

MEDICAL POLICY

| MEDICAL POLICY DETAILS | |
|-------------------------|---|
| Medical Policy Title | Intensity Modulated Radiation Therapy (IMRT) |
| Policy Number | 6.01.24 |
| Category | Technology Assessment |
| Original Effective Date | 02/21/02 |
| Committee Approval Date | 03/20/03, 03/18/04, 02/17/05, 12/15/05, 12/21/06, 12/20/07, 10/23/08, 01/21/10, 08/19/10, 11/17/11, 12/20/12, 01/16/14, 08/21/14, 11/19/15, 12/15/16, 08/17/17, 08/16/18, 05/16/19, 05/21/20, 8/20/20, 06/17/21, 01/20/22, 09/21/23 |
| Current Effective Date | 10/15/21, 01/20/22, 09/21/23 |
| Archived Date | N/A |
| Archive Review Date | N/A |
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POLICY STATEMENTS

- I. Based upon our criteria and assessment of the peer-reviewed literature, intensity modulated radiation therapy (IMRT) is considered **medically appropriate** for individuals with the following cancers when the following criteria have been met:
- A. **Adrenal tumors** for any of the following:
 1. Stage II or III disease
 2. Presence of positive margins
 3. Presence of high-grade or Ki-67 > 10%.
 - B. **Anal cancer** for definitive treatment.
 - C. **Bladder cancer** in the curative setting which overlaps a previously irradiated area or when dose to nearby critical structures may be exceeded.
 - D. **Bone cancer** for any of the following:
 1. Primary bone cancer (i.e, chondrosarcoma, chordoma, Ewing sarcoma, giant cell tumor of bone, osteosarcoma)
 2. Metastases when treatment is overlapping a previously irradiated area
 - E. **Brain metastases** for any of the following:
 1. sole treatment of partial brain therapy in individuals with good prognosis; or
 2. as boost therapy; or
 3. to spare the hippocampi when delivering whole brain radiation therapy (HA-WBRT) in patients who:
 - a. have a prognosis of at least 4 months; and

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 2 of 13

- b. have a Karnofsky Performance Status (KPS) of at least 70 or an Eastern Cooperative Oncology Group (ECOG) Performance Status of at least 2; and
 - c. do not have leptomeningeal disease; and
 - d. whose primary histology is not germ cell, lymphoma or unknown.
- F. **Breast cancer** when:
1. treatment is overlapping a previously irradiated area; or
 2. when dose to nearby critical structures may be exceeded; or
 3. accelerated partial breast irradiation (APBI) following breast-conserving surgery delivered in 10 fractions twice daily or 5 fractions delivered once daily.
- G. **Cervical cancer** with any of the following:
1. positive pelvic nodes on positron emission tomography (PET), magnetic resonance imaging (MRI) or computed tomography (CT) scan being treated to doses of 54 Gy or higher; or
 2. definitive treatment when additional brachytherapy cannot be performed, and the patient is inoperable; or
 3. treatment of the paraaortic nodes; or
 4. as adjuvant (post-operative) treatment in an individual without evidence of distant metastases for positive surgical margins, positive pelvic nodes, positive paraaortic nodes, close vaginal margins less than 0.5 cm, extensive lymphovascular or capillary involvement, deep stromal invasion, large tumor size greater than four cm; or
 5. locoregional recurrence in an individual without evidence of distant metastases when either of the following:
 - a. The paraaortic nodes will be treated; or
 - b. The postoperative setting where the whole pelvis will be treated to 45 Gy or higher; or
 6. In the non-curative setting when symptoms are present and when previous external beam radiation therapy (EBRT) or brachytherapy has been given and normal tissue dose constraints cannot be met with 3D CRT.
- H. **Craniospinal tumors:**
1. Ependymoma, medulloblastoma and primitive neuroectodermal tumors (PNET); or
 2. Benign brain tumors (e.g., pituitary adenomas, acoustic neuromas, schwannomas, craniopharyngiomas, hemangioblastomas, pineocytomas, glomus tumors, and meningiomas); or
 3. Treatment of the following:
 - a. Recurrent glioma, who have an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2
 - b. World Health Organization (WHO) grade I, II tumors
 - c. WHO grade III-IV tumors, using conventional fractionation or hypofractionation for those that have poor performance status or cannot tolerate longer courses of radiation.
 4. Inoperable primary spinal tumor with compression or intractable pain.
- I. **Endometrial cancer;** when:
1. dose to nearby critical structures may be exceeded; or
 2. in the post-hysterectomy setting.
- J. **Esophageal cancer** when normal tissue dose constraints cannot be met with 3D CRT; and
1. as neoadjuvant therapy in stage T1b node-positive or stage T2-T4a; or
 2. as adjuvant therapy, if no pre-operative or prior radiation given; or
 3. as adjuvant therapy in squamous cell carcinoma with at least T2 or node positive; or
 4. as definitive therapy in stage T1b node-positive, stage T2-T4a, or tumors located in the cervical esophagus; or
 5. palliation when dose to nearby critical structures may be exceeded.
- K. **Gastric cancer:**
1. as neoadjuvant therapy of T2-T4 or node positive; or
 2. as adjuvant therapy of at least T2 or node positive, positive margins, microscopic or macroscopic residual disease, or high-risk features (e.g., poor differentiation, lymphovascular invasion, neural invasion, age less than 50); or

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 3 of 13

3. treatment when tumor is inoperable (e.g., co-morbidity); or
 4. palliation when dose to nearby critical structures may be exceeded.
- L. Head and neck cancer:**
1. as definitive therapy in select T1-2, N0 cases as monotherapy; or
 2. as definitive therapy in select T1N1, T2 N0-1 cases as monotherapy; or
 3. as definitive therapy with concurrent chemotherapy in T2-4a, N0-3 cases; or
 4. post-operatively when there are high risk factors (e.g., pT3 or pT4 primary tumors, N2 or N3 nodal disease, positive nodes in levels IV or V, perineural invasion, vascular tumor embolism, or positive surgical margins or residual gross disease; or
 5. as palliative therapy in a previously un-irradiated individual with symptomatic local disease; or
 6. as salvage therapy after prior radiation in cases of recurrent or persistent disease, or for in-field new primary tumors, in cases in which there are no known distant metastases.
- M. Hodgkin Lymphoma:**
1. when used as sole therapy in selected cases of stage I-IIA lymphocyte predominant Hodgkin's lymphoma; or
 2. as adjuvant radiation therapy (combined modality treatment) after chemotherapy in stage III-IV disease to areas of initial bulky involvement or to areas with less than a complete response; or
 3. as salvage radiation therapy after chemotherapy to areas of relapsed bulky involvement; or
 4. as salvage therapy in an individual who relapses after solo chemotherapy for initial stage I/IIA disease; or
 5. as palliative therapy in an individual with advanced or recurrent symptomatic local disease that is not curative.
- N. Liver, primary (hepatocellular [HCC]), cholangiocarcinoma):**
1. as definitive management of medically or technically unresectable localized HCC in an individual with adequate hepatic reserve; or
 2. as definitive management of unresectable localized intrahepatic or extrahepatic bile duct cancer; or
 3. as adjuvant (postoperative) treatment of resected intrahepatic or extrahepatic bile duct cancer.
- O. Lung Cancer when:**
1. Small Cell, when an optimized 3D conformal radiation therapy plan exceeds tolerances for organs at risk; or
 2. Non-Small Cell, in the curative setting which overlaps a previously irradiated area or dose to nearby critical structures may be exceeded.
- P. Multiple Myeloma and Solitary Plasmacytomas** for definitive treatment of a solitary plasmacytoma presenting in the head and neck region.
- Q. Non Hodgkin Lymphoma:**
1. Definitive radiation therapy when disease is located above the diaphragm
 2. extranodal NK/T-cell lymphoma
 3. peripheral T-cell lymphoma, for refractory disease or for primary treatment in an individual not receiving chemotherapy
 4. sub-diaphragmatic disease when normal tissue dose constraints cannot be met with 3D-CRT.
- R. Pancreatic cancer:**
1. as neoadjuvant therapy when cancer is borderline resectable
 2. unresectable/locally advanced
 3. postoperative
 4. palliative treatment when dose to small bowel, liver, heart, lung, kidneys and spinal cord may be exceeded.
- S. Prostate cancer:**
1. clinically localized disease:
 - a. low, intermediate and high-risk: IMRT to be delivered as hypofractionation – 20 to 28 fractions per treatment course in up to 2 phases.
 - b. low, intermediate and high-risk: IMRT to be delivered as conventional fractionation- up to 45 fractions for localized prostate cancer is considered medically necessary for ANY of the following:
 - i. For high-risk or node-positive prostate cancer when the pelvic nodes will be treated;

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 4 of 13

- ii. Inflammatory bowel disease, Crohn's and ulcerative colitis;
 - iii. Previous pelvic radiation therapy;
 - iv. History of rectal, urinary bladder, or urethral fistula or abscess;
 - v. History of anorectal surgery, including but not limited to coloanal anastomosis;
 - vi. Prior local treatment including cryotherapy or high-intensity focused ultrasound (HIFU); or,
 - vii. Prior transurethral resection of prostate (TURP)
2. as adjuvant or salvage therapy after radical prostatectomy in men with adverse pathological features (*refer to Policy Guideline II*) or detectable Prostate-Specific Antigen (PSA) with no evidence of disseminated disease; or combined with brachytherapy for intermediate and high risk disease; total dose of 64-72 Gy in 32-40 fractions;
 3. treatment of pelvic lymph nodes:
 - a. high-risk or node-positive disease with IMRT alone (conventional fractionation or hypofractionation) or combined with brachytherapy.
 4. metastatic disease:
 - a. low volume disease, castration naïve metastatic prostate cancer with three or fewer bone metastases and no visceral disease, in conjunction with androgen deprivation therapy (ADT); total dose of 55 Gy in 20 fractions;
 - b. high volume disease; IMRT considered **not medically necessary** (*refer to policy statement III.e.*)
- T. Rectal Cancer:**
1. extension of tumor to involve the anal canal requiring coverage of the inguinal nodes; or
 2. a dose of greater than 54 Gy is planned for curative treatment in the non-metastatic, medically inoperable setting; or
 3. previous pelvic radiation, or
 4. where tolerance for organs at risk may be exceeded by conventional treatment.
- U. Skin cancer- Non-Melanoma**
1. Extramammary Paget disease, treatment of inguinal lymph nodes
- V. Soft Tissue Sarcomas:**
1. Individuals with stage II-III and non-metastatic stage IV tumors that are unresectable, or in the postoperative setting with gross residual disease
 2. Extremity sarcomas located within the proximal lower extremity (i.e., thigh, groin)
 3. Preoperative treatment of retroperitoneal sarcoma.
- W. Spinal Cord** primary inoperable tumors with compression or intractable pain where tolerance may be exceeded by conventional treatment.
- X. Thymoma and Thymic Cancer**
1. Postoperative treatment of Stage I-IVA* thymoma and thymic carcinoma; and
 - a. Macroscopic positive surgical margins; or
 - b. gross residual disease
 2. Definitive treatment
 - a. unresectable disease
 - b. isolated local recurrence without distant metastatic disease
 - c. curative setting overlapping a previously irradiated area
- *Masaoka-Koga staging system
- Y. Urethral cancer:**
1. curative treatment of inoperable T2- T4 or node positive disease;
 2. Postoperative setting, with gross residual disease, positive margins and/or extranodal extension
 3. Recurrent disease when normal tissue dose constraints cannot be met with 3D CRT.
- Z. Vulvar cancer:**
1. adjuvant therapy following initial surgery; or
 2. preoperative therapy for locally advanced disease; or

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 5 of 13

3. in the definitive setting; or
 4. recurrent vulvar cancer without evidence of distant spread of disease.
- II. Based upon our criteria and assessment of the peer-reviewed literature, biodegradable perirectal spacer (e.g., SpaceOar system) use is **medically appropriate** for individuals with clinically localized prostate cancer (i.e., has not invaded into the rectum or extended beyond the posterior region of the prostate) who are planning to undergo hypofractionated radiation therapy.
- III. Based on our criteria and assessment of the peer-reviewed literature IMRT has not been medically proven to be more effective than 3D CRT and, therefore, is considered **not medically necessary** for all other indications including, but not limited to:
- A. Renal cell cancer, as definitive treatment
 - B. Prostate Cancer, for high volume disease

Refer to Corporate Medical Policy #6.01.16 Brachytherapy or Radioactive Seed Implantation for Prostate Cancer

Refer to Corporate Medical Policy #6.01.30 Brachytherapy After Breast Conserving Surgery, as Boost with Whole Breast Irradiation or Alone as Accelerated Partial Breast Irradiation

POLICY GUIDELINES

- I. Radiation therapy may be delivered by many different techniques depending on the type of cancer being treated, tumor size, location, and dose to be delivered. Therefore, the clinical rationale for use of IMRT must be clearly documented by the treating radiation oncologist. The documentation must reflect the condition of the individual patient, and indicate the medical necessity for which the service was performed. The documentation submitted for review must include:
 - A. A statement by the treating physician, documenting the special need for performing IMRT on the specific patient, rather than performing conventional or 3D treatment planning and delivery.
- II. In prostate cancer, adverse pathological features include:
 - A. Positive surgical margins; and/or
 - B. Extracapsular extension; and/or
 - C. Seminal vesicle involvement; and/or
 - D. Positive lymph nodes; and/or
 - E. Gleason score 8 to 10; and/or
 - F. Detectable or rising postoperative PSA level.
- III. Daily Image-Guided Intensity-modulated radiotherapy (IGRT) is recommended when criteria for IMRT is met.

DESCRIPTION

The ACR –ASTRO Practice Guideline for IMRT (2016) states that a major goal of radiation therapy is the delivery of the desired dose distribution of ionizing radiation to target tissue while limiting the radiation dose to the surrounding normal tissues to an acceptable level and thus achieving optimal patient care outcomes. This can be accomplished using IMRT.

The process of care for IMRT consists of multiple steps for treatment planning and delivery of radiation. Compared to 3D conformal radiation therapy, IMRT combines inverse treatment planning and computer-controlled intensity modulation of the photon radiation beam. Delineation of both the target volume and the surrounding tissues at risk is required to decrease the dose to volumes of non-target structures while achieving prescription doses to the target volume. An optimized treatment plan is developed that respects the target dose requirements as well as the dose constraints of the surrounding dose-limiting structures.

IMRT treatment delivery demands careful, day-by-day reproduction of the treatment plan within the patient as well as, levels of precision and accuracy that surpass the requirements of conventional radiotherapy treatment planning and delivery techniques. The IMRT process requires a coordinated team effort between the radiation oncologist, the medical physicist, the medical dosimetrist, and the radiation therapist.

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 6 of 13

Volumetric Modulated Arc Therapy (VMAT) is an advanced form of IMRT. While IMRT relies on multiple static independent beam angles, VMAT continuously administers the treatment in an arc, with a rotating gantry.

IGRT is the use of imaging at the time of treatment delivery to ensure that the location of the target relative to the treatment beams based on a pre-determined plan is reproduced. At the time of treatment delivery, an IGRT modality is employed to determine the location of the target (and often the surrounding normal organs) at some frequency, most often at the beginning, to as often as nearly continuously throughout delivery. The target location may be determined by a range of methods from soft tissue volumetric imaging (e.g., kV or MV CT, ultrasound, magnetic resonance imaging) to localization of surrogates such as implanted fiducial markers or external surface markers or features (e.g., by planar imaging or fluoroscopy, electromagnetic localization or optical surface imaging). The match or discrepancy between the simulated location and the “live” IGRT measurement at the time of treatment may be determined manually, or in some cases using automated image analysis software. If a discrepancy is found, a correction is applied. Corrections may include repositioning the patient, either through rigid corrections (shift and/or rotation) or readjustment of anatomic relationship (e.g., neck and shoulder manipulations for head/neck treatments), or movement or reshaping of the radiation beam to match the target position, or holding the beam until the target falls in the correct location (e.g., respiratory gating). In this manner, the treatment will be delivered precisely and accurately according to the treatment plan approved by the radiation oncologist.

In summary, the ability of IMRT to deliver the radiation dose preferentially to target structures in close proximity to organs at risk (OAR) and other non-target tissues, while minimizing the dose to normal tissues makes it an alternative to conventional 3D conformational radiation therapy.

Due to its close proximity to the prostate, the rectum may receive unintended doses of radiation which can cause gastrointestinal toxicities. The increasing use of hypofractionation is associated with shorter treatment durations, however, has been shown to increase the risk of acute moderate gastrointestinal (GI) toxicity when compared to conventional fractionation. SpaceOAR (Spacing Organs At Risk (OAR) (Augmenix, Inc, Waltham, MA) is a polyethylene glycol-based hydrogel spacer that received FDA approval in 2015 as a means of reducing the dose of radiation received by the rectum. The spacer is injected into the perirectal space, temporarily positioning the rectum further away from the radiation field reducing the dose of radiation outside of the designated treatment area, and proposes to improve patient’s quality of life by reducing potential toxicities. The hydrogel remains in place for three months after which, it is then absorbed, and excreted through the patient’s urine.

RATIONALE

Clinical evidence supports that IMRT improves health outcomes by allowing adequate radiation therapy while minimizing damage to surrounding structures for adrenal tumors, primary brain tumors, brain metastasis, head and neck cancer, lung cancer, pancreatic cancer and other upper abdominal sites, pituitary tumors, prostate cancer and spinal cord tumors.

Breast Cancer

The American Society for Radiation Oncology (ASTRO) published a 2017 evidence-based guideline on accelerated partial breast irradiation (APBI) (Correa et al), stating that trials have demonstrated that in properly selected breast cancer patients, APBI has provided outcomes similar to whole breast irradiation (WBI). The guidelines state that suitable patients would be ≥ 50 years of age (weak level of evidence), negative margins by at least 2mm, stage Tis or T1, or for individuals with DCIS, it must be screen detected, low to intermediate nuclear grade, size ≤ 2.5 cm, resected with margins negative at ≥ 3 cm.

ASTRO published a 2018 evidence-based guideline on radiation therapy for the whole breast (Smith et al, 2018), recommending hypofractionated WBI to a dose of 4000 cGy in 25 fractions or 4250 Cgy in 16 fractions for women with invasive breast cancer. The authors stated that treatment with 3DCRT with field-in-field technique is recommended, however, IMRT should be reserved for those cases where 3DCRT or other methods cannot meet the dose constraints to the heart or lung.

Meattini and colleagues (2020) published long term results of the randomized phase III APBI-IMRT Florence Trial, evaluating the use of APBI vs. WBI with IMRT in 520 individuals with early breast cancer, >40 years old and a max

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 7 of 13

diameter of 2.5cm in size. The WBI arm received a total dose of 50Gy in 25 fractions, followed by a boost on the surgical bed of 10Gy in 5 fractions. The APBI arm received a total dose of 30Gy in five non-consecutive once-daily fractions. Follow up occurred monthly for three months, every four months for two years, and every six months for a median follow up of ten years. The primary outcomes were ipsilateral breast tumor recurrence (IBTR) rate, defined as measured local recurrence plus new ipsilateral breast tumors. Secondary outcomes included locoregional tumor recurrence (LRR), treatment related toxicity, and cosmetic outcomes. The ten year cumulative incidence of IBTR was 2.5% in the WBI arm and 3.7% in the APBI arm (hazard ratio [HR], 1.56; 95% CI, 0.55 to 4.37; P=.40). Overall survival was 91.9% for both arms(HR, 0.95; 95% CI, 0.50 to 1.79; P = .86), breast cancer specific survival was 96.7% in the WBI and 97.8% in the APBI arm, respectfully. The APBI showed significantly less acute and late toxicity as well as improved cosmetic outcomes rated by both the patient and the physician. The authors concluded that APBI with IMRT utilizing 30Gy in 5 fractions resulted in a IBTR that was not significantly different from patients being treated with WBI, and this schedule should be considered an attractive option to treat patients with low-risk early breast cancer.

Bone Cancer

NCCN Bone Cancer Guidelines Version 3.2023 states, “Patients should be strongly encouraged to have RT at the same specialized center that is providing surgical and systemic interventions. Specialized techniques such as intensity-modulated RT (IMRT); particle beam RT with protons, carbon ions, or other heavy ions; or stereotactic radiosurgery (SRS) should be considered as indicated in order to allow high-dose therapy while maximizing normal tissue sparing.”

Prostate Cancer

An ASTRO/ASCO/AUA evidence-based guideline (Morgan et al. 2018), supports the use of hypofractionated radiation in men with localized prostate cancer and although it is associated with both acute and late GI and genitourinary toxicity, it is similar in severity to conventional fractionation when appropriate normal tissue dose-volume histogram constraints are used. The guidelines state that one dosing regimen is not suggested over another as most schemes have not yet been compared to each other in clinical trials.

The most recent NCCN Guidelines Version 2.2023 for prostate cancer, indicate that external-beam radiotherapy, 3D CRT and IMRT are techniques which allow the volume of tissue receiving high radiation doses to conform more closely to the prostate shape. Overall, the panel believes that hypofractionated IMRT techniques, which are more convenient for patients, can be considered as an alternative to conventionally fractionated regimens when clinically indicated” and that moderate hypofractionation (i.e., 20-28 fractions) is preferred for the treatment of low, intermediate and high-risk disease.

Evidence from randomized trials has emerged that supports the use of adjuvant/salvage radiation therapy after radical prostatectomy in men with adverse laboratory or pathological features or detectable PSA. Adverse pathological features, which include positive surgical margin(s), seminal vesicle invasion, and/or extracapsular extension, place a patient at risk for biochemical recurrence after prostatectomy. Biochemical recurrence after radical prostatectomy is defined in the NCCN guidelines as those whose PSA level fails to fall to undetectable levels after radical prostatectomy, those who achieve an undetectable PSA after radical prostatectomy with a subsequent detectable PSA level that increases on two or more subsequent laboratory determinations or the occasional case with persistent but low PSA levels attributed to slow PSA metabolism or residual benign tissue.

The NCCN Guidelines Panel recommends active surveillance for men with very-low-risk prostate cancer and an estimated life expectancy-greater than or equal to 20 years, and for men with low-risk prostate cancer and estimated life expectancy of greater than or equal to 10 years. Observation is preferred for men with low-risk prostate cancer with life expectancy less than 10 years. The active surveillance recommendation involves monitoring the course of disease with the expectation to intervene with curative intent if the cancer progresses, meaning that the PSA is likely to rise, and that the tumor may grow with time. Patients must be prepared to re-evaluate the decision to defer treatment. The NCCN Guideline Panel recommends treatment in most men who demonstrate a Gleason grade of 4 or 5 on repeat biopsy, or have cancer in greater number or greater extent of prostate biopsies.

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 8 of 13

Clinically localized prostate cancer has been categorized by the risk of recurrence as follows (Gleason system has been compressed into histologic Grade Groups by NCCN):

| Recurrence Risk | Stage | Gleason Score | PSA(ng/ml) | PSADensity (ng/ml/g) | Other/Grade Group |
|-----------------|---------|-------------------------|-----------------|----------------------|---|
| Very Low | T1c | Less than or equal to 6 | Less than 10 | Less than 0.15 | Less than three prostate biopsy cores positive or less than or equal to 50% cancer in any core Grade Group 1 |
| Low | T1-T2a | Less than or equal to 6 | Less than 10 | | Grade Group 1 |
| Intermediate | T2b-T2c | 7 | 10-20 | | Grade Group 2 or 3 |
| High | T3a | 8-10 | Greater than 20 | | Grade Group 4 or 5 |
| Very High | T3b-T4 | 8-10 | any | | Greater than 4 cores with Grade Group 4 or 5 |

The NCCN Guidelines include examples of radiation therapy regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms, and toxicity of therapy.

For individuals who have prostate cancer and are undergoing radiation therapy who receive a hydrogel spacer, the evidence includes a pivotal RCT with a 3-year follow up, observational studies, and systematic reviews. Mariados and colleagues (2015) carried out a manufacturer sponsored, prospective, multi-center, single-blind study, evaluating the percent of the rectal volume receiving 70 Gy in dose planning studies of 222 men randomized 2:1 to either a spacer or control group. All men received IMRT (79.2 Gy in 1.8-Gy fractions) to the prostate. Those with spacer use experienced a lower percentage of rectal volume receiving 70 Gy (3.3% vs. 11.7%). They evaluated the effectiveness of the SpaceOAR system in reducing adverse gastrointestinal events with IMRT, and demonstrated a significant reduction in mean rectal V70 with the device in place. There were no reports of device-related adverse events, rectal perforations, serious bleeding, or infections, and acute rectal adverse events were similar between the two groups, however there was significantly less pain experience reported by the treatment group. A reduction in late rectal toxicity (three to 15 months after RT) has been observed, and no patients treated with the spacer experienced greater than grade 1 toxicity. The 3-year follow up study (Hamstra et al. 2017) involved 63% of the original participants (94 SpaceOAR subjects and 46 control group) and demonstrated a reduction of Grade ≥ 1 adverse events in the treatment group (2% vs. 9%, $p < .03$).

NCCN guidelines (v2.2023) state that biocompatible and biodegradable perirectal spacer materials may be implanted between the prostate and rectum in patients undergoing external radiotherapy with organ-confined prostate cancer in order to displace the rectum from high radiation dose regions. A randomized phase III trial demonstrated reduced rectal bleeding in patients undergoing the procedure, compared to controls. Retrospective data also support its use in similar patients undergoing brachytherapy. Patients with obvious rectal invasion or visible T3 or posterior extension should not undergo perirectal spacer implantation.

Non-small Cell Lung Cancer and Small Cell Lung Cancer

NCCN Guidelines suggest a potential role for radiation therapy in all stages of NSCLC. Given that the goals of modern radiation therapy are to maximize tumor control and to minimize treatment toxicity, IMRT should be used in the setting of prior radiation therapy, potentially with hyperfractionation to reduce the risk of toxicity. This recommendation was based on the RTOG 0617 prospective trial (Chun, et al. 2017) which found that IMRT was associated with a nearly 60% decrease, from 7.9% to 3.5% in high grade radiation pneumonitis as well as similar survival and tumor control outcomes

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 9 of 13

despite a higher proportion of stage IIIb and larger treatment volumes compared to 3D-CRT. The principles of radiation therapy stimulation, planning, and delivery for small cell lung cancer follow the NCCN Guidelines for NSCLC.

Soft-Tissue Sarcomas

ASTRO released a Clinical Practice Guideline for radiation therapy for the treatment of soft tissue sarcoma in 2021. The guideline states that after resection alone, final pathologic exam may reveal unanticipated adverse features that increase risk for local recurrence, and in such cases, postoperative RT is recommended for local control, particularly where further resection is not feasible.

Thymomas and Thymic Carcinoma

Thymomas and thymic carcinoma, are very rare neoplasms (0.13 cases per 100,000 person years) occurring in the anterior mediastinum. The standard of care for thymomas for any stage is surgical resection, but adjuvant radiation post definitive surgery is indicated for positive margin or gross residual disease, with studies indicating improved disease-free survival. Thymomas specifically are associated with autoimmune paraneoplastic diseases (e.g., myasthenia gravis, hypogammaglobulinemia, autoimmune pure red cell aplasia) but the clinical behavioral of both can vary greatly from indolent to metastatic and aggressive, with a five-year survival for inoperable locally advanced carcinoma of 36%; and 24% for metastatic thymoma and thymic carcinoma. NCCN Guidelines 2.2022 for Thymomas and Thymic Carcinomas states that more advanced technologies are appropriate when needed to deliver curative RT safely. These technologies include (but are not limited to) 4D-CT and or PET/CT simulation, IMRT, Volumetric arc therapy, IGRT, motion management and proton therapy. In particular, IMRT is preferred over 3D-CRT.”

Urethral Cancer

The treatment of T2-T4 or node positive disease aligns with NCCN guidelines, that currently recommend definitive radiation therapy for T2-T4 or lymph node positive disease, postoperatively when there is residual disease, positive margins and/or extranodal extension. For post operative treatment and recurrent disease, NCCN notes that the dose may be limited secondary to normal tissue dose constraints. Given the rarity of urethral cancer, there is limited prospective data supporting treatment decisions.

Radiation therapy methods are evolving and there are various other cancers for which the NCCN recommends the use of IMRT in special circumstances.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member’s subscriber contract.*
- ***CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.***
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/appropriate = (NMN).*

CPT Codes

| Code | Description |
|-------------|---|
| 31626 | Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed with placement of fiducial markers, single or multiple |
| 31627 | Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed with computer-assisted, image-guided navigation (List separately in addition to code for primary procedure(s)) |
| 32553 | Placement of interstitial device(s) for radiation therapy guidance (e.g., fiducial markers, dosimeter), percutaneous, intra-thoracic, single or multiple |

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)**Policy Number: 6.01.24****Page: 10 of 13**

| Code | Description |
|-------------|---|
| 49411 | Placement of interstitial device(s) for radiation therapy guidance (e.g., fiducial markers, dosimeter), percutaneous, intra-abdominal, intra-pelvic (except prostate), and/or retroperitoneum, single or multiple |
| 55874 | Transperineal placement of biodegradable material, peri-prostatic, single or multiple injection(s), including image guidance, when performed |
| 77301 | Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications |
| 77338 | Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan |
| 77385 | Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple |
| 77386 | Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; complex |
| 77387 | Guidance for localization of target volume for delivery of radiation treatment delivery, includes intrafraction tracking, when performed |

*Copyright © 2023 American Medical Association, Chicago, IL***HCPSC Codes**

| Code | Description |
|-------------|---|
| G6015 | Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session |
| G6016 | Compensator-based beam modulation treatment delivery of inverse planned treatment using three or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session |
| G6017 | Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (e.g., 3D positional tracking, gating, 3D surface tracking), each fraction of treatment |

ICD10 Codes

| Code | Description |
|-------------|--------------------|
| Numerous | |

REFERENCES

- ACR –ASTRO Practice Guideline for Image Guided-Radiation Therapy (IGRT). 2009. Revised 2019 [<https://www.acr.org/-/media/ACR/Files/Practice-Parameters/IGRT-RO.pdf?la=en>] accessed 07/31/23.
- ACR –ARS Practice parameter for intensity-modulated radiation therapy (IMRT). 2011. Revised 2021 [<https://www.acr.org/-/media/ACR/Files/Practice-Parameters/imrt-ro.pdf?la=en>] accessed 07/31/23.
- ASTRO Model Policies- Intensity modulated radiation therapy. 2019. [<https://www.astro.org/ASTRO/media/ASTRO/Daily%20Practice/PDFs/IMRTMP.pdf>] accessed 07/31/23.

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 11 of 13

- *Alektiar KM, et al. Local control comparison of adjuvant brachytherapy to intensity-modulated radiotherapy in primary high-grade sarcoma of the extremity. Cancer 2011 Jul 15;117(14):3229-34.
- *Alicikus ZA, et al. Ten-year outcomes of high-dose, intensity modulated radiotherapy for localized prostate cancer. Cancer 2011 Apr 1;(117(7):1429-37.
- Armstrong N, et al. SpaceOAR hydrogel spacer for reducing radiation toxicity during radiotherapy for prostate cancer. A systematic review. Urology 2021 May 23;156:e74-e85.
- Chang JS, et al. Intensity modulated radiotherapy and volumetric modulated arc therapy in the treatment of breast cancer: an updated review. J Breast Cancer 2022 Oct;25(5):249-365.
- Chao M, et al. Prospective analysis of hydrogel spacer for patients with prostate cancer undergoing radiotherapy. BJU Int 2018 Sep;122(3):427-433.
- Chao M, et al. The use of hydrogel spacer in men undergoing high-dose prostate cancer radiotherapy: results of a prospective phase 2 clinical trial. World J Urol 2019 Jun;37(6):1111-1116.
- Chao YA, et al. Hydrogel spacers for patients with prostate cancer: a review of clinical effectiveness and cost-effectiveness [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019 Feb. CADTH Rapid Response Reports.
- Choi KH, et al. Postoperative radiotherapy with intensity-modulated radiation therapy versus 3-dimensional conformal radiotherapy in early breast cancer: A randomized clinical trial of KROG 15-03. Radiotherapy and Oncology 2021 Jan; 154:179-186.
- Chun SG, et al. Impact of intensity-modulated radiation therapy technique for locally advanced non-small cell lung cancer: a secondary analysis of the NRG Oncology RTOG 0617 randomized clinical trial. J Clin Oncol 2017;35(1):56-62.
- *Chuong MD, et al. Intensity-modulated radiation therapy vs. 3D conformal radiation therapy for squamous cell carcinoma of the anal canal. Gastrointest Cancer Res 2013 Mar;6(2):39-45.
- *Correa C, et al. Accelerated Partial Breast Irradiation: executive summary for the update of an ASTRO evidence-based consensus statement. Prac Rad Onc 2017 Mar;7(2):73-79.
- Farjam R, et al. Quantifying the impact of SpaceOAR hydrogel on interfractional rectal and bladder dose during 0.35 T MR-guided prostate adaptive radiotherapy. J Applied Clin Med Physics 2021 Jun 6;22(9):49-58.
- *Hamstra DA, et al. Continued benefit to rectal separation for prostate radiation therapy: final results of a phase III trial. Int J Radiat Oncol Biol Phys 2017 Apr 1;97(5):976-85.
- *Hamstra DA, et al. Sexual quality of life following prostate intensity modulated radiation therapy (IMRT) with a rectal/prostate spacer: secondary analysis of a phase 3 trial. Pract Radiat Oncol 2018 Jan-Feb;8(1):e7-e15.
- Karsh LI, et al. Absorbable hydrogel spacer use in prostate radiotherapy: a comprehensive review of phase 3 clinical trial published data. Urology 2018;115:39-44.
- Kibbi N, et al. Evidence-based clinical practice guidelines for extramammary paget disease. JAMA Oncology 2022 Apr 1; 8(4):618-628.
- *Lei RY, et al. Four-year clinical update from a prospective trial of accelerated partial breast intensity-modulated radiotherapy (APBIMRT). Breast Cancer Res Treat 2013;140:119–33.
- *Mariados, et al. Hydrogel spacer prospective multicenter randomized controlled pivotal trial: dosimetric and clinical effects of perirectal spacer application in men undergoing prostate image guided intensity modulated radiation therapy. Int J Radiat Oncol Biol Phys 2015;92:971-977.
- Moningi S, et al. IMRT reduces acute toxicity in patients treated with preoperative chemoradiation for gastric cancer. Advances in Radiation Oncology 2020 May-June;5 (369-3776).

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 12 of 13

*Morgan SC, et al. Hypofractionated radiation therapy for localized prostate cancer: an ASTRO, ASCO, and AUA evidence-based guideline. *J Clin Oncol* 2018 Oct 11;36(34):3411-3430.

National Comprehensive Cancer Network. Practice guidelines in oncology: bone cancer V.3.2023. [https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf] accessed 07/31/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: breast cancer V.4.2023. [http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf] accessed 07/31/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: colon cancer V.2.2023. [http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf] accessed 08/25/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: esophageal and esophagogastric junction cancer V.2.2023. [https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf] accessed 08/25/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: gastric cancer V.1.2023. [http://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf] accessed 08/25/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: non-small cell lung cancer V.3.2023. [http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf] accessed 07/31/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: pancreatic adenocarcinoma V.2.2023. [http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf] accessed 08/25/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: prostate cancer. V.2.2023. [http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf] accessed 07/31/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: small cell lung cancer V.3.2023. [http://www.nccn.org/professionals/physician_gls/pdf/sclc.pdf] accessed 07/31/23.

National Comprehensive Cancer Network. Practice guidelines in oncology: soft tissue sarcoma V.2.2023. [http://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf] accessed 08/25/23.

Pietro P, et al. Clinical outcomes of hydrogel spacer injection Space OAR in men submitted to hypofractionated radiotherapy for prostate cancer. *In vivo* 2021 Nov;25(6):2285-3389.

Quinn TJ, et al. Who benefits from a prostate rectal spacer? Secondary analysis of a phase III trial. *Pract Radiat Oncol* 2020 May-Jun;10(3):186-194.

Seymour ZA, et al. Long-term follow-up after radiotherapy for prostate cancer with and without rectal hydrogel spacer: a pool prospective evaluation of bowel associated quality of life. *BJU Int* 2020 Sep;126(3):367-372.

*Smith BD, et al. Radiation therapy for the whole breast: executive summary of an ASTRO evidence-based guideline. *Prac Rad Onc* 2018 May;8(3):145-152.

*United States Social Security Administration. Actuarial Period of Life table 2016. [https://www.ssa.gov/oact/STATS/table4c6_2016.html] accessed 07/31/23.

*Key Article

KEY WORDS

IMRT, Intensity modulated radiotherapy, Intensity modulated radiation therapy, hypofractionated radiotherapy, SpaceOAR.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

Based on our review, intensity modulated radiation therapy is not addressed in National or Regional Medicare coverage determinations or policies.

Medical Policy: Intensity Modulated Radiation Therapy (IMRT)

Policy Number: 6.01.24

Page: 13 of 13

There is currently a Local Coverage Determination (LCD) for Prostate Rectal Spacers (L37485). Please refer to the following LCD website for Medicare Members: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=37485&ver=17&CtrctrSelected=298*1&Ctrctr=298&s=41&DocType=Active&bc=AAgAAAQAoAAAAAAA&= accessed 08/25/23.