) in select cases with positive margins.

Post-Operative

Indications for IMRT or 3D-CRT [104]

Fractionation

- Conventional Fractionation
  - For patients with an **R0 resection,** treatment in up to 33 fractions (which is the sum of 28 fractions using **IMRT or 3D-CRT** followed by a boost of 5 fractions **using IMRT or 3D-CRT**) for patients with no metastatic disease
  - For patients with an **R1 resection**, treatment in up to 37 fractions (which is the sum of 28 fractions using **IMRT or 3D-CRT** followed by a boost of 9 fractions using **IMRT or 3D-CRT**) for patients with no metastatic disease

Indications for Brachytherapy [104]

Fractionation

- For positive margins (treatment with a combined modality approach)
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** and a boost using a single fraction of **LDR brachytherapy**
  - Treatment in up to 28 fractions using **IMRT or 3D-CRT** and a boost of up to 10 fractions using **HDR brachytherapy**
- For negative margins (treatment with a brachytherapy alone approach)
  - Treatment using 1 fraction of **LDR brachytherapy**
  - Treatment using up to 10 fractions of **HDR brachytherapy**

Unresectable

Indications for IMRT or 3D-CRT [104]

Fractionation

- Conventional Fractionation
  - Treatment in up to 45 fractions using **IMRT or 3D-CRT** for patients with unresectable, non-metastatic disease

NOTE: Soft Tissue Sarcoma - See section on **IORT**

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SKIN CANCERS

Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC)

Indications for Electron Beam Therapy (2D-CRT) or 3D-CRT for Patients with No Metastatic Disease *(107–109)*

Definitive Treatment of Primary Tumor ± Regional Lymph Nodes (No Resection of Primary Tumor and No Lymph Node Dissection)

- Conventional Fractionation or Hypofractionation
  - Treatment in up to 35 fractions using **Electron Beam Therapy (2D-CRT) or 3D-CRT** for patients with no metastatic disease

Adjuvant External Beam Radiotherapy to Primary Tumor Bed ± Regional Lymph Nodes After Resection of Primary Tumor ± Lymph Node Dissection

- Conventional Fractionation
  - **Negative Margins, No Extranodal Extension**
    - Treatment in up to 30 fractions using **2D-CRT or 3D-CRT** for patients with no metastatic disease
  - **Microscopic Residual Disease or Perineural Tumor Spread**
    - Treatment in up to 33 fractions using **2D-CRT or 3D-CRT** for patients with no metastatic disease
  - **Gross Residual Disease**
    - Treatment in up to 35 fractions using 2D-CRT or 3D-CRT for patients with no metastatic disease

Indications for 2D-CRT (Superficial Radiation or Orthovoltage Radiation Therapy) *(110)*

Fractionation

- **Definitive Treatment**
  - Hypofractionation
    - Treatment in up to 25 fractions using a **Superficial Radiation Therapy (50-150 kV)**, or an **Orthovoltage Radiation Therapy (151-500 kV) device** for patients with no metastatic disease

Indications for HDR Brachytherapy with Iridium-192 *(107,108,111)*

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Fractionation

- Hypofractionation
  - Treatment in up to 16 fractions using **HDR brachytherapy** with Iridium-192 for patients with no metastatic disease

NOTE: The use of electronic brachytherapy (50-100 kV) is considered investigational and not medically necessary. (108,109)

Indications for IMRT (108,109)

Treatment using **IMRT** is considered medically necessary ONLY when the treatment includes a lymph node chain.

Fractionation

- Conventional Fractionation
  - Treatment in up to 35 fractions using **IMRT** for patients with no metastatic disease

NOTE: Basal Cell and Squamous Cell Skin Cancers - See section on **Local** Hyperthermia

Dermatofibrosarcoma Protuberans (DFSP)

Indications for 3D-CRT or 2D-CRT (Electron Beam Therapy, Superficial Radiation Therapy, or Orthovoltage Radiation Therapy) (112)

Fractionation

- Adjuvant Treatment
  - Conventional Fractionation
    - Treatment in up to 33 fractions for positive margins or gross tumor using **3D-CRT or 2D-CRT (Electron Beam Therapy)**

Melanoma of the Skin and Eye (Uveal)

Indications for 3D-CRT or 2D-CRT (Electron Beam Therapy, Superficial Radiation Therapy, or Orthovoltage Radiation Therapy) to the Skin (113)

Fractionation

- **Definitive Treatment**
  - Conventional Fractionation

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        - For patients with unresectable disease, Treatment in up to 35 fractions using **3D-CRT** or **2D-CRT (Electron Beam Therapy)** for patients with unresectable, non-metastatic disease
    - Hypofractionation
        - Treatment in up to 28 fractions using **3D-CRT or 2D-CRT (Electron Beam Therapy)** for patients with no metastatic disease
- **Adjuvant Treatment**
    - Conventional Fractionation
        - Treatment in up to 33 fractions using **3D-CRT or 2D-CRT (Electron Beam Therapy)** for patients with no metastatic disease
    - Hypofractionation
        - Treatment in up to 20 fractions using **3D-CRT or 2D-CRT (Electron Beam Therapy)** for patients with no metastatic disease

Indications for IMRT *(113)*

Treatment using **IMRT** is considered medically necessary ONLY when the treatment includes a lymph node chain.

Fractionation

- Conventional Fractionation
    - Treatment in up to 33 fractions using **IMRT** for patients with no metastatic disease
- Hypofractionation
    - Treatment in up to 20 fractions using **IMRT** for patients with no metastatic disease

NOTE: Melanoma of the Skin - See section on **Local** Hyperthermia

Indications for Brachytherapy to the Eye (Uveal) *(114)*

Fractionation

- Treatment using 1 fraction of plaque brachytherapy for patients with no metastatic disease

Merkel Cell Carcinoma (MCC)

Indications for 3D-CRT, or 2D-CRT (Electron Beam Therapy) *(115)*

Fractionation

- **Definitive Treatment**

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- Treatment in up to 30 fractions using **3D-CRT or 2D-CRT (Electron Beam Therapy)** for non-metastatic patients that are postoperative or have unresectable disease

- **Adjuvant Treatment**
  - Treatment in up to 28 fractions using **3D-CRT or 2D-CRT (Electron Beam Therapy)** for patients with negative surgical margins and non-metastatic disease
  - Treatment in up to 30 fractions using **3D-CRT or 2D-CRT (Electron Beam Therapy)** for patients with microscopically or grossly positive surgical margins and non-metastatic disease

Indications for IMRT [115]

Treatment using **IMRT** is considered medically necessary ONLY when the treatment includes a lymph node chain.

Fractionation

- Definitive Treatment
  - Treatment in up to 30 fractions using **IMRT** for patients with no metastatic disease

THYMOMAS AND THYMIC CARCINOMAS

Indications for IMRT or 3D-CRT [116]

Fractionation

- **Definitive Treatment**
  - Conventional Fractionation
    - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease.
- **Adjuvant Treatment**
  - Conventional Fractionation
    - Following an **R0 resection** with negative or close margins, treatment in up to 25 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
    - Following an **R1 resection** with microscopically positive margins, treatment in up to 27 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
    - Following an **R2 resection** with grossly positive margins, treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

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THYROID CARCINOMA

Anaplastic Thyroid Cancer

Indications for IMRT or 3D-CRT *(117)*

Fractionation

- **Salvage treatment following an R2 resection or inoperable patient**
  - Conventional Fractionation
    - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for gross disease in patients with no metastatic disease
    - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for microscopic disease in patients with no metastatic disease
- **Postoperative treatment following an R0 resection or R1 resection**
  - Conventional Fractionation
    - Treatment in up to 33 fractions using **IMRT or 3D-CRT** for microscopic disease in patients with no metastatic disease

Differentiated, Medullary or Poorly Differentiated (Non-Anaplastic) Thyroid Cancer

Indications for IMRT or 3D-CRT *(117)*

Fractionation

- **Unresectable disease**
  - Conventional Fractionation
    - Treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
- **Postoperative Disease**
  - Conventional Fractionation
    - Following an **R1 resection** with microscopically positive margins, treatment in up to 33 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease
    - Following an **R2 resection** with grossly positive margins, treatment in up to 35 fractions using **IMRT or 3D-CRT** for patients with no metastatic disease

Indications for Sodium Iodine-131

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Sodium iodine-131 is used to treat select cases of well-differentiated follicular carcinoma and papillary carcinoma for [118]:

- Remnant ablation of cT1b-T2 (1.1-4.0 cm with minor extrathyroidal extension), cN0-N1a with fewer than 5 lymph node metastases < 2 mm in diameter, cM0 (no distant metastasis) disease **OR**
- Adjuvant therapy for a higher likelihood of residual disease based on operative pathology or pretherapy radioiodine scan **OR**
- Treatment of known disease consisting of proven unresectable or metastatic disease based on pathology or pretherapy radioiodine scan

  NOTE: One sodium iodine-131 treatment is considered medically necessary

UNIQUE TREATMENT MODALITIES

Local Hyperthermia with Radiation Therapy

Indications

Up to 10 local hyperthermia treatments are considered medically necessary when used in connection with radiation therapy for **ANY** of the following indications [113]:

- Primary or metastatic cutaneous or subcutaneous superficial malignancies **OR**
- A chest wall recurrence of breast cancer [119] **OR**
- Recurrent cervical lymph node metastases from head and neck cancer [120]

Intraoperative Radiation Therapy (IORT)

Indications for IORT

- For the treatment of **Breast Cancer**, Intraoperative Radiation Therapy is reviewed on a case-by-case basis. IORT is considered not medically necessary when electronic brachytherapy (50-100 kV) is used. [2]
- For the treatment of **Cervical and Uterine Cancers** in 1 fraction only in the following scenarios [49,52,121]:
  - Unresectable disease **OR**
  - Residual disease (including positive margins) following surgery **OR**
  - Recurrent disease
- For the treatment of **Colon and Rectal Cancers** in 1 fraction only in the following scenarios [25,122]:

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- Unresectable disease **OR**
- Residual disease (including positive margins) following surgery **OR**
- Recurrent disease **OR**
- Initial treatment of T4 tumors penetrating a fixed structure

- For the treatment of **Soft Tissue & Retroperitoneal Sarcoma** in 1 fraction only in the following scenarios [104]:
  - Residual disease (including positive margins) following surgery **OR**
  - Recurrent disease

Selective Internal Radiation Therapy (SIRT)

Indications for SIRT

For Selective Internal Radiation Therapy (SIRT) utilizing yttrium-90 (90Y) microspheres (TheraSphere, SIR-Spheres, or QuiremSpheres) to treat hepatocellular cancer please refer to ***MCP 181 Radioembolization (Selective Internal Radiation Therapy) for Liver Tumors.***

The use of SIRT for the treatment of all other conditions is considered investigational and not medically necessary.

CODING AND STANDARDS

Codes

Code	Description
C2616	Brachytherapy source, nonstranded, yttrium-90, per source
G0562	Therapeutic radiology simulation-aided field setting; complex, including acquisition of PET and CT imaging data required for radiopharmaceutical-directed radiation therapy treatment planning (i.e., modeling)
G0563	Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance and real-time positron emissions-based delivery adjustments to 1 or more lesions, entire course not to exceed 5 fractions

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Code	Description
G0339	Image guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session or first session of fractionated treatment
G0340	Image guided robotic linear accelerator-based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, second through fifth sessions, maximum five sessions per course of treatment
G0458	Low dose rate (LDR) prostate brachytherapy services, composite rate
0395T	High dose rate electronic brachytherapy, interstitial or intracavitary treatment, per fraction, includes basic dosimetry, when performed
19296	Placement of radiotherapy afterloading expandable catheter (single or multichannel) into the breast for interstitial radioelement application following partial mastectomy, includes imaging guidance; on date separate from partial mastectomy
19298	Placement of radiotherapy after loading brachytherapy catheters (multiple tube and button type) into the breast for interstitial radioelement application following (at the time of or subsequent to) partial mastectomy, includes imaging guidance
20555	Placement of needles or catheters into muscle and/or soft tissue for subsequent interstitial radioelement application (at the time of or subsequent to the procedure)
31643	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with placement of catheter(s) for intracavitary radioelement application
32701	Thoracic target(s) delineation for stereotactic body radiation therapy (SRS/SBRT), (photon or particle beam), entire course of treatment
41019	Placement of needles, catheters, or other device(s) into the head and/or neck region (percutaneous, transoral, or transnasal) for subsequent interstitial radioelement application
43499	Unlisted procedure, esophagus
47999	Unlisted procedure, biliary tract

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Code	Description
55860	Exposure of prostate, any approach, for insertion of radioactive substance;
55862	Exposure of prostate, any approach, for insertion of radioactive substance; with lymph node biopsy(s) (limited pelvic lymphadenectomy)
55865	Exposure of prostate, any approach, for insertion of radioactive substance; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric and obturator nodes
55875	Transperineal placement of needles or catheters into prostate for interstitial radioelement application, with or without cystoscopy
55899	Unlisted procedure, male genital system
55920	Placement of needles or catheters into pelvic organs and/or genitalia (except prostate) for subsequent interstitial radioelement application
57155	Insertion of uterine tandem and/or vaginal ovoids for clinical brachytherapy
57156	Insertion of a vaginal radiation afterloading apparatus for clinical brachytherapy
58346	Insertion of Heyman capsules for clinical brachytherapy
61796	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 simple cranial lesion
61798	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 complex cranial lesion
63620	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); 1 spinal lesion
67218	Destruction of localized lesion of retina (e.g., macular edema, tumors), 1 or more sessions; radiation by implantation of source (includes removal of source)
76145	Medical physics dose evaluation for radiation exposure that exceeds institutional review threshold, including report

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Code	Description
76873	Ultrasound, transrectal; prostate volume study for brachytherapy treatment planning (separate procedure)
76965	Ultrasonic guidance for interstitial radioelement application
77011	Computed tomography guidance for stereotactic localization
77261	Therapeutic radiology treatment planning; simple
77262	Therapeutic radiology treatment planning; intermediate
77263	Therapeutic radiology treatment planning; complex
77280	Therapeutic radiology simulation-aided field setting; simple
77285	Therapeutic radiology simulation-aided field setting; intermediate
77290	Therapeutic radiology simulation-aided field setting; complex
77295	3-dimensional radiotherapy plan, including dose-volume histograms
77299	Unlisted procedure, therapeutic radiology clinical treatment planning
77300	Basic radiation dosimetry calculation, central axis depth dose calculation, TDF, NSD, gap calculation, off axis factor, tissue inhomogeneity factors, calculation of non-ionizing radiation surface and depth dose, as required during course of treatment, only when prescribed by the treating physician
77301	Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications
77306	Teletherapy isodose plan; simple (1 or 2 unmodified ports directed to a single area of interest), includes basic dosimetry calculation(s)
77307	Teletherapy isodose plan; complex (multiple treatment areas, tangential ports, the use of wedges, blocking, rotational beam, or special beam considerations), includes basic dosimetry calculation(s)
77316	Brachytherapy isodose plan; simple (calculation[s] made from 1 to 4 sources, or remote afterloading brachytherapy, 1 channel), includes basic dosimetry calculation(s)

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Code	Description
77317	Brachytherapy isodose plan; intermediate (calculation[s] made from 5 to 10 sources, or remote afterloading brachytherapy, 2-12 channels), includes basic dosimetry calculation(s)
77318	Brachytherapy isodose plan; complex (calculation[s] made from over 10 sources, or remote afterloading brachytherapy, over 12 channels), includes basic dosimetry calculation(s)
77321	Special teletherapy port plan, particles, hemibody, total body
77331	Special dosimetry (e.g., TLD, microdosimetry) (specify), only when prescribed by the treating physician
77332	Treatment devices, design and construction; simple (simple block, simple bolus)
77333	Treatment devices, design and construction; intermediate (multiple blocks, stents, bite blocks, special bolus)
77334	Treatment devices, design and construction; complex (irregular blocks, special shields, compensators, wedges, molds or casts)
77336	Continuing medical physics consultation, including assessment of treatment parameters, quality assurance of dose delivery, and review of patient treatment documentation in support of the radiation oncologist, reported per week of therapy
77338	Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan
77370	Special medical radiation physics consultation
77371	Radiation treatment delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; multi-source Cobalt 60 based
77372	Radiation treatment delivery, stereotactic radiosurgery (SRS), complete course of treatment of cranial lesion(s) consisting of 1 session; linear accelerator based

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Code	Description
77373	Stereotactic body radiation therapy, treatment delivery, per fraction to 1 or more lesions, including image guidance, entire course not to exceed 5 fractions
77387	Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed
77399	Unlisted procedure, medical radiation physics, dosimetry and treatment devices, and special services
77402	Radiation treatment delivery; Level 1 (e.g., single-electron field, multiple-electron fields, or 2D photons), including imaging guidance, when performed
77407	Radiation treatment delivery; Level 2, single-isocenter (e.g., 3D or IMRT), photons, including imaging guidance, when performed
77412	Radiation treatment delivery; Level 3, multiple isocenters with photon therapy (e.g., 2D, 3D, or IMRT) or a single-isocenter photon therapy (e.g., 3D or IMRT) with active motion management, or total skin electrons, or mixed-electron/photon field(s), including imaging guidance, when performed
77417	Therapeutic radiology port image(s)
77424	Intraoperative radiation treatment delivery, x-ray, single treatment session
77425	Intraoperative radiation treatment delivery, electrons, single treatment session
77427	Radiation treatment management, 5 treatments
77431	Radiation therapy management with complete course of therapy consisting of 1 or 2 fractions only
77432	Stereotactic radiation treatment management of cranial lesion(s) (complete course of treatment consisting of 1 session)
77435	Stereotactic body radiation therapy, treatment management, per treatment course, to 1 or more lesions, including image guidance, entire course not to exceed 5 fractions

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Code	Description
77436	Surface radiation therapy; superficial or orthovoltage, treatment planning and simulation-aided field setting
77437	Surface radiation therapy; superficial, delivery, ≤150 kV, per fraction (e.g., electronic brachytherapy)
77438	Surface radiation therapy; orthovoltage, delivery, >150-500 kV, per fraction
77469	Intraoperative radiation treatment management
77470	Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation)
77499	Unlisted procedure, therapeutic radiology treatment management
77600	Hyperthermia, externally generated; superficial (ie, heating to a depth of 4 cm or less)
77605	Hyperthermia, externally generated; deep (i.e., heating to depths greater than 4 cm)
77610	Hyperthermia generated by interstitial probe(s); 5 or fewer interstitial applicators
77615	Hyperthermia generated by interstitial probe(s); more than 5 interstitial applicators
77620	Hyperthermia generated by intracavitary probe(s)
77750	Infusion or instillation of radioelement solution (includes 3-month follow-up care)
77761	Intracavitary radiation source application; simple
77762	Intracavitary radiation source application; intermediate
77763	Intracavitary radiation source application; complex
77767	Remote afterloading high dose rate radionuclide skin surface brachytherapy, includes basic dosimetry, when performed; lesion diameter up to 2.0 cm or 1 channel

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Code	Description
77768	Remote afterloading high dose rate radionuclide skin surface brachytherapy, includes basic dosimetry, when performed; lesion diameter over 2.0 cm and 2 or more channels, or multiple lesions
77770	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 1 channel
77771	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 2-12 channels
77772	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; over 12 channels
77778	Interstitial radiation source application, complex, includes supervision, handling, loading of radiation source, when performed
77789	Surface application of low dose rate radionuclide source
77790	Supervision, handling, loading of radiation source
77799	Unlisted procedure, clinical brachytherapy
+19294	Preparation of tumor cavity, with placement of a radiation therapy applicator for intraoperative radiation therapy (IORT) concurrent with partial mastectomy (List separately in addition to code for primary procedure)
+19297	Placement of radiotherapy afterloading expandable catheter (single or multichannel) into the breast for interstitial radioelement application following partial mastectomy, includes imaging guidance; concurrent with partial mastectomy (List separately in addition to code for primary procedure)
+61797	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional cranial lesion, simple (List separately in addition to code for primary procedure)

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Code	Description
+61799	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional cranial lesion, complex (List separately in addition to code for primary procedure)
+61800	Application of stereotactic headframe for stereotactic radiosurgery (List separately in addition to code for primary procedure)
+63621	Stereotactic radiosurgery (particle beam, gamma ray, or linear accelerator); each additional spinal lesion (List separately in addition to code for primary procedure)
+77293	Respiratory motion management simulation (List separately in addition to code for primary procedure)
+77439	Surface radiation therapy; superficial or orthovoltage, image guidance, ultrasound for placement of radiation therapy fields for treatment of cutaneous tumors, per course of treatment (List separately in addition to code for primary procedure)

BACKGROUND

Radiation Oncology is the specialty of medicine that utilizes high-energy ionizing radiation in the treatment of malignant neoplasms and certain non-malignant conditions. Radiation Oncology uses several distinct therapeutic modalities: teletherapy, EBRT (2D-CRT or 3D-CRT) IMRT, brachytherapy, hyperthermia, proton beam therapy, carbon ion therapy, neutron beam therapy, and SBRT.

Radiation Therapy Treatment Process:

- Consultation
- Simulation
- Treatment Planning
- Treatment Delivery

SUMMARY OF EVIDENCE (8,106,124)

3D-CRT: This technique uses imaging to create a three-dimensional representation of the tumor, allowing for precise targeting of radiation. It is particularly useful for treating tumors in

complex areas like the brain and spinal cord, where precision is crucial to minimize damage to surrounding healthy tissue.

IMRT: IMRT is an advanced form of 3D-CRT that modulates the intensity of the radiation beams. This allows for even more precise targeting, which is beneficial for tumors located near sensitive structures. IMRT is commonly used for head and neck cancers, prostate cancer, and certain types of brain tumors.

SRS and SBRT: These techniques deliver high doses of radiation in fewer sessions. SRS is typically used for brain tumors, while SBRT is used for tumors in the body, such as lung and liver cancers. The high precision of these methods reduces the risk of damage to surrounding tissues.

Brachytherapy: This involves placing radioactive sources directly into or near the tumor. It is often used for prostate cancer, cervical cancer, and certain types of breast cancer. Brachytherapy allows for high doses of radiation to be delivered to the tumor while sparing surrounding healthy tissue.

IORT: IORT is administered during surgery, allowing for direct application of radiation to the tumor site. This technique is beneficial for certain types of cancers, such as pancreatic and colorectal cancers, where it can help to control local disease.

Hypofractionation and Hyperfractionation: Hypofractionation involves delivering larger doses of radiation over fewer sessions, while hyperfractionation involves smaller doses over more sessions. These approaches can be tailored to the specific needs of the patient and the type of cancer being treated.

ANALYSIS OF EVIDENCE (8,106,124)

Breast Cancer

Breast cancer is the most frequently diagnosed cancer among women globally. An estimated 2.3 million new cases were reported in 2020. (1) The incidence rates vary by region, with higher rates in developed countries due to better screening and diagnostic practices.

The survival rates for breast cancer have improved significantly over the years, thanks to advancements in early detection and treatment (1):

- Early-Stage Breast Cancer: The 5-year survival rate for localized breast cancer (cancer that has not spread beyond the breast) is about 99%.
- Regional Breast Cancer: When the cancer has spread to nearby lymph nodes, the 5-year survival rate drops to approximately 86%.

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- Distant Breast Cancer: For metastatic breast cancer (cancer that has spread to other parts of the body), the 5-year survival rate is around 28%.

Accelerated PBI is recommended for its shorter treatment duration, which can improve patient convenience and adherence to therapy. It is suitable for patients with low-risk, early-stage breast cancer. [2,3] Techniques such as brachytherapy and EBRT have been used effectively in APBI. [2,3]

Electronic brachytherapy recommendations for its use are weak based upon lack of long term data from reputable studies and the concern for delivery of the dose covering the entire clinical target volume. Studies indicate that at 1 cm from the applicator, the dose of electronic brachytherapy is 28%, whereas when compared to 100% with high dose rate which is prescribed to 1 cm. [3] Electronic brachytherapy treatment is currently considered investigational and experimental.

IMRT is recommended for its precision in delivering radiation doses, which helps in sparing surrounding healthy tissues and reducing side effects. This is particularly useful for patients with complex anatomy or those requiring treatment of the internal mammary lymph nodes. [8]

IORT is used to deliver a concentrated dose of radiation during surgery, which can be beneficial for patients who may have difficulty completing a full course of external beam radiation therapy. It may be useful for patients with early-stage breast cancer. [2,3]

However, IORT alone is associated with higher ipsilateral breast recurrence (IBR) rates compared to whole breast irradiation (WBI). [2,3,125]

The ELIOT Trial evaluated electron IORT (IOERT) and found that it had inferior IBTR rates compared to WBI with a boost. The 15-year IBTR rate was 12.6% for IOERT versus 2.4% for WBI. [8] The TARGIT-A Trial assessed low-energy photon IORT (kV IORT) and found that it was associated with a higher IBTR rate compared to WBI. The 5-year IBTR rate was 3.3% for kV IORT versus 1.3% for WBI. [8] Currently, the use of IORT in the treatment of breast cancer is not recommended.

AccuBoost is a non-invasive, image-guided form of brachytherapy used to deliver targeted radiation to treat early-stage breast cancer after a lumpectomy. The technique uses a mammography platform to immobilize the breast and pinpoint the treatment area. It uses an HDR Ir-192 source via specialized external applicators, unlike other types of brachytherapy that require catheters or balloons to be implanted in the breast. In a registry study of 154 patients, the authors concluded that "longer follow up is needed to confirm late end points." [126] AccuBoost treatment is considered investigational and experimental. [3]

SBRT

To date, there have been no published phase III randomized clinical trials of SBRT for the treatment of breast cancer. Study data is limited to several phase I-II trials. SBRT is not recommended for treatment of non-metastatic breast cancer. [127–129]

CNS Tumors

The incidence of CNS cancers varies globally, with an estimated 3-5 cases per 100,000 people annually. The most common types of CNS cancers include gliomas, meningiomas, and pituitary tumors. Gliomas, which arise from glial cells, are the most common primary brain tumors and include subtypes such as astrocytomas, oligodendrogliomas, and glioblastomas. [4,10,11]

Survival rates for CNS cancers depend on several factors, including the type of tumor, its location, the patient's age, and the extent of surgical resection. Here are some key points [4,10,11]:

- Glioblastomas are the most aggressive and common type of primary brain tumors in adults. The median survival rate for glioblastoma patients is approximately 12-15 months, with a 5-year survival rate of less than 5%.
- Astrocytomas and Oligodendrogliomas tumors have better prognoses compared to glioblastomas. The 5-year survival rate for low-grade astrocytomas is around 40-60%, while for oligodendrogliomas, it can be as high as 70-90% depending on the grade and molecular characteristics.
- Meningiomas are generally benign tumors with a high survival rate. The 5-year survival rate for benign meningiomas is over 90%, while atypical and malignant meningiomas have lower survival rates, around 50-70%.
- Medulloblastomas common in children, these tumors have a 5-year survival rate of about 70-80% with current treatment protocols.
- Primary CNS Lymphomas have a variable prognosis, with a 5-year survival rate ranging from 20-40% depending on the patient's response to treatment.

Several factors influence the survival rates of CNS cancer patients [4,10,11]:

- Age: Younger patients generally have better survival rates
- Tumor Grade: Lower-grade tumors have better prognoses
- Extent of Resection: Complete surgical resection often leads to better outcomes

Molecular Markers: Certain genetic mutations and molecular markers can influence prognosis and treatment response

Adjuvant Radiation Therapy

For patients with high-risk features, adjuvant radiation therapy is recommended to improve local control and survival outcomes. The guidance emphasizes the importance of advanced radiation techniques to minimize long-term adverse effects. [6,14] Dose recommendations are based on histology and grade, ensuring that the radiation dose is optimized for maximum effectiveness while minimizing toxicity. [6,14]

Adjuvant radiation therapy combined with chemotherapy is recommended for high-risk grade 2 gliomas and grade 3 gliomas to improve overall survival (OS) and progression-free survival (PFS). [4,5,13]

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A clinical trial evaluated the use of 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) and/or radiotherapy in patients with histologically confirmed anaplastic glioma. The trial included 303 patients divided into four groups. Patients receiving radiotherapy had a median survival of 36 weeks, significantly higher than the 14 weeks for those receiving best conventional care. The combination of BCNU and radiotherapy resulted in a median survival of 34.5 weeks. [130]

A randomized phase III trial by the European Organization for Research and Treatment of Cancer (EORTC) and National Cancer Institute of Canada Clinical Trials Group (NCIC) reported improved median and 2-year survival for patients with glioblastoma treated with concomitant and adjuvant temozolomide and radiotherapy. [131] Overall, the survival rate was 27.2% at 2 years, 16.0% at 3 years, 12.1% at 4 years, and 9.8% at 5 years with temozolomide. However, the survival rates with radiotherapy alone were 10.9%, 4.4%, 3.0%, and 1.9%.

Brachytherapy

GammaTile brachytherapy is recommended for recurrent glioblastomas due to its ability to provide high local control rates and favorable survival outcomes. The treatment involves the placement of radioactive seeds within the tumor bed, delivering a high dose of radiation directly to the tumor while sparing surrounding healthy tissue. [7,10,12] The safety profile of GammaTile brachytherapy is comparable to other treatment options, with low rates of complications and adverse effects. [7,10,12]

Brachytherapy has shown mixed results in treating cystic craniopharyngiomas (CPs). The 1-year, 2-3 years, and 5-year PFS rates are 75%, 62%, and 57%, respectively. [11]

Brachytherapy is more effective for cystic components but may not be suitable for tumors with solid components. [10]

IMRT

The use of advanced radiation techniques such as IMRT is recommended to minimize exposure to healthy brain tissue and reduce the risk of long-term side effects. [14]

SRS and Fractionated Stereotactic Radiosurgery (FSRT)

Hypofractionated SRS for intracranial arteriovenous malformations (AVMs) has shown high rates of radiation necrosis, especially with larger intracranial AVM volumes. This necrosis can lead to significant complications and is a major concern when using high-dose radiation. [5]

For large tumors, single-fraction SRS is not recommended due to the increased risk of radiation-induced edema and necrosis. FSRT is preferred in such cases. [4] For larger vestibular schwannomas, single-fraction SRS is not recommended due to the higher risk of complications. Fractionated approaches are preferred to reduce the risk of adverse effects. [7] SRS for pituitary tumors and caution should be used for lesions larger than 2.5-3 cm or involving the anterior optic pathway. [12]

Some radiation therapies, such as single-dose radiosurgery, may not provide adequate tumor control for certain types of CNS cancers. For example, craniopharyngiomas with cystic components may not respond well to single-dose treatments, leading to incomplete tumor control and the need for additional interventions. [9]

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Gastrointestinal Cancers

Gastrointestinal cancers involve malignant lesions in the esophagus, stomach, intestines, and accessory organs such as the liver, gall bladder, and pancreas. The incidence of gastric cancer varies globally, with higher rates observed in Eastern Asia, Central and Eastern Europe, and South America. In 2020, there were more than 1 million new cases globally, resulting in approximately 768,793 deaths. [29] Colorectal cancer is one of the most commonly diagnosed cancers worldwide, with an estimated 1.4 million cases and nearly 700,000 deaths in 2012. [132] Pancreatic cancer incidence is also high, with fewer than 20% of patients presenting with tumors amenable to resection. [133] In contrast, the incidence of biliary tract cancers is low, accounting for less than 1% of all human cancers. [134] In the United States, the incidence rate of invasive anal carcinoma is rising, showing an increase of approximately 1.9-fold for males and 1.5-fold for females between 1973-1979 and 1994-2000, which have continued to rise since then, [17] particularly in patients aged 50 years and older. [135]

Survival rates for gastrointestinal cancers are also variable and heavily dependent upon disease location and progression. OS rates for esophageal cancer have risen from 5% in 1970 to 12% in 2010 and currently stand at ~22%. [136] The 5-year survival rate for esophageal cancer varies depending on the stage at diagnosis. For localized disease, the 5-year survival rate is approximately 47%, while for regional disease, it is around 25%. For distant metastatic disease, the 5-year survival rate drops to about 5%. [27] For localized gastric cancer, survival rates are significantly better, with the 5-year survival rate being ~90%, though the rate drops to ~71% and 14% for regional and distance metastatic disease, respectively. [29] For anal cancer, patients with localized disease have an 80% 5-year survival rate, those with regional lymph node involvement have a 60% 5-year survival rate, and those with distant metastasis have a 30.5% 5-year survival rate. [17] In contrast, the 5-year overall rate for pancreatic cancer is typically less than 25% for patients with localized disease. [133]

IMRT

IMRT allows for detailed beam shaping to target specific volumes and limit the exposure of normal tissue has been shown to improve local control and reduce the rates of adverse gastrointestinal effects compared to conventional radiation and is therefore preferred over 3D-CRT for most gastrointestinal cancers, including esophageal, [27,136] gastric, [29,137] pancreatic, [133,138] colorectal, [25,122,132,139] liver, cholangiocarcinoma, and anal [17] cancers.

SBRT

SBRT is increasingly studied for its high local control rate, especially in cases where surgery is not feasible (ie, unresectable tumors), and is recommended for patients with liver cancer, particularly intrahepatic cholangiocarcinoma (iCCA) and patients who are contraindicated to surgery, as it offers a high local control rate and can also be used in the palliative setting. [24,30,134,140] SBRT is not recommended for colon, rectal, or anal cancer patients with extensive disease or those who cannot meet normal organ constraints. [25,132] IORT is, however, indicated for the treatment of pancreatic, cholangiocarcinoma, and liver cancers.

Brachytherapy

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Brachytherapy as a primary treatment modality for esophageal [27] and anal [17,135,136] cancers is not recommended due to insufficient evidence demonstrating its benefit.

IORT

IORT is not recommended for esophageal, [136] pancreatic, liver, cholangiocarcinoma, and pancreatic cancers due to a lack of clear evidence demonstrating its benefit. IORT is, however, indicated for the treatment of colorectal cancers. [25,122]

Genitourinary Cancers

Prostate Cancer

Radiation therapy, including EBRT and brachytherapy, is effective in treating localized prostate cancer. It targets the prostate gland and any nearby cancer cells, reducing the risk of recurrence. Studies like the FLAME trial have shown that a focal boost to the intraprostatic tumor improves biochemical disease-free survival without significantly increasing toxicity. [39,141] Hypofractionated radiation therapy, which involves delivering higher doses of radiation in fewer sessions, has been found to be as effective as conventional fractionation. It offers the advantage of shorter treatment duration, which can improve patient convenience and reduce healthcare costs. Advances in imaging and radiation delivery techniques, such as MRI-guided radiotherapy and SBRT, have improved the precision and effectiveness of radiation therapy. These technologies allow for better targeting of the tumor while sparing healthy tissues, reducing the risk of side effects. Additionally, dose escalation, where higher doses of radiation are delivered to the prostate, has been associated with better biochemical control. The SPARC trial and other studies have shown that dose escalation to the dominant intraprostatic lesion (DIL) can improve outcomes in high-risk disease while limiting toxicity. [35,142]

Modality-Specific Findings

The choice of radiation therapy modality depends on various factors, including the patient's risk profile, baseline urinary function, and the presence of any prior treatments. Each modality offers unique benefits and challenges, and the decision should be guided by clinical judgment and patient preferences.

- **Hypofractionated IMRT (HIMRT)**
    - Hypofractionation involves delivering higher doses of radiation in fewer sessions. Pollack et al [38] found no significant difference in BCDF between HIMRT and conventional fractionation IMRT (CIMRT). However, HIMRT was delivered in 2.5 fewer weeks, making it a more convenient option for patients. Men with compromised urinary function before treatment may not be ideal candidates for this approach. Neerhut et al [39] reviewed the genitourinary toxicity in patients who underwent TURP prior to receiving HIMRT for localized prostate cancer. The review found that while acute toxicity was not significantly increased, there was a notable

risk of late toxicity, particularly hematuria. Factors such as poor baseline urinary function and prostate volume were identified as influencing genitourinary outcomes

- **Focal Radiotherapy Boost**
  - Focal radiotherapy boost targets the DIL identified by MRI, aiming to improve biochemical disease-free survival (bDFS) without significantly increasing toxicity. Dornisch et al [141] reviewed seven studies and found that MRI-guided EBRT with a focal boost improved bDFS without significantly increasing toxicity.
- **SBRT with Focal Boost** [143,144]
  - SBRT with dose escalation to the DIL is an approach that can improve outcomes in high-risk disease while limiting toxicity. The SPARC Phase 2 trial evaluated the use of SBRT with a simultaneous focal boost to the DIL in patients with intermediate- to high-risk localized prostate cancer. The study found that this approach was well-tolerated, with acceptable rates of acute and late genitourinary and gastrointestinal toxicity. The trial also reported no cases of biochemical relapse to date. [142]

Recommendations by Risk Group

Treatment recommendations and associated outcomes vary by risk group, but urinary function should also be considered. Low-risk patients may benefit from hypofractionation due to its convenience, while intermediate- and high-risk patients may benefit from focal boosts and combination therapies to improve biochemical control and reduce toxicity. Fractionation plays little role in outcomes for low and intermediate risk groups, [38] making toxicity and convenience of treatment potentially more significant considerations. Urinary function in intermediate and high-risk groups may dictate treatment options, as HIMRT was not well tolerated in men with compromised urinary function. [38] For intermediate-risk patients with compromised urinary function, SBRT with a focal boost may be preferred. [142] This also may be true for high-risk groups, as both Dornish et al [141] and Yasar et al [142] found that a focal boost added to either MRI-guided EBRT [141] or SBRT [142] had acceptable rates of toxicity, HIMRT increased the likelihood of late toxicity in high-risk groups, particularly for patients with compromised urinary function. [39] Androgen deprivation therapy should be considered in conjunction with radiation therapy, particularly for high-risk patients, as it can aid in shrinking tumors and potentially improve urinary function. [35] In short:

- Hypofractionated IMRT (HIMRT) is recommended for **low-risk patients** due to its convenience and shorter treatment duration. [38]
- SBRT with a simultaneous focal boost to the DIL or HIMRT is recommended for **intermediate-risk patients**. [38,142]
- Hypofractionated radiotherapy, focal radiotherapy boost to MRI-visible tumors, or SBRT with a simultaneous focal boost to the DIL is recommended for **high-risk patients**. [39,141,142]
  - HIMRT is recommended primarily for high-risk patients with localized cancer post-TURP due to the increased risk of late toxicity and hematuria.

Penile Cancer

Radiation therapy (RT) is a significant treatment option for penile cancer, particularly for those who wish to avoid surgery or are not suitable candidates for it. RT allows for organ preservation, which can allow a patient to maintain urinary and sexual functions, can achieve local control of the tumor, and is suitable for multiple disease stages. [33,145–148]

There are multiple viable radiation therapy modalities for treating penile cancer. Recommendations and outcomes vary by modality and disease stage. [33,145,147,148]

- **Patient Health**: Overall health and comorbidities should be considered when selecting the appropriate modality.
- **Tumor Characteristics**: The clinical stage, depth of tumor invasion, grade of tumor, and location of the primary tumor are critical factors.
    - Brachytherapy is ideal for tumors less than 4 cm in diameter and with less than 1 cm of invasion. The disease should be limited to the glans for optimal results
    - EBRT is suitable for tumors that are less than 4 cm in size and localized to the glans or coronal sulcus. Tumors that are superficial or exophytic are particularly good candidates.
- **Patient Preference**: Patients who wish to avoid penectomy or are elderly and frail may opt for EBRT.
- **Patient Compliance**: Patients must be willing to comply with the treatment regimen and follow-up care.

Early-Stage Disease (Tis, Ta, T1a)

- **Brachytherapy**: This modality is highly effective for early-stage penile cancer. Studies have shown that brachytherapy can achieve a 5-year local control rate of around 70-90% and a penile preservation rate of approximately 66-86%. [33,145,147,148] For instance, Martz et al. [147] reported a 5-year local recurrence-free survival (LRFS) rate of 82% and a penile preservation rate of 79.3%.
- **External Beam Radiation Therapy (EBRT)**: EBRT is less commonly used for early-stage disease but can be effective. The 5-year local control rates range from 37-62%, and penile preservation rates are between 36-66%. However, EBRT is associated with higher rates of late toxicities such as urethral stenosis and penile necrosis.

Intermediate-Stage Disease (T1b, T2)

- **Brachytherapy**: For intermediate-stage disease, brachytherapy continues to show good outcomes with 5-year local control rates of 75-78% and penile preservation rates similar to those in early-stage disease. [33,145,147,148] The outcomes are slightly lower than those for early-stage disease but still favorable.

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- **EBRT**: The outcomes for EBRT in intermediate-stage disease are less favorable compared to brachytherapy. The local control rates are around 50-60%, and penile preservation rates drop to 18-67.3% at 10 years.

Advanced-Stage Disease (T3, T4)

- **Brachytherapy**: The effectiveness of brachytherapy decreases with more advanced stages. The 5-year local control rates for T3 disease are around 50-71%. [33,145,147,148] The penile preservation rates are also lower compared to early and intermediate stages.
- **EBRT**: For advanced-stage disease, EBRT is often used in combination with chemotherapy. The local control rates are around 41-60%, and penile preservation rates are significantly lower.

Under various clinical scenarios, several types of radiation treatment are often not recommended in the treatment of penile cancer. This includes:

EBRT [145–148]

- **Tumor Size and Location**: EBRT is not recommended for tumors larger than 4 cm or those that have invaded deeply into the penile shaft or surrounding structures.
- **Previous Radiation Therapy**: Patients who have previously received radiation therapy to the pelvic or inguinal regions may not be suitable candidates for EBRT due to the increased risk of severe toxicity.
- **Severe Comorbidities**: Patients with severe cardiovascular, pulmonary, or other systemic diseases may not tolerate the side effects of EBRT.
- **Poor Performance Status**: Patients with a poor performance status (eg, ECOG score ≥ 3) may not be able to tolerate the treatment.
- **Infection or Ulceration**: Active infection or ulceration in the treatment area can be a contraindication due to the risk of exacerbating the condition.

Brachytherapy [145–148]

- **Tumor Size and Invasion**: Brachytherapy is contraindicated for tumors larger than 4 cm or those with more than 1 cm of invasion.
- **Tumor Location**: Tumors located in areas that are difficult to access or treat with brachytherapy, such as the penile shaft, are not suitable candidates.
- **Previous Radiation Therapy**: Previous radiation therapy to the pelvic or inguinal regions can be a contraindication.
- **Severe Comorbidities**: Patients with severe systemic diseases may not tolerate the procedure and its side effects.
- **Poor Performance Status**: Patients with a poor performance status may not be able to undergo the procedure.

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- **Infection or Ulceration**: Active infection or ulceration in the treatment area can be a contraindication.

Bladder and Urethral Cancer

In treating bladder and urethral cancers, RT can provide locoregional control when used in combination with chemotherapy, or as adjuvant therapy after surgery. Tumor characteristics, patient health, and treatment goals are all relevant to the selection of modality. [31,149,150]

IMRT

Advantages: IMRT allows for more precise targeting of the tumor while sparing surrounding healthy tissues. This precision reduces the risk of acute and late toxicities, particularly gastrointestinal and genitourinary toxicities. [149] This is particularly important for urethral cancer, where the proximity of critical structures can make treatment challenging. [151] Larger or more advanced tumors may benefit from more precise modalities like IMRT to minimize damage to surrounding tissues. [149,150]

Outcomes: Studies have shown that IMRT can achieve similar or better locoregional control compared to 3D-CRT, with a lower incidence of severe toxicities. For example, the study by James et al. [150] highlights that synchronous chemotherapy with fluorouracil and mitomycin C combined with radiotherapy significantly improves locoregional control of muscle-invasive bladder cancer, and the meta-analysis by Zalay et al. [151] found that adjuvant radiotherapy significantly reduces locoregional recurrence risk in patients with locally advanced or margin-positive disease following surgery.

3D-CRT

Advantages: 3D-CRT is a well-established technique that uses imaging to create a three-dimensional representation of the tumor, allowing for more accurate targeting than conventional radiotherapy.

Outcomes: While 3D-CRT is effective in treating bladder cancer, it is associated with a higher risk of acute and late toxicities compared to IMRT. [149,151] This may be exacerbated in patients with other health issues. For example, those with poor renal function may not be suitable for treatments that require high doses of radiation. [150]

Under various clinical scenarios, several types of radiation treatment are often not recommended in the treatment of bladder and urethral cancers. This includes:

Bladder Cancer [150]:

- **Severe Hydronephrosis**: Patients with moderate to severe hydronephrosis are generally not considered good candidates for radiation therapy due to the risk of worsening renal function.
- **High-risk Non-Muscle Invasive Bladder Cancer (NMIBC):** the NCCN Guidelines recommend considering concurrent chemoradiotherapy for patients who are not candidates for cystectomy or prefer to avoid surgery.

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- **Extensive Carcinoma in Situ (CIS)**: The presence of extensive CIS associated with muscle-invasive tumors can complicate radiation therapy and reduce its effectiveness.
- **Poor Renal Function**: Impaired renal function can limit the use of certain radiosensitizing agents like cisplatin, which are often used in combination with radiation therapy.
- **Previous Pelvic Radiation**: Prior radiation therapy to the pelvic region can increase the risk of severe toxicity and complications.
- **Inflammatory Bowel Disease**: Conditions like Crohn's disease or ulcerative colitis can be exacerbated by radiation therapy, leading to severe gastrointestinal complications.

Urethral Cancer [151]:

- **Severe Comorbidities**: Patients with significant comorbid conditions, such as uncontrolled cardiovascular disease or severe pulmonary disease, may not tolerate the side effects of radiation therapy.
- **Previous Radiation Therapy**: Similar to bladder cancer, prior radiation therapy to the pelvic region can increase the risk of severe toxicity and complications.
- **Poor Performance Status**: Patients with a poor performance status (eg, bedridden or severely limited in their daily activities) may not be able to tolerate the side effects of radiation therapy.

Testicular Cancer

Radiation therapy is primarily recommended as a treatment option for less advanced stages of testicular cancer, at relatively low doses. [152] At more advanced disease stages, the choice between radiation therapy or chemotherapy relies on specific disease and patient characteristics. [153] The risk of distant metastases, as well as the increased risk of secondary neoplasms associated with radiation therapy, makes chemotherapy preferable as a treatment option for the most advanced disease stages. [45]

- **Stage I Testicular Cancer** [152,154]:
  - For Stage I testicular seminoma, adjuvant radiotherapy is one of the management strategies post-orchiectomy.
  - Modern radiotherapy techniques are preferred due to their lower risk of long-term complications.
  - Conventional radiotherapy is effective in reducing relapse rates but is associated with long-term risks such as second malignant neoplasms (SMNs) and cardiovascular disease (CVD) mortality.
- **Stage II Testicular Cancer** [45,153]:

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- For Stage II testicular seminoma, the choice between radiotherapy and multi-agent chemotherapy (MACT) depends on various factors, including the extent of the disease and patient characteristics.
- Radiation therapy is preferred for non-bulky Stage IIB cases (≤ 3 cm) due to its effectiveness in local control.
- For Stage IIA and IIB seminoma, conventional radiotherapy involves treating the para-aortic and ipsilateral iliac lymph nodes.
- For Stage IIA patients, radiotherapy has shown a 5-year survival rate of 99.0% compared to 93.0% for multi-agent chemotherapy (MACT).

Under various clinical scenarios, several types of radiation treatment are often not recommended in the treatment of testicular cancer. This includes [45,153,154]:

- **Pre-existing Conditions**: Patients with pre-existing conditions that could be exacerbated by radiation therapy, such as cardiovascular disease, are generally contraindicated for this treatment.
- **Second Malignant Neoplasms (SMNs)**: Patients with a history of SMNs or those at high risk for developing SMNs may be contraindicated for radiation therapy due to the increased risk of secondary cancers.
- **Infection and Immunosuppression**: Patients with active infections or those who are immunosuppressed may not be suitable candidates for radiation therapy.
- **Specific Contraindications by Stage** [45,152]:
  - **Stage I Testicular Cancer**: Radiation therapy is generally not recommended for patients with Stage I testicular cancer who have other effective treatment options, such as active surveillance or single-agent carboplatin.
  - **Stage II Testicular Cancer**: For Stage IIB and IIC testicular cancer, radiation therapy is less favored due to the higher risk of distant metastases and the effectiveness of chemotherapy in these stages.
  - **Advanced Stages (IIC and III)**: Radiation therapy is generally contraindicated for advanced stages of testicular cancer (Stage IIC and III) due to the higher risk of distant metastases and the preference for chemotherapy as the primary treatment modality.

Gynecological Cancers [48]

Incidence

- Cervical cancer is one of the most common gynecological cancers worldwide. It is primarily caused by persistent infection with high-risk human papillomavirus (HPV) types. [121]
- Uterine cancer, particularly endometrial carcinoma, is the most common gynecological

cancer in developed countries. It is often associated with obesity, unopposed estrogen exposure, and genetic factors. (49)

- Ovarian cancer is less common but is the most lethal gynecological cancer due to its late diagnosis. Risk factors include family history, genetic mutations (eg, BRCA1/2), and reproductive history. (53,155)
- Vulvar cancer is relatively rare and is often associated with HPV infection and chronic inflammatory conditions like lichen sclerosus. (48)
- Vaginal cancer is very rare and is often linked to HPV infection. It can also be secondary to cervical or vulvar cancer. (50)

Survival Rate

- The survival rate varies depending on the stage at diagnosis. Early-stage cervical cancer has a high survival rate, with a 5-year survival rate of over 90% for localized cases. However, the survival rate decreases significantly for advanced stages. (121)
- The 5-year survival rate for localized uterine cancer is around 95%. For regional and distant stages, the survival rates are approximately 69% and 17%, respectively. (49)
- The overall 5-year survival rate for ovarian cancer is about 47%. Early-stage ovarian cancer has a higher survival rate, while advanced-stage disease has a significantly lower survival rate. (53)
- The 5-year survival rate for localized vulvar cancer is around 86%. The survival rate decreases to about 54% for regional disease and 16% for distant metastases. (48)
- The 5-year survival rate for localized vaginal cancer is approximately 84%. For regional and distant stages, the survival rates are around 58% and 18%, respectively. (52)

Brachytherapy

- HDR brachytherapy is not recommended for certain gynecological cancers due to the potential for short- and long-term injury to normal tissues from large HDR doses per treatment. The radiation oncologist must carefully assess and minimize doses to organs at risk (OARs) to avoid toxicity. Higher doses per fraction with fewer fractions per regimen can increase toxicity. Specifically, doses greater than 7 Gy per fraction should be used carefully due to the potential for higher rates of complications. (48)
- In patients with tumors extremely close to the rectum or anus may not be suitable for brachytherapy and may require an IMRT boost instead. (52)
- In early-stage vaginal cancer, brachytherapy is used for its precision in targeting the tumor and sparing healthy tissues. (52) Vaginal Brachytherapy alone is not recommended for patients with high-risk histologies such as serous carcinoma, clear cell carcinoma, and carcinosarcoma. These patients benefit more from a combination of EBRT and chemotherapy to address both locoregional and distant recurrence risks. (50)

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- The RetroEMBRAVE Cohort Study assessed outcomes of Image-Guided Adaptive Brachytherapy (IGABT) for Primary Vaginal Cancer and showed high local control rates (86% at two years) and acceptable morbidity, with better outcomes in patients with larger tumors (T2–T4) when higher doses (≥ 80 Gy EQD2) were delivered to the clinical target volume. The study concluded that IGABT plays an important role in treating vaginal cancer, with improved local control and reduced morbidity compared to traditional 2D radiograph-based brachytherapy. (156)

- In advanced cervical cancer, tumors that extensively involve the vagina or extend to the side wall may not be suitable for intracavitary brachytherapy alone and may require interstitial brachytherapy. (48)
- In recurrent uterine carcinoma, small, unifocal, thin vaginal recurrences from uterine cancer may not be suitable for brachytherapy alone and should be combined with pelvic EBRT. (48)

EBRT AND Brachytherapy

- In vulvar cancer, EBRT and Brachytherapy are recommended for their effectiveness in treating vulvar cancer, especially when combined with concurrent chemotherapy. This combination helps in controlling the disease locally and improving survival rates. Postoperative radiation therapy is suggested for patients with high-risk features to reduce the risk of recurrence. (53)
- In uterine cancer, EBRT and Brachytherapy are recommended for their ability to target the tumor bed and reduce the risk of local recurrence in endometrial cancer. For advanced stages, combining systemic therapy with radiation is suggested to manage both local and distant disease. (49)
- In locally advanced cervical cancer, EBRT alone may not be sufficient as the combination of EBRT with brachytherapy to improve local control and survival rate. (46,121)
  - The EMBRACE II study aimed to benchmark high levels of local, nodal, and systemic control while limiting morbidity using advanced EBRT (IMRT and image-guided RT [IGRT]) and brachytherapy (IC/IS) techniques. The study demonstrated that image-guided adaptive brachytherapy (IGABT) in locally advanced cervical cancer resulted in excellent local control, especially in limited and well-responding tumors. The study highlighted the importance of dose prescription and technique, with evidence showing that higher doses and advanced techniques lead to better clinical outcomes. The EMBRACE II study also emphasized the need for systematic contouring, prescription, and reporting for tumor and node-related EBRT CTVs, ITV, PTVs, and OARs. (157)
- In vaginal cancer with significant residual thickness, combination of EBRT with brachytherapy is preferred to achieve better local control and reduce the risk of recurrence. (52)

IORT

- IORT is indicated for the treatment of cervical and uterine cancers. There is insufficient evidence to support IORT for the treatment of other gynecological cancers.

Concurrent Chemoradiation

- In cervical cancer, concurrent chemoradiation is the standard of care for locally advanced cervical cancer. The combination of cisplatin-based chemotherapy or platinum-based chemotherapy with radiation enhances the effectiveness of treatment. (46,121)
- In vaginal cancer, chemoradiation is recommended for its effectiveness in treating advanced vaginal cancer. The combination of chemotherapy with radiation helps in better tumor control, particularly for stages II-IV. (52)
- EBRT with concurrent chemotherapy followed by adjuvant chemotherapy is conditionally recommended for FIGO stage III to IVA endometrial cancer. (50)
    - An NRG Oncology/GOG prospective randomized multi-center clinical trial concluded that adding chemotherapy did not improve PFS compared to radiation therapy alone in patients with low-grade tumors and recurrences at the vaginal apex. Patients treated with radiation alone had a median PFS that was not reached, while those receiving chemoradiation had a median PFS of 73 months. The trial also found higher rates of acute toxicity in the chemoradiation group. (158)
- In vulvar cancer, the use of concurrent chemoradiation and EBRT for locally advanced disease is recommended as radiation therapy alone may not be sufficient for controlling the disease, especially in cases with positive lymph nodes or extranodal extension. (53)
    - GROINSS-V III/ NRG-GY024 study investigated the safety of replacing inguinofemoral lymphadenectomy with chemoradiation in early-stage vulvar cancer patients with macrometastasis (> 2 mm) and/or extracapsular extension in the sentinel node. The study hypothesized that combining 56 Gy of radiation to the inguinal site with concurrent cisplatin chemotherapy will be feasible and safe, with low groin recurrence rates. The findings suggest that inguinofemoral radiotherapy is a safe alternative to inguinofemoral lymphadenectomy in patients with sentinel node micrometastasis, but not for those with macrometastasis. The addition of chemotherapy to radiotherapy increases the effectiveness of treatment by 20-25%, translating to a 10% absolute benefit in complete remission/local control. (159)

IMRT (46,50)

- IMRT is recommended to decrease acute and chronic toxicity, with studies showing improved patient-reported outcomes.
- IMRT is recommended for postoperative RT and conditionally recommended for definitive RT to reduce acute and late toxicity. Dosimetric studies have shown that IMRT decreases the volumes of the bladder, rectum, bowel, and bone marrow receiving clinically significant doses of RT.
    - NRG Oncology–RTOG 1203 study compared patient-reported acute toxicity and

health-related quality of life during treatment with standard pelvic RT versus IMRT in women with cervical and endometrial cancer. The findings indicated that IMRT was associated with significantly less gastrointestinal (GI) and urinary toxicity compared to standard RT. Specifically, 51.9% of women receiving standard RT reported frequent or almost constant diarrhea, compared to 33.7% in the IMRT group. Additionally, IMRT resulted in a smaller decline in physical function and fewer treatment-related concerns. [160]

Head and Neck Cancers

Head and neck cancers encompass a variety of malignancies that occur in the oral cavity, pharynx, larynx, nasal cavity, and salivary glands. The incidence and survival rates for these cancers can vary significantly based on factors such as the specific type of cancer, stage at diagnosis, and treatment modalities.

Incidence

- **Nasopharyngeal Carcinoma (NPC):** This type of cancer has a high prevalence in Southeastern Asia, with age-standardized rates of 22.2 to 27.2 per 100,000 male patients. [161] Incidences of synchronous distant metastasis in endemic NPC range from 6% to 8% at the time of presentation. [161]
- **Oropharyngeal Squamous Cell Carcinoma (OPSCC):** The increasing prevalence of OPSCC is mostly due to the widespread infection of human papillomavirus (HPV). [162] HPV-positive tumors show a higher survival rate compared to HPV-negative counterparts. [162]

Survival Rates

- **NPC:** The median OS for de novo metastatic NPC is approximately 29.1 months with gemcitabine and cisplatin (GP) chemotherapy. [161] The 24-month OS was 76.4% in patients receiving chemotherapy plus radiotherapy, compared to 54.5% in those receiving chemotherapy alone. [161]
- **OPSCC:** The cumulative survival rate for patients treated with IMRT was 83.6%, while it was 91.3% for those treated with transoral robotic surgery (TORS). [163] Disease-free survival (DFS) was significantly different between IMRT (79.6%) and TORS (89.4%). [162]

Modality-Specific Considerations

Elective Neck Irradiation: Elective neck irradiation did not show a significant benefit in reducing the risk of locoregional failure (LRF) or improving OS in patients with recurrent or

second primary squamous carcinoma of the head and neck. [164] It was associated with increased acute toxicity in the postoperative setting. [164]

Hyperfractionation: Hyperfractionation (twice daily radiation) did not improve LRF or OS and was associated with higher rates of late toxicity in the postoperative setting. [164]

IMRT

- **Definitive Re-IMRT:** For patients with recurrent or second primary squamous cell carcinoma of the head and neck, definitive re-irradiation using IMRT at doses ≥ 66 Gy has been associated with improved clinical outcomes, particularly in those with high performance status. [164] This approach underscores the importance of dose intensity in achieving therapeutic benefit during re-treatment.
- **Postoperative Re-IMRT:** Following surgical removal of gross disease, postoperative IMRT doses ranging from 50 to 66 Gy are considered adequate and effective. [164] This dosing strategy supports local control while minimizing unnecessary toxicity in the postoperative setting.
- **IMRT vs. 2D/3D-RT:** Compared to conventional external beam radiotherapy, IMRT offers superior long-term tumor control and a lower incidence of late toxicities. [163] The enhanced precision of IMRT makes it the preferred modality, as 2D/3D-RT is increasingly discouraged due to its higher toxicity profile and reduced efficacy. [163]

Tailored Radiation Dose: High-dose radiation is recommended for specific cases, emphasizing the importance of tailoring the radiation dose to the individual patient's condition to optimize outcomes

Elective Nodal Irradiation: The guidelines suggest that elective nodal irradiation may not be necessary in certain cases, as it does not significantly improve outcomes and can increase toxicity. [161]

Chemoradiotherapy: Adding radiotherapy to chemotherapy significantly improves OS in patients with metastatic nasopharyngeal carcinoma (mNPC). This combination therapy is recommended for its efficacy in improving patient outcomes. [55]

Chemotherapy Alone vs. Chemoradiotherapy: The study found that adding radiotherapy to chemotherapy significantly improved OS in patients with mNPC. [55] However, the role of radiotherapy in chemotherapy non-responders remains unclear. [55]

Lung Cancer

The incidence of lung cancer is the leading cause of cancer death for both men and women in the United States, with more than 158,000 deaths expected in 2016. [57] Approximately 85% to 90% of lung cancer cases are caused by voluntary or involuntary (second-hand) cigarette smoking. [58] The number of lung cancers in individuals who do not smoke is increasing

worldwide, necessitating more research to identify relevant risk factors such as environmental exposures, chronic lung diseases, and family history. [58]

Survival rates for NSCLC vary depending on the stage at diagnosis and the treatment received. The five-year survival rates for patients with stage I NSCLC can exceed 50% after standard surgery. [165] SCLC represents about 15% of all lung cancers and is characterized by its highly invasive capacity and early metastatic behavior. [62]

There are several indications in which radiation therapy may not be appropriate. For Stage IVB (M1c) with pleural or disseminated metastases, radiation therapy is generally not recommended for patients with widespread metastatic disease, as systemic therapy is preferred. [57] Patients with significant comorbidities (underlying health conditions that could be exacerbated by radiation therapy) may not be suitable candidates. [57] Patients with poor performance status (eg, ECOG 3 or 4) may not tolerate the side effects of radiation therapy. [57]

Modality-Specific Considerations

Accelerated Hypofractionated Radiotherapy

The use of accelerated HIMRT for centrally located lung tumors not suitable for SBRT, chemoradiotherapy, or high-risk patients. [59,166] It is associated with a higher risk of toxicity, especially for larger and centrally located tumors. Larger tumor size (> 3.5 cm) is associated with higher risk of local failure and distant progression at 24 months of 14.2%. [59]

The National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) BR.25 investigated an accelerated hypofractionated regimen of 60 Gy in 15 fractions yielded local control of 87.4% and OS of 68.7% at two years. [59] The Zeng 2023 trial was similar to NCIC CTG study in which they evaluated 60 Gy in 15 fractions in peripheral T1-3N0M0 NSCLC and reported a local failure rate of 12.6% at 2 years. [59]

Brachytherapy

Brachytherapy involves placing radioactive material directly inside or next to the tumor. It is not commonly recommended for lung cancer due to the difficulty in accurately placing the radioactive sources within the lung tissue and the potential for significant damage to surrounding healthy tissues and organs. [56,57,62] Small Cell Lung Cancer often involves larger areas and multiple sites that are not suitable for the localized approach of brachytherapy. [62]

Hypofractionated IGRT

Hypofractionated IGRT is recommended for patients with stage II/III non-small cell lung cancer (NSCLC) who cannot receive concurrent chemoradiotherapy due to comorbidities or poor performance status. The Iyengar 2021 study found that hypofractionated IGRT (60Gy in 15 fractions) was not superior to conventionally fractionated RT (CFRT) (60Gy in 30 fractions) in terms of OS. The Iyengar 2021 study found no significant difference in 1-year OS between the two groups (37.7% for IGRT vs. 44.6% for CFRT) and no significant differences in median OS, PFS, or time to local failure. [61] However, hypofractionated IGRT may offer a more convenient treatment option for well-selected patients with peripheral primary tumors and limited mediastinal/hilar adenopathy. [61]

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The Iyengar 2021 trial compared hypofractionated IGRT with CFRT in patients with stage II/III NSCLC who could not receive concurrent chemoradiotherapy. The study found no statistically significant difference in 1-year overall survival between the two groups. (61)

IMRT

Pleural IMRT is recommended for carefully selected patients at centers with experience in this technique (56) While IMRT is beneficial for reducing doses to adjacent normal tissues, it is more complex to plan and deliver compared to 3D-CRT. The complexity and potential for increased low-dose exposure to larger volumes of normal tissue can be a concern. (165)

The NRG Oncology RTOG 0617 trial compares IMRT with 3D-CRT for locally advanced NSCLC it finds that IMRT can improve radiation coverage of tumors and enhance the therapeutic ratio by avoiding adjacent organs at risk. (165) With reducing severe grade 3 or greater pneumonitis risk and lowering heart doses the use of IMRT may be associated with improved outcomes. The study revealed that high-dose radiation therapy, such as 74 Gy, has been associated with increased toxicity without a significant improvement in overall survival compared to standard doses (60 Gy). (165)

IORT

IORT delivers a concentrated dose of radiation to a tumor site during surgery. While it can be effective for certain cancers, it is not typically recommended for lung cancer because of the challenges in delivering a uniform dose to the irregular and often mobile lung tissue. Additionally, the risk of complications and damage to surrounding structures is higher. (56,57,62)

BID (twice daily) Radiation Therapy

Twice-Daily Radiotherapy regimen was recommended in both NCCN and Gronberg 2021 for limited-stage small cell lung cancer (LS-SCLC) as it has been shown to improve survival compared to once-daily RT. The twice-daily schedule is considered more effective due to the radiosensitivity of SCLC cells and the reduction in tumor cell repopulation. (62) The Gronberg study 2021 found that high-dose twice-daily thoracic radiotherapy (60Gy) significantly improved 2-year survival and median overall survival compared to the standard dose (45 Gy). The high-dose arm showed a significant improvement in 2-year survival (75% vs. 51.3%) and median overall survival (37.2 months vs. 24.0 months) compared to the standard-dose arm. The higher dose did not result in increased radiotoxicity, making it an attractive option for patients. (167)

Sequential Hypofractionated Radiotherapy

The therapy is recommended as an alternative to concurrent twice-daily RT for LS-SCLC. The study found that sequential hypofractionated RT had comparable survival outcomes and less toxicity compared to the concurrent twice-daily regimen. (168) This suggests that sequential hypofractionated RT can be an alternative, especially for patients who may not tolerate the more intensive concurrent regimen. (167,168)

SBRT

SBRT is a highly precise form of RT that delivers high doses of radiation to a small, well-defined tumor area. While SBRT is effective for early-stage, node-negative lung cancer, it is not

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recommended for larger tumors or those with nodal involvement due to the increased risk of toxicity and complications and SBRT should be used with caution for centrally located tumors due to the risk of severe toxicity. (56,57,62)

There are current evidence-based recommendations for SBRT in early-stage NSCLC when medically inoperable and limited other treatment options. (58) While SBRT is effective for early-stage NSCLC, it carries significant risks when used for centrally located tumors. (57,58) The use of 3-fraction regimens should be avoided due to the higher risk of severe toxicity, including fatal pulmonary hemorrhage. (59,165) For central tumors, SBRT should be delivered in 4 or 5 fractions, and adherence to dose constraints is crucial to optimize safety. (59)

While SBRT is effective for early-stage NSCLC, it is not recommended for SCLC due to the aggressive nature and rapid spread of this type of cancer. SCLC typically requires a more comprehensive approach that includes systemic therapy and concurrent chemoradiation to address both the primary tumor and potential metastases. (62)

Lymphoma

Lymphoma is a type of cancer that begins in the lymphatic system, which is part of the body's immune system. There are two main types of lymphoma: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). (67)

NHL is more common than HL. In the United States, NHL is one of the most common cancers, with an estimated incidence of about 19.6 cases per 100,000 people per year. HL is less common, with an incidence of about 2.7 cases per 100,000 people per year in the United States. (67,69)

HL is an uncommon malignancy of B-cell origin. Most patients are diagnosed between the ages of 15 and 30 years, with another peak in adults aged 55 years and older. In 2025, it is estimated that 8,720 people will be diagnosed with HL in the United States, and 1,150 people will die from the disease. (66)

The incidence of NHL varies globally, with higher rates in developed countries. The incidence of NHLs is estimated to be 80,350 new cases in 2025, with approximately 19,390 deaths due to the disease. (68) The incidence and survival rates for lymphoma can vary based on the type and stage of the disease. The survival rates for HL have significantly improved over the past few decades due to advancements in treatment. HL generally has a high survival rate, especially when diagnosed early. The overall 5-year relative survival rate for HL is about 87%. For early-stage HL, the 5-year survival rate can be as high as 90-95%. (66,67) The survival rate for NHL varies widely depending on the subtype, stage at diagnosis, and other factors. The overall 5-year relative survival rate for NHL is approximately 73%. However, this can range from about 60% for aggressive subtypes to over 90% for indolent (slow-growing) subtypes. (169)

Lymphomas, including primary cutaneous lymphomas, are highly radiosensitive, meaning they respond well to radiation therapy. This makes radiation an effective treatment option either as a standalone therapy or as part of a multimodal approach. (70)

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Radiation therapy may not be effective for all types of lymphoma. For instance, certain aggressive lymphomas may not respond well to radiation alone and may require a combination of chemotherapy and radiation or other systemic therapies. [68,69] The decision to use radiation therapy can also depend on individual patient factors, such as age, overall health, and the presence of other medical conditions. For example, older patients or those with significant comorbidities may not tolerate radiation therapy well.

In cases where the lymphoma is located in areas where radiation could cause significant damage to critical structures (eg, heart, lungs), alternative treatments may be preferred. [70]

IMRT

IMRT allows for highly conformal dose distributions, which are especially important for patients treated with curative intent or those with long life expectancies. This precision helps to spare OARs and reduce the risk of late complications from normal tissue damage. [66]

Techniques such as volumetric modulated arc therapy (VMAT), deep-inspiratory breath hold (DIBH), and IGRT are often used in conjunction with IMRT to further enhance precision and reduce incidental dose to critical structures such as the heart and lungs or the parotid glands in the head and neck region. [66]

SBRT & IORT
SBRT and IORT are not recommended for the routine treatment of lymphoma. [66]

Systemic Therapy

Radiation therapy is generally recommended as part of combined modality therapy (CMT) for better PFS and freedom from progression (FFP) for Hodgkin Lymphoma Stage I-II. However, chemotherapy alone may be preferred for patients assigned female at birth with intact breast tissue, especially if they are under 30 years old and the recommended breast dose-volume histogram (DVH) constraints are exceeded, or if cardiac constraints cannot be met. [66]

For patients with advanced-stage lymphoma, systemic therapy is often preferred over radiation therapy due to the widespread nature of the disease. [67]

Diffuse Large B-Cell Lymphoma (DLBCL), Leg Type, tends to relapse in extra-cutaneous sites, and while radiation therapy can be used, it is often combined with systemic treatments like R-CHOP (rituximab, cyclophosphamide, adriamycin, vincristine, and prednisone) for better outcomes. [67]

Total Skin Electron Beam Therapy (TSEBT)

This technique is used primarily for cutaneous T-cell lymphomas like mycosis fungoides. It involves directing electron beams at the entire skin surface to treat widespread skin involvement. [70]

Metastatic Cancer

Metastatic disease, also known as metastatic cancer, occurs when cancer cells spread from the primary site (where the cancer started) to other parts of the body. This spread can happen

through the bloodstream or the lymphatic system. The incidence and survival rates for different types of metastatic disease vary significantly and depend on the type of cancer and site of metastasis. [170]

EBRT

EBRT is particularly effective as a palliative treatment for spinal bone metastases by reducing pain and potentially preventing new skeletal events [73]

SBRT

In spinal bone metastases, SBRT is effective for achieving a durable pain response, preventing local metastasis progression, and contributing to long-term disease control in selected patients, and offers higher rates of overall and complete pain response compared to conventional palliative RT [171]

Advances in SBRT are also effective for oligometastatic malignancies, [172] such as colorectal cancer, where SBRT treatments have been shown to result in a five-year overall survival rate of 45%, local PFS of 83%, and distant PFS of 27% [75]

SRS

SRS is strongly recommended for patients with up to four intact brain metastases because it provides effective intracranial control without the neurocognitive decline associated with whole-brain radiation therapy (WBRT). [4,173,174]

WBRT with 3D or IMRT

WBRT is recommended as primary treatment for patients with brain metastases who are ineligible for surgery or SRS and have a favorable prognosis. [4,173,174] IMRT should be used with WBRT to avoid treating the hippocampal structures (if clinically possible).

EBRT

While EBRT is effective for managing pain from bone metastases, it is not always the best option for patients with spinal cord or cauda equina compression. In such cases, surgery followed by postoperative RT is conditionally recommended over RT alone due to better outcomes in maintaining and regaining ambulatory status. [73]

SBRT

Due to a lack of high-quality evidence, SBRT is not recommended for routine use in non-oligo metastatic diseases, [175] or those with more than five lesions due to significantly worse outcomes. [172,176]

SRS

SRS is not recommended for brain tumors greater than 6 cm due to limited evidence for its effectiveness. [4,173,174]

WBRT

For brain metastases, WBRT should avoid hippocampal involvement to preserve neurocognitive function. Adjuvant WBRT added to SRS is also not recommended for patients with limited brain metastases. (4,173,174)

Myeloma

Multiple myeloma is characterized by the proliferation of malignant plasma cells in the bone marrow. It is a relatively common hematologic malignancy, accounting for about 1% of all cancers and approximately 10% of hematologic malignancies. (177,178) The introduction of novel therapies such as proteasome inhibitors, immunomodulatory drugs, anti-CD38 monoclonal antibodies, bispecific antibodies, and CAR-T cell therapies has significantly improved the survival rates for multiple myeloma, with the median overall survival being approximately 5-7 years. (177,178)

Solitary Plasmacytoma is a less common plasma cell disorder compared to multiple myeloma and accounts for about 5-10% of all plasma cell neoplasms.(76) Solitary Plasmacytoma can be classified into two types: Solitary Bone Plasmacytoma (SBP) and Solitary Extramedullary Plasmacytoma (SEP). SBP occurs more frequently in the axial skeleton, while SEP is often found in the head and neck region. (76) The 10-year PFS rate for SBP is approximately 30-50%, while the overall survival rate is around 50-70%. (76) For SEP, the 10-year PFS rate is higher, ranging from 60-80%, with an overall survival rate of 70-90%. (76)

Radiation therapy is well-established for multiple myeloma, and is effective in palliating bony pain, promoting bone recalcification, and reducing skeletal-related events such as pathological fractures and spinal cord compression. (177) Definitive radiation therapy is the standard treatment for solitary plasmacytoma, providing long-term local control and is potentially curative in extramedullary cases. (178)

Scenarios in which radiation therapy may not be appropriate for multiple myeloma and solitary plasmacytoma include:

- **Multiple Myeloma (MM)**:
  - **Advanced Systemic Disease**: Radiation therapy is primarily used for localized control and palliation of symptoms. In cases where the disease is widespread and systemic, systemic therapies such as chemotherapy, immunotherapy, or targeted therapies are preferred (76,177)
  - **High Risk of Recurrence at Initial Radiation Site**: Concerns about the risk of recurrence at the initial radiation site and the effect of radiation therapy on peripheral blood stem cell harvest for autologous stem cell transplantation (ASCT) are noted (177)
  - **Peripheral Blood Stem Cell Harvest**: RT, particularly to the pelvic/lumbosacral region, can negatively impact peripheral blood stem cell yields for ASCT (177)
- **Solitary Plasmacytoma (SP)**:
  - **Minimal Marrow Involvement**: For solitary plasmacytoma with minimal marrow

involvement, systemic therapy might be indicated in patients with a high risk of progression based on clinical context [76]

- **High Risk of Progression**: Systemic therapy may be considered in patients with a high risk of progression based on clinical context [76]
- **Neurologic Compromise**: In cases of neurologic compromise due to spinal cord compression, surgical intervention might be preferred over RT [178]
- **Pathologic Fracture or Surgical Instability**: Surgical stabilization is indicated for pathologic fractures or surgical instability of weight-bearing bones [178]

Palliation

Radiation therapy is often ordered as a palliative care option for patients with advanced cancer. Palliative radiation therapy (PRT) can alleviate symptoms and improve quality of life. PRT can effectively reduce pain caused by bone metastases and other painful malignant lesions, [71,179,180] help achieve hemostasis for patients experiencing bleeding from tumors, such as hemoptysis, hematemesis, or bleeding from fungating lesions, [179,180] exert local tumor control in critical areas like the brain, spine, head and neck, and pelvis, [173,179,181] and alleviate various symptoms caused by advanced cancers, including obstruction, compression, and ulceration, [179,180] subsequently improving quality of life in cancer patients.

A number of radiation therapy modalities can be employed for PRT, although individualized treatment planning is crucial to choosing a palliative care plan that is beneficial to the patient.

EBRT

This is the most common form of radiation therapy for palliation, and is effective for pain relief, controlling bleeding, and reducing tumor size to alleviate symptoms such as obstruction or compression. Dose must be considered, as high-dose radiation therapy, such as those used in curative settings, may not be appropriate for palliative care due to the increased risk of severe side effects and the prolonged treatment duration.

SRS

SRS delivers a high dose of radiation precisely to the tumor in one or a few sessions. It is particularly useful for brain metastases and small tumors in the body. SRS can provide rapid symptom relief with minimal damage to surrounding tissues. It may not be suitable for larger tumors due to the risk of radiation necrosis and other complications.

Hypofractionated Radiation Therapy

This approach involves giving larger doses of radiation over fewer sessions. It is beneficial for patients with a limited life expectancy as it reduces the number of hospital visits and provides quicker symptom relief. Hypofractionated regimens are commonly used for bone metastases, brain metastases, and other symptomatic sites.

Brachytherapy

This type of radiation therapy involves placing radioactive sources directly into or near the

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tumor. Brachytherapy is effective for controlling bleeding and providing local tumor control in cancers such as cervical, prostate, and esophageal cancers. However, certain tumors, such as renal cell carcinoma and melanoma, are less responsive to radiation therapy. Using radiation therapy for these types of tumors may not provide significant symptom relief.

Whole Brain Radiation Therapy

WBRT is used for patients with multiple brain metastases. It helps control symptoms such as headaches, seizures, and neurological deficits by treating the entire brain. However, it may have more side effects compared to SRS, and it can lead to significant neurocognitive decline, especially in patients with limited life expectancy.

While PRT can be an effective palliative treatment for many patients, it is important to carefully consider the individual patient's condition, prognosis, and preferences. There are certain situations where it may not be the best option. For patients with a very limited life expectancy or severe comorbidities, the benefits of PRT may not outweigh the burdens and side effects. In cases where the disease is too advanced and widespread, or for certain types of tumors that may not respond well to radiation therapy, PRT may not provide meaningful symptom relief or improve quality of life. The treatment may also delay other important aspects of end-of-life care, and the need for frequent visits to a radiation therapy center can be a significant burden for patients with limited mobility or those living far from treatment facilities. Ultimately, some patients may prefer to avoid the side effects and inconvenience of radiation therapy, opting instead for other palliative measures such as pain management, hospice care, or other supportive therapies.

Re-irradiation [103]

Re-irradiation is defined as the use of additional radiation treatment to treat an area of the body that has already received prior radiation to that same area. Reirradiation can provide symptom palliation, local tumor control, and potentially cure recurrent cancer. [188] It is particularly beneficial for nasopharynx cancer and glioma, where hyperfractionated radiotherapy has emerged as a preferred option, [188] and advances in radiotherapy techniques, such as image-guided brachytherapy and stereotactic body radiotherapy, have made reirradiation more feasible for other cancers, as well. [189] However, serious toxicity remains a concern after high cumulative doses [188] and an accurate understanding of the clinical implications of reirradiation is essential for improving patient outcomes. [190]

Patient selection criteria should consider numerous factors, including disease type and stage, previous treatment response, and the time interval between initial radiation therapy and reirradiation, as insufficient recovery time between radiotherapy courses can increase the risk of severe toxicity. [188,190] Patients who experienced severe toxicity (grade 3 or higher) from the initial radiotherapy are generally not considered suitable for reirradiation [188], and a short interval between the initial radiotherapy and the proposed reirradiation can increase the risk of cumulative toxicity. [188] Furthermore, reirradiation is contraindicated if critical OARs are within the high-dose region and cannot be adequately spared or contraindicated if there is significant overlap of irradiated volumes that could lead to excessive cumulative doses. [188,190] Additional patient selection considerations vary by modality.

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- **Hyperfractionated Radiotherapy**: This modality is preferred for recurrent, inoperable nasopharynx cancer due to its better therapeutic ratio. [103,188] Patients should have a stable performance status and no severe radiation-induced complications from previous treatments. [188] It is ideal for patients requiring high doses in fewer fractions. [103]
- **Image-Guided Brachytherapy**: Advances in this technique have made reirradiation more feasible by allowing high-dose focal irradiation to a limited target volume with minimal normal tissue reirradiation. [103,189,190] This makes it suitable for patients with localized tumors where high-dose focal irradiation can be delivered with minimal normal tissue reirradiation. [189]
- **VMAT**: This technique enables precise targeting of tumors while minimizing damage to surrounding healthy tissues and is best for patients with small target volumes and localized tumors. [189,190]
- **SBRT**: This modality is used for its precision and ability to deliver high doses to small target volumes. [103,189]
- **IMRT**: This technique is used for its ability to create highly conformal dose distributions, making reirradiation more feasible. Suitable for patients requiring highly conformal dose distributions. [190]

Sarcoma

Incidence [104,105]

- Soft tissue sarcomas are relatively rare, accounting for about 1% of all adult cancers.
- Bone sarcomas are also rare, with osteosarcoma being the most common type.
- Gastrointestinal Stromal Tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal tract.
- Uterine sarcomas are rare, accounting for about 3-7% of all uterine cancers.
- DFSP is a rare type of soft tissue sarcoma that typically occurs in the dermis layer of the skin
- HIV-associated Kaposi sarcoma (KS) is significantly higher than in the general population, with an estimated 540 cases diagnosed in the United States in 2020.
- Classic KS is most common in people of Mediterranean, Eastern European, Middle Eastern, and/or Jewish origins, with a mean age of 74 years at diagnosis.
- Iatrogenic KS occurs in the context of immunosuppressive therapy, often appearing 2 to 8 months after initiation of immunosuppression.
- Endemic KS occurs in children and younger adults in equatorial Africa and may also occur in immigrants from the region,

Survival Rate [104,105]

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- In soft tissue sarcoma, the 5-year survival rate varies significantly depending on the stage at diagnosis. For localized disease, the survival rate is around 81%, while for regional and distant metastases, the rates drop to 56% and 16%, respectively.
- The 5-year survival rate for localized osteosarcoma is approximately 70%, but it decreases significantly if the cancer has spread to other parts of the body.
- The 5-year survival rate for localized GISTs is about 76%, while it is around 48% for regional disease and 34% for distant metastases.
- The 5-year survival rate for localized uterine sarcomas is approximately 63%, but it drops to 36% for regional disease and 14% for distant metastases.
- The 5-year survival rate for DFSP is very high, around 99%, due to its low metastatic potential.
- The 5-year survival rate of HIV-associated KS has improved significantly in the post-ART era, reaching as high as 88%.
- The survival rate is generally good in classic KS, but synchronous primary malignancies are more likely to be the cause of death.
- The survival rate can be good in iatrogenic KS if immunosuppression is reduced or switched to mTOR inhibitors.
- The survival rate varies in endemic KS, but it is generally more aggressive than classic KS.

IORT

- IORT is indicated in the treatment of sarcoma for several clinical scenarios

Radiation Therapy

- RT is generally not recommended for low-grade tumors due to their lower risk of metastasis and the potential for long-term side effects [104]
    - Retroperitoneal/Intra-Abdominal Sarcoma: Adjuvant RT following surgery is discouraged for retroperitoneal/intra-abdominal sarcoma. If RT is not given prior to surgical resection, follow-up with possible neoadjuvant RT at the time of localized recurrence is recommended.
    - Desmoid Tumors: Definitive RT is primarily reserved for patients who cannot tolerate or progress through systemic therapy and where surgery would be too morbid or result in positive margins.
        - Keus 2013 phase II trial [191] investigated the use of moderate dose radiotherapy (56 Gy in 28 fractions) for inoperable desmoid-type fibromatosis (DF). The study found that this regimen was effective, with a 3-year local control rate of 81.5% and a significant proportion of patients achieving complete or partial response. The treatment was associated with manageable acute and late toxic effects,

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making moderate dose radiotherapy a recommended option for patients with inoperable DF.

- Soft Tissue Sarcoma: RT to plantar and palmar surfaces should be approached with caution due to potential long-term wound healing issues, particularly in the presence of coexisting lymphedema.

- Radiation therapy is not recommended as the first-line therapy for disseminated disease whenever systemic therapy is feasible in Kaposi Sarcoma. It should be reserved for circumstances when systemic therapy is not feasible, with the goal of palliation or short-term disease management until systemic therapy may be delivered [105]
  - Tsao 2016 retrospective review [192] examined the use of radiotherapy for treating skin KS. The findings indicated that radiotherapy is effective in treating KS skin lesions, with 87% of untreated sites responding to radiation (30% complete response and 57% partial response). The study also noted that repeat radiotherapy for KS lesions that progressed despite initial treatment resulted in partial responses in 50% of cases
- For neoadjuvant radiation therapy, preoperative radiation is generally preferred over postoperative radiation due to lower total radiation dose, shorter treatment time, smaller field sizes, and potential for reduced late toxicities such as fibrosis, edema, and joint stiffness. It also has the potential for tumor downstaging. A preoperative dose of 50 to 50.4 Gy EBRT is recommended per NCCN guidance. For adjuvant radiation therapy, EBRT (50–50.4 Gy) to a larger volume followed by a 10- to 16-Gy boost to a reduced volume encompassing the tumor bed. [104]
  - A randomized trial by O'Sullivan 2002 [193] compared preoperative and postoperative radiotherapy for soft tissue sarcoma of the limbs. The study found that preoperative radiotherapy was associated with a higher risk of wound complications compared to postoperative radiotherapy. However, preoperative radiotherapy required smaller field sizes and lower doses, which could be beneficial in certain anatomical sites. The study concluded that the choice between preoperative and postoperative radiotherapy should consider the timing of surgery, tumor size, and anatomical site
  - RTOG-0630 trial [194] focused on the use of IGRT for treating extremity soft tissue sarcoma (STS). The trial found that preoperative IGRT to a reduced target volume significantly reduced late toxicities such as subcutaneous fibrosis, joint stiffness, and edema compared to traditional preoperative radiation therapy without IGRT. The study concluded that IGRT is effective in reducing radiation morbidity while maintaining local control of the disease.
  - Kalbasi 2020 phase II study [195] evaluated a five-day neoadjuvant radiation therapy regimen (30 Gy in five fractions) for high-risk primary soft tissue sarcoma (STS). The findings indicated that this condensed regimen resulted in favorable rates of wound complications and grade ≥ 2 toxicity, with a local recurrence rate of 5.7% and a significant increase in the utilization of neoadjuvant RT at the institution. The study also identified potential germline biomarkers for predicting wound complications,

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suggesting that this shorter regimen could improve access to care and reduce treatment burden

- Bedi 2022 phase II trial [196] investigated a hypofractionated preoperative radiation therapy regimen (35 Gy in 5 fractions) for localized STS. The study reported excellent local control rates (100% at 3 years) and acceptable toxicity profiles, with major acute postoperative wound complications occurring in 25% of patients. The findings support the use of hypofractionated radiation therapy as an effective and convenient option for treating STS, potentially reducing treatment time and improving patient convenience.

- Definitive Radiation Therapy for Unresectable Disease provides a reasonable option for non-surgical candidates, although long-term local control from radiation alone may be inferior to multimodality therapy. Initial volume doses should be 50 Gy with a boost of at least 63 Gy; higher doses of 70 to 80 Gy can be considered based on tolerance of normal structures.

Skin Cancers

Incidence [108,109,112–115]

- BCC is the most common type of skin cancer, with a high incidence rate. It is primarily caused by chronic exposure to ultraviolet (UV) radiation. SCC is the second most common type of skin cancer. It also results from chronic UV exposure and other risk factors such as immunosuppression. Nonmelanoma skin cancer (NMSC), which includes BCC and SCC, account for over 95% of all skin cancer diagnoses in the United States, with an incidence rate of over 5 million cases annually.
- Melanoma is one of the most common types of skin cancer. It can occur anywhere on the skin but is most commonly found on the trunk in men and on the legs in women.
- Uveal melanoma is a rare type of melanoma that occurs in the eye. It is the most common primary intraocular malignancy in adults, with new cases occurring in 5 to 10 people per million per year.
- Merkel Cell Carcinoma (MCC) is a rare but aggressive type of skin cancer. Approximately 2,488 individuals are affected per year in the United States.
- DFSP is an uncommon, low-grade sarcoma of fibroblast origin with an incidence rate of 4.1 to 4.5 cases per million persons per year in the United States
- Fibrosarcomatous Transformation of DFSP (FS-DFSP) is associated with a higher metastasis risk of 15%–20%

Survival Rate [108,109,112–115]

- BCC has a very high survival rate, with most cases being successfully treated. The five-year survival rate is nearly 100% for localized BCC. The survival rate for SCC is generally high, especially when detected early. The five-year survival rate for localized

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SCC is around 95%, but it can decrease significantly if the cancer spreads to lymph nodes or other organs.

- The survival rate for melanoma varies depending on the stage at diagnosis. Early-stage melanoma has a high survival rate, with a 5-year survival rate of about 99% for localized melanoma. However, the survival rate decreases significantly for advanced stages. For regional melanoma, the 5-year survival rate is about 66%, and for distant metastatic melanoma, it is around 27%.
- The survival rate for uveal melanoma also varies by stage. The 5-year survival rate for localized uveal melanoma is around 85%, but it drops significantly for metastatic disease. The 5-year survival rate for metastatic uveal melanoma is less than 20%.
- MCC has a high mortality rate, exceeding that of melanoma. The 5-year relative survival rates range from 41% to 77%, depending on the stage at presentation. Early-stage MCC has a better prognosis, while advanced stages have significantly lower survival rates.
- DFSP rarely metastasizes. When metastasis occurs, it is typically in the lung, bone, or regional lymph nodes. The local recurrence rate for wide local excision (WLE) of DFSP ranges from 10% to 60%, whereas the rate of development of regional or distant metastatic disease is only 1% and 4-7.4%, respectively
- FS-DFSP has a significantly higher risk of local recurrence (29.8% vs. 13.7%), metastasis (14.4% vs. 1.1%), and death (14.7% vs. 0.8%) compared to DFSP.

Radiation Therapy

- Recommended for treating BCC in cases where surgery might compromise function or cosmesis, especially in anatomically sensitive areas like the face, for patients with gross perineural spread that is clinically or radiologically apparent, and for patients with high-risk BCC, especially those with aggressive histologic subtypes or extensive disease. Postoperative RT is suggested for patients with close or positive margins that cannot be corrected with further surgery due to morbidity or adverse cosmetic outcomes [107,108]
    - Radiation therapy is contraindicated for genetic conditions predisposing to skin cancer, such as ataxia telangiectasia, basal cell nevus syndrome (Gorlin syndrome) or Li-Fraumeni syndrome and relatively contraindicated for patients with connective tissue diseases like scleroderma.
    - Radiation therapy is not recommended for patients with superficial basal cell skin cancer as non-surgical modalities like topical imiquimod, topical 5-fluorouracil, photodynamic therapy, or cryotherapy may be considered, although cure rates are approximately 10% lower than for surgical treatment modalities.
    - Re-irradiation should not be routinely utilized for recurrent disease within a prior radiation field due to higher complication rates.
- Recommended for patients with SCC who cannot undergo or decline surgical resection, for patients with SCC in the setting of recurrence after a prior margin-negative resection., and for patients with extensive perineural invasion or other poor prognostic features.

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Postoperative radiation therapy is recommended for patients with SCC having close or positive margins that cannot be corrected with further surgery. [107,109]

- Radiation therapy is not recommended for patients with genetic conditions predisposing to heightened radiosensitivity, such as ataxia telangiectasia, nevoid BCC syndrome (Gorlin syndrome), or Li-Fraumeni syndrome. Poorly controlled connective tissue disorders are also a relative contraindication.

- Zaorsky 2017 study [197] focused on hypofractionated radiation therapy for basal and squamous cell skin cancer. It found that hypofractionated RT regimens, such as 50 Gy in 15 fractions, 36.75 Gy in 7 fractions, or 35 Gy in 5 fractions, resulted in good cosmetic outcomes in 80% of patients. The study concluded that hypofractionated RT is a favorable option for patients with skin BCCs/SCCs due to its convenience and effectiveness. Marconi 2016 study [198] reported on the use of superficial X-ray therapy (SXRT) for head and neck non-melanoma skin cancer (N-MSC) and compared outcomes by prescribed fractionation schedules. The findings showed that SXRT is well tolerated and achieves excellent local control, with fractionation schedules using more than 2.0 Gy daily being associated with improved local control
- Recommended for melanoma in cases where surgery is not feasible or as an adjuvant treatment to reduce the risk of recurrence. It is particularly useful for treating in-transit metastases and nodal disease. [113]
  - Radiation therapy is not appropriate for patients with early-stage melanoma (Stage 0, IA, IB) unless there are specific high-risk features. It is also not recommended for patients with melanoma who have had a complete surgical resection with clear margins or in patients with a single, small (less than 3 cm) cervical lymph node harboring carcinoma without extracapsular extension.
  - Radiation therapy is not recommended for patients with SCC as non-surgical options like topical 5-fluorouracil, topical imiquimod, photodynamic therapy, or vigorous cryotherapy may be considered.
  - Re-irradiation should not be routinely utilized for recurrent disease within a prior radiation field due to higher complication rates.
- Radiation therapy, including plaque brachytherapy and particle beam therapy, is recommended for uveal melanoma due to its ability to deliver precise doses to the tumor while preserving vision. [114]
  - Radiation therapy is not recommended if the tumor is small and can be managed with observation or local therapies. It is also not appropriate for patients with extensive extraocular extension where surgery or other systemic therapies are more suitable.
  - Systematic review by Echegaray 2017 [199] investigated the optimal radiation dose for iodine-125 brachytherapy in treating uveal melanoma. The review suggested that lower radiation doses might yield similar local control rates to the standard 85.0 Gy used in the Collaborative Ocular Melanoma Study (COMS) trial. The findings

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indicated that a dose reduction could potentially reduce radiation-related complications while maintaining effective local control.

- Recommended for MCC as an adjuvant treatment to surgery or as a primary treatment when surgery is not feasible. It helps in achieving local control and reducing the risk of recurrence. (115)
    - Radiation therapy is not recommended for patients with MCC who have had a complete surgical resection with clear margins. It is also not appropriate for patients with extensive comorbidities where the risks of radiation outweigh the benefits.
    - Liu 2022 study (200) analyzed clinical outcomes after shorter course hypofractionated and standard-course radiotherapy for stage I-III MCC. The findings showed no significant difference in cumulative incidence of in-field locoregional relapse or MCC-specific survival between hypofractionated radiotherapy (hypo-RT) and conventionally-fractionated radiotherapy (conv-RT). However, hypo-RT was more convenient for elderly and medically frail patients
- Recommended for DFSP in cases where surgical margins are positive or narrow, and further resection is not feasible. It is also considered for recurrent or metastatic disease. (112)
    - Radiation therapy is not recommended if Mohs surgery or other forms of complete margin assessment have been performed and margins are clear. It is also not appropriate for patients with positive margins if further resection is feasible.

Superficial radiation therapy (SRT) (201)

- Recommended as a first option for treating appropriate types of NMSC in suitable patients. SRT is considered superior to EBRT and electronic brachytherapy for treating most cases of NMSC due to its better cosmesis and lower lateral edge beam drop-off. SRT is particularly recommended for treating NMSC in anatomical areas where tissue-sparing is important, such as the nasal alar rim, ear, and perioral and periorbital areas. SRT is particularly beneficial for elderly patients and those with comorbidities, as it avoids the need for surgery
    - Contraindications to the use of SRT include aggressive tumor histology or deep tumor invasion, previously irradiated lesions, and some types of NMSC occurring on organ transplant recipients.

Brachytherapy (111)

- Recommended for treating skin cancers, especially in elderly and frail patients, due to its non-invasive or minimally invasive nature and shorter overall treatment duration. Brachytherapy is advantageous for tumors located on curved surfaces and for deeper or very irregular tumors. Brachytherapy is recommended for treating keloids, with the treatment starting as soon as possible after surgery to prevent regrowth
    - Brachytherapy is not suitable for tumors thicker than 5 mm within any surface, including very irregular. Brachytherapy is not recommended for large, deep tumors

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as it may not provide adequate dose coverage of the tumor. Higher doses per fraction are not recommended for very thin skin or underlying cartilage, such as the nose, to avoid poor cosmetic long-term results.

- Haseltine 2016 study [202] compared HDR brachytherapy, hypofractionated EBRT, and standard fractionation EBRT for NMSC such as BCC and SCC. The findings indicated that all three modalities are effective for treating NMSC with good cosmetic outcomes and acceptable toxicity profiles. However, standard fractionation EBRT showed higher grade toxicity and a greater portion of patients experiencing toxicity.

Thymomas and Thymic Carcinomas

Thymomas and thymic carcinomas are rare tumors originating in the thymus. The incidence of thymomas is approximately 1.5 cases per million people annually, making them a relatively uncommon type of tumor. [203] Thymic carcinomas are even rarer and more aggressive compared to thymomas. [203]

In terms of survival rates, thymomas generally have a better prognosis than thymic carcinomas. Patients with thymomas have a 5-year survival rate of approximately 90%. However, the survival rate can vary depending on the stage of the disease. For example, patients with stage I thymomas have an excellent prognosis with a 10-year survival rate of around 90%, while those with stage II thymomas have a 10-year survival rate of about 70%. [203]

Thymic carcinomas, on the other hand, have a poorer prognosis. The 5-year survival rate for thymic carcinomas is approximately 60%. The survival rate also varies depending on the stage and resectability of the tumor. [203] However, for those with advanced stages or unresectable tumors, the survival rates are significantly lower.

Modality-Specific Considerations

IMRT

IMRT is recommended over 3D-CRT because it allows for precise targeting of the tumor while minimizing radiation exposure to surrounding healthy tissues such as the heart and lungs. This precision helps reduce the risk of radiation-induced damage to these critical organs. [203–205]

Conventional Fractionated Radiation Therapy

This approach involves delivering radiation in small doses over several weeks. Studies have shown that this method is effective in achieving local control of the tumor while minimizing acute and late complications such as radiation pneumonitis and esophagitis. It is recommended for its effectiveness in controlling tumor growth while allowing normal tissues time to repair between treatments. [203,205]

Elective Nodal Irradiation (ENI)

Although not recommended for thymomas and thymic carcinomas due to the low likelihood of lymph node metastasis, ENI can be considered in specific cases where there is a high risk of nodal involvement. [203–205]

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High-Dose Radiation

Escalating radiation doses beyond 60-66 Gy is generally not recommended as it has not shown improved outcomes and may increase the risk of toxicity. [203,205] However, high-dose radiation (60-70 Gy) is recommended for **unresectable** disease or gross residual disease after surgery. It has been shown to improve local control of the tumor while balancing the risk of severe toxicity to the heart, lungs, and esophagus and increase the chances of long-term survival. [203,204]

Concurrent Chemotherapy with Radiation

Combining chemotherapy with radiation therapy is recommended for locally advanced unresectable thymic carcinomas. This approach enhances the effectiveness of treatment by targeting both the primary tumor and potential microscopic disease. Clinical trials have shown that this approach can improve local control rates, although it also increases the risk of severe side effects. [203–205]

Consolidative Systemic Therapy

Routine use of consolidative high-dose cytotoxic chemotherapy after curative-intent surgical resection is not recommended due to the high risk of toxicity and lack of evidence for improved outcomes. [204,205]

Thyroid

Thyroid cancer is relatively common, with an estimated 52,890 new cases diagnosed in the United States in 2020. [206] The majority of these cases are differentiated thyroid cancers (DTCs), such as papillary or follicular thyroid cancer. [206]

The incidence of thyroid cancer has been increasing over the years, and it is now the fifth leading cause of cancer in women in the United States. [207] The majority of thyroid cancers are differentiated, with papillary and follicular histologies accounting for over 90% of new diagnoses. [207]

The survival rate for thyroid cancer is generally excellent, especially for differentiated thyroid cancers. The 5-year survival rate for patients with DTC is very high, often exceeding 90%. [207] However, the prognosis can vary depending on the type and stage of the cancer. For instance, anaplastic thyroid cancer (ATC) is highly aggressive and has a much poorer prognosis, with a historical median survival of about 5 months and a 1-year overall survival of 20%. [117]

In summary, while the incidence of thyroid cancer is increasing, the survival rate for most types of thyroid cancer remains high, particularly for differentiated thyroid cancers. However, more aggressive forms like ATC have significantly lower survival rates.

Modality-Specific Considerations

Locoregional Control: Radiation therapy, particularly IMRT, is effective in controlling locoregional disease. This is especially important in cases where the disease is unresectable or there is gross residual disease after surgery. Studies have shown that IMRT can achieve high rates of locoregional PFS and OS in patients with non-anaplastic thyroid cancer. [207,208]

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Clinical trials have shown that IMRT combined with chemotherapy (CC-IMRT) provides excellent locoregional control in patients with non-anaplastic thyroid cancer. For instance, a prospective phase II trial demonstrated that CC-IMRT achieved a 2-year locoregional PFS rate of 78.3%, with no in-field locoregional failures in the CC-IMRT cohort. (206,208)

Combination with Chemotherapy: Concurrent chemoradiation therapy (CC-IMRT) using agents like doxorubicin has been shown to improve locoregional control and overall survival compared to IMRT alone. Patients treated with CC-IMRT had higher rates of locoregional PFS and overall survival (OS) compared to those treated with IMRT alone. (206,208) This combination therapy is particularly beneficial for patients with high-risk pathology, such as poorly differentiated thyroid cancer (PDTC) and tall cell variant papillary thyroid cancer. (207,208)

Safety and Tolerability: Modern radiation therapy techniques, such as IMRT, have been shown to be safe and well-tolerated. Acute and late toxicities are generally manageable, and functional outcomes, such as swallowing function, are preserved. Patient-reported quality of life (PRQOL) also returns to baseline levels within a few months after treatment. (206–208)

Multidisciplinary Approach: The decision to use radiation therapy is often made in a multidisciplinary setting, involving input from surgeons, radiation oncologists, and medical oncologists. This collaborative approach ensures that the treatment plan is tailored to the individual patient's needs and maximizes the chances of achieving the best possible outcomes. (117,206)

In summary, radiation therapy is recommended for treating thyroid cancer in select cases where it significantly improves locoregional control, overall survival, and quality of life. Its effectiveness and safety are further enhanced when combined with chemotherapy and modern techniques like IMRT.

Some clinical indications where radiation therapy is not recommended for treating thyroid cancer:

- **Differentiated Thyroid Cancers (DTCs)**: Radiation therapy, such as EBRT, is generally not recommended for differentiated thyroid cancers like papillary or follicular thyroid cancer. These types of cancers often respond well to surgical resection and radioactive iodine (RAI) therapy, making EBRT unnecessary unless the disease is unresectable or there is gross residual disease. (207,208)
- **Early-Stage Disease**: For early-stage thyroid cancers, the prognosis is excellent with surgery and RAI therapy alone. The addition of EBRT in these cases does not significantly improve outcomes and may expose patients to unnecessary risks. (207,208)
- **Specific Histological Types**: Certain histological types of thyroid cancer, such as anaplastic thyroid cancer (ATC), may not respond well to conventional radiation therapy. ATC is highly aggressive and often requires a combination of surgery, chemotherapy, and targeted therapies. (117,207,208)
- **Potential for Significant Toxicity**: Radiation therapy can lead to significant acute and late toxicities. For example, IMRT combined with chemotherapy (CC-IMRT) has been associated with higher rates of acute dermatitis, mucositis, and dysphagia. (206–208) These

side effects can impact the patient's quality of life and may not be justified if other effective treatments are available.

- **Limited Benefit in Specific Cases**: Radiation therapy is not recommended for patients with small, localized tumors that can be effectively managed with surgery and RAI therapy alone. For early-stage thyroid cancers, the prognosis is generally excellent with surgery and RAI therapy alone. The addition of EBRT in these cases does not significantly improve outcomes and may expose patients to unnecessary risks. The risks associated with radiation therapy may outweigh the benefits in these cases. [207,208]

In summary, radiation therapy is generally reserved for more advanced or specific cases where other treatments are not sufficient. It is important to consider the type and stage of cancer, potential side effects, and overall treatment goals when deciding on the use of radiation therapy for thyroid cancer. It is often reserved for more advanced or specific cases where other treatments are not sufficient.

Unique Treatment Modalities

IORT

Cervical Cancer [121]

- Locoregional Recurrence: IORT is recommended for patients with recurrent disease in the central pelvis following radiation therapy. It is particularly useful for delivering a single, highly focused dose of radiation to an at-risk tumor bed or isolated unresectable residual disease during an open surgical procedure.
    - Howlett 2024 study [209] examined the use of IORT for recurrent cervical and endometrial cancer. The findings indicated that IORT can be a useful treatment modality for patients with recurrent gynecologic malignancies, particularly in cases of isolated recurrence in the pelvis or retroperitoneal lymph nodes. The study highlighted that IORT offers the ability to target the field at the highest risk of recurrence while sparing healthy tissues, making it 2-3 times as effective as the same dose delivered in fractionated EBRT doses. Factors such as ECOG performance status, neoadjuvant chemotherapy/immunotherapy, pelvic sidewall involvement, and resection margin status influence the risk of morbidity and mortality. The overall survival at 3 years was 48.6%, with a median survival of 2.8 years
- Advanced-Stage Disease: For patients with advanced-stage disease (Stage IIB and above), IORT can be considered in cases where pelvic exenteration is performed. This is especially relevant when there is documented evidence of persistent or recurrent small volume cervical disease after radiation/chemoradiation and no metastatic disease.
- Surgical Exploration: IORT is also recommended during surgical exploration for patients with recurrent or persistent disease in the central pelvis. It helps in achieving negative margins by manually displacing overlying normal tissue from the region at risk.

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Uterine Neoplasms [49]

- Locoregional Recurrence: IORT is recommended for patients with isolated vaginal/pelvic recurrence who have not received prior radiation therapy to the site of recurrence. It is used in conjunction with surgical exploration and resection to ensure complete removal of the tumor.
- High-Risk Histologies: For high-risk histologies such as serous carcinoma, clear cell carcinoma, and carcinosarcoma, IORT is considered during surgical resection to manage any residual disease and improve local control.
- Advanced-Stage Disease: In cases of advanced-stage disease (Stage III and IV), IORT is recommended as part of a multimodal approach that includes systemic therapy and EBRT. It is particularly useful for treating gross upper abdominal residual disease

Soft Tissue & Retroperitoneal Sarcoma [104]

- Retroperitoneal/Intra-Abdominal Sarcomas: IORT is recommended for retroperitoneal/intra-abdominal sarcomas, particularly when neoadjuvant radiation therapy has been previously delivered. It is used to boost known or suspected positive margins at the time of surgery. The recommended doses are 10 to 12.5 Gy for microscopically positive disease and 15 Gy for gross disease.
- Extremity/Body Wall, Head/Neck Sarcomas: IORT is also recommended for extremity/body wall, head/neck sarcomas when there are oncologically appropriate margins. It is suggested only after neoadjuvant radiation therapy. This approach helps in achieving better local control by delivering a concentrated dose of radiation directly to the tumor bed during surgery.

Colon Cancer [210–212]

- For carefully selected patients—such as those with T4 tumors invading adjacent fixed structures or with locally recurrent disease—neoadjuvant or adjuvant radiation therapy administered concurrently with fluoropyrimidine-based chemotherapy may be appropriate. The treatment volume should encompass the tumor bed, as determined by preoperative imaging and/or the placement of surgical clips. When available, IORT can be employed to deliver an additional boost dose. If IORT is not accessible, an extra 10 to 20 Gy may be delivered to a restricted field using EBRT and/or brachytherapy.
- For patients with locally unresectable tumors or those medically unfit for surgery, definitive chemoradiation is an option. Following such treatment, surgical resection with or without IORT may be reconsidered, or the patient may proceed to further systemic therapy depending on response and overall condition.

Rectal Cancer [213–215]

- For individuals with T4 lesions, locally recurrent disease, or tumors with close or positive surgical margins, the use of IORT may be appropriate as an adjunctive boost to enhance local control and support complete resection. IORT allows targeted irradiation of the tumor area during surgery, delivering radiation directly to the exposed tissues while

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shielding surrounding normal structures from unnecessary exposure.

Hyperthermia

Hyperthermia, when combined with radiotherapy, has been shown to significantly improve therapeutic outcomes for several cancer types:

- **Head and Neck Cancers:** The addition of hyperthermia to radiotherapy increases the complete response rate to 62.5%, compared to 39.6% with radiotherapy alone, without notable increases in toxicity. (120)
- **Cutaneous Melanoma:** Clinical guidelines and trials indicate that hyperthermia combined with radiotherapy can achieve complete response rates ranging from 55% to 66%, which is substantially higher than the 16% to 47% observed with chemo-radiotherapy alone. (113)
- **Chest Wall Recurrence of Breast Cancer:** Hyperthermia enhances the effects of radiotherapy, resulting in a complete response rate of 66% versus 42% for radiotherapy alone, and provides more durable local control, especially in previously irradiated areas. (119)

Hyperthermia in combination with radiotherapy varies by cancer type and clinical scenario, but consistently demonstrates higher complete response and survival rates compared to radiotherapy alone, particularly for patients with recurrent disease or prior irradiation. (113,119,120)

Clinical trials have demonstrated that hyperthermia enhances the effectiveness of radiotherapy by inhibiting DNA repair, sensitizing hypoxic tumor cells, and improving oxygenation, resulting in improved therapeutic outcomes without significant additional toxicity. (120)

Modality-Specific Considerations

Head and Neck Cancers: Hyperthermia can enhance the effectiveness of radiotherapy by inhibiting DNA damage repair, sensitizing hypoxic cells, and improving oxygenation. These effects lead to better therapeutic outcomes without significant additional toxicities A meta-analysis of 451 cases found that the complete response rate with thermoradiotherapy was 62.5%, compared to 39.6% with radiotherapy alone. (120)

Yet, hyperthermia is not always recommended due to the potential for increased toxicity and the need for specialized equipment and expertise. (120)

Cutaneous Melanoma: Guidelines and clinical studies show that combining hyperthermia with radiotherapy improves local control and reduces recurrence risk, with complete response rates ranging from 55% to 66%, notably higher than the 16% to 47% seen with chemo-radiotherapy alone. (113)

While hyperthermia can be beneficial when combined with radiotherapy, it is not always recommended due to the risk of increased side effects and the need for precise temperature control to avoid damage to surrounding healthy tissues. (113)

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Chest Wall Recurrence of Breast Cancer: Hyperthermia blocks DNA repair and increases tumor oxygenation, leading to higher complete response rates and more durable local control, especially in previously irradiated areas; clinical trials report a complete response rate of 66% with hyperthermia plus radiotherapy versus 42% with radiotherapy alone. (119)

However, while hyperthermia can enhance the effects of radiotherapy, it is not always recommended due to the potential for severe side effects, including skin burns and tissue damage. Additionally, the availability of hyperthermia treatment is limited to specialized centers. (119)

In summary, the main clinical trial findings supporting the recommendation of radiation therapies with hyperthermia include enhanced radiotherapy effectiveness, improved local control, reduced recurrence risk, and the ability to use lower radiation doses, all contributing to better patient outcomes. (113,119,120)

APPROVAL HISTORY

10/21/2026	IMRT added to Breast Cancer sections, Added indications to the Post Lumpectomy section and clarified indicated cancer stages and characteristics, Indications for Partial Breast Irradiation updated to include brachytherapy and subsequent clinical indications updated, Central Nervous System Tumors fractionation section added Craniospinal-Irradiation delivered over 13-20 fractions, Updated treatment fractions for Meningioma Grade 3, Pituitary Adenoma, Colon Cancer, Esophageal Cancer (cervical), Primary Brain and Spinal Cord Cancers conventional fractionation indications updated to include high-risk features, High Grade Adult Glioma fractionation section added Karnofsky Performance Status and indication for Gamma-Tile brachytherapy updated to include high-grade glioma, Primary CNS Lymphoma conventional fractionation updated to include WBRT may be used as consolidation therapy, Primary Spinal Cord Tumors updated conventional fractionation indication to include IMRT or 3D-CRT for tumors below the conus medullaris, Prophylactic Cranial Irradiation fractionation section added radiation therapy delivered as WBRT, Trigeminal Neuralgia added indications, Anal Cancer updated to include cT1-T2, cN0 with No Residual Primary Tumor after 25 Fractions of IMRT or 3D-CRT, Carcinoid (Neuroendocrine) Tumors section added with indications, Clarified indicated cancer stages and characteristics for Bladder Cancer, Penile Cancer, Urethral Cancer, Regional Disease, Added Kidney Cancer and MCRPC sections for related indications, Added indications for brachytherapy to Penile Cancer and Favorable/Unfavorable Intermediate Risk Prostate Cancer, Reorganized Prostate Cancer section for readability and clarified definitions of favorable/unfavorable intermediate risk, low-volume metastases, and regional disease, Updated indications under Prostate Cancer sections (Low-Volume Metastases, Post-Prostatectomy Radiation Therapy, Prophylactic Breast Irradiation for Patients Receiving ADT, Regional Disease) and Testicular Cancer, Clarified indications under Nonsurgical Vaginal Cancer, Clarified and expanded indications under Nonsurgical and Postoperative Vulvar Cancer, Added Melanoma section under Vulvar Cancer section for related indications, Updated treatment stages and fraction used in conventional

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	fractionation IMRT/3D-CRT for Glottic Larynx Cancer, Added Maxillary Sinus Tumors indication, Added treatment stages in conventional fractionation IMRT/3D-CRT for Oral Cavity Cancer, Specified treatment stages for NSCLC and SCLC, Added SBRT fractionation for patients with cT3, cN0, cM0, Stage IIB NSCLC cancers, Removed indications: stage IIA NSCLC preoperative, patients with EMZL of the orbit and salivary gland, PTCLD in Cutaneous Lymphomas, Updated hypofractionation treatment in patients at limited stage SCLC, Updated treatment fractions for patients with a partial response/refractory disease (Deauville 4–5) (in Hodgkin's Lymphoma), PTCL non-Hodgkin's lymphoma, PC-ALCL, PCFCL, PCMZL, PCNKTCL, and SBRT Spinal Bone Metastases, Expanded low energy x-rays range from 100 kV to 50-300 kV, Added SPTCL treatment fraction indication in Cutaneous Lymphomas, Added conditions (Castleman's Disease, Hyperthyroidism) to the Other Non-Cancerous Conditions section, Updated treatment fractions for Lentigo Maligna, Orbital Pseudotumor, Pterygium, Total Body Irradiation, and Basal Cell and Squamous Cell Carcinoma, Updated treatment fractions for Basal Cell and Squamous Cell Carcinoma using Electron Beam Therapy (2D-CRT) or, 3D-CRT, or IMRT for Patients with No Metastatic Disease, Melanoma of the Skin and Eye (Uveal), Merkel Cell Carcinoma, and Thymoma and Thymic Carcinomas, and partitioned indications into Definitive and Adjuvant treatment sections, Added indications for using IMRT to treat Merkel Cell Carcinoma and Melanoma of the Skin and Eye (Uveal), Added an indication for using IMRT or 3D-CRT to treat Anaplastic Thyroid Cancer in non-metastatic patients with microscopic disease, Added indications for using Sodium Iodine-131 to treat well-differentiated follicular carcinoma and papillary carcinoma
02/11/2026	Added E/I/U statement for all non-cancerous indications other than those listed in the policy.
12/10/2025	Updated fractions according to societal guidance throughout policy; Radiation doses (i.e., Grays (Gy)) were removed;'Exclusion' sections were removed; Palliative care indications were consolidated; Unnecessary wording was removed; Added a Summary of Evidence and Analysis of Evidence; Updated references
06/11/2025	Removed SIRT therapy guidelines for Hepatocellular Carcinoma and routed the criteria to reference MCP 181
12/11/2024	New Policy.

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