Clinical Policy Title: Intensity modulated radiation therapy

Clinical Policy Number: 05.02.03

Effective Date: March 1, 2015
Initial Review Date: October 15, 2014
Most Recent Review Date: October 19, 2017
Next Review Date: October 2018

Policy contains:
- Intensity modulated radiation therapy (IMRT).
- Conformal radiotherapy.

Related policies:

CP 05.02.01 Proton beam therapy

ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas considers the use of intensity modulated radiation therapy in instances where sparing the surrounding normal tissue is of added benefit to be clinically proven and, therefore, medically necessary when the following criteria are met (Frenzel 2015, Ricco 2016, Chen 2016, Hayes 2016):

- Intensity modulated radiation therapy is being used for treatment of:
  - Primary, metastatic and benign tumors of the central nervous system, including tumors of the spine where conventional treatment may compromise the cord
  - Primary, metastatic and benign tumors of the head and neck
  - Prostate cancer
  - Lung cancer (i.e., non-small cell cancers fixed to the spine, superior sulcus or involving bilaterally the mediastinum) and appropriate thoracic and abdominal malignancies
  - Breast cancer (i.e., non-routine cases proximate to the heart and great vessels)
  - Anal cancer
- Intensity modulated radiation therapy is required to reduce morbidity and avoid damage to critical
structures adjacent to the cancer.

- An immediately adjacent target lesion has been irradiated and abutting portals must be established with high precision.
- Gross tumor volume margins are concave or convex and in close proximity to critical structures which must be protected to avoid unacceptable morbidity and radiation exposure.
- When only intensity modulated radiation therapy techniques would decrease the probability of grade 2 or grade 3 radiation toxicity as compared to conventional radiation in greater than 15 percent of radiated similar cases.

**Limitations:**

All other uses of intensity modulated radiation therapy are not medically necessary, including:

- Intrafraction localization and tracking of target or patient motion during delivery of radiation therapy.
- Treating all diagnoses not listed above as proven, including:
  - Colon cancer.
  - Gastric cancer.
  - Gynecological cancer (except where noted above).
  - Lung cancer (except where noted above).
  - Lymphoma.
  - Pelvic bone cancer.
  - Primary or secondary liver cancer.
  - Rectal cancer.
  - Secondary bone and articular cartilage cancer.
  - Soft tissue sarcoma and all other neoplasms not listed above as proven.

Because of limited studies, small sample sizes and weak study designs, there is insufficient data to conclude intensity modulated radiation therapy is safe or effective for treating the neoplasms listed above. There is also little evidence to indicate intensity modulated radiation therapy increases survival in patients with these neoplasms.

**Alternative covered services:**

- Standard surgical therapies.
- Radiation therapies.
- Chemotherapies as appropriate for the clinical condition.
- Proton beam therapy.

**Background**

Intensity modulated radiation therapy is the use of beams with non-uniform fluence to deliver radiation to a target organ. It typically involves the use of techniques where the target is specified, organs at risk for
collateral radiation scatter are identified, and a computer calculates the most appropriate field and fluence arrangement.

Currently, the most useful device for delivery of radiotherapy beams with dynamic modulation of energy fluence is the multileaf collimator. This is computer-controlled, and may be aimed at stationary targets (multisegmented static fields) or targets in motion (dynamic delivery). The latter technique requires rapidly moving multileaf collimator leaves (over 2 cm per second) and requires additional resources to measure the position of leaves and ensure accuracy. The former technique is easier to implement, as it requires fewer resources, but faces issues with beam “on” and “off” cycling and takes longer to deliver.

A third technique is intensity modulated arc therapy. In this technique, the gantry rotates around the patient with the beam on, and the multileaf collimator leaves shift dynamically during treatment. This has the benefit of rapid treatment delivery but increases the volume of tissue being exposed to radiation.

Historically, the maximum radiation dose that could be given to a tumor site has been restricted by the tolerance and sensitivity of the surrounding nearby healthy tissues. When a tumor or condition is not eligible for treatment with normal stereotactic radiosurgery, conformal radiation may be used in one or more sessions. Three-dimensional conformal radiation therapy is less than 10 years old. It is only available with linear accelerator-based technology.

The Calypso® 4D Localization System is regulated as a component of a medical linear accelerator. This device received Food and Drug Administration 510(k) approval on July 28, 2006, as an adjunct to radiation therapy in patients who have undergone permanent implantation of at least two Beacon transponders. Intra-fraction localization and tracking systems, such as the Calypso 4D Localization System, are unproven for use in guiding radiotherapy. Results of available studies suggest the Calypso System can provide continuous information to guide prostate radiotherapy. However, although this technology has the potential to reduce complications of radiotherapy and improve local tumor control, none of the available studies reported clinical information related to the safety or efficacy of radiation therapy guided by the Calypso System.

Examples of approved devices and systems are the NOMOS Slit Collimator (BEAK™) (NOMOS Corp.); the Peacock™ System (NOMOS Corp.); the Varian Multileaf Collimator with dynamic arc therapy feature (Varian Oncology Systems); the Saturne Multileaf Collimator (GE Medical Systems); the Mitsubishi 120 Leaf Multileaf Collimator (Mitsubishi Electronics America Inc.); the Stryker Leibinger Motorized Micro Multileaf Collimator (Stryker Leibinger); the Mini Multileaf Collimator, model KMI (MRC Systems GMBH); and the Preference® Intensity Modulated Radiation Therapy Treatment Planning Module (Northwest Medical Physics Equipment Inc.). The RayPilot® system (Micropos Medical, Sweden) is not Food and Drug Administration approved for marketing in the United States.

More precise techniques using one-session Gamma Knife® machines and other one-session linac technology are best utilized within the brain. Several manufacturers currently offer beneficial treatments with high-level linac technology that can perform both one-session radiosurgery and radiotherapy. The most well-recognized brand names at this time are the Novalis Tx® (Varian Medical Systems Inc. and
BrainLab Inc.); Synergy S® (Elekta Inc.); and CyberKnife® (Accuray Inc.). All of these machines are robotic and image-guided, and can perform intensity modulated radiation therapy.

**Searches**

AmeriHealth Caritas searched PubMed and the databases of:

- UK National Health Services Center for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on September 19, 2017. Searched terms were: "intensity modulated radiation therapy (MeSH)", "intensity modulated radiation therapy (MeSH)", and "cancer."

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines** based on systematic reviews.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

There is a great deal of contemporary interest regarding intensity modulated radiation therapy for cancer of the prostate, spine, lung, breast, kidney, pancreas, liver, larynx, tongue, and sinus. As with conventional radiation therapy, treatment with intensity modulated radiation therapy involves a radiation oncologist and physicist. Should the treatment site be within the brain, a neurosurgeon is recommended to be a part of the team as well.

A new study (Patel 2014) of proton beam therapy in the treatment of a variety of advanced head and neck cancers compared to intensity modulated radiation therapy has found proton beam therapy significantly improved disease-free survival and tumor control when compared to intensity modulated radiation therapy. Researchers found disease-free survival to be significantly higher at five years for patients receiving proton therapy than for patients receiving intensity modulated radiation therapy (72 percent versus 50 percent). Tumor control did not differ between treatment groups at five years; however, tumor control was higher for patients receiving proton therapy than for intensity modulated radiation therapy at the longest follow-up (81 percent versus 64 percent).
Men with localized prostate cancer treated with intensity modulated radiation therapy have more than one quarter (26 percent) fewer late bowel and rectal side effects and a statistically improved lower dose of radiation to the bladder and rectum, compared to those who undergo 3 dimensional conformal radiation therapy (Mychalski 2013). The authors also found there is a significant increase (15 percent) in rectal side effects associated with Caucasian men, compared to other races, regardless of the radiation treatment.

Intensity modulated radiation therapy treatment for localized prostate cancer is better than conventional conformal radiation therapy for reducing certain side effects (i.e., gastrointestinal and rectal toxicity) and preventing cancer recurrence (Sheets 2012).

There is no evidence from randomized controlled trials comparing intensity modulated radiation therapy with 3 dimensional conformal radiation therapy for treatment of anal cancer. However, non-randomized studies of intensity modulated radiation therapy consistently demonstrate reduced toxicity and comparable tumor control for malignancies of the anal canal.

As for other abdominal (e.g., gastric, pancreatic, hepatobiliary) and pelvic (e.g., rectal, gynecologic) cancers, there is currently no evidence from randomized controlled trials comparing intensity modulated radiation therapy with other radiation modalities for the treatment of abdominal and pelvic cancers.

There is insufficient published evidence to assess the safety and/or impact on health outcomes or patient management of intensity modulated radiation therapy for the treatment of colon cancer.

Ricco (2016) retrospectively reviewed 270 consecutive men treated with either stereotactic body radiation therapy \( (n = 150) \) or intensity modulated radiation therapy \( (n = 120) \) at a community hospital with organ confined prostate cancer from 2007 – 2012. There was no significant difference in freedom from biochemical failure between stereotactic body radiation therapy versus intensity modulated radiation therapy \( (p = 0.46) \) with six-year actuarial freedom from biochemical failure of 91.9% for stereotactic body radiation and 88.9% for intensity modulated radiation therapy. Overall toxicity was low.

Chen (2016) retrospectively evaluated the distant metastatic outcomes in 91 of 530 nasopharyngeal carcinoma patients treated with intensity modulated radiation therapy plus chemotherapy from June 2006 – December 2011. Patients were treated with one fraction of intensity modulated radiation therapy daily for five days a week for 69.96–74.09 Gy, while 473 (89.2 percent) of patients also received chemotherapy. Patients were followed for a median follow-up duration of 49 months (range from five to 98 months). Chemotherapy failed to reduce cancer distant metastasis in early stage patients, the distant metastasis rate was 17.5 percent in stage III and 24.2 percent in stage IVA–B diseases, after intensity modulated radiation therapy and chemotherapy. The multivariate analysis showed that cancer remission duration, treatment modality, and metastatic site \( (p < 0.001, p = 0.027 \text{ and } p = 0.022, \text{ respectively}) \) were all independent predictors for overall survival of nasopharyngeal carcinoma patients after intensity modulated radiation therapy and chemotherapy.

Hayes (2016) reviewed 13 peer-reviewed studies, including six studies on intensity modulated radiation
therapy for anal cancer and seven studies on intensity modulated radiation therapy for rectal cancer and determined that clinical outcomes following intensity modulated radiation therapy are similar to those seen with standard conformal radiotherapy for treating anal cancer and locally advanced rectal cancer, suggesting that intensity modulated radiation therapy may have similar efficacy. However, the use of intensity modulated radiation therapy to treat anal or rectal cancer did not consistently result in any additional benefit relative to traditional radiotherapy. Intensity modulated radiation therapy may have a better toxicity profile since it resulted in fewer high-grade toxicities. Furthermore, evidence of low quality suggests that intensity modulated radiation therapy may have a better safety profile than standard radiotherapy, and that it may be as effective as standard radiotherapy for some patients with anal cancer. Evidence of very low quality suggests that intensity modulated radiation therapy may have a better safety profile than standard radiotherapy for rectal cancer, and that it may be as effective for local control; however, there is a lack of comparative data on long-term outcomes.

Policy updates:

The German Association of Medical Physicists surveyed its membership (n=26,779) employing intensity modulated radiation therapy in various oncologic conditions to assess the regularity and quality of this intervention in Germany (Frenzel 2015). The most frequently employed intensity modulated radiation therapy techniques were volumetric modulated arc therapy (58.37 %) and step-and-shoot intensity modulated radiation therapy (14.66 %), dynamic multileaf collimator (dMLC: 14.53 %), TomoTherapy (9.25 %), and 3.2 % unspecified interventions. Patients were included in the survey; 44 % were treated using intensity modulated radiation therapy techniques. Intensity modulated radiation therapy was most frequently used for anal cancer, craniospinal irradiation, head and neck cancer, prostate cancer, pelvic and gynecologic tumors (except for breast cancer), and brain tumors.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frenzel (2015)</td>
<td><strong>Key points:</strong></td>
</tr>
</tbody>
</table>
| The use of intensity modulated radiation therapy in Germany. | - A survey (n=26,779) sought to understand intensity modulated radiation therapy use in various oncologic conditions to assess the regularity and quality of this intervention in Germany  
- The most frequently employed intensity modulated radiation therapy techniques were volumetric modulated arc therapy (58.37 %) and step-and-shoot intensity modulated radiation therapy (14.66 %), dynamic multileaf collimator (dMLC: 14.53 %), TomoTherapy (9.25 %), and 3.2 % unspecified interventions. Patients were included in the survey; 44 % were treated using intensity modulated radiation therapy techniques.  
- Intensity modulated radiation therapy was most frequently used for anal cancer, craniospinal irradiation, head and neck cancer, prostate cancer, pelvic and gynecologic tumors (except for breast cancer), and brain tumors. |
<p>| Ricco (2016)        | <strong>Key points:</strong>                                                                                  |
| The comparison of   | - Retrospective review of 270 consecutive men treated with either stereotactic (n = 150) or     |</p>
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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</thead>
<tbody>
<tr>
<td>Patel (2014)</td>
<td>Systematic review of 41 observational studies of treatment for malignant tumors arising within the nasal cavity and paranasal sinuses. Overall survival and disease-free survival was significantly higher at five years for charged</td>
</tr>
<tr>
<td>Citation</td>
<td>Content, Methods, Recommendations</td>
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| sinus and nasal cavity malignant diseases: a systematic review and meta-analysis | particle therapy than for photon therapy.  
• Analysis comparing proton beam therapy with intensity-modulated radiation therapy showed significantly higher disease-free survival at five years. |
| Hong (2014) | **Key points:**  
• Study of technique for administering intensity modulated radiation therapy to head and neck cancers.  
• Authors demonstrated that smaller leafs within the midleaf collimator delivered an irradiation beam that can provide better dosimetric outcomes in intensity modulated radiation therapy.  
• Set a baseline for minimum requirements of treatment when assigning or introducing equipment for the treatment of head and neck cancers. |
| Chang (2014) | **Key points:**  
• Comparison of intensity modulated radiation therapy versus 3 dimensional conformal radiotherapy for administering treatment to non-small cell lung cancer.  
• Authors demonstrated an increasing tendency to use intensity modulated radiation therapy versus 3D in the treatment of non-small cell lung cancer, with a market penetration rate of 26.8% in 2009.  
• However, among patients receiving potentially curative radiation there was no significant difference in overall survival or time spent hospitalized following treatment. |
| Sheets (2012) | **Key points:**  
• Study of intensity modulated radiation therapy, proton therapy, and conformal radiation therapy for primary prostate cancer from 2000 – 2009.  
• Primary complications noted were gastrointestinal and urinary morbidity, erectile dysfunction, hip fractures, and additional cancer therapy.  
• intensity modulated radiation therapy patients were less likely to receive additional cancer therapy compared to conformal radiotherapy. |
| Michalski (2011) | **Key points:**  
• Clinical trial inclusive of 763 patients of 3-dimensional conformal radiotherapy and intensity modulated radiation therapy.  
• There was a statistically significant decrease in gastrointestinal and genitourinary toxicity for intensity modulated radiation therapy. |
| Bauman (2010) | **Key points:**  
• Systematic review of studies performed years 2000 –2009 inclusive of ≥ 50 patients |
modulated radiation therapy in prostate cancer

- evaluating intensity modulated radiation therapy in treating prostate cancer.
  - Intensity modulated radiation therapy recommended over 3 dimensional conformal radiotherapy for localized prostate cancer where dose escalation (>70 Gy) is required.
  - Insufficient evidence for postoperative radical prostatectomy use was documented.

Ramaekers (2010)

Systematic review and meta-analysis of radiotherapy in various head and neck cancers: comparing photons, carbon-ions, and protons

- Systematic review of studies performed years 1990–2010 inclusive of ≥ 10 patients evaluating intensity modulated radiation therapy in treating head and neck cancer.
- Found tumor control and survival similar for intensity modulated radiation therapy and proton beam therapy to be similar.
- Proton beam therapy was associated with lower toxicity rates than intensity modulated radiation therapy.

**Key points:**

**References**

**Professional society guidelines/other:**


Bauman G, Rumble RB, Chen J, Loblaw A, Warde P. intensity modulated radiation therapy indications expert panel. The role of intensity modulated radiation therapy in prostate cancer. Toronto (ON): Cancer Care Ontario (CCO); 2010 Oct 27.


Peer-reviewed references:


**CMS National Coverage Determination (NCDs):**

No NCDs were identified as of the writing of this policy.

**Local Coverage Determinations (LCDs):**


**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.
<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comment</th>
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<tbody>
<tr>
<td>77301</td>
<td>Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications.</td>
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<tr>
<td>77338</td>
<td>Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (intensity modulated radiation therapy), design and construction per intensity modulated radiation therapy plan.</td>
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<tr>
<td>77385</td>
<td>Intensity modulated radiation treatment delivery (intensity modulated radiation therapy), includes guidance and tracking, when performed; simple</td>
<td></td>
</tr>
<tr>
<td>77386</td>
<td>Intensity modulated radiation treatment delivery (intensity modulated radiation therapy), includes guidance and tracking, when performed; complex</td>
<td></td>
</tr>
<tr>
<td>77387</td>
<td>Guidance for localization of target volume for delivery of radiation treatment delivery, includes intrafraction tracking, when performed</td>
<td></td>
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<tr>
<td>4165F</td>
<td>3-dimensional conformal radiotherapy (3D-CRT) or intensity modulated radiation therapy (intensity modulated radiation therapy) received (PRCA)</td>
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<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
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<tr>
<td></td>
<td>Too many to list</td>
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<thead>
<tr>
<th>HCPCS Level II Code</th>
<th>Description</th>
<th>Comment</th>
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<tbody>
<tr>
<td>G6002</td>
<td>Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy</td>
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<tr>
<td>G6015</td>
<td>Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session</td>
<td></td>
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<tr>
<td>G6016</td>
<td>Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session</td>
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</table>