



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

## Subject Intensity-Modulated Radiation Therapy (IMRT)

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- Proton Beam Therapy for Prostate Cancer
- Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiation Therapy (SBRT)

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## Coverage Policy

CIGNA covers intensity-modulated radiation therapy (IMRT) as medically necessary for the treatment of a radiation-sensitive tumor when there is reasonable concern about damage to an adjacent organ or vital tissue with the use of conventional external beam radiation therapy or three-dimensional conformal radiation therapy (3D CRT).

CIGNA does not cover intrafraction localization systems (e.g., Calypso<sup>®</sup> 4D Localization System<sup>™</sup>, AlignRT<sup>®</sup> Radiotherapy Positioning System) because it is considered experimental, investigational or unproven.

## General Background

External beam radiation therapy involves the delivery of electromagnetic radiation (e.g., x-rays, gamma rays) or particulate radiation (e.g., electrons, protons) from a linear accelerator or radionuclide source. Intensity-

modulated radiation therapy (IMRT), a type of external beam radiation, involves variation in the intensity of the x-ray output from a linear accelerator and the use of multiple shaped treatment fields. This allows for more conformal radiation dose distributions to the target while reducing exposure of adjacent non-target structures. The planning process is significantly more labor intensive than conventional radiation therapy (RT) and requires the use of more sophisticated modeling software for optimization. Older techniques may include compensator-based IMRT. Currently, IMRT is generally delivered via conventional linac-plus-multileaf collimator (MLC) with photons, such as multiple static segment (step-and-shoot) treatment, dynamic segment (sliding-window) treatment, intensity-modulated arc treatment, and binary-collimator "tomotherapy".

### **Localization Techniques**

Image-guided radiation therapy (IGRT) refers to an approach which may be applied to various RT techniques including IMRT, in which modern imaging modalities such as CT and MRI have been directly incorporated into radiation delivery machines, allowing for frequent confirmation of the tumor location and patient positioning. IGRT can be performed to enhance either 3-dimensional conformal radiation therapy (3DCRT) or IMRT and is considered a necessary, integral component of stereotactic body radiation therapy (SBRT). The conventional location technique is interfraction localization, locating the tumor between radiation treatments with frequent imaging. A newer technique is Intrafraction or "real time" localization which refers to locating the tumor during a given radiation treatment session. The Calypso® Four-dimensional (4D) Localization System™ (Calypso Medical Technologies, Inc., Seattle, WA) was developed with the goal of improving prostate cancer targeting during (intrafraction) radiation. To use this system, Beacon® Electromagnetic Transponders are transrectally implanted into the patient's prostate. AlignRT® Radiotherapy Positioning System (Vision RT, Ltd., London UK) uses a video-based 3D imaging system during radiotherapy throughout the body.

### **Indications**

Because IMRT maximizes radiation dose distributions to the target while reducing exposure of adjacent non-target structures, it is more commonly utilized when there is particular concern about damage to an adjacent organ or vital tissue. Currently, IMRT is being used most extensively to treat cancers of the prostate, head and neck, and central nervous system. IMRT has also been used in limited situations to treat breast, thyroid, lung, as well as in gastrointestinal, gynecologic malignancies and certain types of sarcomas. IMRT may also be beneficial for treating pediatric malignancies (Radiological Society of North America, 2010).

### **U.S. Food and Drug Administration (FDA)**

The FDA has approved a number of medical charged-particle RT system devices and RT treatment planning system devices. Some RT devices include integrated or add-on imaging devices. A few examples include: the TomoTherapy Hi-Art System® (TomoTherapy Inc., Madison, WI); the Peacock™ System (NOMOS Corp., Sewickley, PA); and Trilogy™ and SmartBeam™ IMRT (Varian Medical Systems, Inc. Palo Alto, CA), and Elekta VMAT (Volumetric Intensity Modulated Arc Therapy) (Stockholm, Sweden).

The Calypso® 4D Localization Systems (Calypso Medical Technologies, Inc., Seattle, WA) was cleared for marketing by the FDA based on a 510(k) application for use in prostate cancer. Cited predicate devices include tracking systems and implanted fiducials. It is intended for use as an adjunct in treatment planning and RT, to align and monitor the patient's position relative to the isocenter of a linear accelerator. Beacon transponders are indicated for use to radiographically and electromagnetically mark soft tissue for future therapeutic procedures. Permanent Beacon transponders are indicated for permanent implantation in the prostate and the peri-prostatic tissue.

AlignRT® Radiotherapy Positioning System (Vision RT, Ltd., London UK) was FDA approved in January 2006. AlignRT uses a video-based imaging system, mapping the skin surface in three-dimensional (3D) before and during radiotherapy treatment to position patients undergoing types of external beam radiation therapy. It is used to position patients at the isocenter of the linear accelerator for radiation therapy procedures.

The RayPilot®, previously called Micropos 4DRT system, (Micropos Medical AB, Sweden) is not FDA approved.

### **Literature Review**

Many clinical studies have verified that IMRT provides superior dose distribution over 3D CRT. Since the goal of IMRT is to increase the therapeutic ratio, delivering a higher tumor dose relative to normal tissues, IMRT can be used to escalate the tumor volume to a higher dose while maintaining normal tissue toxicity at a tolerable level.

Staffurth et al. (2010) conducted a systematic review of 61 comparative studies (including six randomized controlled trials [RCTs]), comparing IMRT and conventional radiotherapy. The RCT included three trials in head and neck cancer (205 patients) and three in breast cancer (664 patients). The six RCTs in breast and locally advanced head and neck cancers have all shown a significant improvement in their normal tissue-focused primary end points. Other areas studied included endometrial and cervical cancer, central nervous system tumors, anal cancer and lung cancer. The results of these studies supported those of the RCTs with benefits reported in acute and late toxicity, health-related quality of life and tumor control end points.

**Breast Cancer:** Evidence in the published, peer-reviewed scientific literature supports the use of IMRT for the treatment of breast cancer (Barnett, et al., 2011; Livi, et al., 2010; Pignol, et al., 2008; Rusthoven, et al., 2008; Donovan, et al., 2007; Harsolia, et al., 2007; Formenti, et al., 2007; Leonard, et al., 2007; Bhatnagar, et al., 2006).

The National Comprehensive Cancer Network<sup>®</sup> (NCCN<sup>®</sup>) Clinical Practice Guidelines in Oncology<sup>™</sup> breast cancer guideline states under local-regional treatment, whole breast radiation including the majority of the breast tissue is recommended. Breast irradiation should be performed following CT-based treatment planning so as to limited irradiation exposure of the heart and lungs and to assure adequate coverage of the primary tumor and surgical site. Tissue wedging, forward planning with segments (step and shoot), or IMRT is recommended (NCCN, v.2.2011).

**Central Nervous System (CNS) Cancers:** The NCCN Guidelines<sup>™</sup> on CNS cancers note “every attempt should be made to decrease the radiation dose outside the target volume. This can be achieved with 3D planning or IMRT” (NCCN, v.2.2011).

**Colon Cancer:** The NCCN Guidelines<sup>™</sup> on colon cancer note that conformal external beam should be routinely used and IMRT reserved only for unique clinical situations. In patients with a limited number of liver or lung metastases, radiotherapy can be considered in highly selected cases or in the setting of a clinical trial. Radiotherapy should not be used in the place of surgical resection. Radiotherapy should be delivered in a highly conformal manner. The techniques can include 3DCRT, IMRT or SBRT (NCCN, v.2.2011).

**Esophageal Cancer:** The NCCN Guidelines<sup>™</sup> on esophageal cancer state that IMRT is currently being investigated, noting “retrospective planning studies comparing 3DCRT versus IMRT treatment plans for esophagus cancer have generally shown superior dose conformity and homogeneity with IMRT and reduction of radiation dose to the lungs and heart” (NCCN, v.2.2010).

**Gastric Cancer:** The NCCN Guidelines<sup>™</sup> on gastric cancer note that IMRT has a great potential to reduce radiation-related toxicity by delivering large doses of radiation to target tissues. The use of this technique in gastric cancer remains investigational (NCCN, v.2.2010).

**Gynecological Cancers:** There are promising studies regarding the use of IMRT in patients with gynecological cancer. Definitive IMRT-specific results are difficult to obtain as chemotherapy and brachytherapy are often utilized in addition to external beam RT. In a prospective cohort study, Kidd et al. (2009) reported on a facility that utilized standard external beam (n=317), then on a set date in time changed to IMRT (n=135), to treat newly diagnosed cervical cancer patients. It should be noted that patients also underwent brachytherapy, and 85% of patients received concurrent chemotherapy. Results showed the IMRT group demonstrated better overall and cause-specific survivals ( $p < 0.0001$ ). Additionally, eight patients (6%) in the IMRT group developed a Grade 3 or greater bowel or bladder complication; this was significantly fewer than the 54 (17%) observed in the non-IMRT group ( $p = 0.0017$ ). The mean overall time to developing such a complication was 16.2 months for all patients (16.5 months for non-IMRT, 14.0 months for IMRT). These results led the authors to conclude that IMRT improved survival and demonstrated less treatment-related toxicity compared to non-IMRT radiotherapy.

Chen et al. (2007) conducted a prospective cohort study including 68 patients at high risk of cervical cancer after hysterectomies that were treated with adjuvant pelvic RT and concurrent chemotherapy. Of the 68, 35 underwent conventional four-field RT, followed by 33 receiving adjuvant IMRT. The authors reported that IMRT patients had a statistically significant lower incidence of Grade 1-2 toxicity (30% vs. 60%). Also, there were statistically significant improvements for the bladder, rectum, and small bowel observed in the IMRT patients at the mean dose. For the rectum and small bowel, these differences remained significant down to 50% of prescribed dose. Therefore, IMRT planning significantly decreased acute and chronic GI toxicity and acute GU

toxicity, and provided good locoregional control compared with conventional RT. Beriwal et al. (2006) evaluated the use of IMRT for adjuvant treatment of endometrial cancer in 47 patients for a median follow-up of 20 months. The authors reported IMRT dosimetry showed excellent coverage of the planning target volume (PTV), with excellent local control and low toxicity. The authors acknowledged the need for larger number of patients and longer-term follow-up.

The NCCN Guidelines™ on cervical cancer state under the subheading of Planning Treatment Fields, “IMRT is becoming more widely used; however, issues regarding target definition, immobilization, and reproducibility remain to be validated” (NCCN, v.1.2011).

**Head and Neck Tumors:** Evidence in the published, peer-reviewed scientific literature supports the use of IMRT for the treatment of head and neck cancers (Nutting, et al., 2011; Fang, et al., 2008; Milker-Zabel, et al., 2007; Kam, et al., 2007; Pow, et al., 2006; Pacholke, et al., 2005; Lee, et al., 2003; Chao, et al., 2001).

The NCCN Guidelines™ on head and neck cancer state IMRT, 3D, and 2D conformal techniques may be used as appropriate depending on the stage, tumor location, physician training/experience, and available physics support. IMRT has been shown to be particularly useful in reducing long-term toxicity in oropharyngeal, paranasal sinus, and nasopharyngeal cancers by reducing the dose to salivary glands, temporal lobes, auditory structures (including cochlea), and optic structures. The application of IMRT to other sites (e.g., oral cavity, larynx, hypopharynx, salivary glands) is evolving and may be used at the discretion of treating physicians. IMRT is the preferred technique for cancers of the oropharynx, nasopharynx, maxillary, paranasal or ethmoid sinus tumors to minimize dose to critical structures (NCCN, v.1.2011).

**Lung Cancer:** Evidence in the published, peer-reviewed scientific literature supports the use of IMRT for the treatment of non-small cell lung cancer (Liao, et al. 2010; Sura, et al., 2008; Yom, et al., 2007; Murshed, et al., 2004).

The NCCN Guidelines™ on non-small cell lung cancer (NSCLC) note that where there is a large volume of normal lung being irradiated or tumors are located close to critical structures ( i.e. spinal cord), IMRT may be considered for high-dose radiation to avoid overdose to normal tissue. Significantly lower risk of radiation pneumonitis and improved overall survival has been observed with IMRT compared with 3DCRT for lung cancer (NCCN, v.3.2011).

The NCCN Guidelines™ on small cell lung cancer (SCLC) state 3DCRT or IMRT are preferred for limited disease. If IMRT is utilized, four dimensional imaging should also be performed to assure tumor movement of less than one centimeter is achievable (NCCN, v.2011).

**Mesothelioma (Malignant Pleural):** The NCCN guideline notes that IMRT allows a more conformal high-dose RT and improved coverage to the hemithorax. When IMRT is applied, the National Cancer Institute (NCI)/American Society for Radiation Oncology (ASTRO) guidelines should be followed strictly. Special attention should be paid to minimize radiation to the contralateral lung as the risk of fatal pneumonitis with IMRT is excessively high when strict limits are not applied (NCCN, v.1.2011).

**Occult Primary:** The NCCN Guidelines™ on occult primary state that in patients with disseminated metastases, specialized approaches may include novel forms of RT such as intraoperative radiation therapy (IORT), IMRT, IGRT, or proton therapy (NCCN, v.2.2011).

**Pancreatic Adenocarcinoma:** The NCCN Guidelines™ state “Increasingly, IMRT is being applied for therapy of pancreatic adenocarcinoma. There is no clear consensus on appropriate maximum dose of radiation in either the adjuvant setting or in the setting of locally advanced disease” (NCCN, v.2.2010).

**Prostate Cancer:** Evidence in the published, peer-reviewed scientific literature supports the use of IMRT for the treatment of prostate cancer (Kuban, et al., 2010; Cahlon, et al., 2008; Zelefsky, et al., 2008; Vora, et al., 2007; Martin, et al., 2007; De Meerleer, et al., 2007; Pollack, et al., 2006; Peeters, et al., 2006; Zietman, et al., 2005; Brabbins, et al., 2005; Martinez, et al., 2001; Zelefsky, et al., 2000).

In a systematic review of the literature, Hummel et al. (2010) concluded “Comparative data of IMRT versus 3DCRT seem to support the theory that higher doses, up to 81 Gray (Gy), can improve biochemical survival for

patients with localized prostate cancer, concurring with data on conformal RT. The data also suggest that toxicity can be reduced by increasing conformality of treatment, particularly with regard to GI toxicity, which can be more easily achieved with IMRT than 3DCRT.”

The NCCN Guidelines™ on prostate cancer state 3D conformal and IMRT techniques should be employed. The second generation 3D technique, IMRT, is now state-of-the-art and required (NCCN, v.1.2011).

**Rectal/Anal Cancer:** The NCCN Guidelines™ on rectal cancer state that IMRT should only be used in the setting of a clinical trial. In patients with a limited number of liver or lung metastases, radiotherapy can be considered in highly selected cases or in the setting of a clinical trial. Radiotherapy should not be used in the place of surgical resection. Radiotherapy should be delivered in a highly conformal manner. The techniques can include 3DCRT, IMRT or SBRT (NCCN, v.2.2011). The NCCN anal cancer recommendations for the primary treatment of anal canal cancer state the consensus of the panel is IMRT may be used in place of 3D CRT in the treatment of anal carcinoma. Multiple pilot studies have demonstrated reduced toxicity while maintaining local control using IMRT (NCCN, v.2.2011).

**Sarcoma:** The NCCN Guidelines™ on soft tissue sarcoma state that advances in RT technology such as IMRT have led to the improvement in treatment outcomes in patients with soft tissue sarcoma. Post-operative IMRT following limb-sparing surgery is associated with excellent local control in selected patients with high-risk features (NCCN, v.1.2011).

**Thymic Malignancies:** The NCCN Guidelines™ note that RT should be given by 3D conformal technique to reduce surrounding normal tissue damage (e.g., heart, lungs, esophagus, and spinal cord). IMRT may further improve the dose distribution and decrease dose to normal tissue (NCCN, v.1.2011).

**Intrafraction localization systems:** Locating a tumor during a given radiation treatment session is intrafraction localization. Studies in the peer-reviewed scientific literature suggest that intrafraction or “real time” localization systems such as Calypso® or AlignRT™ can safely provide continuous information to guide RT; however, the studies are not comparative; they do not demonstrate that continuous (intrafraction) positional monitoring decreases adverse events and improves patient outcomes over interfraction positional monitoring of implanted fiducial markers (Sandler, et al., 2010; Tanyi, et al., 2010; Krengli, et al., 2009; Quigley, et al., 2009; Kupelian, et al., 2007).

### **Professional Societies/Organizations**

**American College of Radiology (ACR):** The ACR Practice Guideline for IMRT (2007) states “Through the modulation of radiation dose intensities across treatment fields, IMRT makes possible conformal radiation dose distributions to the target while reducing exposure of adjacent non-target structures, beyond the capabilities of traditional two-dimensional or 3D CRT techniques.”

**American Society for Radiation Oncology (ASTRO):** Implementing IMRT in Clinical Practice, a joint document with the American Association of Physicists in Medicine (2004) states that the advantages of IMRT are noted as most obvious when “a critical structure (e.g., the optic nerve) invaginates a target by creating a concavity in its surface (taken here as the planning target volume, or PTV) or when the critical structure is completely surrounded by that target” (Galvin, et al., 2004).

### **Summary**

While the supporting data are not robust for some cancer types and anatomic locations, there is sufficient evidence in the published, peer-reviewed scientific literature supporting IMRT as a safe and effective treatment option for a subset of individuals with radiation-sensitive tumors when there is reasonable concern about damage to surrounding tissue with the use of conventional external beam or three-dimensional (3D) conformal radiation therapy.

There is insufficient evidence to determine whether guidance of radiation therapy with an intrafraction localization system (e.g., Calypso, AlignRT) benefits patients. Preliminary studies do not demonstrate that these systems provide any improved clinical value such as local control or survival, over guidance of radiation therapy with interfraction localization.

## Coding/Billing Information

**Note:** This list of codes may not be all-inclusive.

### Covered when medically necessary:

CPT®* Codes	Description
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
77418	Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
0073T	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

ICD-9-CM Diagnosis Codes	Description
140.0-149.9	Malignant Neoplasm of Lip, Oral Cavity, and Pharynx
150.0-159.9	Malignant neoplasm of digestive organs and peritoneum
160.0-169.9	Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
170.0-176.9	Malignant neoplasm of bone, connective tissue, skin and breast
179	Malignant neoplasm of uterus, part unspecified
180.0-189.9	Malignant neoplasm of genitourinary organs
190.0-199.2	Malignant neoplasm of other and unspecified sites
200.00-200.88	Lymphosarcoma and reticulosarcoma and other specified malignant tumors of lymphatic tissue
201.00-201.98	Hodgkin's disease
202.00-202.98	Other malignant neoplasms of lymphoid and histiocytic tissue
209.00-209.79	Neuroendocrine tumors
210.0-229.9	Benign neoplasms
230.0-234.9	Carcinoma in situ
235.0-238.3	Neoplasms of uncertain behavior
239.0-239.9	Neoplasms of unspecified nature
V15.3	Personal history of irradiation, presenting hazards to health

### Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description
0197T	Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (eg, 3D positional tracking, gating, 3D surface tracking), each fraction of treatment

ICD-9-CM Diagnosis Codes	Description
	All codes

\*Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.

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## Policy History

<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	5/15/2008	0088	Intensity-Modulated Radiation Therapy (IMRT)

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