The Role of Radiation Therapy in the Treatment of Medullary Thyroid Cancer

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Key Words
Medullary thyroid cancer, thyroid cancer, external-beam radiation, IMRT, radiotherapy

Abstract
Medullary thyroid cancer (MTC) is a neuroendocrine tumor derived from parafollicular or C cells of the thyroid gland. Surgical resection is the mainstay of treatment for MTC. External-beam radiation treatment (EBRT) has traditionally played a limited role in the management of MTC. Despite aggressive surgery, patients at high risk for local recurrence may benefit from adjuvant EBRT. With improvements in radiation technique, adequate dose can be effectively delivered to the region at risk while minimizing dose to surrounding critical structures. Although the role of EBRT in the management of these tumors has thus far been poorly defined, EBRT should be considered as a treatment option for patients with locally advanced MTC to optimize locoregional control. (JNCCN 2010;8:532–541)

Learning Objectives
Upon completion of this activity, participants will be able to:
• Identify the primary marker for MTC used to follow disease activity
• Describe treatment options for MTC
• Distinguish the clinical presentations of the sporadic and familial forms of MTC
• Describe the added value of external beam radiation therapy (EBRT) for patients with MTC
• Identify options for the palliative treatment of MCT

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Medullary thyroid cancer (MTC) is a neuroendocrine tumor that develops from parafollicular or C cells of the thyroid gland. C cells secrete calcitonin which is used as a marker for this malignancy. C cells constitute approximately 1% of thyroid cells, and MTC accounts for approximately 4% of thyroid cancers. Both familial (FMTC) and sporadic forms of MTC exist; FMTC is associated with the autosomal dominant hereditary syndromes, including multiple endocrine neoplasia (MEN) type 2A, MEN type 2B, and non-MEN familial type MTC. The RET proto-oncogene, a tyrosine kinase receptor, has been identified as the germline mutation responsible for these hereditary cases.

Surgical resection is the primary modality used for treatment of MTC. Radioactive iodine, although typically used in the first-line treatment of differentiated thyroid cancer, is not useful in the treatment of MTC as these tumors do not concentrate iodine. The indications for the use of external-beam radiation treatment (EBRT) in the treatment of MTC are controversial and poorly defined. Data evaluating the role of EBRT in the management of MTC are scarce, and thus EBRT has generally been reserved for patients with locally advanced disease and limited treatment options.

Clinical Presentation

MTCs are generally indolent tumors, although aggressive variants have been described. Regional lymph node metastases are identified in up to 75% of patients, particularly in large primary tumors. Lymph nodes with MTC are most frequently located in the central compartment at levels VI and VII and the ipsilateral neck at levels II to V. The contralateral cervical chain and upper mediastinal nodes are also at risk for locoregional spread of disease.

As opposed to FMTC, the sporadic form of MTC most often presents as a palpable nodule. Locally advanced disease may cause dysphagia, hoarseness, or respiratory complaints, including stridor (see Figure 1). Serum calcitonin level is a sensitive and specific marker for MTC; high levels are associated with diarrhea. Carcinoembryonic antigen (CEA) is also a good tumor marker and helpful in follow-up. Distant metastases are present in approximately 10% of patients at diagnosis.

Nearly 100% of hereditary MTCs are associated with germline RET proto-oncogene mutations, whereas somatic RET proto-oncogene mutations are associated with 25% of sporadic cases. FMTCs typically present with multifocal or bilateral disease in individuals younger than 20 years. MEN 2A, the most common syndrome affiliated with MTC, is associated with hyperparathyroidism and pheochromocytoma. MEN 2B syndrome includes MTC, pheochromocytoma, mucosal ganglioneuromatosis, and a marfanoid habitus. FMTC is characterized by the presence of MTC. Because MTC has high penetrance in all 3 familial forms, first-degree relatives of a family member with the mutation should receive genetic counseling and testing if the patient index demonstrates the RET mutation. The presentation of MTC varies according to the specific mutation of the RET codon gene. MTC affiliated with MEN 2B tends to be most aggressive, with the development of invasive cancer in patients as young as 1 year. FMTC is the least aggressive, with invasive cancer not presenting until 20 to 30 years of age. Genetic screening should be performed for all patients presenting with MTC because surgery for early-stage disease is curative. Before surgery, patients must undergo screening for pheochromocytoma and hyperparathyroidism. Treatment of pheochromocytoma should be performed before management of MTC. Parathyroidectomy can be performed at surgery for MTC if hyperparathyroidism is identified.

Figure 1 Axial CT scan identifying a locally advanced thyroid mass with tracheal deviation. A fine needle aspiration performed identified medullary thyroid cancer.
Surgical Considerations

Surgical resection for both familial and sporadic forms of MTC is the mainstay of treatment for multiple reasons. MTC is typically considered to have a more aggressive natural history than differentiated thyroid cancer. It is not amenable to radioactive iodine, and nodal involvement is common. Furthermore, MTC is frequently multifocal, particularly in the hereditary form, but can also be multifocal in the sporadic form in approximately 20% of patients. Early prophylactic thyroidectomy is routinely performed in patients with MEN 2 with RET proto-oncogene mutations.\(^\text{15,16,18}\) All thyroid tissue must be removed given the multifocal nature of MEN-associated MTC, because any remaining C cells are a potential source of malignancy. Recommendations for surgical management, and guidance on the age for intervention, are based on the RET codon mutations identified, which are correlated with the presentation of disease.\(^\text{10}\) RET mutations have been classified as highest-, high-, and/or intermediate-risk depending on the observed aggressiveness of the phenotype.\(^\text{8}\)

In patients with sporadic MTC, total thyroidectomy and nodal dissection of the central compartment with dissection of levels II to V in the ipsilateral, and often contralateral neck, is also routinely performed.\(^\text{3,19}\) Consideration is also given to parathyroidectomy with autotransplantation.\(^\text{8,19–21}\) Both the completeness of surgical resection and monitoring for recurrence of disease can be assessed by postoperative calcitonin levels and CEA levels.\(^\text{22–24}\) However, calcitonin may remain elevated up to 3 to 4 months after surgery because of the postoperative stimulation of calcitonin synthesis.\(^\text{25}\)

The major surgical considerations in MTC recognize its high-risk nature. These considerations include large size, extrathyroidal extension, recurrent laryngeal nerve involvement, tumor adherent to the tracheal wall where surgical resection was unsatisfactory, multiple positive nodes, and extranodal spread in nodal metastasis. These factors must be evaluated at surgery, and appropriate consideration may be given, depending on the surgeon’s concerns, to postoperative radiation therapy. Bulky metastatic disease at level II or VI is always of concern. Patients with bulky nodal disease at levels VI or VII are more likely to have mediastinal disease, which may be very difficult to control without external radiation therapy.

Role of Radiation Treatment

Although persistent or recurrent disease may be managed surgically, EBRT can play a role in patients at high risk for local recurrence despite the prevailing view in the literature that EBRT minimally impacts the control of MTC. High-risk patients may still be referred postoperatively for consideration of EBRT. Although the biology and natural history of MTC is distinct from well-differentiated thyroid cancers, the risk factors for locoregional recurrence are considered similar, including extrathyroidal extension, postoperative residual disease, high clinical stage, and lymph node involvement.\(^\text{26–28}\)

Although the role of EBRT in the management of this disease has been minimal, the American College of Surgeons Commission on Cancer reported that 13.9% of patients with sporadic MTC and 15.4% with FMTC underwent EBRT postoperatively.\(^\text{29}\) EBRT has also traditionally played a limited role in the management of well-differentiated thyroid cancer. Only a small number of patients present with MTC in most published series on nonanaplastic thyroid cancer. As a result, data specifically evaluating the role of EBRT in the management of MTC are scarce.

Several series have suggested that EBRT may play a role in local control of MTC in patients with poor prognostic factors predictive of local recurrence. A recent series from M. D. Anderson Cancer Center reported their experience treating 34 consecutive patients with stage IVA to IVC MTC with EBRT postoperatively; 10 had recurrent disease, 12 had positive margins, and 16 had mediastinal involvement. Distant metastases were also identified in 10 patients. Patients were treated to a median radiation dose of 60 Gy with conformal techniques. In this patient cohort with locally advanced disease at significant risk for local recurrence, the 5-year locoregional relapse-free survival rate was 87%, and the 5-year disease-specific and overall survival rates were 62% and 56%, respectively. EBRT also locoregionally controlled gross residual disease in all 3 patients (100%) at a minimum follow-up of 28 months.\(^\text{30}\)

Fife et al.\(^\text{31}\) evaluated 51 patients treated with radiation between 1960 and 1992. Lymph node–positive patients had a lower locoregional recurrence-free survival rate on univariate analysis, but postoperative residual disease status was the only factor that remained significant on multivariate analysis.
(P = .0005). In this series, the 5-year local control rate was 100% in patients with no residual disease, 65% of those with microscopic residual disease, and 24% in those with gross residual disease. Nguyen et al.32 also reported on the outcome of 59 patients treated with EBRT, most of whom underwent total thyroidectomy. In this series, 44 patients presented with positive lymph nodes and 11 had residual tumors. Thirty percent of patients experienced local recurrence primarily within the radiation field; 35 patients remained alive at analysis and 24 had no evidence of disease. Thus, EBRT may be valuable to provide control in properly selected patients, particularly when there are few viable treatment options.

Brierley et al.26 also analyzed the records of 73 patients with a median follow-up of 7.9 years treated for MTC between 1954 and 1992. The patient population included 40% with gross residual and 37% with microscopic residual disease; 8 patients were deemed inoperable. Primary tumor size was 1 to 4 cm in 53%, and larger than 4 cm in 37%; 46 patients were irradiated to a median dose of 40 Gy. Extraglandular extension was identified in 56% of patients. On multivariate analysis, gross residual disease and extraglandular extension were predictive of cause-specific survival. Although overall no difference was seen in the locoregional relapse-free rate between patients receiving and not receiving EBRT, a statistically significant locoregional relapse rate was seen in patients considered at high risk for local recurrence. The 10-year locoregional relapse-free rate in patients with microscopic residual disease, extraglandular extension, or lymph node involvement was 86% in those who underwent postoperative EBRT and 52% in patients who did not (P = .049). Therefore, selected patients may benefit from EBRT in the postoperative setting. However, EBRT has not been shown to reduce calcitonin levels in this population.26,31

Several larger series of patients that predominantly include differentiated thyroid cancers also include a subgroup of patients with MTC treated with EBRT, because the risk factors for local recurrence are similar for both populations. In a large series reported by Tubiana et al.,33 115 of 539 patients had thyroid cancer differentiated for MTC, and 35 of these underwent postoperative cervical EBRT. All patients selected for EBRT were considered at high risk for local recurrence and presented with gross residual disease, extensive pathologic lymph node involvement, or incomplete surgical resection. Relapse-free and overall survivals were not significantly different between patients who underwent EBRT and those who underwent surgery alone. However, the patients who underwent surgery alone had less-extensive disease overall than those who underwent EBRT.

In a series published from Memorial Sloan-Kettering Cancer Center (MSKCC), 76 patients with nonanaplastic thyroid cancer considered at high risk for local recurrence were treated with EBRT predominantly in the postoperative setting. Among these, 12 presented with MTC and 84% had T4 disease. The 4-year locoregional control rate was 72% and no significant differences in locoregional control, disease-free survival, or overall survival were seen in patients with medullary compared with non-medullary disease. All 5 patients with unresectable MTC were locally controlled at a median follow-up of 18 months.35

Although EBRT may impact locoregional control, studies have been unsuccessful in presenting convincing evidence that postoperative EBRT impacts survival in patients with MTC. Jensen et al.36 reported a 5-year survival of 97% in a small series of patients who underwent radiation compared with 62% in patients who underwent surgery alone. However, Samaan et al.37 showed decreased survival in patients with MTC who underwent EBRT compared with those who did not undergo radiation treatment despite being matched for age, extent of disease, and surgery. Fersht et al.38 retrospectively assessed 51 patients who had persistently elevated calcitonin after initial surgery despite the absence of clinical or radiographic evidence of disease. In this cohort, 24 patients underwent EBRT because of locally advanced disease on presentation. No significant difference in survival was seen between the patients who did and did not undergo EBRT. However, local relapse was significantly lower in those patients who underwent EBRT (29% vs. 59%, respectively). The 20-year local recurrence-free survival rate was 66% in the group who underwent EBRT and 30% in the group who did not, although the patients in the radiotherapy group had a higher percentage of positive nodes and pT3 or pT4 tumors.33 Thus, although no impact on survival has been convincingly shown, multiple studies have shown that the addition of EBRT reduces local recurrence rates.

Studies evaluating the role of EBRT in MTC
include small numbers of patients, and therefore showing a statistically significant benefit in overall survival with the use of EBRT will be difficult in underpowered series. These studies are also retrospective in nature and show clear selection bias because patients who are referred for EBRT with MTC after surgery are generally those at high risk for locoregional failure. Furthermore, patients with locally advanced disease may also harbor micrometastatic disease, in which case adjuvant local treatment is unlikely to address systemic disease that may ultimately cause death.

Although EBRT has not been shown to confer a survival benefit, locoregional control is a valid end point to address in these patients, because progression in the cervical region can have a significant impact on quality of life. Locoregional progression of disease in the neck can cause substantial morbidity, including airway, laryngeal speech, and swallowing compromise. Uncontrolled growth of a cervical tumor can also lead to neurovascular impingement, resulting in symptoms such as pain and bleeding. Therefore, although a survival benefit has not been shown, local therapy is important to consider for these patients, who may otherwise have significant symptoms from locoregional progression. EBRT can provide a clinically meaningful benefit in preserving quality of life through protecting the airway, esophagus, and surrounding neurovascular structures. In the setting of low-volume metastatic disease, a definitive course of local therapy using EBRT may be indicated particularly if a protracted survival time is possible. However, the potential for toxicity with full-dose EBRT must be weighed against the expected benefits of local therapy to maintain quality of life. Therefore, for patients in whom a shorter survival time is likely given widespread disseminated disease with multiorgan involvement, a shorter palliative course of EBRT may be preferred to minimize the potential acute toxicities of treatment.

EBRT has been used in the palliative treatment of metastatic disease, because effective systemic therapy has been limited. Single-agent doxorubicin has been delivered in the metastatic setting along with chemotherapy combinations using 5FU and cisplatin. Somatostatin analogs such as octreotide have been used to inhibit neuroendocrine tumor growth and have shown a measurable response in small numbers of patients. Tyrosine kinase inhibitors are also under active investigation. EBRT has a well-known role in the local treatment of painful bony metastases. Mediastinal or lung disease may also cause symptoms, such as dyspnea or hemoptysis. A dose of 30 Gy given in 10 fractions or 20 Gy given in 5 fractions is generally delivered for palliative treatment in these circumstances to provide symptomatic relief.

Despite the literature suggesting that EBRT can be effective for local control, EBRT use in patients with MTC remains controversial. Surgical resection remains standard treatment for gross disease that can be removed without significant morbidity. However, postoperative EBRT should be considered in patients with an incomplete resection if further surgery is not an option. Patients at high risk for relapse, including those with extrathyroidal extension and a persistent detectable postoperative calcitonin level, should also be referred for discussion of EBRT. However, the recently published management guidelines of the American Thyroid Association do not recommend using EBRT to treat a persistently elevated serum calcitonin in the absence of positive margins or extrathyroidal soft tissue extension. Patients with advanced age or poor performance status may not be ideal candidates for radiotherapy. The decision to recommend EBRT in these patients must be individualized and the potential benefits of treatment of local control weighed against the possible acute and late toxicities. A prospective multi-institutional trial is needed to clarify the effect of EBRT on locoregional control and survival, particularly for patients at high risk for local relapse.

**Radiation Treatment Planning**

The radiation dose and fractionation delivered to this patient population varies based on institutional preference. However, it is generally accepted that approximately 60 Gy delivered over 6 weeks using 4- to 6-MV photon beams should be delivered to the thyroid bed for eradication of microscopic disease. Gross residual disease likely requires a higher dose up to 70 Gy for effective local control. Treatment planning should include use of CT.

The target volume for external-beam radiation must encompass the thyroid bed extending from the hyoid to the carina. The central compartment lymph node region should be included within the treatment
volume, including levels VI and VII. Azrif et al. recently reported on patterns of relapse after EBRT for differentiated thyroid cancer. In this series, 49 patients underwent EBRT and radioactive iodine after thyroidectomy or biopsy. All mediastinal recurrences occurred in the superior mediastinum in level VII. Although this study did not focus on MTC, level VII lymph nodes are similarly at risk for regional disease and therefore should be included in the treatment volume. The ipsilateral and contralateral levels II to V cervical lymph nodes should also be encompassed within the target.

Treatment of this target volume can be accomplished with conventional techniques. However, the dose is often limited because of the proximity of normal structures, such as the spinal cord and esophagus. Conformal techniques are ideally suited for treating the head and neck region. Dosimetric studies have been performed and have shown that dose escalation to the thyroid bed can be accomplished using intensity-modulated radiotherapy (IMRT) while simultaneously sparing normal tissues, such as the spinal cord (see Figure 2). IMRT is now used routinely to deliver a high radiation dose to the target volume with acceptable toxicity. The availability of imaging with CT, MRI, and PET is invaluable to ensure accurate target volume delineation.

At MSKCC, IMRT using “dose painting” is used to integrate different dose levels in the treatment of gross residual disease, microscopic residual disease, and regions at risk for subclinical spread. The low-risk clinical target volume (CTV) typically includes levels II to V in the node-negative neck and the upper mediastinum to the level of the carina. The high-risk CTV includes the preoperative thyroid gland volume, operative bed, tracheoesophageal grooves, central nodal compartment, and levels II through V in the node-positive neck (see Figure 3). The operative bed with a close or positive margin is typically treated to 63 to 66 Gy, and gross residual or unresectable disease is treated to a higher dose of 66 to 70 Gy, if feasible.

Using IMRT, dose escalation to the target volume can be accomplished as normal tissue doses are constrained. Normal structures contoured for treatment planning include the bilateral parotid glands, larynx, esophagus, bilateral lungs, and spinal cord. The parotid dose is limited, if possible, to a mean dose less than 26 Gy. In most cases, particularly when the high level II neck nodes are not included in the treatment field, a mean parotid dose lower than 26 Gy can be accomplished. The maximum spinal

Figure 2 A CT coronal and sagittal slice showing the conformality of intensity-modulated radiotherapy delivered to a 29-year-old man after thyroidectomy with bilateral positive cervical lymph nodes. The yellow isodose curve represents the volume treated to 60 Gy. This patient had involved high cervical level II lymph nodes, and therefore the treatment volume included coverage of the cervical neck above the level of the hyoid. Coverage of the high cervical neck is advisable when there is positive lymph node involvement in this region. The royal blue and red isodose curves represent the area that received 45 and 30 Gy, respectively, showing the rapid dose fall-off beyond the 60 Gy volume. The light blue contours represent the bilateral parotid glands that receive relatively minimal dose given their proximity to the level II lymph nodes encompassed within the high-dose volume.
Acute toxicity of this treatment includes skin erythema and desquamation, mucositis, esophagitis, and laryngeal edema. Because of odynophagia and dysphagia, some patients will require a percutaneous gastrostomy (PEG) tube for nutrition. For most patients, the PEG is removed after acute toxicity has resolved within 2 to 3 months after completion of EBRT. Late toxicities include skin hyperpigmentation, telangiectasias, and neck fibrosis. Voice hoarseness and xerostomia may also result from EBRT to the neck, although the parotid glands are better spared with the use of IMRT. Long-term esophageal stricture may occur. Esophageal stricture can be a devastating complication of neck radiation. Every attempt should be made to avoid this complication, however, no set guidelines exist. The experience from organ preservation protocols, in which a high incidence of esophageal stricture is seen, can be viewed as a concern for MTC and radiation therapy. Appropriate dilatation of the esophagus may help.

In the study reported by Schwartz et al., 2 patients (9%) experienced chronic EBRT morbidity: the first had late grade 2 xerostomia after treatment with conventional techniques and the second had multiply recurrent disease and was referred for EBRT with concurrent chemotherapy for gross disease. The second patient experienced posttreatment complications, including fibrosis, trismus, and carotid artery bleeding requiring carotid artery embolization and surgery. Despite the potential acute and late toxicities, radiation is fairly well-tolerated. Scarring and fibrosis from EBRT may make further surgeries more complicated and difficult, but surgical resection still remains feasible after EBRT. Therefore, reoperation is generally reserved for completion of an inadequate primary surgical resection or management of recurrent disease, particularly if there is evidence of potential local extension into critical structures.

Although prospective trials for the use of external radiation therapy in MTC do not currently exist or are likely to be undertaken, the major decision-making factor is the surgeon’s satisfaction with the operation. If the surgeon believed that all gross tumor was removed and any future recurrence could be easily surgically treated, then the role of radiation therapy is questionable. However, recurrent disease in critical areas, including the cricoid cartilage, cri-cothyroid junction, or cricothyroid area where recurrent disease may mean total laryngectomy, indicates that patients would be best treated with postoperative radiation therapy. As with thyroid cancers, such as those that are poorly differentiated, radiation therapy helps reduce the incidence of local recurrence. Most surgeons would make a critical decision at the first surgical procedure or reoperative surgery about the likelihood of recurrence and whether future surgery is possible. Truly high-risk patients benefit from external radiation therapy.

**Conclusions**

Surgical resection is the primary modality in the treatment of MTC. Despite aggressive surgery, certain patients remain at high risk for local recurrence because of locally advanced disease. Although data are limited, postoperative EBRT has been shown to improve locoregional control in patients with risk factors, including residual disease, extraglandular extension, and lymph node involvement. Although EBRT is not routinely recommended for the treat-
ment of MTC, it should be considered in patients with limited treatment options and poor prognostic factors with high likelihood of recurrence after surgical resection.

References

47. Cohen MS, Hussain HB, Moley JF. Inhibition of medullary thyroid carcinoma cell proliferation and RET phosphorylation by tyrosine kinase inhibitors. Surgery 2002;132:960–966; discussion 966–967.
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1. Which of the following is a reliable marker of disease activity in patients with medullary thyroid cancer (MTC)?
   A. Parathyroid hormone
   B. Thyroid stimulating hormone
   C. Calcitonin
   D. All of the above

2. Which of the following modalities is considered the gold standard for the treatment of MTC?
   A. External beam radiation therapy (EBRT)
   B. Surgery
   C. Surgery with chemotherapy
   D. Radio-iodine

3. A 45-year-old man presents with stridor, dysphagia, hoarseness, and diarrhea and examination shows a solitary thyroid nodule with associated ipsilateral lymphadenopathy. MTC is suspected. Which form of MTC is most likely?
   A. Sporadic
   B. Autosomal dominant
   C. Autosomal recessive
   D. Polygenic

4. A 30-year-old man undergoes surgical excision for unilateral MTC but has gross residual disease after surgery. Which of the following benefits is EBRT most likely to add to his management?
   A. Improved survival
   B. Prevention of contralateral spread
   C. Reduction in locoregional recurrence
   D. Prevention of metastases

5. A 42-year-old woman has mediastinal and lung metastases 3 years after surgical resection of MTC. Which of the following is most appropriate for symptomatic relief of hemoptysis and dyspnea?
   A. 5-FU and cisplatin
   B. EBRT
   C. Octreotide
   D. Doxorubicin

Activity Evaluation

1. The activity supported the learning objectives.
   Strongly Disagree Strongly Agree
   1 2 3 4 5

2. The material was organized clearly for learning to occur.
   Strongly Disagree Strongly Agree
   1 2 3 4 5

3. The content learned from this activity will impact my practice.
   Strongly Disagree Strongly Agree
   1 2 3 4 5

4. The activity was presented objectively and free of commercial bias.
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   1 2 3 4 5

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