Radiation Therapy for Cutaneous T-Cell Lymphomas

Daniel J. Tandberg, MD, Oana Craciunescu, PhD, Chris R. Kelsey, MD*

INTRODUCTION

Cutaneous T-cell lymphomas (CTCLs) are comprised of several histologic subtypes of non-Hodgkin lymphoma characterized by localization of malignant lymphocytes to the skin. Mycosis fungoides (MF) is the most common type of CTCL, accounting for 54% of CTCL diagnoses from 2001 to 2005 in one Surveillance, Epidemiology, and End Results registry review.1 Other subtypes of CTCL include cutaneous CD30+ T-cell lymphoproliferative disorders and primary cutaneous peripheral T-cell lymphomas.

Radiation therapy (RT) is one of the most effective treatment modalities for CTCL. Lymphocytes are among the most radiosensitive of all cells. Low doses of radiation yield impressive local responses with minimal side effects. For patients with MF, RT has several different clinical applications. For the rare patient with unilesional disease, RT alone is potentially curative. For patients with more advanced cutaneous disease, RT to local lesions or to the entire skin can effectively palliate symptomatic disease and provide local disease control. Finally, symptomatic nodal or visceral disease can also be palliated with RT if necessary. This article reviews basic information regarding the administration of RT and reviews the published literature supporting the use of such for MF and primary cutaneous anaplastic large cell lymphoma (cALCL). Cutaneous peripheral T-cell lymphomas are rare and are not discussed further.

MYCOSIS FUNGOIDES

Local Radiation Therapy

In rare circumstances, MF presents as a solitary lesion, or small number of clustered lesions, that are amenable to a definitive course of therapy where the goal of treatment is long-term disease control. More commonly, patients with MF have more diffuse presentations where symptom palliation...
and local disease control are the fundamental goal of treatment. In circumstances where other modalities are not effective or a rapid response is desired, local RT can be efficacious. These circumstances include cosmetically disfiguring lesions on the face; tumors and thick plaques where radiation can effectively treat to the necessary depth; and lesions that are painful, pruritic, or weeping.

Clinical applications of local radiation therapy

Minimal stage IA disease Patients with patches or plaques covering less than 10% of the body surface area without significant blood, nodal, or visceral involvement have clinical stage IA MF. These patients have a favorable prognosis with survival similar to age-matched control subjects without MF. In a retrospective cohort analysis including 121 patients with clinical stage IA disease, the median survival had not been reached after more than 32 years of follow-up. Three (2%) of 122 patients had died of MF during the study period.

The subgroup of patients with “minimal” stage IA MF (ie, unilesional or up to three close lesions) have an especially favorable prognosis. Patients with this disease may experience long-term remission or ostensibly even “cure” with local RT alone. Several small studies have reported outcomes of local RT in minimal stage IA disease. Results of these studies are summarized in Table 1. Wilson and colleagues evaluated 21 patients with minimal disease treated with local RT. Thirteen patients had unilesional MF. The complete response (CR) rate to localized RT was 97%. Disease-free survival (DFS) for the entire group at 5 and 10 years was 75% and 64%, respectively. Improved DFS at 10 years was reported in patients with unilesional disease (85%) and those receiving doses of at least 20 Gy (91%).

Micaliy and colleagues reported on the outcomes of 18 patients with unilesional stage IA MF. This represented only 5% (18 of 325) of patients with MF treated at the study institution. Most patients received 30.6 Gy of local RT. The CR rate was 100%. Relapse-free survival (RFS) and overall survival at 10 years was 86% and 100%, respectively. Two relapses occurred, both confined to the skin at distant sites and subsequently treated with topical nitrogen mustard.

Finally, Piccinno and colleagues evaluated 15 patients with minimal stage MF treated with a median dose of 22 Gy. Complete remission of treated lesions was observed in 95% with the other 5% achieving a partial remission. At 5 and 10 years the overall relapse-free rate was 51%.

In summary, less than 5% of patients present with minimal stage IA MF. This unique subgroup may be managed effectively with local RT alone. Available studies report excellent responses to local RT with 95% to 100% of lesions experiencing a CR. Many patients have a prolonged disease-free interval with the best outcomes seeming to be with RT doses of 20 to 30 Gy.

Palliation of individual lesions Local RT is an effective palliative therapy for patients with all stages of MF with symptomatic cutaneous lesions. Local RT is often used to treat MF lesions refractory to other skin-directed or systemic therapies. Several retrospective studies have demonstrated very high rates of CR (>95%) of individual MF lesions with fractionated courses of RT. A dose–response relationship has emerged with higher doses being associated with higher rates of CR and local control. Cotter and colleagues evaluated the impact of radiation dose on local control in 111 MF lesions (53% plaques, 47% tumors). They demonstrated a CR to treatment in all lesions receiving greater than 20 Gy. Local recurrence was inversely associated with dose. The rate of local in-field recurrence was 42% with doses less than or equal to 10 Gy, 32% for doses 10 to 20 Gy, 21% for doses 20 to 30 Gy, and 0% when the dose was greater than 30 Gy. There was no difference in response rates between plaques and tumors. It was suggested that tumor doses equivalent to 30 Gy at 2 Gy per fraction were required for adequate control of MF lesions.

Palliation of individual skin lesions with very short courses of RT has also been reported. Short courses of radiation are more convenient for

<table>
<thead>
<tr>
<th>Study (Ref)</th>
<th>Extent of Disease</th>
<th>No. of Patients</th>
<th>No. of Sites</th>
<th>RT Dose (Median)</th>
<th>CR Rate</th>
<th>Relapse in RT Field</th>
<th>DFS 5 y</th>
<th>DFS 10 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson et al,3 1998</td>
<td>1–3 lesions</td>
<td>21</td>
<td>32</td>
<td>20 Gy</td>
<td>97%</td>
<td>3/31</td>
<td>75%</td>
<td>64%</td>
</tr>
<tr>
<td>Micaliy et al,4 1998</td>
<td>1 lesions</td>
<td>18</td>
<td>18</td>
<td>30.6 Gy</td>
<td>100%</td>
<td>0/18</td>
<td>NR</td>
<td>86%</td>
</tr>
<tr>
<td>Piccinno et al,5 2009</td>
<td>1–4 lesions</td>
<td>15</td>
<td>22</td>
<td>22 Gy</td>
<td>95%</td>
<td>4/22</td>
<td>51%</td>
<td>51%</td>
</tr>
</tbody>
</table>

Abbreviations: CR, complete response; DFS, disease-free survival.
patients and are potentially more cost effective compared with multiple fractions. Thomas and colleagues\(^7\) reported their experience treating 270 CTCL lesions (primarily MF) with a single fraction of local RT. Of the 58 patients included in the study, 21 (36\%) had patch/plaque disease, 34 (59\%) had tumor-stage disease, and 3 (5\%) had erythroderma only. Most patients (97\%) were treated with a single dose of greater than or equal to 7 Gy. A CR was observed in 94\% of lesions and the rate of relapse in the radiation field was 1\% with a median follow-up of 41.8 months. Large-cell transformation and tumor morphology were associated with a lower CR rate. Neelis and colleagues\(^8\) reported a CR rate of 92\% when patients with MF were treated to a total dose of 8 Gy in two fractions. Local relapse occurred in 8\% of treated sites. Of note, only 30\% of lesions treated with 4 Gy in two fractions achieved a CR. Patients who either did not have a CR or failed locally were retreated with 20 Gy in eight fractions without complication. No significant acute or long-term toxicities were reported in either study.

In summary, local RT is very effective in the palliation of MF skin lesions. Short courses of one to two fractions (7–8 Gy) have yielded favorable results and can be used for patients requiring rapid palliation or who would have a difficult time coming in for a more conventional regimen. Generally, smaller lesions are optimally suited for a single fraction of treatment, whereas larger lesions are often better managed with a more protracted fractionated approach.

**Palliation of nodal and visceral disease** Most patients with MF never develop symptomatic nodal or visceral disease. However, just as with other malignancies, local RT can be used in this setting for symptom palliation. Patients with advanced-stage MF may experience pain, swelling, or other local symptoms secondary to bulky lymphadenopathy. Visceral metastatic disease can impact the function of an involved organ. RT in these circumstances is typically performed with computed tomography (CT)–based three-dimensional planning with megavoltage photon RT. Typical doses used in our institution range from 20 to 30 Gy using 2- to 3-Gy fractions.

**Side effects**

Acute and long-term side effects of local RT directed at skin lesions are minimal. Patients may develop erythema and occasionally dry or moist desquamation within the treatment field. Ulcerated lesions sometimes appear worse shortly after starting RT. The skin generally heals rapidly after a course of radiation. Nothing more than topical symptom management is typically necessary during treatment. In the long-term patients may have pigmentation changes and alopecia in the treated areas. There is a theoretic risk of secondary cutaneous malignancies, although reports of this in the literature are rare.\(^9\)

**Technique and administration**

Local RT is typically delivered by means of a linear accelerator (Fig. 1). Most linear accelerators can produce high-energy photon (x-rays) and electron beams. Both photons and electrons can be used depending on the clinical circumstances. Electrons have unique properties that make them particularly suited to treating cutaneous lesions. Electron beam therapy delivers dose close to the skin surface after which the dose falls off extremely rapidly, limiting radiation exposure to deeper tissues. Increasing electron energies can be chosen to treat deeper lesions. The association between the depth dose and electron energy is plotted in Fig. 2.

Most electron beam treatments for superficial skin lesions are planned clinically rather than with imaging modalities, such as CT or MRI (Fig. 3). The radiation oncologist delineates a margin of 1- to 2-cm around visible and/or palpable disease. A lead cutout is then created conforming to the shape of the target. The lead cutout is inserted into the treatment machine thus focusing the radiation beam to the desired shape. As electrons begin depositing their dose on contact with the skin, there can be some degree of “skin sparing” with electron beam therapy (see Fig. 2). To address this phenomenon, material referred to as bolus is placed over skin lesions before treatment. Bolus is a tissue-equivalent material that starts the process of dose deposition allowing the maximum dose to be at the skin surface. The radiation dose is often fractionated, or divided into multiple smaller doses. Patients are treated daily excluding weekends until their course is completed. Each treatment, including time for set-up, lasts approximately 15 minutes.

Photon radiation is often used to treat nodal and visceral disease because the dose penetrates deeper than electrons. Photon beams are occasionally required to treat thick cutaneous tumors. Patients receiving photon radiation must first undergo a radiation planning session termed a simulation. The patient is immobilized and a planning CT is performed. The radiation oncologist then uses the planning CT scan and advanced treatment planning software to plan the radiation treatment. The gross disease is identified and contoured on the planning scan. Margins are created around this volume to account for...
Fig. 1. Medical linear accelerator used to generate and deliver external beam radiation therapy.

Fig. 2. Plot of percentage of radiation dose (%) versus depth (mm) for various electron beam energies from 6 to 22 MeV.
subclinical disease and variations in daily set-up. The optimal number and configuration of radiation beams to treat the target volume and limit dose to normal sensitive tissues is then determined. Patients are treated daily in the same position as their planning scan. Proper positioning is ensured by alignment to skin markings placed at the time of planning scan. Proper positioning is ensured by alignment to skin markings placed at the time of planning and imaging taken immediately before treatment.

**Total Skin Electron Beam Therapy**

Many patients with MF present with diffuse cutaneous disease or develop such during the course of their illness. Multiple systemic and skin-directed therapies have been used for diffuse disease, including total skin electron beam therapy (TSEBT). TSEBT is used when RT is recommended and the distribution of disease is such that the entire skin surface requires treatment.

TSEBT is a technically challenging procedure where radiation is delivered to the entire skin surface. It requires special commissioning (ie, configuring) of a linear accelerator and significant support from medical physics. Thus, this treatment is generally only available at larger centers that treat many patients a year. As with local RT, TSEBT is very effective with nearly all patients experiencing significant clinical improvement. Continued research is exploring dose reduction of TSEBT and concurrent and adjuvant therapies.

**Clinical indications**

**Early stage (T1)**

TSEBT has shown favorable results in early stage MF. Ysebaert and colleagues\(^\text{10}\) demonstrated an 88% CR rate in patients T1 MF treated to a mean dose of 30 Gy. Five-year RFS was 75%. Hoppe and colleagues\(^\text{11}\) showed complete regression of all skin lesions in 86% of patients with limited plaque disease. Finally, Jones and colleagues\(^\text{12}\) reported a CR rate of 95% in patients with stage IA MF treated with 31 to 36 Gy. Progression-free survival (PFS) at 15 years was 35%. However, because there are numerous other effective therapies with less acute side effects, TSEBT is generally not recommended as first-line treatment of patients with limited or localized skin involvement (T1).\(^\text{13,14}\)
**Advanced stage (T2-T3)** The major indication for TSEBT is the palliation of patients with severe skin symptoms or generalized thick plaque or tumor disease (T2-T3). These patients have often had a poor response to previous therapies. Clinical responses are correlated to tumor stage at presentation (T2 vs T3) and the extent of skin involvement. For patients with T2 disease the rate of CR has been reported to be 75% to 85% with 50% RFS at 5 years but only 10% at 10 years. With T3 disease, CR rates of 43% to 78% have been reported with nearly all patients eventually experiencing recurrent disease.

The largest reported series on TSEBT in T2 and T3 MF was published by Navi and colleagues from Stanford. They included 103 patients with T2 MF and 77 patients with T3 MF, all treated with doses greater than 30 Gy. All patients had clinically significant improvement in their disease (>50% improvement in skin involvement). The CR rate was 63%, including 75% in patients with T2 MF and 43% in patients with T3 MF. The median duration of response (in complete responders) was 29 months in patients with T2 disease and 9 months for patients with T3 disease. The 5- and 10-year overall survival rates for the cohort were 59% and 40%, respectively.

Ysebaert and colleagues reported an 85% CR to TSEBT in patients with T2 MF. Five-year RFS was 28%. Quiros and colleagues reported the outcomes of 46 patients with T3 MF treated with TSEBT. A total of 36 of 46 patients (78%) had a cutaneous CR. DFS was 12% at 36 months.

**Erythrodermic (T4) disease** There is limited experience of TSEBT for patients with erythrodermic (T4) MF. Jones and colleagues reported the outcomes of 45 patients with T4 disease treated with TSEBT without neoadjuvant, concurrent, or adjuvant therapies. The rate of complete cutaneous remission was 60% with 26% remaining disease-free at 5 years. Improved outcomes were seen in patients with stage III disease without blood involvement and in patients treated with a more intensive TSEBT regimen (32–40 Gy). Another retrospective study demonstrated improved PFS and cancer-specific survival with the addition of extracorporeal photophoresis (ECPP) to TSEBT in T4 MF.

**Special circumstances with total skin electron beam therapy**

**Retreatment** A second course of TSEBT is feasible and safe in most circumstances. Ideal candidates for such include those who achieved a good response to the first course of TSEBT with reasonable response duration, failure of subsequent treatments, and generalized symptomatic skin involvement.

Several small studies support the tolerability and efficacy of multiple courses of TSEBT in MF. In general, the dose of a second (and sometimes third) course of TSEBT should be reduced. Becker and colleagues described the experience of 15 patients treated with a second course of TSEBT to a mean of 23.4 Gy (mean of first course was 32.6 Gy). A CR to the first course was achieved in 11 of 15. Six patients had a CR and nine achieved a partial response to the second course. Long-term toxicities were mild and consisted of generalized xerosis, scattered telangiectasias, pigmentation changes, and partial alopecia.

Wilson and colleagues reported on 14 patients with recurrent MF treated with multiple courses of TSEBT (two to three courses). The median cumulative dose for the entire cohort was 57 Gy. After the first course, 13 of 14 patients had a CR. After the second course, 12 of 14 had a CR, again showing that a good response can be achieved even when disease relapses after prior RT. The median disease-free interval after the first course of therapy for those with a CR was 20 months and 11.5 months after the second course. Overall the repeat treatments were well tolerated with no severe toxicities.

**Adjuvant therapies** Patients with advanced MF receiving TSEBT inevitably relapse. Several studies have attempted to lengthen the disease-free interval after TSEBT by using adjuvant therapies, such as topical nitrogen mustard, oral psoralen plus ultraviolet light, oral etretinate, ECPP, interferon, and cytotoxic chemotherapy. Unfortunately, most of these studies are small, retrospective, and from single institutions. Prospective, randomized data are needed to confirm their results.

Chinn and colleagues initially demonstrated a longer freedom from relapse in patients with T2 disease treated with adjuvant topical nitrogen mustard compared with observation after TSEBT. However, a larger more recent series from the same institution showed no clinical advantage to adjuvant topical nitrogen mustard. Quiros and colleagues reported a significant benefit in DFS but no significant overall survival advantage in patients receiving adjuvant psoralen plus ultraviolet A. Roberge and colleagues demonstrated concurrent and adjuvant alpha interferon to be tolerable but there was no significant difference in PFS or overall survival. A more recent study similarly showed no clinical benefit with the addition of interferon to TSEBT. Wilson and colleagues have reported on their experience with concurrent/adjuvant ECPP in patients with...
Treatment of Cancer (EORTC) has published consensus guidelines regarding the use of TSEBT. Adjuvant systemic chemotherapy (cyclophosphamide/doxorubicin) has been shown to have no benefit for RFS or overall survival in one study, but to improve RFS among stage I/II patients in another. In short, the data are mixed whether adjuvant therapies after TSEBT are clinically beneficial.

**Total skin electron beam therapy before stem cell transplant** Select patients with advanced-stage, refractory MF are deemed appropriate candidates for an autologous or allogeneic stem cell transplant. Patients should, ideally, be in CR before initiating the conditioning regimen for transplant. TSEBT can be used to control cutaneous disease and achieve remission in the skin. Total-body irradiation can also be used in the conditioning regimen.

Duvic and colleagues reported their experience with 19 patients who received TSEBT (36 Gy) immediately before allogeneic transplantation for refractory MF (median of four prior therapies). Three patients had stage IIB disease (all with large cell transformation), six had stage IVA disease, and 10 had stage IVB disease. The rate of CR was 58% after TSEBT and transplant. At 2 years, overall survival was 79% and PFS 53%. The authors also suggested that TSEBT may have helped to reduce the severity of posttransplantation cutaneous graft-versus-host disease.

**Technique and administration**

The European Organization for Research and Treatment of Cancer (EORTC) has published consensus guidelines regarding the use of TSEBT in MF. The goal of TSEBT is to deliver a relatively uniform dose of radiation to the entire skin while limiting acute and long-term toxicities. Modern TSEBT as delivered by linear accelerator was largely developed at Stanford and today the “Stanford technique” is commonly used. Many modifications of this technique now exist.

The patient is positioned standing approximately 3 to 4 m from the linear accelerator. A 6- to 9-MeV electron beam is used. A polycarbonate screen is often placed between the linear accelerator and the patient, which attenuates or scatters the beam to increase the dose to the skin surface.

The patient is treated in six different standing positions including anterior, posterior, right posterior oblique, left posterior oblique, left anterior oblique, and right anterior oblique (Fig. 4). All six positions are treated over the course of 2 treatment days, three positions on Day 1 and three positions on Day 2. This cycle is repeated twice per week. Treatment of each position is accomplished with a dual-field technique where the linear accelerator is angled up to treat the superior field and down to treat the inferior field. The use of angled beams helps to fit the patient in the radiation treatment field. The EORTC recommends that the 80% isodose line extend to 4 mm below the skin surface.

Certain areas of the body are more susceptible to side effects from RT and may require shielding during portions of the treatment. Internal or external eye shields are used to protect the eyes during treatment (Fig. 5). Internal lead shields placed underneath the eyelids are used when there is disease on the face. External eye shields can be used for portions of the treatment, especially in the absence of disease on the face. At our institution we also commonly use mouth shields covering the lips and oral mucosa to prevent the development of mucositis. Blisters can occasionally develop on the feet, which can cause significant disability and delay patients from completing the treatment as planned. At our institution, the hands and feet are shielded in the TSEBT fields and treated separately with photon fields.

Certain areas of the body may be underdosed or even overdosed during TSEBT because of shadowing, body habitus, or peculiarities inherent in treating with TSEBT. In a study by Weaver and colleagues, thermoluminescent monitors were placed on several body locations to record the dose received during TSEBT. Areas that routinely receive a lower dose include the top of head, perineum, upper inner thighs, and inframammary fold region in women. These areas may be treated with supplemental local electron beam either during or after completion of the TSEBT. For patients with tumors, a supplemental course of local RT can be given at the start of TSEBT to rapidly reduce the thickness of the tumor allowing for better dosimetry through the course of therapy.

Some patients cannot be treated with the modified Stanford technique because of their inability to stand safely or comfortably for extended periods. An alternative technique exists where the patient is treated in three supine and three prone positions (lying-on-the-floor position). This technique has shown comparable radiation quality and uniformity with the modified Stanford technique.

**Dose**

When RT is delivered to discrete lesions, larger daily doses can be safely administered. In contrast, treating the entire skin surface with
TSEBT necessitates a lower dose of radiation per fraction to prevent significant toxicity. This typically consists of 1 to 1.5 Gy each day. When lower daily doses are used, higher total doses are necessary to achieve comparable tumor responses.

Similar to local RT, a dose–response relationship has been observed with TSEBT. Hoppe and colleagues\textsuperscript{11} correlated the rate of CR with TSEBT dose. He demonstrated a CR rate of 18% with less than 10 Gy, 55% with 10 to 20 Gy, 66% with 20 to 25 Gy, 75% with 25 to 30 Gy, and 94% with doses from 30 to 36 Gy. These data provide the rationale for the recommendation that the total TSEBT dose ranges from 30 to 36 Gy.\textsuperscript{14,17} At our institution, the typical TSEBT prescription is 36 Gy at 1.5 Gy per fraction using 6-MeV electrons. Treatment is delivered over 6 weeks. Daily doses of 1 Gy per fraction are also commonly used with treatments delivered over 9 weeks.

More recent experience has also shown reasonable clinical outcomes with lower doses of TSEBT. Harrison and colleagues\textsuperscript{33} reviewed the Stanford experience with low-dose (<30 Gy) TSEBT. Overall response rates (defined as >50% improvement) were 90% in patients receiving 5 to 10 Gy, 98% in patients receiving 10 to 20 Gy, and 97% in patients receiving 20 to 30 Gy. When compared with the standard dose of greater than or equal to 30 Gy, CR rates were reduced in the lower-dose groups. However, PFS was comparable among the low-dose groups and the standard dose. Furthermore, a pooled analysis of three phase II clinical trials including 33 patients treated with 12-Gy TSEBT demonstrated an overall response rate of 88%.\textsuperscript{34} The median duration of response was 71 weeks. These data suggest low-dose TSEBT may be a reasonable option for patients desiring palliation of diffuse disease and who may not tolerate the side effects and time commitment of the standard course. Patients who receive the low-dose TSEBT may also benefit from the ability to repeat the regimen multiple times without considerable toxicity.

\textbf{Fig. 4.} The six treatment positions used for total skin electron beam therapy. (From Smith BD, Wilson LD. Management of mycosis fungoides. Part 2: treatment. Oncology 2003;17(10):1424; with permission.)
Side effects

TSEBT is given over a 6- to 10-week time period, which can be logistically and emotionally challenging for patients. Furthermore, it is also associated with more acute toxicities compared with local RT. However, most patients successfully complete the planned course of therapy without high-grade toxicity and long-term toxicities are generally mild. Some patients might require a 10- to 14-day break after 18 to 30 Gy to recover from the acute toxicities of TSEB. Lloyd and colleagues described the type and grade of acute treatment toxicities in 82 patients receiving TSEB courses from 30 to 36 Gy. The most common toxicities included erythema/desquamation (76%), blisters (52%), hyperpigmentation (50%), and skin pain (48%). In their series, 32% of patients had clinical evidence of a skin infection, which was treated with antibiotics. There were no grade 4 or 5 acute toxicities.

Close surveillance of patients by a multidisciplinary team is required to manage the acute side effects of TSEBT. Patients receiving TSEBT are seen formally by the radiation oncologist during weekly treatment check visits. Symptomatic treatments include moisturizers, topical and oral analgesics, antibiotics when clinical infections develop, and appropriate wound care. Close collaboration with a wound care specialist is important in promoting wound healing and preventing infection.

Side effects that may develop following completion of TSEBT include alopecia (temporary vs permanent based on dose), dystrophic nails, decreased ability to sweat, chronically dry skin, cataracts, and telangiectasias. TSEBT has also been associated with increased rates of secondary skin cancers.

Primary cutaneous CD30 lymphoproliferative disorders are less common than MF and include lymphomatoid papulosis (LyP) and primary cutaneous anaplastic large cell lymphoma (cALCL). The Dutch Cutaneous Lymphoma Group published a detailed report on a large series of patients with CD30 lymphoproliferative disorders with long-term follow-up. In addition, a more recent consensus publication by the International Society for Cutaneous Lymphoma, EORTC Cutaneous Lymphoma Task Force, and the United States Cutaneous Lymphoma Consortium has addressed treatment of these conditions. Based on their observations and that of the National Comprehensive Cancer Network, there are clinical guidelines for diagnosis and treatment of the CD30 lymphoproliferative disorders.

LyP is an indolent lymphoproliferative disorder. Clinically this disorder is characterized by multifocal skin lesions that regress spontaneously within 3 to 12 weeks. The prognosis of LyP is excellent with a 5- and 10-year disease-related survival of 100%. Of note, within the Dutch cohort, 19% of patients with LyP had other associated malignant lymphomas before, after, or concurrent with LyP. There is no clear role for RT for LyP.

In contrast to LyP, cALCL typically presents as a solitary lesion or a localized group of lesions. The prognosis of patients with localized disease is excellent. Local RT is the first choice of treatment in patients with a solitary or few localized nodules or tumors (Fig. 6). A series from Stanford demonstrated a CR in six of seven patients treated with RT alone. Yu and colleagues reported on

Fig. 5. Patient undergoing total skin electron beam therapy. Both internal eye and mouth shields are used. The hands and feet are shielded and treated separately with photon fields.
eight patients with cALCL treated with 34- to 44-Gy local RT. The CR was 100% and there was no evidence of disease recurrence at a median follow-up of 12 months. Finally, in the Dutch study, 99% of patients had a CR to initial therapy, 48% of which were treated with local RT. Fifty-one percent of patients developed recurrent disease with the skin only being the most common site of relapse (80% of patients with recurrent disease). Relapses are almost always outside the previous radiation field.

REFERENCES