8.01.48	Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid		
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Section:	8.0 Therapy	**Page:**	Page 1 of 24

Policy Statement

I. Intensity-modulated radiotherapy (IMRT) may be considered **medically necessary** for the treatment of head and neck cancers when the cancer to be treated is **one or more** of the following:
   A. Oral cavity and lip
   B. Larynx
   C. Hypopharynx
   D. Oropharynx
   E. Nasopharynx
   F. Paranasal sinuses and nasal cavity
   G. Salivary glands
   H. Occult primaries in the head and neck region

II. Intensity-modulated radiotherapy may be considered **medically necessary** for the treatment of thyroid or other head and neck cancers when dosimetric planning with standard 3-dimensional conformal radiotherapy predicts that the radiation dose to an adjacent organ (e.g.: esophagus, salivary glands, spinal cord) would result in unacceptable normal tissue toxicity, as documented by **one or more** of the following:
   A. The target volume is in close proximity to critical structures that must be protected and **both** of the following: * (see source below)
      1. Planned 3D-CRT exposure to critical adjacent structures is above normal tissue constraints
      2. Planned IMRT exposure to these critical adjacent structures does not exceed normal tissue constraints
   B. An immediately adjacent area has been previously irradiated and abutting portals must be established with high precision

III. Intensity-modulated radiotherapy is considered **not medically necessary** for the treatment of thyroid or other head and neck cancers for all indications not meeting the criteria above.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

For this policy, head and neck cancers are those arising from the oral cavity and lip, larynx, hypopharynx, oropharynx, nasopharynx, paranasal sinuses and nasal cavity, salivary glands, thyroid and occult primaries in the head and neck region.

Cancers of the central nervous system (brain, brain stem, spinal cord and some cochlea and eye cancers) are not addressed in this policy; see Blue Shield of California Medical Policy: Intensity-Modulated Radiotherapy: Central Nervous System Tumors.

*The following Normal Tissue Constraint Guidelines are derived from the textbook: Radiation Oncology: A Question-Based Review published by Lippincott Williams & Wilkins, 2010 [author: Hristov et al., 2010]). According to the author, most dosages were derived from randomized studies or consensus guidelines; however, pediatric dose constraints will vary greatly from protocol to protocol. Sources used in the development of the guidelines included the American Brachytherapy Society (ABS); Clinical practice guidelines from Johns Hopkins Hospital (JHH); the

International Journal of Radiation Oncology *Biology* Physics (IJROBP); the National Comprehensive Cancer Network (NCCN), Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC); and the Radiation Therapy Oncology Group (RTOG) protocols at the time of publication.

The following guidelines are only intended to serve as a guide and may not be applicable to all clinical scenarios.

Organ	Constraints
Central Nervous System (1.8-2.0 Gray/fraction [Gy/fx])	
• Spinal Cord	max 50 Gy (full cord cross-section); tolerance increases by 25% 6 mos after 1st course (for re-irradiation)
• Brain	max 72 Gy (partial brain); avoid >2 Gy/fx or hyperfractionation
• Chiasm/Optic Nerves	max 55 Gy
• Brainstem	Entire brainstem <54 Gy, V59 Gy <1–10 cc
• Eyes (globe)	mean <35 Gy, max 54 Gy
• Lens	max 7 Gy
• Retina	max 50 Gy
• Lacrimal Gland	max 40 Gy
• Inner ear/cochlea	mean </=45 Gy (consider constraining to </=35 Gy with concurrent cisplatin)
• Pituitary gland	max 45 Gy (for panhypopituitarism, lower for GH deficiency)
• Cauda equina	max 60 Gy
Central Nervous System (single fraction)	
• Spinal Cord	max 13 Gy (if 3 fxs, max 20 Gy)
• Brain	V12 Gy <5–10 cc
• Chiasm/Optic Nerves	max 10 Gy
• Brainstem	max 12.5 Gy
• Sacral plexus	V18 <0.035 cc, V14.4 <5 cc
• Cauda equina	V16 <0.035 cc, V14 <5 cc
Head and Neck (1.8–2.0 Gy/fx)	
• Parotid gland(s)	mean <25 Gy (both glands) or mean <20 Gy (1 gland)
• Submandibular gland(s)	mean <35 Gy
• Larynx	mean </=44 Gy, V50 </=27%, max 63–66 Gy (when risk of tumor involvement is limited)
• TMJ/mandible	max 70 Gy (if not possible, then V75 <1 cc)
• Oral cavity	Non-oral cavity cancer: mean <30 Gy, avoid hot spots >60 Gy Oral cavity cancer: mean <50 Gy, V55 <1 cc, max 65 Gy
• Esophagus (cervical)	V45 <33%
• Pharyngeal constrictors	mean <50 Gy
• Thyroid	V26 <20%
Thoracic (1.8–2.0 Gy/fx)	
• Brachial plexus	max 66 Gy, V60 <5%
• Lung (combined lung for lung cancer treatment)	mean <20–23 Gy, V20 <30%–35%
• Lung (ipsilateral lung for breast cancer treatment)	V25 <10%
• Single lung (after pneumonectomy)	V5 <60%, V20 <4–10%, MLD <8 Gy
• Bronchial tree	max 80 Gy
• Heart (lung cancer treatment)	Heart V45 <67%; V60 <33%
• Heart (breast cancer treatment)	V25 <10%
• Esophagus	V50 <32% ;V60 <33%
Thoracic (hypofractionation) Note: the max dose limits refer to volumes >0.035 cc (~3 mm^3).	
• Spinal cord	1 fraction: 14 Gy 3 fractions: 18 Gy (6 Gy/fx)

Organ	Constraints
	4 fractions: 26 Gy (6.5 Gy/fx) 5 fractions: 30 Gy (6 Gy/fx)
• Esophagus	1 fraction: 15.4 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 30 Gy (7.5 Gy/fx) 5 fractions: 32.5 Gy (6.5 Gy/fx)
• Brachial plexus	1 fraction: 17.5 Gy 3 fractions: 21 Gy (7 Gy/fx) 4 fractions: 27.2 Gy (6.8 Gy/fx) 5 fractions: 30 Gy (6 Gy/fx)
• Heart/Pericardium	1 fraction: 22 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 34 Gy (8.5 Gy/fx) 5 fractions: 35 Gy (7 Gy/fx)
• Great vessels	1 fraction: 37 Gy 3 fractions: 39 Gy (13 Gy/fx) 4 fractions: 49 Gy (12.25 Gy/fx) 5 fractions: 55 Gy (11 Gy/fx)
• Trachea/Large Bronchus	1 fraction: 20.2 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 34.8 Gy (8.7 Gy/fx) 5 fractions: 40 Gy (8 Gy/fx)
• Rib	1 fraction: 30 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 32 Gy (7.8 Gy/fx) 5 fractions: 32.5 Gy (6.5 Gy/fx)
• Skin	1 fraction: 26 Gy 3 fractions: 30 Gy (10 Gy/fx) 4 fractions: 36 Gy (9 Gy/fx) 5 fractions: 40 Gy (8 Gy/fx)
• Stomach	1 fraction: 12.4 Gy 3 fractions: 27 Gy (9 Gy/fx) 4 fractions: 30 Gy (7.5 Gy/fx) 5 fractions: 35 Gy (7 Gy/fx)
Gastrointestinal (GI) (1.8–2.0 Gy/fx)	
• Stomach	TD 5/5 whole stomach: 45 Gy
• Small bowel	V45 <195 cc
• Liver (metastatic disease)	mean liver <32 Gy (liver = normal liver minus gross disease)
• Liver (primary liver cancer)	mean liver <28 Gy (liver = normal liver minus gross disease)
• Colon	45 Gy, max dose 55 Gy
• Kidney (bilateral)	mean <18 Gy, V28 <20%, V23 Gy <30%, V20 <32%, V12 <55%. If mean kidney dose to 1 kidney >18 Gy, then constrain remaining kidney to V6 <30%.
Gastrointestinal (GI) (single fraction)	
• Duodenum	V16 <0.035 cc, V11.2 <5 cc
• Kidney (Cortex)	V8.4 <200 cc
• Kidney (Hilum)	V10.6 <66%
• Colon	V14.3 <20 cc, V18.4 <0.035 cc
• Jejunum/Ileum	V15.4 <0.035 cc, V11.9 <5 cc
• Stomach	V16 <0.035 cc, V11.2 <10 cc
• Rectum	V18.4 <0.035 cc, V14.3 <20 cc
Genitourinary (GU) (1.8-2.0 Gy/fx)	
• Femoral heads	V50 <5%
• Rectum	V75 <15% , V70 <20%, V65 <25%, V60 <35%, V50 <50%
• Bladder	V80 <15%, V75 <25%, V70 <35%, V65 <50%
• Testis	V3 <50%

Organ	Constraints
• Penile bulb	Mean dose to 95% of the volume <50 Gy. D70 </=70 Gy, D50 </=50 Gy
Genitourinary (GU) (LDR prostate brachytherapy)	
• Urethra	Volume of urethra receiving 150% of prescribed dose (Ur150) <30%
• Rectum	Volume of rectum receiving 100% of prescribed dose (RV100) <0.5 cc
Gynecological (GYN)	
• Bladder point (cervical brachytherapy)	Max 80 Gy (LDR equivalent dose)
• Rectal point (cervical brachytherapy)	Max 75 Gy (LDR equivalent dose)
• Proximal vagina (mucosa) (cervical brachytherapy)	Max 120 Gy (LDR equivalent dose)
• Distal vagina (mucosa) (cervical brachytherapy)	Max 98 Gy (LDR equivalent dose

Coding

The following CPT codes are used for simple and complex intensity-modulated radiotherapy delivery:

- **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

The Centers for Medicare & Medicaid Services (CMS) decided not to implement these CPT codes and instead created HCPCS G codes with the language of the previous CPT codes. The following codes may be used for IMRT:

- **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 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session

Code 77301 remains valid:

- **77301**: Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications

Code 77338 is to be reported only once per IMRT plan:

- **77338**: Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan

The following codes may also be used:

- **77261**: Therapeutic radiology treatment planning; simple
- **77262**: Therapeutic radiology treatment planning; intermediate
- **77263**: Therapeutic radiology treatment planning; complex
- **77293**: Respiratory motion management simulation (List separately in addition to code for primary procedure)
- **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
- **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)

- **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)
- **77334**: Treatment devices, design and construction; complex (irregular blocks, special shields, compensators, wedges, molds or casts)
- **77370**: Special medical radiation physics consultation
- **77470**: Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation)
- **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
- **77427**: Radiation treatment management, 5 treatments
- **77014**: Computed tomography guidance for placement of radiation therapy fields
- **77417**: Therapeutic radiology port image(s)
- **77387**: Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed
- **G6001**: Ultrasonic guidance for placement of radiation therapy fields
- **G6002**: Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy
- **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

Allowable Codes and Frequencies for IMRT/Proton

Description	Code	Maximum per course of treatment	Notes
Clinical Treatment Planning	77261, 77262 or 77263	1	
Simulation	77280, 77285, 77290	0	May not be billed with 77301. 1 unit of 77290 + 1 boost is allowed for proton therapy when using 77295 instead
Verification Simulation	77280	0	One per simulation allowed
Respiratory Motion Management	77293	0	1 for breast, lung, and upper abdominal or thoracic cancer areas
3D CRT Plan	77295	0	May not be billed with 77301. 1 unit may be allowed for proton therapy.
IMRT Plan	77301	1	If comparison 3D plan is generated, it is included in 77301
Basic Dosimetry	77300	4+ 1 boost, up to a max of 10 with documentation	0 if billed with 77306, 77307, 77321, 0394T or 0395T
Teletherapy Isodose Plan, Simple	77306	1 for mid-Tx change in volume/contour	Not on the same day as 77300; may not bill 77306 and 77307 together; documentation of medical necessity is required for more than 1
Teletherapy Isodose Plan, Complex	77307	1 for mid-Tx change in volume/contour	Not on the same day as 77300; may not bill 77306 and 77307 together; documentation of medical necessity is required for more than 1
Special Dosimetry Calculation	77331	0	Needs documentation for review
Treatment Devices, Designs, and Construction	77332, 77333, 77334	1, 5 or 10	-If billed w/ MLC (77338): 1 -If billed w/o MLC: 5 (any combination) -More may be allowed when documentation of medical necessity is provided (such as additional beams), maximum of 10
Multi-leaf Collimater (MLC)	77338	1	MLC may not be reported in conjunction with HCPCS G6016

Description	Code	Maximum per course of treatment	Notes
Special Radiation Physics Consult	77370	0	May allow x 1; documentation of medical necessity required
Special MD Consultation (Special Tx Procedure)	77470	0	May allow x 1; documentation of medical necessity required
Medical Physics Management	77336	8	Allowed once per 5 courses of therapy
Radiation Treatment Management	77427	8	Allowed once per 5 courses of therapy
Radiation (IMRT or Proton) Delivery, prostate and breast cancer	IMRT 77385 or G6015; Proton 77520, 77522, 77523	Using IMRT or Proton: 28 for prostate cancer Using IMRT only: -16 for breast cancer without boost -24 for breast cancer with boost (IMRT only)	Prostate cancer: Documentation of medical necessity needed for more than 28 treatments Breast cancer: documentation of medical necessity needed for treatments beyond 16 IMRT delivery sessions without boost and/or 24 IMRT delivery sessions with boost.
Radiation (IMRT or Proton) Delivery, all other cancers	IMRT 77385, 77386; or G6015-G6016: Proton 77520, 77522, 77523, 77525	No limit	All cancers other than hypofractionated prostate or breast

Description

Radiotherapy (RT) is an integral component in the treatment of head and neck cancers. Intensity-modulated radiotherapy (IMRT) has been proposed as a method to allow adequate radiation to the tumor, minimizing the radiation dose to surrounding normal tissues and critical structures.

Related Policies

- Radiation Oncology
- Stereotactic Radiosurgery and Stereotactic Body Radiotherapy

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

In general, IMRT systems include intensity modulators, which control, block, or filter the intensity of radiation, and RT planning systems, which plan the radiation dose to be delivered.

A number of intensity modulators have been cleared for marketing by the FDA through the 510(k) process. Intensity modulators include the Innocure Intensity Modulating Radiation Therapy Compensators (Innocure) and Decimal Tissue Compensator (Southeastern Radiation Products), cleared in 2006 and 2004, respectively. FDA product code: IXI. Intensity modulators may be added to standard linear accelerators to deliver IMRT when used with proper treatment planning systems.

Radiotherapy treatment planning systems have also been cleared for marketing by the FDA through the 510(k) process. They include the Prowess Panther (Prowess) in 2003, TiGRT (LinaTech) in 2009, and the Ray Dose (RaySearch Laboratories). FDA product code: MUJ.

Fully integrated IMRT systems also are available. These devices are customizable and support all stages of IMRT delivery, including planning, treatment delivery, and health record management. One such device cleared for marketing by the FDA through the 510(k) process is the Varian IMRT system (Varian Medical Systems). FDA product code: IYE.

Rationale

Background

Head and Neck Cancers

This evidence review focuses on cancers affecting the oral cavity and lip, larynx, hypopharynx, oropharynx, nasopharynx, paranasal sinuses and nasal cavity, salivary glands, and occult primaries in the head and neck region.

Radiotherapy Techniques

Radiation therapy may be administered externally (i.e., a beam of radiation is directed into the body) or internally (i.e., a radioactive source is placed inside the body, near a tumor).[1,] External radiotherapy (RT) techniques include "conventional" or 2-dimensional (2D) RT, 3-dimensional (3D) conformal RT, and intensity-modulated radiation therapy (IMRT).

Conventional External-Beam Radiotherapy

Methods to plan and deliver RT have evolved that permit more precise targeting of tumors with complex geometries. Conventional 2D treatment planning utilizes X-ray films to guide and position radiation beams.[1,] Bony landmarks visualized on X-ray are used to locate a tumor and direct the radiation beams. The radiation is typically of uniform intensity.

Three-Dimensional Conformal Radiotherapy

Radiation treatment planning has evolved to use 3D images, usually from computed tomography (CT) scans, to more precisely delineate the boundaries of the tumor and to discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Three-dimensional conformal RT (3D-CRT) involves initially scanning the patient in the position that will be used for the radiation treatment.[1,] The tumor target and surrounding normal organs are then outlined in 3D on the scan. Computer software assists in determining the orientation of radiation beams and the amount of radiation the tumor and normal tissues receive to ensure coverage of the entire tumor in order to minimize radiation exposure for at risk normal tissue and nearby organs. Other imaging techniques and devices such as multileaf collimators (MLCs) may be used to "shape" the radiation beams. Methods have also been developed to position the patient and the radiation portal reproducibly for each fraction and to immobilize the patient, thus maintaining consistent beam axes across treatment sessions.

Intensity-Modulated Radiotherapy

Intensity-modulated radiotherapy is the more recent development in external radiation. Treatment planning and delivery are more complex, time-consuming, and labor-intensive for IMRT than for 3D-CRT. Similar to 3D-CRT, the tumor and surrounding normal organs are outlined in 3D by a scan and multiple radiation beams are positioned around the patient for radiation delivery.[1,] In IMRT, radiation beams are divided into a grid-like pattern, separating a single beam into many smaller "beamlets". Specialized computer software allows for “inverse” treatment planning. The radiation oncologist delineates the target on each slice of a CT scan and specifies the target's prescribed radiation dose, acceptable limits of dose heterogeneity within the target volume, adjacent normal tissue volumes to avoid, and acceptable dose limits within the normal tissues. Based on these parameters and a digitally reconstructed radiographic image of the tumor, surrounding tissues, and organs at risk, computer software optimizes the location, shape, and intensities of the beam ports to achieve the treatment plan's goals.

Increased conformality may permit escalated tumor doses without increasing normal tissue toxicity and is proposed to improve local tumor control, with decreased exposure to surrounding, normal tissues, potentially reducing acute and late radiation toxicities. Better dose homogeneity within the target may also improve local tumor control by avoiding underdosing within the tumor and may decrease toxicity by avoiding overdosing.

Other advanced techniques may further improve RT treatment by improving dose distribution. These techniques are considered variations of IMRT. Volumetric modulated arc therapy delivers radiation from a continuous rotation of the radiation source. The principal advantage of volumetric modulated arc therapy is greater efficiency in treatment delivery time, reducing radiation exposure, and improving target radiation delivery due to less patient motion. Image-guided RT involves the incorporation of imaging before and/or during treatment to more precisely deliver RT to the target volume.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Head and Neck Cancers

Clinical Context and Therapy Purpose

The purpose of intensity-modulated radiotherapy (IMRT) in patients who have head and neck cancers is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of IMRT improve the net health outcome in patients with head and neck cancers?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with head and neck cancers. Head and neck cancers account for about 4% of all cancer cases in the U.S.[2] The generally accepted definition of head and neck cancers includes those arising from the oral cavity and lip, larynx, hypopharynx, oropharynx, nasopharynx, paranasal sinuses and nasal cavity, salivary glands, and occult primaries in the head and neck region. Cancers generally not considered as head and neck cancers include uveal and choroidal melanoma, cutaneous tumors of the head and neck, esophageal cancer, and tracheal cancer.

Interventions
The test being considered is IMRT. A proposed benefit of IMRT is to reduce toxicity to adjacent structures, allowing dose escalation to the target area and fewer breaks during treatment to reduce side effects.

Comparators
The following practices are currently being used to treat cancer of the head and neck: 3-dimensional conformal radiotherapy (3D-CRT) and 2-dimensional radiotherapy (2D-RT).

Outcomes
The general outcomes of interest are overall survival (OS), functional outcomes, and treatment-related morbidity (e.g. xerostomia). Evaluation of patient-reported outcomes and quality of life measures are also of interest.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Systematic Reviews
Systematic reviews have evaluated IMRT compared to 2D-RT or 3D-CRT in patients with head and neck cancers. A comparison of the trials in more recent systematic reviews that included outcomes of interest is shown in Table 1. These systematic reviews included a total of 22 articles published between 2006 and 2018. Characteristics and results of these reviews are summarized in Tables 2 and 3. Overall, Du et al (2019)[3] and Luo et al (2019)[4] reported significantly improved OS, locoregional free survival/control, and progression- or disease-free survival (PFS or DFS) with IMRT versus 2D-RT or 3D-CRT among patients with nasopharyngeal carcinoma (NPC). Marta et al (2014)[5] concluded that IMRT, when compared with 2D-RT or 3D-CRT, had no significant impact on OS or loco-regional control in previously untreated patients with non-metastatic head and neck cancers. The incidence of xerostomia was significantly reduced with IMRT as compared to patients undergoing 2D-RT or 3D-CRT.[5,3]

There are inherent limitations to the data within some of these systematic reviews, including the prevalence of retrospective and nonrandomized study designs. Some studies had small sample sizes of 20 to 50 subjects. Studies also varied considerably with regard to tumor stage, length of follow-up, and radiological dose. All of these variations contributed to heterogeneity of the

data. Additionally, 1 of the reviews specifically noted the existence of publication bias for the OS outcome.[3]

Table 1. Trials Included in Systematic Reviews of IMRT Versus 2D-RT or 3D-CRT.

Trials	Systematic Reviews		
	Marta et al (2014)[5]	Luo et al (2019)[4]	Du et al (2019)[3]
Kam et al (2007)[6]	●		●
Lai et al (2011)[7]		●	●
Peng et al (2012) [8]	●	●	●
Zhou et al (2013)[9]			●
Moon et al (2016)[10]		●	●
Zhang et al (2015)[11]		●	●
Qiu et al (2017)[12]		●	●
Tang et al (2015)[13]			●
Lee et al (2014)[14]			●
Zhong et al (2013)[15]			●
OuYang et al (2016)[16]		●	
Jiang et al (2015)[17]		●	
Fang et al (2008)[18]		●	
Kuang et al (2012)[19]		●	
Huang et al (2013)[20]		●	
Chen et al (2014)[21]		●	
Zou et al (2015)[22]		●	
Bisof et al (2018)[23]		●	
Pow et al (2006)[24]	●		
Nutting et al (2011)[25]	●		
Gupta et al (2011)[26]	●		
Gupta et al (2012)[27]	●		

2D-RT: 2-dimensional radiotherapy; 3D-CRT: 3-dimensional conformal radiotherapy; IMRT: intensity-modulated radiotherapy.

Table 2. Summary of Systematic Reviews of IMRT versus 2D-RT or 3D-CRT.

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Du et al 2019[3]	To December 1, 2018	10	Patients with nasopharyngeal carcinoma who underwent IMRT or 2D-RT	13,304 (56 to 7081)	2 RCTs; 8 nonrandomized trials	Follow-up data evaluated up to 5 years for certain outcomes
Luo et al 2019[4]	To November 20, 2018	13	Patients with nasopharyngeal carcinoma who underwent IMRT or CRT	14,745 (24 to 7081)	1 RCT; 1 prospective study; 11 retrospective studies	Mean follow-up: 42 to ≥ 60 months
Marta et al 2014[5]	To December 20, 2012	5 (6 publications corresponding to 5 trials)	Previously untreated patients with non-metastatic head and neck cancers treated with RT either primarily or combined with surgery or chemotherapy with or without brachytherapy boost	871 (45 to 616)	Prospective RCTs; 4 studies compared 2D-RT with IMRT	Follow-up data evaluated up to 5 years for certain outcomes

2D-RT: two-dimensional radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy; CRT: conformal radiotherapy; IMRT: intensity-modulated radiotherapy; RCT: randomized controlled trial; RT: radiotherapy.

Table 3. Results of Systematic Reviews of IMRT versus 2D-RT or 3D-CRT.

Study	Overall survival	Locoregional free survival/ control rate	Progression- or disease-free survival	Metastasis-free survival	Xerostomia
Du et al (2019)[3]		Local-regional free survival			
Total N	10,851	13,003	9380	10,432	1764
Pooled effect OR (95% CI)	1.70 (1.36 to 2.21) at 5 years	2.08 (1.82 to 2.37) at 5 years	1.40 (1.26 to 1.56) at 5 years	1.11 (0.99 to 1.24)	0.21 (0.09 to 0.51)
I^2; p value	68.7%;.007	20.7%;.272	0%;.446	17.9%;.301	87.3%;.00
Luo et al (2019)[4]		Locoregional control			
Total N	13,018	13,899	2464	4171	
Pooled effect OR (95% CI); p value	0.51 (0.41 to 0.65); <.00001	0.59 (0.52 to 0.67); <.00001	0.77 (0.65 to 0.91);.002	0.71 (0.54 to 0.94);.01	
I^2; p value	63%;.002	44%;.06	38%;.15	54%;.03	
Marta et al (2014)[5]		Locoregional control			
Total N	770	770			826
Pooled effect HR (95% CI); p value	1.12 (0.97 to 1.29);.11	1.07 (0.93 to 1.23);.35			0.76 (0.66 to 0.87); <.0001
I^2; p value		0%; NR			0%; NR

2D-RT: two-dimensional radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy; CI: confidence interval; HR: hazard ratio; NR: not reported; OR: odds ratio.

In addition, to the systematic reviews summarized in Tables 1 to 3, Ursino et al (2017) published a systematic review of 22 studies (N=1311 patients) that focused specifically on swallowing outcomes in patients treated with 3D-CRT or IMRT for head and neck cancer.[28] The heterogeneity of the population limited analysis, but reviewers concluded that IMRT produced markedly better results than 3D-CRT in terms of swallowing impairments, aspiration, pharyngeal residue, and functional parameters, especially when swallowing-related organs at risk were specifically taken into account during IMRT treatment planning. The analysis was limited by a lack of standardized evaluation questionnaires, objective instrumental parameter scores, amount and consistency of bolus administration, and timing of evaluations.

Ge et al (2020) recently evaluated the effects of IMRT as compared to conventional RT with regard to quality of life and xerostomia severity in 761 patients with head and neck cancer.[29] This meta-analysis included data from 7 studies: 3 RCTs, 2 prospective studies, 1 prospective case control study, and 1 retrospective study. Overall, patients who underwent IMRT had a better global health status (pooled standardized mean difference [SMD], 0.80; 95% CI: 0.26 to 1.35; p=.004) and improved cognitive function (pooled SMD, 0.30; 95% CI: 0.06 to 0.54; p=.013) as compared to patients who underwent conventional RT. Intensity-modulated radiotherapy was also associated with significantly lower scores for xerostomia than conventional RT (pooled SMD, -0.60; 95% CI; -0.97 to -0.24; p=.001). There were no differences between the groups with regard to emotional function (p=.531) and social function (p=.348). The analysis was limited by a small number of included studies, heterogeneity of data, and relatively small sample sizes.

Randomized Controlled Trials

Beyond the trials included in the systematic reviews, Tandon et al (2018) published a non-blinded RCT, which compared 2 fractionation schedules of IMRT for locally advanced head and neck cancer —simultaneous integrated boost (SIB-IMRT) and simultaneous modulated accelerated radiotherapy (SMART)—with the endpoint measures of toxicity, PFS, and OS.[30] Characteristics and results of this RCT are summarized in Tables 4 and 5. The SIB-IMRT group received 70, 63, and 56 gray (Gy) in 35 fractions to clinical target volumes 1, 2, and 3, respectively. The SMART group received 60 and 50 Gy to clinical target volumes 1 and clinical target volumes 3, respectively. No statistically significant differences in acute or late toxicities were found between the groups

except in fatigue, which was experienced by 66.7% of the control group and 40.0% of the study group (p=.038). At 2 years post-treatment, PFS and OS were improved for the SMART versus SIB-IMRT group (Table 5). The small sample sizes within subgroups, which result in greater standard errors and less power, may have prevented any meaningful interpretation of subgroup analysis. Also, due to cost, human papillomavirus (HPV) status was not part of the pre-treatment workup; the treatment response and prognosis for HPV-positive tumors are considerably different compared to HPV-negative tumors, but this factor could not be included in the analysis. Relevance, study design, and conduct limitations of the RCT are detailed in Tables 6 and 7.

Table 4. Characteristics of a RCT Comparing SIB-IMRT versus SMART.

Study	Countries	Sites	Dates	Participants	Interventions
Tandon et al (2018)[30]	India	1	June 2014 to March 2016	Adults (18 to 65 years) with Stage III or non-metastatic Stage IV locally advanced head and neck cancer	RT using standard SIB-IMRT fractionation RT using SMART boost technique

RCT: randomized controlled trial; RT: radiotherapy; SIB-IMRT: simultaneous integrated boost-intensity-modulated radiotherapy; SMART: simultaneous modulated accelerated radiotherapy.

Table 5. Results of the SIB-IMRT versus SMART RCT.

Study	Overall survival (2 years)	Progression-free survival (2 years)
Tandon et al (2018)[30]		
N	NR	NR
SIB-IMRT	60%	53.3%
SMART	86.7%	80%
p	.02	.28

NR: not reported; SIB-IMRT: simultaneous integrated boost-intensity-modulated radiotherapy; SMART: simultaneous modulated accelerated radiotherapy.

Table 6. Study Relevance Limitations of the SIB-IMRT versus SMART RCT.

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of follow-up[e]
Tandon et al (2018)[30]	4. Small sample sizes within each subgroup			1. Locoregional control not addressed	

SIB-IMRT: simultaneous integrated boost-intensity-modulated radiotherapy; SMART: simultaneous modulated accelerated radiotherapy.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a]Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b]Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c]Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d]Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e]Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 7. Study Design and Conduct Limitations of the SIB-IMRT versus SMART RCT.

Study	Allocation[a]	Blinding[b]	Selective reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Tandon et al (2018)[30]	3. Allocation using "chit method"	1, 2		1. During follow-up, there were 11 disease-related deaths (7 SIB-IMRT; 4 SMART) and 4	3. Sample size calculated based on historical trials; power analysis done	1. Survival statistics required still median follow-up for deriving

Study	Allocation[a]	Blinding[b]	Selective reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
				non-disease-related deaths each in both arms	to detect a difference in incidence of toxicity not survival	clinically meaningful results

SIB-IMRT: simultaneous integrated boost-intensity-modulated radiotherapy; SMART: simultaneous modulated accelerated radiotherapy.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Nonrandomized Comparative Studies

Nonrandomized comparative studies have evaluated late toxicities and quality-of-life after treatment with IMRT, 2D-RT, and 3D-CRT.

Qiu et al (2017) published a retrospective, single-center study comparing 2D-CRT and IMRT as treatments for NPC in children and adolescents.[12] All 176 patients (74 treated with 2D-CRT, 102 with IMRT) identified for the study were between 7 and 20 years old and treated at a single institution. The OS rate at 5 years was significantly higher for IMRT than 2D-CRT (90.4% vs. 76.1%, respectively; hazard ratio [HR], 0.30; 95% CI, 0.12 to 0.78; p=.007), as well as the 5-year DFS rate (85.7% vs. 71.2%, respectively; HR, 0.47; 95% CI, 0.23 to 0.94; p=.029). Grade 2, 3, and 4 xerostomia (52.7% vs. 34%, respectively; p=.015) and hearing loss (40.5% vs. 22.5%, respectively; p=.01) were also significantly lower with IMRT than with 2D-CRT. The duration of follow-up for late-onset radiation-induced toxicity and small sample size are limitations of the report.

A cross-sectional study by Huang et al (2016) assessed patients who had survived more than 5 years after treatment for NPC.[31] Of 585 NPC survivors, data were collected on 242 patients who met study selection criteria (no history of tumor relapse or second primary cancers, cancer-free survival >5 years, completion of the self-reported questionnaire). Treatments were given from 1997 to 2007, with the transition to the IMRT system in 2002. One hundred patients were treated with IMRT. Prior to use of IMRT, treatments included 2D-RT (n=39), 3D-CRT (n=24), and 2D-RT plus 3D-CRT boost (n=79). Patients had scheduled follow-ups at 3- to 4-month intervals until 5 years posttreatment; then, at 6-month intervals thereafter. Late toxicities (e.g., neuropathy, hearing loss, dysphagia, xerostomia, neck fibrosis) were routinely assessed at clinical visits. At the time of the study, the mean follow-up was 8.5 years after 2D-RT or 3D-CRT, and 6.4 years after IMRT. The IMRT group had statistically and clinically superior results for both clinician-assessed and patient-assessed (global quality-of-life, cognitive functioning, social functioning, fatigue, and 11 scales of a head and neck module) outcomes with moderate effect sizes after adjusting for covariates (Cohen *d* range, 0.47 to 0.53). Late toxicities were less severe in the IMRT group, with adjusted odd ratios (ORs) of 3.2, 4.8, 3.8, 4.1, and 5.3 for neuropathy, hearing loss, dysphagia, xerostomia, and neck fibrosis, respectively. No significant differences in late toxicities were observed between the 2D-RT and the 3D-CRT groups.

Section Summary: Head and Neck Cancer
The literature on IMRT for head and neck cancer includes systematic reviews as well as RCTs and nonrandomized comparative studies. Some of the most recently published systematic reviews compared IMRT to 2D-RT and 3D-CRT in patients with NPC. Results revealed a significant improvement in clinical oncologic outcomes (e.g., OS, PFS, locoregional control/survival) and toxicities such as xerostomia with IMRT in this patient population. A 2014 systematic review concluded that IMRT, when compared with 2D-RT or 3D-CRT, had no significant impact on OS or locoregional control in previously untreated patients with non-metastatic head and neck cancers; however, a significant improvement in xerostomia was observed with IMRT. Non-randomized comparative studies have compared IMRT with 3D-CRT or with 2D-RT plus 3D-CRT boost. These studies support the findings that both short- and long-term xerostomia is reduced with IMRT. Health-related quality of life was also improved with IMRT compared with 3D-CRT or with 2D-RT plus 3D-CRT boost. Comparators in these nonrandomized studies were generally older technologies (e.g., 2D-RT) with older treatment protocols, both of which limit interpretation of the results. For the outcomes of PFS and OS, another RCT compared 2 fractionation schedules of IMRT and found SMART superior to SIB-IMRT in the areas of 2-year PFS and OS.

Thyroid Cancer
Clinical Context and Therapy Purpose
The purpose of IMRT in patients who have thyroid cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of IMRT improve the net health outcome in patients with thyroid cancer?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is patients with thyroid cancer in close proximity to organs at risk. Anaplastic thyroid cancer occurs in less than 2% of patients with thyroid cancer.[32.]

Interventions
The test being considered is IMRT. A proposed benefit of IMRT is to reduce toxicity to adjacent structures, allowing dose escalation to the target area and fewer breaks during treatment to reduce side effects.

Comparators
The following practices are currently being used to treat cancer of the thyroid: 3D-CRT and 2D-RT. Conventional external-beam radiotherapy is uncommonly used in the treatment of thyroid cancers, but may be considered in patients with anaplastic thyroid cancer and for locoregional control in patients with incompletely resected high-risk or recurrent differentiated (papillary, follicular, or mixed papillary-follicular) thyroid cancer. In particular, for patients with anaplastic thyroid cancer variants, which are uncommon but have often demonstrated local invasion at the time of diagnosis, RT is a critical part of locoregional therapy.

Outcomes
The general outcomes of interest are OS, functional outcomes, and treatment-related morbidity. Evaluation of patient-reported outcomes and quality of life measures are also of interest. Locoregional control and OS should be assessed at 1 and 5 years.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Case Series

The best available evidence for this indication consists of case series. For example, Bhatia et al (2010) published a series that reviewed institutional outcomes for anaplastic thyroid cancer treated with 3D-CRT or IMRT in 53 consecutive patients.[33] Thirty-one (58%) patients were irradiated with curative intent. Median radiation dose was 55 Gy (range, 4 to 70 Gy). Thirteen (25%) patients received IMRT to a median of 60 Gy (range, 39.9 to 69.0 Gy). The Kaplan-Meier estimate of OS at 1 year for definitively irradiated patients was 29%. Patients without distant metastases receiving 50 Gy or more had superior survival outcomes; in this series, use of IMRT or 3D-CRT did not influence toxicity.

Schwartz et al (2009) retrospectively reviewed single-institution outcomes for patients treated for differentiated thyroid cancer with postoperative conformal external-beam RT.[34] One hundred thirty-one consecutive patients with differentiated thyroid cancer who underwent RT between 1996 and 2005 were included. Histologic diagnoses included 104 papillary, 21 follicular, and 6 mixed papillary-follicular types. Thirty-four (26%) patients had high-risk histologic types, and 76 (58%) had recurrent disease. Extraglandular disease progression was seen in 126 (96%) patients, microscopically positive surgical margins were seen in 62 (47%) patients, and gross residual disease was seen in 15 (11%) patients. Median RT dose was 60 Gy (range, 38 to 72 Gy). Fifty-seven (44%) patients were treated with IMRT to a median dose of 60 Gy (range, 56 to 66 Gy). Median follow-up was 38 months (range, 0 to 134 months). Kaplan-Meier estimates of loco-regional relapse-free survival, disease-specific survival, and OS at 4 years were 79%, 76%, and 73%, respectively. On multivariate analysis, high-risk histologic features, M1 (metastatic) disease, and gross residual disease were predictors for inferior disease-specific survival and OS. Intensity-modulated radiotherapy did not impact survival outcomes, but was associated with less frequent severe late morbidity (12% vs. 2%, respectively), primarily esophageal stricture.

Section Summary: Thyroid Cancer

The evidence on IMRT in individuals who have thyroid cancer includes case series data. High-quality studies that differentiate the superiority of any type of external-beam RT technique to treat thyroid cancer are not available. Limitations of published evidence include patient heterogeneity, variability in treatment protocols, short follow-up periods, inconsistency in reporting important health outcomes (e.g., OS vs PFS or tumor control rates), and inconsistency in reporting or collecting outcomes. However, the published evidence plus additional dosimetry considerations together suggest IMRT for thyroid tumors may be appropriate in some circumstances (e.g., anaplastic thyroid carcinoma) or for thyroid tumors located near critical structures (e.g., salivary glands, spinal cord), similar to the situation for head and neck cancers. Given the rarity of both anaplastic thyroid cancer and papillary thyroid cancers that are not treatable by other methods, high-quality trials are unlikely. Thus, when adverse events could result if nearby critical structures receive toxic radiation doses, the ability to improve dosimetry with IMRT may be accepted as meaningful evidence for its benefit.

Summary of Evidence

For individuals who have head and neck cancer who receive IMRT, the evidence includes systematic reviews, RCTs, and nonrandomized comparative studies. Relevant outcomes are OS, functional outcomes, quality of life, and treatment-related morbidity. Recently published systematic reviews compared IMRT to 2D-RT and CRT in patients with NPC. Results revealed a significant improvement in clinical oncologic outcomes (e.g., OS, PFS, locoregional control/survival) and toxicities such as xerostomia with IMRT in this patient population. A 2014 systematic review concluded that IMRT, when compared with 2D-RT or 3D-CRT, had no significant impact on OS or locoregional control in previously untreated patients with non-metastatic head and neck cancers; however, IMRT was associated with a significant improvement in xerostomia. One

RCT compared 2 fractionation schedules of IMRT for locally advanced head and neck cancer and found a survival benefit in using SMART boost over SIB-IMRT. Nonrandomized cohort studies have supported the findings that both short- and long-term xerostomia are reduced with IMRT. Overall, evidence has shown that IMRT significantly and consistently reduces both early and late xerostomia and improves quality of life domains related to xerostomia compared with 2D-RT or 3D-CRT. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have thyroid cancer in close proximity to organs at risk who receive IMRT, the evidence includes case series data. Relevant outcomes include OS, functional outcomes, quality of life, and treatment-related morbidity. High-quality studies that differentiate the superiority of any type of external beam RT to treat thyroid cancer are not available. However, the published evidence plus additional dosimetry considerations together suggest IMRT may be appropriate for thyroid tumors in some circumstances, such as for anaplastic thyroid carcinoma or thyroid tumors located near critical structures (e.g., salivary glands, spinal cord), similar to the situation for head and neck cancers. Thus, when adverse events could result if nearby critical structures receive toxic radiation doses, the ability to improve dosimetry with IMRT might be accepted as meaningful evidence for its benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests from Blue Cross Blue Shield Association, input was received from 2 physician specialty societies (3 reviewers) and 4 academic medical centers in 2012. There was a uniform consensus that intensity-modulated radiotherapy (IMRT) is appropriate for the treatment of head and neck cancers. There was a near uniform consensus that IMRT is appropriate in select patients with thyroid cancer. Respondents noted IMRT for head, neck, and thyroid tumors may reduce the risk of exposure to radiation in critical nearby structures (e.g., spinal cord, salivary glands), thus decreasing risks of adverse effects (e.g., xerostomia, esophageal stricture).

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Comprehensive Cancer Network
The NCCN (v.3.2021) guideline on head and neck cancer notes that: "Advanced radiation therapy technologies such as IMRT, tomotherapy, volumetric modulated arc therapy (VMAT), image-guided radiation therapy (IGRT), and proton beam therapy (PBT) may offer clinically relevant advantages in specific circumstances to spare important organs at risk (OARs)...and decrease the risk for late, normal tissue damage while still achieving the primary goal of local tumor control.[35] The demonstration of clinically significant dose-sparing of these OARS reflects best clinical practice." The NCCN guideline also notes that "randomized studies to test [advanced radiation therapy technologies] are unlikely to be done since specific clinical scenarios represent complex combinations of multiple variables. In light of that, the modalities

and techniques that are found best to reduce the doses to the clinically relevant OARs without compromising target coverage should be considered."

The NCCN (v.1.2021) guideline for thyroid cancer states, "External-beam radiotherapy (EBRT) or IMRT can increase short-term survival in some patients with anaplastic thyroid carcinoma; EBRT or IMRT can also improve local control and can be used for palliation (e.g., to prevent asphyxiation)." Additionally, the guideline notes, "IMRT may be useful to reduce toxicity" in these patients.[36] The NCCN also states that the use of IMRT can be considered if an unresectable, gross residual disease or locoregional recurrence threatens vital structures in the neck.

American Thyroid Association

The American Thyroid Association published guidelines for the management of patients with anaplastic thyroid cancer in 2021.[37] These guidelines contained the following recommendations regarding use of IMRT:

- Following R0 or R1 resection, we recommend that good performance status patients with no evidence of metastatic disease who wish an aggressive approach should be offered standard fractionation IMRT with concurrent systemic therapy.
  Strength of recommendation: strong; Quality of evidence: low.
- We recommend that patients who have undergone R2 resection or have unresectable but nonmetastatic disease with good performance status and who wish an aggressive approach be offered standard fractionation IMRT with systemic therapy.
  Strength of recommendation: strong; Quality of evidence: low.
- Among patients who are to receive radiotherapy for unresectable thyroid cancer or in the postoperative setting, IMRT is recommended.
  Strength of recommendation: strong; Quality of evidence: low.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

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

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 8.

Table 8. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01220583	A Randomized Phase II/Phase III Study of Adjuvant Concurrent Radiation and Chemotherapy Versus Radiation Alone in Resected High-Risk Malignant Salivary Gland Tumors	252	Oct 2028

NCT: national clinical trial.

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Documentation for Clinical Review

Please provide the following documentation:

- (click here >>>) Fax Back Form for Radiation Oncology Services

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	77014	Computed tomography guidance for placement of radiation therapy fields
	77261	Therapeutic radiology treatment planning; simple
	77262	Therapeutic radiology treatment planning; intermediate
	77263	Therapeutic radiology treatment planning; complex
	77293	Respiratory motion management simulation (List separately in addition to code for primary procedure)
	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)
	77331	Special dosimetry (e.g., TLD, microdosimetry) (specify), only when prescribed by the treating physician

Type	Code	Description
	77332	Treatment devices, design and construction; simple (simple block, simple 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
	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, includes intrafraction tracking, when performed
	77417	Therapeutic radiology port image(s)
	77427	Radiation treatment management, 5 treatments
	77470	Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation)
HCPCS	G6001	Ultrasonic guidance for placement of radiation therapy fields
	G6002	Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy
	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

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
03/30/2015	Policy title change from Intensity Modulated Radiation Therapy (IMRT) BCBSA Medical Policy adoption Policy revision without position change
10/01/2016	Policy revision without position change
09/01/2017	Policy revision without position change
09/01/2018	Policy revision without position change
09/01/2019	Policy revision without position change
06/01/2020	Administrative update. Policy statement and guidelines updated.
10/01/2020	Annual review. No change to policy statement. Literature review updated. Coding update.
11/20/2020	Policy statement and guidelines updated.
08/01/2021	Annual review. No change to policy statement. Policy guidelines updated.

Effective Date	Action
12/01/2021	Administrative update. No change to policy statement. Policy guidelines and literature updated.
08/01/2022	Annual review. No change to policy statement.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE **Red font: Verbiage removed**	**AFTER** **Blue font: Verbiage Changes/Additions**
Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid 8.01.48 **Policy Statement:** Intensity-modulated radiotherapy (IMRT) may be considered **medically necessary** for the treatment of head and neck cancers when the cancer to be treated is **one or more** of the following: I. Oral cavity and lip II. Larynx III. Hypopharynx IV. Oropharynx V. Nasopharynx VI. Paranasal sinuses and nasal cavity VII. Salivary glands VIII. Occult primaries in the head and neck region Intensity-modulated radiotherapy may be considered **medically necessary** for the treatment of thyroid or other head and neck cancers when dosimetric planning with standard 3-dimensional conformal radiotherapy predicts that the radiation dose to an adjacent organ (e.g.: esophagus, salivary glands, spinal cord) would result in unacceptable normal tissue toxicity, as documented by **one or more** of the following: I. The target volume is in close proximity to critical structures that must be protected and **both** of the following: * (see source below) A. Planned 3D-CRT exposure to critical adjacent structures is above normal tissue constraints B. Planned IMRT exposure to these critical adjacent structures does not exceed normal tissue constraints II. An immediately adjacent area has been previously irradiated and abutting portals must be established with high precision	**Intensity-Modulated Radiotherapy: Cancer of the Head and Neck or Thyroid 8.01.48** **Policy Statement:** I. Intensity-modulated radiotherapy (IMRT) may be considered **medically necessary** for the treatment of head and neck cancers when the cancer to be treated is **one or more** of the following: A. Oral cavity and lip B. Larynx C. Hypopharynx D. Oropharynx E. Nasopharynx F. Paranasal sinuses and nasal cavity G. Salivary glands H. Occult primaries in the head and neck region II. Intensity-modulated radiotherapy may be considered **medically necessary** for the treatment of thyroid or other head and neck cancers when dosimetric planning with standard 3-dimensional conformal radiotherapy predicts that the radiation dose to an adjacent organ (e.g.: esophagus, salivary glands, spinal cord) would result in unacceptable normal tissue toxicity, as documented by **one or more** of the following: A. The target volume is in close proximity to critical structures that must be protected and **both** of the following: * (see source below) 1. Planned 3D-CRT exposure to critical adjacent structures is above normal tissue constraints 2. Planned IMRT exposure to these critical adjacent structures does not exceed normal tissue constraints B. An immediately adjacent area has been previously irradiated and abutting portals must be established with high precision

POLICY STATEMENT	
BEFORE **Red font: Verbiage removed**	**AFTER** **Blue font: Verbiage Changes/Additions**
Intensity-modulated radiotherapy is considered **not medically necessary** for the treatment of thyroid or other head and neck cancers for all indications not meeting the criteria above.	III. Intensity-modulated radiotherapy is considered **not medically necessary** for the treatment of thyroid or other head and neck cancers for all indications not meeting the criteria above.