Intensity-modulated radiation therapy (IMRT) has been proposed as a method of radiation therapy that allows adequate radiation therapy to the tumor while minimizing the radiation dose to surrounding normal tissues and critical structures.

Background

Radiation techniques

Conventional external-beam radiation therapy. Over the past several decades, methods to plan and deliver radiation therapy have evolved in ways that permit more precise targeting of tumors with complex geometries. Most early trials used 2-dimensional treatment planning based on flat images and radiation beams with cross-sections of uniform intensity that were sequentially aimed at the tumor along 2 or 3 intersecting axes. Collectively, these methods are termed “conventional external-beam radiation therapy.”

3-dimensional conformal radiation (3D-CRT). 3D-CRT involves treatment planning evolved by using 3-dimensional images, usually from computed tomography (CT) scans, to delineate the boundaries of the tumor and discriminate tumor tissue from adjacent normal tissue and nearby organs at risk for radiation damage. Computer algorithms were developed to estimate cumulative radiation dose delivered to each volume of interest by summing the contribution from each shaped beam. Methods also were developed to position the patient and the radiation portal reproducibly for each fraction and immobilize the patient, thus maintaining consistent beam axes across treatment sessions. Collectively, these methods are termed 3-dimensional conformal radiation therapy (3D-CRT).

Intensity-modulated radiation therapy (IMRT). IMRT, which uses computer software and computed tomography (CT) images, offers better conformality than 3D-CRT as it is able to modulate the intensity of the overlapping radiation beams projected on the target and to use multiply-shaped treatment fields. It uses a device (a multileaf collimator, MLC) which, coupled to a computer algorithm, 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 and surrounding tissues and organs at risk, computer software optimizes the location, shape and intensities of the beams ports, to achieve the treatment plan’s goals.

Increased conformity may permit escalated tumor doses without increasing normal tissue toxicity and thus may 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.

Since most tumors move as patients breathe, dosimetry with stationary targets may not accurately reflect doses delivered within target volumes and adjacent tissues in patients. Furthermore, treatment planning and delivery are more complex, time consuming and labor-intensive for IMRT than for 3D-CRT. (1) Thus, clinical studies must test whether IMRT improves tumor control or reduces acute and late toxicities when compared with 3D-CRT.

Multiple-dose planning studies have generated 3D-CRT and IMRT treatment plans from the same scans, then compared predicted dose distributions within the target and in adjacent organs at risk. Results of such planning studies show that IMRT improves on 3D-CRT with respect to conformity to, and dose homogeneity within, the target. Dosimetry using stationary targets generally confirms these predictions. Thus, radiation oncologists hypothesized that IMRT may improve treatment outcomes compared with those of 3D-CRT. However, these types of studies offer indirect evidence on treatment benefit from IMRT, and it is difficult to relate results of dosing studies to actual effects on health outcomes.

Comparative studies of radiation-induced side effects from IMRT versus alternative radiation delivery are probably the most important type of evidence in establishing the benefit of IMRT. Such studies would answer the question of whether the theoretical benefit of IMRT in sparing normal tissue translates into real health outcomes. Single-arm series of IMRT can give some insights into the potential for benefit, particularly if an adverse effect that is expected to occur at high rates is shown to decrease by a large amount. Studies of treatment benefit are also important to establish that IMRT is at least as good as other types of delivery, but in the absence of such comparative trials, it is likely that benefit from IMRT is at least as good as with other types of delivery.

Note: This policy only addresses the use of IMRT for thyroid cancers.

Related Policies
8.01.46 Intensity-Modulated Radiation Therapy (IMRT) of the Lung
8.01.49 Intensity-Modulated Radiation Therapy (IMRT): Abdomen and Pelvis
8.01.59 Intensity-Modulated Radiation Therapy (IMRT): Central Nervous System Tumors
Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Intensity-modulated radiation therapy may be considered medically necessary for the treatment of thyroid cancers in close proximity to organs at risk (esophagus, salivary glands, and spinal cord) and 3-D CRT planning is not able to meet dose volume constraints for normal tissue tolerance. (see Policy Guidelines)

Policy Guidelines

Organs at risk are defined as normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed radiation dose. These organs at risk may be particularly vulnerable to clinically important complications from radiation toxicity. The following table outlines radiation doses that are generally considered tolerance thresholds for these normal structures in the area of the thyroid.

Radiation tolerance doses for normal tissues

<table>
<thead>
<tr>
<th>Site</th>
<th>Portion of organ involved</th>
<th>TD 5/5 (Gy)a</th>
<th>TD 50/5 (Gy)b</th>
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<tbody>
<tr>
<td></td>
<td>Portion of organ involved</td>
<td>1/3</td>
<td>2/3</td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td>60</td>
<td>58</td>
</tr>
<tr>
<td>Salivary glands</td>
<td></td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>50 (5-10 cm)</td>
<td>NP</td>
<td>47 (20 cm)</td>
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*TD 5/5, the average dose that results in a 5% complication risk within 5 years
rTD 50/5, the average dose that results in a 50% complication risk within 5 years
NP: not provided
cm=centimeters

The tolerance doses in the table are a compilation from the following two sources:
Kehwar TS, Sharma SC. Use of normal tissue tolerance doses into linear quadratic equation to estimate normal tissue complication probability. http://www.rooj.com/Radiation%20Tissue%20Tolerance.htm

Rationale

Introduction

Intensity-modulated radiation therapy (IMRT) methods to plan and deliver radiation therapy are not uniform. IMRT may use beams that remain on as the multileaf collimators (MLC) that move around the patient (dynamic MLC), or that are turned off during movement and turned on when the MLC reaches prespecified positions (“step and shoot” technique). A third alternative uses a very narrow single beam that moves spirally around the patient (tomotherapy). Each of these methods uses different computer algorithms to plan treatment and yields somewhat different dose distributions in and outside the target. Patient position can alter target shape and thus affect treatment plans. Treatment plans are usually
based on one imaging scan, a static 3-dimensional computed tomography (CT) image. Current methods seek to reduce positional uncertainty for tumors and adjacent normal tissues by various techniques. Patient immobilization cradles and skin or bony markers are used to minimize day-to-day variability in patient positioning. In addition, many tumors have irregular edges that preclude drawing tight margins on CT scan slices when radiation oncologists contour the tumor volume. It is unknown whether omitting some tumor cells or including some normal cells in the resulting target affects outcomes of IMRT.

**Thyroid Cancer**

Studies on use of IMRT for thyroid cancers are few. In thyroid cancer, radiation therapy is generally used for 2 indications. The first indication is treatment of anaplastic thyroid cancer, and the second indication is potential use for locoregional control in patients with incompletely resected high-risk or recurrent differentiated (papillary, follicular, or mixed papillary-follicular) thyroid cancer. Anaplastic thyroid cancer occurs in a minority (less than 5%) of thyroid cancer. The largest series comparing IMRT to 3D-CRT was published by Bhatia and colleagues. (2) This study reviewed institutional outcomes for anaplastic thyroid cancer treated with 3D-CRT or IMRT for 53 consecutive patients. Thirty-one (58%) patients were irradiated with curative intent. Median radiation dose was 55 gray (Gy; range, 4-70 Gy). Thirteen (25%) patients received IMRT to a median 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 higher had superior survival outcomes; in this series, use of IMRT versus 3D-CRT did not influence toxicity. The authors concluded that outcomes for anaplastic thyroid cancer treated with 3D-CRT or IMRT remain equivalent to historic results and that healthy patients with localized disease who tolerate full-dose irradiation can potentially enjoy prolonged survival.

Schwartz and colleagues reviewed institutional outcomes for patients treated for differentiated thyroid cancer with postoperative conformal external beam radiotherapy. (3) This was a single-institution retrospective review of 131 consecutive patients with differentiated thyroid cancer who underwent RT between January 1996 and December 2005. Histologic diagnoses included 104 papillary, 21 follicular, and 6 mixed papillary-follicular types. Thirty-four patients (26%) had high-risk histologic types and 76 (58%) had recurrent disease. Extraglandular disease spread was seen in 126 patients (96%), microscopically positive surgical margins were seen in 62 patients (47%), and gross residual disease was seen in 15 patients (11%). Median RT dose was 60 Gy (range, 38-72 Gy). Fifty-seven patients (44%) 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 predicted for inferior disease-specific and OS. IMRT did not impact on survival outcomes but was associated with less frequent severe late morbidity (12% vs. 2%, respectively), primarily esophageal stricture. The authors concluded that conformal external beam radiotherapy provides durable locoregional disease control for patients with high-risk differentiated thyroid cancer if disease is reduced to microscopic burden and that IMRT may reduce chronic radiation morbidity, but additional study is required.
Clinical Trials

No clinical trials on IMRT for thyroid cancer were identified.

Practice Guidelines and Position Statements

NCCN guidelines for thyroid cancer state that when considering external-beam radiation therapy for the treatment of anaplastic thyroid cancer, IMRT may be useful to reduce toxicity. (4)

Summary

There are limited data on use of IMRT for thyroid cancer. The published literature consists of small case series with limited comparison among techniques for delivering radiation therapy. Due to the limitations in this evidence, clinical input was obtained. There was near-uniform consensus that the use of IMRT for thyroid tumors may be appropriate in some circumstances such as for anaplastic thyroid carcinoma or for thyroid tumors that are located near critical structures such as the salivary glands or spinal cord. When possible adverse events could result if nearby critical structures receive toxic radiation doses, the ability to improve dosimetry with IMRT can be accepted as meaningful evidence for its benefit. The results of the vetting, together with a strong indirect chain of evidence and the potential to reduce harms, led to the decision that IMRT may be considered medically necessary for the treatment of thyroid cancers in close proximity to organs at risk (esophagus, salivary glands and spinal cord) and 3-dimensional conformal radiation (3-D CRT) planning is not able to meet dose volume constraints for normal tissue tolerance.

Medicare National Coverage

No national coverage determination.

References

Section: Therapy
Effective Date: November 1, 2013
Subsection: Therapy
Original Policy Date: September 13, 2012
Subject: Intensity-Modulated Radiation Therapy (IMRT): Cancer of the Thyroid
Page: 6 of 6

Policy History

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<th>Date</th>
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<tr>
<td>September 2013</td>
<td>Updated Policy</td>
<td>Policy updated with literature review, no change to policy statements.</td>
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Keywords
Radiation Therapy, Thyroid
Thyroid Radiation Therapy

This policy was approved by the FEP Pharmacy and Medical Policy Committee on September 20, 2013 and is effective November 1, 2013.

Signature on file
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