

# Radiation Therapy for Cutaneous Melanoma

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## KEYWORDS

- Cutaneous melanoma • Radiation therapy • Lentigo maligna • Desmoplastic melanoma • Adjuvant
- High-risk • Nodal recurrence • Palliation

## KEY POINTS

- Radiation therapy is infrequently used in the care of patients with cutaneous melanoma, despite research suggesting a benefit in certain clinical scenarios.
- Definitive radiation therapy may be a viable treatment option for lentigo maligna and lentigo maligna melanoma.
- Adjuvant radiation therapy to the site of a resected neurotropic melanoma may improve local control of the tumor.
- Adjuvant radiation therapy to the site of resected lymph node metastases from melanoma at high risk for recurrence may improve regional control of lymphatic metastases.
- Palliative radiation therapy is likely to yield a response in patients with distant metastases.

## INTRODUCTION

In 2002, the Collaboration for Cancer Outcomes Research and Evaluation of Australia estimated that over the course of their disease approximately 23% of patients diagnosed with cutaneous melanoma (CM) would be appropriately treated with radiation therapy (RT) based on the best available evidence. Using population registry data, these investigators found that RT was part of the treatment of 13% of patients in New South Wales, Australia, and 1% to 6% of patients in the United States.<sup>1</sup> Others have noted the infrequent and dwindling use of RT for CM over time.<sup>2,3</sup> Awareness of the evidence supporting the use of RT for the treatment of CM is vital to delivering the optimal care of patients with this potentially lethal disease.

Several general aspects of RT for melanoma are not addressed in this review. The myth that melanoma is not responsive to RT has been adequately described and dispelled elsewhere.<sup>3-5</sup> The curative

and organ-preserving potential of RT for uveal melanoma has been demonstrated by the Collaborative Ocular Melanoma Study<sup>6</sup> and is beyond the scope of this review. Likewise, the role of RT in the management of mucosal melanoma is beyond the scope of this article. Herein, data providing the highest levels of evidence supporting the use of RT for CM are presented and discussed, acknowledging a significant dearth of high-level evidence in many situations.

## RADIATION THERAPY FOR THE PRIMARY TUMOR

Although the effective use of RT as definitive local therapy for primary CM has been described,<sup>7-10</sup> the therapeutic modality of choice for resectable CM in the medically operable patient is surgery. At present, pathologic staging by surgery provides the most valuable prognostic information available for early-stage CM. However, there are situations

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in which surgery might preclude acceptable functional or cosmetic outcomes to some patients.

### **Definitive Radiation Therapy for Lentigo Maligna and Lentigo Maligna Melanoma**

Most frequently, RT for the primary tumor is considered for lentigo maligna (LM) and lentigo maligna melanoma (LMM). Because patients with LM and LMM are often elderly and present with large, superficial lesions on the face, alternatives to surgery are often considered to optimize cosmetic and functional outcome. **Table 1** summarizes the outcome of RT for LM and LMM from the largest updated retrospective series from around the world.<sup>11–17</sup> Although follow-up has been limited, the pooled results demonstrate that the efficacy of RT compares favorably with other treatment modalities. Of note, relatively high rates of local recurrence have been noted in several series from North America, and may be related to RT technique. Although toxicity generally depends on the technique used, the outcome of skin RT is generally acceptable to elderly patients,<sup>18</sup> in whom LM and LMM are most common.

A recent retrospective comparative study of clinical outcomes in the management of CM in situ revealed no statistically significant difference in outcome between surgical excision and RT.<sup>19</sup> In this study, 15 patients were given RT to primary CM in situ in the head and neck region with a 10-kV superficial unit, to a total dose of 120 Gy in 6 fractions, with a security margin of 5 mm. Patients treated with RT were older than patients treated with surgical excision (mean 79 vs 59 years). The majority of patients undergoing excision had non-head and neck primary lesions. Among all patients, statistically significant higher rates of local recurrence were noted in patients older than 62 years or with head and neck lesions. Five-year rates of local recurrence were higher in patients treated with RT when compared with surgery (13.2% vs 6.8%), but this difference was not statistically significant. Statistically significant higher rates of 5-year of local recurrence were noted in patients treated with cryotherapy (34.3%,  $n = 22$ ) and laser therapy (42.9%,  $n = 8$ ) in comparison with surgery (6.8%,  $n = 1041$ ).<sup>19</sup>

Use of RT for LM or LMM varies widely. As noted in **Table 1**, higher rates of recurrence have been observed in North American centers and may be part of the reason for geographic variations. Even within a single geographic region, there is evidence of disparate opinions about the appropriateness of RT of LM and LMM. For example, guidelines from the United Kingdom suggest that RT may be an appropriate treatment method,<sup>20</sup> but a survey of dermatologists in the United Kingdom found that

few (18%) ever recommended RT for LM or LMM while only 13% considered it the treatment of choice for patients older than 70 years.<sup>21</sup>

### **Adjuvant Radiation Therapy After Resection of Primary Cutaneous Melanoma**

Although adjuvant RT to the site of a resected primary tumor at high risk for local recurrence has been advocated, a single phase II study has assessed this prospectively. From 1983 to 1992, 174 patients were enrolled on a single-center study at the M.D. Anderson Cancer Center (MDACC). Patients with CM of the head or neck were eligible if they fulfilled criteria for 1 of 3 groups of patients (**Table 2**) thought to be at high risk for local (at the site of the excised primary tumor) or regional (in dermal or nodal lymphatics) recurrence. All patients in this study received adjuvant RT (before or after surgery) to the site of the excised primary, unless the primary tumor had been excised more than 1 year before nodal recurrence. A dose of 24 to 30 Gy in 4 to 5 fractions over 2.5 to 3 weeks was delivered, using mostly high-energy (9–12 MeV) electrons.

Overall, dermal recurrence was noted in 10 patients (5.7%). Among patients in group 1, a large proportion of patients harbored advanced tumors (61% with  $\geq T2$ , 27% with T4, by current American Joint Committee on Cancer staging criteria), and 2 (2.5%) experienced any dermal recurrence. Whether dermal recurrence represented tumor recurrence at the site of primary tumor excision site or in-transit dermal lymphatics was not specified by the report. Nevertheless, these favorable local control rates in high-risk patients suggest a benefit of adjuvant RT to the site of the primary tumor. Because of this study, a phase III trial (9302) of adjuvant RT for high-risk CM of the head and neck was initiated by the Radiation Therapy Oncology Group (RTOG) and the Eastern Cooperative Oncology Group (ECOG) in 1994, but this was subsequently closed because of poor accrual.

### **Adjuvant Radiation Therapy After Resection of Neurotropic Cutaneous Melanoma**

Desmoplastic melanoma is an unusual subtype of CM that frequently occurs in the head and neck where adequate surgical margins can be difficult to obtain. Moreover, desmoplastic melanoma frequently exhibits neurotropism, which may increase the likelihood of local recurrence. For these reasons, many have used RT to the site of tumor (before, after, or in lieu of resection). The retrospective research presented in **Table 3** suggests a benefit of adjuvant RT in patients with neurotropic CM with adverse features (ie, recurrent

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