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 is considered not medically necessary for the treatment of thyroid or other head and neck cancers for all indications not meeting the criteria above.

Policy Guidelines

*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 (IJ ROBP); 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.
<table>
<thead>
<tr>
<th>Organ</th>
<th>Constraints</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central Nervous System (1.8-2.0 Gray/fraction [Gy/fx])</strong></td>
<td></td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>max 50 Gy (full cord cross-section); tolerance increases by 25% 6 mos after 1st course (for re-irradiation)</td>
</tr>
<tr>
<td>Brain</td>
<td>max 72 Gy (partial brain); avoid &gt;2 Gy/fx or hyperfractionation</td>
</tr>
<tr>
<td>Chiasm/Optic Nerves</td>
<td>max 55 Gy</td>
</tr>
<tr>
<td>Brainstem</td>
<td>Entire brainstem &lt;54 Gy, V59 Gy &lt;1-10 cc</td>
</tr>
<tr>
<td>Eyes (globe)</td>
<td>mean &lt;35 Gy, max 54 Gy</td>
</tr>
<tr>
<td>Lens</td>
<td>max 7 Gy</td>
</tr>
<tr>
<td>Retina</td>
<td>max 50 Gy</td>
</tr>
<tr>
<td>Lacrimal Gland</td>
<td>max 40 Gy</td>
</tr>
<tr>
<td>Inner ear/cochlea</td>
<td>mean &lt;=45 Gy (consider constraining to &lt;=35 Gy with concurrent cisplatin)</td>
</tr>
<tr>
<td>Pituitary gland</td>
<td>max 45 Gy (for panhypopituitarism, lower for GH deficiency)</td>
</tr>
<tr>
<td>Cauda equina</td>
<td>max 60 Gy</td>
</tr>
<tr>
<td><strong>Central Nervous System (single fraction)</strong></td>
<td></td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>max 13 Gy (if 3 fx, max 20 Gy)</td>
</tr>
<tr>
<td>Brain</td>
<td>V12 Gy &lt;5-10 cc</td>
</tr>
<tr>
<td>Chiasm/Optic Nerves</td>
<td>max 10 Gy</td>
</tr>
<tr>
<td>Brainstem</td>
<td>max 12.5 Gy</td>
</tr>
<tr>
<td>Sacral plexus</td>
<td>V18 &lt;0.035 cc, V14.4 &lt;5 cc</td>
</tr>
<tr>
<td>Cauda equina</td>
<td>V16 &lt;0.035 cc, V14 &lt;5 cc</td>
</tr>
<tr>
<td><strong>Head and Neck (1.8-2.0 Gy/fx)</strong></td>
<td></td>
</tr>
<tr>
<td>Parotid gland(s)</td>
<td>mean &lt;25 Gy (both glands) or mean &lt;20 Gy (1 gland)</td>
</tr>
<tr>
<td>Submandibular gland(s)</td>
<td>mean &lt;35 Gy</td>
</tr>
<tr>
<td>Larynx</td>
<td>mean &lt;=44 Gy, V50 &lt;=27%, max 63-66 Gy (when risk of tumor involvement is limited)</td>
</tr>
<tr>
<td>TMJ/mandible</td>
<td>max 70 Gy (if not possible, then V75 &lt;1 cc)</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>Non-oral cavity cancer: mean &lt;30 Gy, avoid hot spots &gt;60 Gy Oral cavity cancer: mean &lt;50 Gy, V55 &lt;1 cc, max 65 Gy</td>
</tr>
<tr>
<td>Esophagus (cervical)</td>
<td>V45 &lt;33%</td>
</tr>
<tr>
<td>Pharyngeal constrictors</td>
<td>mean &lt;50 Gy</td>
</tr>
<tr>
<td>Thyroid</td>
<td>V26 &lt;20%</td>
</tr>
<tr>
<td><strong>Thoracic (1.8-2.0 Gy/fx)</strong></td>
<td></td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>max 66 Gy, V60 &lt;5%</td>
</tr>
<tr>
<td>Lung (combined lung for lung cancer treatment)</td>
<td>mean &lt;20-23 Gy, V20 &lt;30%-35%</td>
</tr>
<tr>
<td>Lung (ipsilateral lung for breast cancer treatment)</td>
<td>V25 &lt;10%</td>
</tr>
<tr>
<td>Single lung (after pneumonectomy)</td>
<td>V5 &lt;60% V20 &lt;4-10% MLD &lt;8 Gy</td>
</tr>
<tr>
<td>Bronchial tree</td>
<td>max 80 Gy</td>
</tr>
<tr>
<td>Heart (lung cancer treatment)</td>
<td>Heart V45 &lt;67%, V60 &lt;33%</td>
</tr>
<tr>
<td>Heart (breast cancer treatment)</td>
<td>V25 &lt;10%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>V50 &lt;32%, V60 &lt;33%</td>
</tr>
<tr>
<td><strong>Thoracic (hypofractionation)</strong></td>
<td></td>
</tr>
<tr>
<td>Note: the max dose limits refer to volumes &gt;0.035 cc (~3 mm³).</td>
<td></td>
</tr>
<tr>
<td>Spinal cord</td>
<td>1 fraction: 14 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 18 Gy (6 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 26 Gy (6.5 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>5 fractions: 30 Gy (6 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>1 fraction: 15.4 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 30 Gy (10 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 30 Gy (7.5 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>5 fractions: 32.5 Gy (6.5 Gy/fx)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>1 fraction: 17.5 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 21 Gy (7 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 27.2 Gy (6.8 Gy/fx)</td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>1 fraction: 17.5 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 21 Gy (7 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 27.2 Gy (6.8 Gy/fx)</td>
</tr>
</tbody>
</table>
### Organ Constraints

<table>
<thead>
<tr>
<th>Organ</th>
<th>Constraints</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart/Pericardium</strong></td>
<td>1 fraction: 22 Gy (6 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 30 Gy (10 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 34 Gy (8.5 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>5 fractions: 35 Gy (7 Gy/fx)</td>
</tr>
<tr>
<td><strong>Great vessels</strong></td>
<td>1 fraction: 37 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 39 Gy (13 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 49 Gy (12.25 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>5 fractions: 55 Gy (11 Gy/fx)</td>
</tr>
<tr>
<td><strong>Trachea/Large Bronchus</strong></td>
<td>1 fraction: 20.2 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 30 Gy (10 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 34.8 Gy (8.7 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>5 fractions: 40 Gy (8 Gy/fx)</td>
</tr>
<tr>
<td><strong>Rib</strong></td>
<td>1 fraction: 30 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 30 Gy (10 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 32 Gy (7.8 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>5 fractions: 32.5 Gy (6.5 Gy/fx)</td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>1 fraction: 26 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 30 Gy (10 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 36 Gy (9 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>5 fractions: 40 Gy (8 Gy/fx)</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>1 fraction: 12.4 Gy</td>
</tr>
<tr>
<td></td>
<td>3 fractions: 27 Gy (9 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>4 fractions: 30 Gy (7.5 Gy/fx)</td>
</tr>
<tr>
<td></td>
<td>5 fractions: 35 Gy (7 Gy/fx)</td>
</tr>
<tr>
<td><strong>Gastrointestinal (GI) (1.8–2.0 Gy/fx)</strong></td>
<td>TD 5/5 whole stomach: 45 Gy</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>V45 &lt;195 cc</td>
</tr>
<tr>
<td><strong>Small bowel</strong></td>
<td>mean liver &lt;32 Gy (liver = normal liver minus gross disease)</td>
</tr>
<tr>
<td><strong>Liver (metastatic disease)</strong></td>
<td>mean liver &lt;28 Gy (liver = normal liver minus gross disease)</td>
</tr>
<tr>
<td><strong>Liver (primary liver cancer)</strong></td>
<td>mean liver &lt;18 Gy, V28 &lt;20%, V23 Gy &lt;30%, V20 &lt;32%, V12 &lt;55% if mean kidney dose to 1 kidney &gt;18 Gy, then constrain remaining kidney to V6 &lt;30%</td>
</tr>
<tr>
<td><strong>Gastrointestinal (GI) (single fraction)</strong></td>
<td>V16 &lt;0.035 cc, V11.2 &lt;5 cc</td>
</tr>
<tr>
<td><strong>Duodenum</strong></td>
<td>V8.4 &lt;200 cc</td>
</tr>
<tr>
<td><strong>Kidney (Cortex)</strong></td>
<td>V10.6 &lt;66%</td>
</tr>
<tr>
<td><strong>Kidney (Hilum)</strong></td>
<td>V14.3 &lt;20 cc, V18.4 &lt;0.035 cc</td>
</tr>
<tr>
<td><strong>Jejunum/Ileum</strong></td>
<td>V15.4 &lt;0.035 cc, V11.9 &lt;5 cc</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>V16 &lt;0.035 cc, V11.2 &lt;10 cc</td>
</tr>
<tr>
<td><strong>Rectum</strong></td>
<td>V18.4 &lt;0.035 cc, V14.3 &lt;20 cc</td>
</tr>
<tr>
<td><strong>Genitourinary (GU) (1.8–2.0 Gy/fx)</strong></td>
<td>V50 &lt;5%</td>
</tr>
<tr>
<td><strong>Femoral heads</strong></td>
<td>V75 &lt;15%, V70 &lt;20%, V65 &lt;25%, V60 &lt;35%, V50 &lt;50%</td>
</tr>
<tr>
<td><strong>Rectum</strong></td>
<td>V80 &lt;15%, V75 &lt;25%, V70 &lt;35%, V65 &lt;50%</td>
</tr>
<tr>
<td><strong>Bladder</strong></td>
<td>V3 &lt;50%</td>
</tr>
<tr>
<td><strong>Testis</strong></td>
<td>Mean dose to 95% of the volume &lt;50 Gy. D70 &lt;70 Gy, D50 &lt;50 Gy</td>
</tr>
<tr>
<td><strong>Genitourinary (GU) (LDR prostate brachytherapy)</strong></td>
<td>Volume of urethra receiving 150% of prescribed dose (Ur150) &lt;30%</td>
</tr>
<tr>
<td><strong>Urethra</strong></td>
<td>Volume of rectum receiving 100% of prescribed dose (RV100) &lt;0.5 cc</td>
</tr>
<tr>
<td><strong>Rectum</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Gynecological (GYN)**
### Constraints

<table>
<thead>
<tr>
<th>Organ</th>
<th>Constraints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder point (cervical brachytherapy)</td>
<td>Max 80 Gy (LDR equivalent dose)</td>
</tr>
<tr>
<td>Rectal point (cervical brachytherapy)</td>
<td>Max 75 Gy (LDR equivalent dose)</td>
</tr>
<tr>
<td>Proximal vagina (mucosa) (cervical brachytherapy)</td>
<td>Max 120 Gy (LDR equivalent dose)</td>
</tr>
<tr>
<td>Distal vagina (mucosa) (cervical brachytherapy)</td>
<td>Max 98 Gy (LDR equivalent dose)</td>
</tr>
</tbody>
</table>

### 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)
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.

### Allowable codes and frequencies for IMRT:

<table>
<thead>
<tr>
<th>Description</th>
<th>Code</th>
<th>Maximum per course of treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Planning</td>
<td>77261, 77262 or 77263</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Respiratory motion management</td>
<td>77293</td>
<td>0</td>
<td>Only for breast and lung cancer; otherwise documentation of medical necessity is required</td>
</tr>
<tr>
<td>IMRT radiotherapy plan</td>
<td>77301</td>
<td>1</td>
<td>If comparison 3D plan is generated, it is included in 77301</td>
</tr>
<tr>
<td>Basic Dosimetry</td>
<td>77300</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Isodose plan, simple</td>
<td>77306</td>
<td>1</td>
<td>Not on the same day as 77300; may not bill 77306 and 77307 together</td>
</tr>
<tr>
<td>Isodose plan, complex</td>
<td>77307</td>
<td>1</td>
<td>Same as above</td>
</tr>
<tr>
<td>Special Dosimetry</td>
<td>77331</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Treatment devices</td>
<td>77331, 77332,</td>
<td>1</td>
<td>Maximum of one of these codes per course of treatment</td>
</tr>
<tr>
<td>Treatment devices</td>
<td>77334</td>
<td>1</td>
<td>Only allowed for compensator-based IMRT; with delivery code G6016</td>
</tr>
<tr>
<td>Multi-leaf collimator</td>
<td>77338</td>
<td>1</td>
<td>Only allowed with delivery codes 77385 or 77386; not allowed with G6015</td>
</tr>
<tr>
<td>Special radiation physics consult</td>
<td>77370</td>
<td>0</td>
<td>May allow x 1; documentation of medical necessity required</td>
</tr>
<tr>
<td>Special physician consult</td>
<td>77470</td>
<td>0</td>
<td>May allow x 1; documentation of medical necessity required</td>
</tr>
<tr>
<td>Medical physics management</td>
<td>77336</td>
<td>8</td>
<td>Allowed once per 5 courses of therapy</td>
</tr>
<tr>
<td>Radiation therapy management</td>
<td>77427</td>
<td>8</td>
<td>Allowed once per 5 courses of therapy</td>
</tr>
<tr>
<td>Radiation delivery</td>
<td>77385 or G6015</td>
<td>28</td>
<td>Documentation of medical necessity needed for more than 28 treatments</td>
</tr>
</tbody>
</table>

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

- Charged-Particle (Proton or Helium Ion) Radiotherapy for Neoplastic Conditions
- 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 exterally (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). 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. Bony landmarks—bones 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. 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**

IMRT 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. 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 conformity 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 that 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. RCTs 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 Test 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.

Patients
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. 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.

IMRT is performed by radiation oncologists in an outpatient clinical setting.

Comparators
The following practices may be used to make decisions about the treatment of head and neck cancers: 3-dimensional conformal radiotherapy (3D-CRT) and 2-dimensional radiotherapy (2D-RT).

3D-CRT and 2D-RT are performed by radiation oncologists in an outpatient clinical setting.

Outcomes
The general outcomes of interest are locoregional control, overall survival (OS), 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) and Luo et al reported significantly improved OS, loco-regional 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) 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.

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.

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

<table>
<thead>
<tr>
<th>Trials</th>
<th>Systematic Reviews</th>
</tr>
</thead>
</table>

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N (Range)</th>
<th>Design</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Du et al 2019</td>
<td>To December 1, 2018</td>
<td>10</td>
<td>Patients with nasopharyngeal carcinoma who underwent IMRT or 2D-RT</td>
<td>13,304 (56 to 7081)</td>
<td>2 RCTs; 8 nonrandomized trials</td>
<td>Follow-up data evaluated up to 5 years for certain outcomes</td>
</tr>
<tr>
<td>Luo et al 2019</td>
<td>To November 20, 2018</td>
<td>13</td>
<td>Patients with nasopharyngeal carcinoma who underwent IMRT or CRT</td>
<td>14,745 (24 to 7081)</td>
<td>1 RCT; 1 prospective study; 11 retrospective studies</td>
<td>Mean follow-up: 42 to ≥ 60 months</td>
</tr>
<tr>
<td>Marta et al 2014</td>
<td>To December 20, 2012</td>
<td>5 (6 publications corresponding to 5 trials)</td>
<td>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</td>
<td>871 (45 to 616)</td>
<td>Prospective RCTs; 4 studies compared 2D-RT with IMRT</td>
<td>Follow-up data evaluated up to 5 years for certain outcomes</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Study</th>
<th>Overall survival</th>
<th>Local-regional free survival/ control rate</th>
<th>Progression-or disease-free survival</th>
<th>Metastasis-free survival</th>
<th>Xerostomia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Du et al (2019)</td>
<td>10,851</td>
<td>Local-regional free survival</td>
<td>13,003</td>
<td>9380</td>
<td>10,432</td>
</tr>
<tr>
<td>Total N</td>
<td></td>
<td></td>
<td>2.08 (1.82 to 2.37) at 5 years</td>
<td>1.40 (1.26 to 1.56) at 5 years</td>
<td>1.11 (0.99 to 1.24)</td>
</tr>
<tr>
<td>Pooled effect (95% CI)</td>
<td>OR 1.70 (1.36 to 2.21) at 5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I² (p)</td>
<td>68.7% 0.007</td>
<td></td>
<td>20.7% 0.272</td>
<td>0% 0.446</td>
<td>17.9% 0.301</td>
</tr>
<tr>
<td>Luo et al (2019)</td>
<td>13,018</td>
<td>Locoregional control</td>
<td>13,899</td>
<td>2464</td>
<td>4171</td>
</tr>
<tr>
<td>Total N</td>
<td></td>
<td></td>
<td>0.59 (0.52 to 0.67); &lt;0.00001</td>
<td>0.77 (0.65 to 0.91); 0.002</td>
<td>0.71 (0.54 to 0.94); 0.01</td>
</tr>
<tr>
<td>Pooled effect (95% CI)</td>
<td>OR 0.51 (0.41 to 0.65); &lt;0.00001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I² (p)</td>
<td>63% 0.002</td>
<td></td>
<td>44% 0.06</td>
<td>38% 0.15</td>
<td>54% 0.03</td>
</tr>
<tr>
<td>Marta et al (2014)</td>
<td>770</td>
<td>Locoregional control</td>
<td>770</td>
<td>826</td>
<td></td>
</tr>
<tr>
<td>Total N</td>
<td></td>
<td></td>
<td>1.07 (0.93 to 1.23); 0.35</td>
<td>0.76 (0.66 to 0.87); &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Pooled effect (95% CI)</td>
<td>HR 1.12 (0.97 to 1.29); 0.11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I² (p)</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td>0%</td>
</tr>
</tbody>
</table>

2D-RT: two-dimensional radiotherapy; 3D-CRT: three-dimensional conformal radiotherapy; CI: confidence interval; HR: hazard ratio; 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.

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.29 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 = 0.038). 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>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tandon et al (2018)</td>
<td>India</td>
<td>1</td>
<td>June 2014 to March 2016</td>
<td>Adults (18 to 65 years) with Stage III or non-metastatic Stage IV locally advanced head and neck cancer</td>
<td>RT using standard SIB-IMRT fractionation RT using SMART boost technique</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Overall survival (2 years)</th>
<th>Progression-free survival (2 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tandon et al (2018)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>SIB-IMRT</td>
<td>60%</td>
<td>53.3%</td>
</tr>
<tr>
<td>SMART</td>
<td>86.7%</td>
<td>80%</td>
</tr>
<tr>
<td>p</td>
<td>0.02</td>
<td>0.28</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Population¹</th>
<th>Intervention²</th>
<th>Comparator³</th>
<th>Outcomes⁴</th>
<th>Duration of follow-up⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tandon et al (2018)</td>
<td>4. Small sample sizes within each subgroup</td>
<td>1. Loco-regional control not addressed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

 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.

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocation</th>
<th>Blinding</th>
<th>Selective Reporting</th>
<th>Data Completeness</th>
<th>Power</th>
<th>Statistical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tandon et al (2018)</td>
<td>3. Allocation using &quot;chit method&quot;</td>
<td>1, 2</td>
<td>1. During follow-up, there were 11 disease-related deaths (7 SIB-IMRT; 4 SMART) and 4 non-disease-related deaths each in both arms</td>
<td>3. Sample size calculated based on historical trials; power analysis done to detect a difference in incidence of toxicity not survival</td>
<td>1. Survival statistics required still median follow-up for deriving clinically meaningful results</td>
<td></td>
</tr>
</tbody>
</table>

SIB-IMRT: simultaneous integrated boost-intensity-modulated radiotherapy; SMART: simultaneous modulated accelerated radiotherapy.


 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. 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; HR, 0.30; 95% CI, 0.12 to 0.78; p = 0.007), 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 = 0.029). Grade 2, 3, and 4 xerostomia (52.7% vs 34% respectively; p = 0.015) and hearing loss (40.5% vs 22.5%, respectively; p = 0.01) 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. 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's d range, 0.47-0.53). Late toxicities were less severe in the IMRT group, with adjusted 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 3 systematic reviews as well as RCTs and nonrandomized comparative studies. 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. Another 2014 systematic review 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; 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. HRQOL was also improved with IMRT compared with 3D-CRT 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 Test 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.

Patients
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.

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.

IMRT is performed by radiation oncologists in an outpatient clinical setting.

Comparators
The following practices may be used to make decisions about the treatment of thyroid cancer: 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 locoregional control, OS, 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. Thirty-one (58%) patients were irradiated with curative intent. Median radiation dose was 55 Gy (range, 4-70 Gy). Thirteen (25%) patients received IMRT to a median of 60 Gy (range, 39.9-69.0 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. 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, 38-72 Gy). Fifty-seven (44%) patients were treated with IMRT to a median dose of 60 Gy (range, 56-66 Gy). Median follow-up was 38 months (range, 0-134 months). Kaplan-Meier estimates of locoregional 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. IMRT 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, randomized controlled trials (RCTs), and nonrandomized comparative studies. Relevant outcomes are overall survival (OS), functional outcomes, quality-of-life, and treatment-related morbidity. Recently published systematic reviews compared IMRT to 2-dimensional radiotherapy (2D-RT) and conformal radiotherapy (CRT) in patients with nasopharyngeal carcinoma (NPC). Results revealed a significant improvement in clinical oncologic outcomes (e.g., OS, progression-free survival (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 loco-regional 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 SB-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 a meaningful 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 a meaningful improvement in the net health outcome.

Supplemental Information
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 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
National Comprehensive Cancer Network
The NCCN (v.1.2020) 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. 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.2.2019) 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. 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.

**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

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrolment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>A Randomized Phase II/Phase III Study of Adjuvant Concurrent Radiation and Chemotherapy Versus Radiation Alone in Resected High-Risk Malignant Salivary Gland Tumors</td>
<td>120</td>
<td>Oct 2028</td>
</tr>
<tr>
<td>NCT02048254</td>
<td>A Randomized Control Trial (RCT) of Using Iodine-125 Brachytherapy Versus Intensity-modulated Radiation Therapy (IMRT) to Treat Inoperable Salivary Gland Cancer</td>
<td>90</td>
<td>Jun 2018 No related publications</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

**References**

**Documentation for Clinical Review**

Please provide the following documentation:

- History and physical and radiation oncology consultation report including:
  - Medical necessity for performing IMRT rather than conventional or 3D treatment planning
  - Past history of radiation (site) (if applicable)
  - Past surgical procedures (pertaining to request)
  - Primary cancer type and location
- Goals/requirements of the IMRT treatment plan and proposed IMRT treatment dose (dose volume histogram [DVH] -in color preferred; organs at risk)
- Comparison 3D-CRT dose volume histogram (DVH) (in color preferred; organs at risk) (as applicable)
- Radiology report(s) for the past 2 months

**Post Service (in addition to the above, please include the following):**

- Procedure report(s)

**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. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT®</td>
<td>77014</td>
<td>Computed tomography guidance for placement of radiation therapy fields</td>
</tr>
<tr>
<td></td>
<td>77261</td>
<td>Therapeutic radiology treatment planning; simple</td>
</tr>
<tr>
<td></td>
<td>77262</td>
<td>Therapeutic radiology treatment planning; intermediate</td>
</tr>
<tr>
<td></td>
<td>77263</td>
<td>Therapeutic radiology treatment planning; complex</td>
</tr>
<tr>
<td></td>
<td>77293</td>
<td>Respiratory motion management simulation (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td></td>
<td>77300</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>77301</td>
<td>Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications</td>
</tr>
<tr>
<td></td>
<td>77306</td>
<td>Teletherapy isodose plan; simple (1 or 2 unmodified ports directed to a single area of interest), includes basic dosimetry calculation(s)</td>
</tr>
<tr>
<td></td>
<td>77307</td>
<td>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)</td>
</tr>
<tr>
<td></td>
<td>77331</td>
<td>Special dosimetry (e.g., TLD, microdosimetry) (specify), only when prescribed by the treating physician</td>
</tr>
</tbody>
</table>
### Type Codes

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>77332</td>
<td>Treatment devices, design and construction; simple (simple block, simple bolus)</td>
</tr>
<tr>
<td></td>
<td>77334</td>
<td>Treatment devices, design and construction; complex (irregular blocks, special shields, compensators, wedges, molds or casts)</td>
</tr>
<tr>
<td></td>
<td>77336</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td>77338</td>
<td>Multi-leaf collimator (MLC) device(s) for intensity modulated radiation therapy (IMRT), design and construction per IMRT plan</td>
</tr>
<tr>
<td></td>
<td>77370</td>
<td>Special medical radiation physics consultation</td>
</tr>
<tr>
<td></td>
<td>77385</td>
<td>Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple</td>
</tr>
<tr>
<td></td>
<td>77387</td>
<td>Guidance for localization of target volume for delivery of radiation treatment, includes intrafraction tracking, when performed</td>
</tr>
<tr>
<td></td>
<td>77417</td>
<td>Therapeutic radiology port image(s)</td>
</tr>
<tr>
<td></td>
<td>77427</td>
<td>Radiation treatment management, 5 treatments</td>
</tr>
<tr>
<td></td>
<td>77470</td>
<td>Special treatment procedure (e.g., total body irradiation, hemibody radiation, per oral or endocavitary irradiation)</td>
</tr>
<tr>
<td></td>
<td>77385</td>
<td>Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; simple</td>
</tr>
<tr>
<td></td>
<td>77386</td>
<td>Intensity modulated radiation treatment delivery (IMRT), includes guidance and tracking, when performed; complex</td>
</tr>
</tbody>
</table>

### HCPCS Codes

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G6001</td>
<td>Ultrasonic guidance for placement of radiation therapy fields</td>
</tr>
<tr>
<td>G6002</td>
<td>Stereoscopic x-ray guidance for localization of target volume for the delivery of radiation therapy</td>
</tr>
<tr>
<td>G6015</td>
<td>Intensity modulated treatment delivery, single or multiple fields/arc,s, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session</td>
</tr>
<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>
</tr>
<tr>
<td>G6017</td>
<td>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</td>
</tr>
</tbody>
</table>

### Policy History

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

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/30/2015</td>
<td>Policy title change from Intensity Modulated Radiation Therapy (IMRT) BCBSA Medical Policy adoption</td>
</tr>
<tr>
<td>10/01/2016</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>09/01/2017</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>09/01/2018</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>09/01/2019</td>
<td>Policy revision without position change</td>
</tr>
<tr>
<td>06/01/2020</td>
<td>Administrative update. Policy statement and guidelines updated.</td>
</tr>
<tr>
<td>10/01/2020</td>
<td>Annual review. No change to policy statement. Literature review updated. Coding update.</td>
</tr>
</tbody>
</table>
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.