International Journal of
Radiation Oncology
biology • physics

www.redjournal.org

Clinical Investigation: Lymphoma

Outcome of Patients Treated With a Single-Fraction Dose of Palliative Radiation for Cutaneous T-Cell Lymphoma

Tarita O. Thomas, MD, PhD,* Priya Agrawal, BA,* Joan Guitart, MD,† Steven T. Rosen, MD,‡ Alfred W. Rademaker, PhD,§ Christiane Querfeld, MD, PhD,‖ John P. Hayes, MD,* Timothy M. Kuzel, MD,‡ and Bharat B. Mittal, MD*

*Departments of *Radiation Oncology and †Dermatology, ‡Division of Hematology/Oncology, Department of Medicine, and §Department of Preventive Medicine, Northwestern University, Robert H. Lurie Comprehensive Cancer Center, Chicago, Illinois; and ‖ Department of Medicine/Dermatology Service, Memorial Sloan-Kettering Cancer Center, New York, New York*

Received Apr 6, 2012, and in revised form May 18, 2012. Accepted for publication May 22, 2012

Summary

Multifractionated radiation therapy has been used to palliatively treat cutaneous T-cell lymphoma (CTCL) lesions. This is a review of 270 CTCL lesions treated with a single fraction of radiation to provide rapid palliation. We found a complete response rate of 94.4% over a mean follow-up of 41.3 months. Patient and tumor characteristics influenced response to radiation. Single-fraction radiation is cost-effective and convenient to the patient.

Purpose: Cutaneous T-cell lymphoma (CTCL) is a radiosensitive tumor. Presently, treatment with radiation is given in multiple fractions. The current literature lacks data that support single-fraction treatment for CTCL. This retrospective review assesses the clinical response in patients treated with a single fraction of radiation.

Methods and Materials: This study reviewed the records of 58 patients with CTCL, primarily mycosis fungoides, treated with a single fraction of palliative radiation therapy (RT) between October 1991 and January 2011. Patient and tumor characteristics were reviewed. Response rates were compared using Fisher's exact test and multiple logistic regressions. Survival rates were determined using the Kaplan-Meier method. Cost-effectiveness analysis was performed to assess the cost of a single vs a multifractionated treatment regimen.

Results: Two hundred seventy individual lesions were treated, with the majority (97%) treated with ≥700 cGy; mean follow-up was 41.3 months (range, 3-180 months). Response rate by lesion was assessed, with a complete response (CR) in 255 (94.4%) lesions, a partial response in 10 (3.7%) lesions, a partial response converted to a CR after a second treatment in 4 (1.5%) lesions, and no response in 1 (0.4%) lesion. The CR in lower extremity lesions was lower than in other sites ($P = .0016$). Lesions treated with photons had lower CR than those treated with electrons ($P = .017$). Patients with lesions exhibiting large cell transformation and tumor morphology had lower CR ($P = .04$ and $P = .035$, respectively). Immunophenotype did not impact response rate ($P = .23$). Overall survival was significantly lower for patients with Sézary syndrome ($P = .0003$) and erythroderma ($P < .0001$). The cost of multifractionated radiation was >200% higher than that for single-fraction radiation.

Conclusions: A single fraction of 700 cGy-800 cGy provides excellent palliation for CTCL lesions and is cost effective and convenient for the patient. © 2013 Elsevier Inc.

Reprint requests to: Bharat B. Mittal, MD, 251 E Huron, LC-178, Chicago, IL 60611. Tel: (312) 926-3399; Fax: (312) 926-6524; E-mail: bmittal@nmh.org

Conflict of interest: none.

Statistical support was provided by National Institutes of Health grant 5P50CA06553.

Acknowledgment—We acknowledge Aleksandar Zafirovski, M.B.A., and Paul J. Williams, M.B.A. for their assistance with the cost analysis as well as Bing Bing Weitner, M.S., for statistical programming.

Int J Radiation Oncol Biol Phys, Vol. 85, No. 3, pp. 747–753, 2013
0360-3016/$ - see front matter
http://dx.doi.org/10.1016/j.ijrobp.2012.05.034

Introduction

Cutaneous T-cell lymphoma (CTCL) is a heterogeneous group of malignancies of mature-memory T lymphocytes, categorized as an extranodal non-Hodgkin lymphoma (1). Mycosis fungoides (MF) and Sézary syndrome (SS) are the most common types of CTCL (2). The mature T-cell phenotype for neoplastic cells in MF is usually $CD4^+$, $CD8^-$, and $CD30^-$ (3); however, a $CD4^-/CD8^+$ or $CD4^-/CD8^-$T-cell phenotype is found in some cases. While the cell morphology is small to intermediate in most early stage cases, large cell transformation portends an aggressive clinical course and shortened survival (2).

Most patients with MF are treated with skin-directed therapies with or without systemic treatment (4). Radiation therapy is an effective treatment for early stage MF and has been shown to result in long-term disease-free intervals and has even shown curative potential (5). Total skin electron treatment has been used to treat the entire skin surface in patients with MF (6).

For patients with unilesional disease or a group of a few lesions in close geographical proximity, localized superficial radiation therapy (RT) has been shown to result in a complete response (CR) rate of >90% (7). Kim et al (8) observed that the percentage of tumor volume remaining after an exposure of 700 rads was significantly lower than that with 300-500 rads, using a single fraction of radiation. In another study, the authors noted that total dose equivalent to at least 3000 cGy at 200 cGy per fraction could ensure adequate local control (9). Neelis et al (10) showed in a small cohort of patients with MF that low-dose involved-field RT results in a high response rate without toxicity. Phase II clinical trials with romidepsin, a histone deacetylase inhibitor, and low-dose electron therapy for CTCL have shown that patients who received RT demonstrated fast and durable responses (11). These recent publications underscore the evolving role of low-dose RT for symptomatic palliation of refractory MF lesions.

In 1991, we began to treat patients with refractory MF lesions using single-fraction radiation to provide rapid palliation. This retrospective analysis describes the largest series of patients with MF treated with a single fraction of localized radiation for palliation.

Methods and Materials

This study was approved by the Institutional Review Board. Between October 1991 and January 2011, 58 patients with CTCL were treated with localized single-fraction palliative RT to 270 individual lesions by a single radiation oncologist (B.B.M.). The World Health Organization-European Organization for Research and Treatment of Cancer criteria for CTCL (2) was used to confirm diagnoses of MF for all patients. For staging, the system of the International Society for Cutaneous Lymphomas was used. Patients and tumor characteristics were assessed at initial consultation with a radiation oncologist or medical oncologist. All patients had disease refractory to prior topical and/or systemic treatment before their referral for radiation treatment. Duration of follow-up after RT ranged from 3-180 months, with a mean of 41.3 months. Patients returned for follow-up 1 month after treatment and then every 3-6 months. Patients were excluded from the study if they had received previous radiation to the index site. Dermatologic pathology reports for each of the 58 patients were reviewed with the dermatopathologist to determine the immunophenotype, the MF variant, and/or the presence of large cell transformation.

Each lesion to receive radiation was categorized based on its location. The RT parameters that were assessed included total dose, dose/fraction, electron/photon energy, and bolus thickness. The RT regimen consisted of 400-900 cGy delivered in a single fraction. However, only 9 of 270 (3%) lesions were treated with <700 cGy because of minimal disease or location close to critical structures such as the eye. Local RT consisted of electrons for 215 lesions with an energy ranging from 6-20 MeV and photons for 55 lesions with energy ranging from 4-10 MV. En-face electron field arrangement was used for superficial lesions on flatter surfaces, and deeper, bulkier or circumferential tumors were treated with parallel opposed photon fields. To bring surface dose to 100% of prescribed dose, bolus was used.

Because this was a retrospective study, the currently used modified Severity Weighted Assessment Tool (mSWAT) or the Composite Assessment of Index Lesion Severity (CAILS) (12), which are recommended for prospective studies, were not available. Instead, we defined CR as 100% reduction, a partial response (PR) as >50% but <100% reduction, and no response (NR) as <50% reduction in lesion size. Survival was calculated using the log-rank test (13). Variables were related to response by using Fisher's exact test (13). Multivariate analyses were done using multiple logistic regressions (13).

Cost analysis was performed for 10 patients randomly selected from the study group; the cost for these patients who received single-fraction radiation was compared with the current "standard" cost of multifractionated radiation given in 10 treatments. Current procedural terminology (CPT) codes for each course of treatment were identified for technical fees based on Medicare facility fee reimbursements via MedAssets, Website version 2011. Each CPT code billed was given a wage-adjusted ambulatory payment classification. Mean and median payments were then calculated. CPT codes for professional fees were identified using the Medicare Physician Fee Schedule.

Results

Patient and tumor characteristics

This study consisted of 35 men and 23 women, ages 24-97 years (median, 62 years) at initial RT consultation. Among the 58 CTCL patients, 47 patients had MF; 4 had MF with lymphomatoid papulosis; 3 patients had cutaneous gamma-delta T-cell lymphoma; 2 patients had Sézary syndrome; 1 patient had MF with Sézary syndrome; and 1 patient had small/medium-sized pleomorphic T-cell lymphoma. All patients were seen for palliation of symptomatic lesions. At initial diagnosis, 29 (50%) patients had stage I disease; 22 (38%) patients had stage II disease; and 7 (12%) patients had stage IV disease.

Of 58 patients, 21 had only patches and plaques, 4 patients had only tumor lesions, 3 patients had only erythroderma, 26 patients had patches/plaques and tumors, and 4 patients had patches/plaques, tumors, and erythroderma. Twenty-three (36%) patients were found to have a large cell transformation in at least 1 lesion, 1 patient had a small/medium-sized pleomorphic cell morphology (2%), and in the remaining patients (n=34) no large cell transformation was reported. Seventy-four percent of patients (n=44) had a $CD4^+/CD8^-$ immunophenotype, whereas 9% (n=5) of

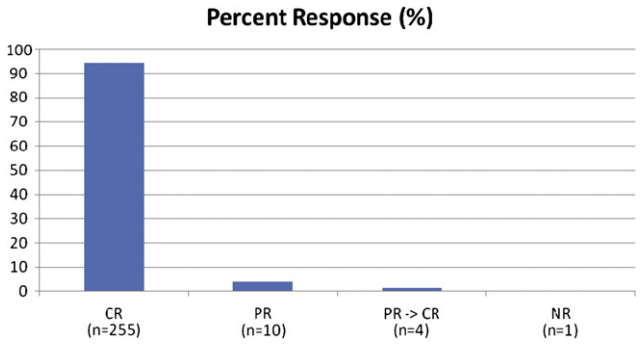

Fig. 1. Percentage of response to treatment. Response is based on the number of lesions with CR, PR, partial response that became CR (PR→CR), or NR.

patients were $CD4^-/CD8^+$; 3% (n=2) were $CD4^-/CD8^-$; and immunophenotypic information was not available for the remaining patients.

Response rates based on number of CTCL lesions

A total of 270 lesions were treated among 58 patients. Response rate by lesion was assessed, with CR in 255 (94.4%) lesions, PR in 10 (3.7%) lesions, PR converted to CR after a second single-fraction treatment in 4 (1.5%) lesions, and NR in 1 (0.4%) lesion (Fig. 1). The time interval between first and second fractions in patients with PR ranged from 1-14 months (median, 3 months). The number of lesions treated per patient ranged from 1-29 (median, 3 lesions). The initial response rate based on location indicated that lesions on the back, feet, buttocks, hands, and scalp had 100% CR. CR was achieved in 96% of lesions on the face/neck, 84% of lower extremity lesions, and 92% of lesions in the axilla (Table 1). There was a significant difference in CR when lesions from all sites were compared with the lesions on the lower extremities ($P=.0016$).

Because all treatments were carried out by a single radiation oncologist, evaluation of the lesions determined the dose prescribed and was based on tumor bulk and location. Lesions were treated with 400 cGy (1 site), 500 cGy (2 sites), 600 cGy (6 sites), 700 cGy (42 sites), 750 cGy (8 sites), 800 cGy (210 sites), or 900 cGy (1 site). Five of 6 lesions in the 600-cGy treatment group achieved CR; 196 of 210 lesions in the 800-cGy group achieved CR. The other dose groups all achieved CR (Table 1). Because most sites were treated with >700 cGy, CR was compared between the <700 cGy and ≥700 cGy groups for statistical significance. There was no statistically significant difference ($P=.41$) between the 2 groups, which could be due to the disparate lesion bulk treated at different dose levels.

Lesions were treated with either electrons or photons. There was 96% CR for lesions treated with electrons and 87% CR for lesions treated with photons ($P=.017$). Six of 10 lesions that achieved PR were treated with photons, and the remaining 4 lesions were treated with electrons. The 1 lesion with NR was treated with electrons. On multivariate analysis of modality, location, and dose, only tumor location (lower extremities vs non-lower extremities) and treatment modality

Table 1 Response rate per number of cutaneous T-cell lymphoma lesions (n=270)

Characteristic	CR	PR	PR→CR	Overall CR	NR
No. of lesions (n=270)	255 (94.4%)	10 (3.7%)	4 (1.5%)	259 (95.9%)	1 (0.4%)
Location*					
Face/neck (n=57)	55 (96%)	2 (4%)	0	55 (96.5%)	0
Lower extremities (n=49)	41 (84%)	7 (14%)	1 (2%)	42 (85.7%)	0
Upper extremities (n=40)	39 (98%)	0	1 (3%)	40 (100%)	0
Back (n=24)	24 (100%)	0	0	24 (100%)	0
Abdomen/thorax (n=19)	18 (95%)	0	1 (5%)	19 (100%)	0
Feet (n=16)	16 (100%)	0	0	16 (100%)	0
Pelvis/perineum (n=16)	14 (88%)	0	1 (6%)	15 (93.8%)	1 (6%)
Axilla (n=13)	12 (92%)	1 (8%)	0	12 (92.3)	0
Buttocks (n=13)	13 (100%)	0	0	13 (100%)	0
Hands (n=12)	12 (100%)	0	0	12 (100%)	0
Scalp (n=11)	11 (100%)	0	0	11 (100%)	0
Radiation dose (cGy) †					
400 (n=1)	1 (100%)	0	0	1 (100%)	0
500 (n=2)	2 (100%)	0	0	2 (100%)	0
600 (n=6)	5 (83%)	1 (17%)	0	5 (83.3%)	0
700 (n=42)	42 (100%)	0	0	42 (100%)	0
750 (n=8)	8 (100%)	0	0	8 (100%)	0
800 (n=210)	196 (93%)	9 (4%)	4 (2%)	200 (95.2%)	1 (1%)
900 (n=1)	1 (100%)	0	0	1 (100%)	0
Radiation modality‡					
Electrons (n=215)	207 (96%)	4 (2%)	3 (1%)	210 (97.7%)	1 (1%)
Photons (n=55)	48 (87%)	6 (11%)	1 (2%)	49 (89.1%)	0

Abbreviations: CR = complete response; NR = no response; PR = partial response; PR→CR = partial response converted to complete response.
* CR for all sites vs lower extremities $P=.0016$.
† CR for <700 cGy vs ≥700 cGy $P=.41$.
‡ CR for photons vs electrons $P=.017$.

(photons vs electrons) remained significant at a P value of <.05. Dose continued to show no significance, most likely because of the disparity in the number of lesions treated at lower doses and in patient selection, where higher doses were prescribed to patients with bulkier lesions. Relapse was defined as recurrence within the radiation field based on clinical assessment from radiation oncology or dermatology follow-up notes. The mean time to relapse was 9.25 months (range, 5-14 months). There were no unifying characteristics of the relapsed sites.

Response rates per number of patients

Response rate was evaluated on the basis of patient-specific characteristics (Table 2). CR was lower in patients with LCT vs those with no LCT (P=.04) and tumor stage vs no tumor stage (P=.035). There were no significant differences in response based on sex (P=.99), stage of disease (P=.79), presence of Sézary syndrome (P=.44), or immunophentoype (P=.23).

Figure 2a shows histopathologic findings of a band-like infiltrate with epidermotropism of atypical lymphocytes from a tissue sample taken from a patient with MF without LCT, followed by the clinical photograph of a representative lesion shown before and 9 months after treatment with 800 cGy in 1 fraction. Figure 2b shows histopathologic findings of a dense infiltrate of large atypical lymphocytes from a tissue sample taken from a patient with MF with LCT, followed by the clinical photograph of the tumor lesion shown before and more than 2 years after treatment with 800 cGy in 1 fraction. Although skin discoloration persisted, there was no evidence of tumor on palpation or recurrence observed on follow-up.

Toxicity

Possible effects of toxicity were assessed at follow-up visits with the radiation oncologist. No significant acute or long-term side effects requiring more than topical management of skin reaction from radiation therapy were reported from these treatments.

Table 2 Response rate per number of patients (n=58)

Characteristic	CR in all sites treated	PR in at least 1 site treated	PR→CR in at least 1 site treated	Overall CR	NR in at least 1 site treated
No. of patients (n=58)	48 (82.8%)	8 (13.8%)	1 (1.7%)	49 (84.5%)	1 (1.7%)
Large cell transformation*					
At least 1 site with LCT (n=23)	16 (70%)	6 (26%)	0	16 (69.6%)	1 (4%)
Small/medium cell transformation (n=1)	1 (100%)	0	0	1 (100.0%)	0
No sites with LCT (n=34)	31 (91%)	2 (6%)	1 (3%)	32 (94.1%)	0
Sex†					
Male (n=35)	29 (83%)	4 (11%)	1 (3%)	30 (85.7%)	1 (3%)
Female (n=23)	19 (83%)	4 (17%)	0	19 (82.6%)	0
Stage of disease at initial presentation‡					
I (n=29)	25 (86.2%)	3 (10.3%)	1 (3.4%)	26 (89.7%)	0
II (n=22)	17 (77%)	4 (18%)	0	17 (77.3%)	1 (5%)
III (n=0)	0	0	0	0 (0.0%)	0
IV (n=7)	6 (86%)	1 (14%)	0	6 (85.7%)	0
Sézary syndrome§					
Yes (n=3)	2 (67%)	1 (33%)	0	2 (66.7%)	0
No (n=55)	46 (83.6%)	7 (12.7%)	1 (1.8%)	47 (85.5%)	1 (1.8%)
Morphology‖					
P/P (n=21)	20 (95%)	1 (5%)	0	20 (95.2%)	0
T (n=4)	3 (75%)	0	0	3 (75.0%)	1 (25%)
E (n=3)	3 (100%)	0	0	3 (100.0%)	0
P/P&T (n=26)	19 (73%)	6 (23%)	1 (4%)	20 (76.9%)	0
P/T/E (n=4)	3 (75%)	1 (25%)	0	3 (75.0%)	0
Immunophenotype¶					
$CD4^+/CD8^-$(n=44)	38 (86.3%)	5 (11.4%)	1 (2.3%)	39 (88.6%)	0
$CD4^-/CD8^+$ (n=5)	2 (40%)	2 (40%)	0	2 (40.0%)	1 (20%)
$CD4^-/CD8^-$ (n=2)	1 (50%)	1 (50%)	0	1 (50.0%)	0
Unknown (n=7)	7 (100%)	0	0	7 (100.0%)	0

Abbreviations: CR = complete response; E = erythroderma; LCT = large cell transformation; NR = no response; P/P = patches and plaques; PR = partial response; PR→CR = partial response converted to complete response; T = tumor.

* CR for at least 1 site with LCT vs no sites with LCT P=.04.

† CR for men vs that for women P=.99.

‡ CR for stage I vs stage II vs stage IV P=.79.

§ CR for Sézary vs non-Sézary P=.44.

‖ CR for tumor stage vs non-tumor stage P=.035.

¶ CR for $CD4^+$ vs $CD4^-$ P=.23.

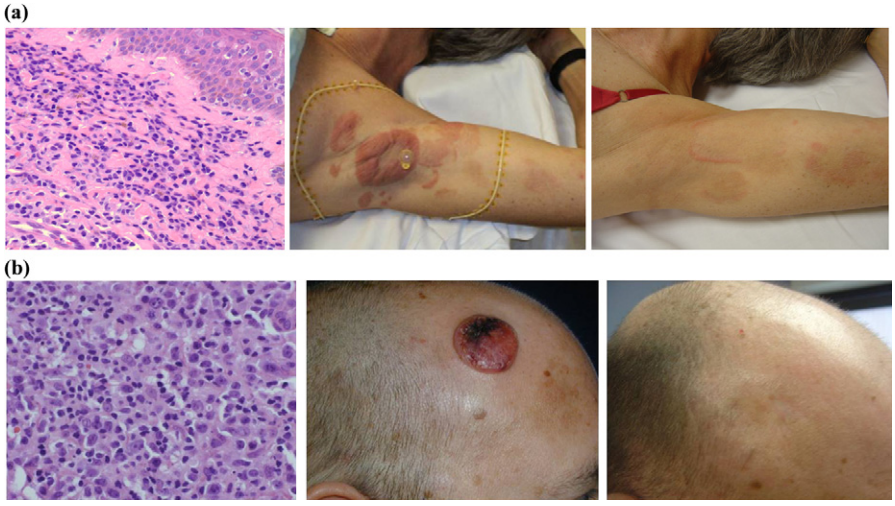

Fig. 2. Histologic sections from a patient's lesion (far left) and representative images prior to and following treatment (right). Post-treatment discoloration persisted without evidence of tumor recurrence on extended follow-up. (a) Patient without large cell transformation. (b) Patient with large cell transformation.

Overall survival

Overall survival was assessed depending on phenotypic characteristics, including patches/plaques, tumor-stage lesions, LCT, CD4/CD8 count, or CD30 count, and was not found to be significant. Overall survival was significantly different on the basis of Sézary count ($P=.0003$) and the presence or absence of erythroderma ($P<.0001$). There was a trend toward reduced survival with advancing stage ($P=.06$).

Cost analysis

The mean technical fee for a single treatment at our center was $887 in today's dollars vs $2072 for 10 fractions. The mean professional charge for a single- vs 10-fraction treatment was $476 vs $761, respectively. The combined mean technical and professional charge for a single treatment was $1364 vs $2833 for 10 treatments, an increased expenditure of 208% (Table 3). This analysis does not include inconvenience to patients, loss of productivity, travel time, and socioeconomic issues related to travel to the radiation oncology center.

Table 3 Cost analysis of technical and professional charges for a single treatment vs 10 fractions

Service	Cost (USD) for single fraction	Cost (USD) for 10 fractions
Technical		
Mean	$887	$2072
Median	$866	$2050
Professional		
Mean	$476	$761
Median	$514	$799
Technical and professional		
Mean	$1364	$2833
Median	$1380	$2849

Discussion

Localized RT and total skin electron treatment play an important role in the management of CTCL, particularly for management of MF. The common practice of providing a total dose of 2000-4000 cGy in multiple fractions to individual lesions generally results in good response rates. These multiple visits are particularly burdensome for a debilitated CTCL patient population. In 1991, we started to use a single fraction to provide rapid palliation to patients with CTCL.

Most lesions treated in this study achieved CR. Characteristics of the partial responders were assessed to determine what may have led to an incomplete response. We found that 70% of the partial responder lesions were those located on a lower extremity, for which several reasons are possible. Sixty percent of these patients had LCT, and 65% had tumor stage disease, suggesting a more aggressive lesion type that could be less responsive. Tumor hypoxia may also have contributed to a lower response rate, as the lower extremity is more prone to peripheral artery disease, which may impact radiation responsiveness and wound healing. Lesions in the lower extremity could also have been bulkier than those in other locations, as we found that these lesions were treated 10% more often with photons than lesions on non-lower extremity sites. Variants of CTCL that are more aggressive and more resistant to traditional treatment are preferentially located in the lower extremities and have also been described (14). These lesions could represent more aggressive and possibly less responsive disease requiring a higher radiation dose.

Because different fraction sizes were used for palliation, we analyzed the data to see if a particular fraction size produced a durable palliative response. The initial CR in patients who received $\geq$700 cGy was 94.6% vs 89% in patients who received $<$700 cGy ($P=.41$). Treatment dose was based on clinical assessment of tumor bulk. Because this was a retrospective review, the number of patients treated at each dose level was not evenly distributed. Therefore, the number of patients treated with $<$700 cGy made up only 3% of the study population, suggesting a selection bias. Although selection bias likely exists, our results

suggest that a dose of ≥700 cGy can provide robust, sustained palliation.

Treatment of lesions with electrons produced a higher rate of CR, 96%, than with photons, 87% ($P = .017$). A possible explanation for this difference could be that photons were used to treat bulky lesions. These lesions are likely to be more aggressive and represent possibly less responsive disease. Modern treatment using computed tomography-based planning is helpful in choosing an adequate margin around tumor and electron and photon energy to prevent marginal failures.

Certain patient-specific characteristics influenced response rate. Historically, patients with Sézary syndrome, erythroderma, and large cell transformation have been correlated with a poor prognosis (1). Large cell transformation is known to be associated with a more aggressive clinical course and shortened survival (15). We found lower CR in patients with at least 1 site with LCT than in patients without any history of LCT ($P = .04$). In addition, we found that tumor stage disease had a 73.5% CR rate compared to disease in patients with either patch/plaque or erythroderma with a CR rate of 95.8% ($P = .035$). CD4 status did not correspond to decreased CR ($P = .23$). These results suggest that prior to initiating treatment, we could potentially stratify patients based on LCT, tumor-stage disease, and location to determine which patients were more likely to respond to RT or will require higher fraction size.

A critical review of the literature yields few studies where different fractionation schedules were used to treat localized CTCL lesions for either palliative or curative intent (Table 4). In the report by Micaily et al (5), 18 patients were treated with localized RT to a total of 18 lesions. Thirteen patients had previous medical therapy, and none had previously received RT. Each site had CR, and 2 sites had local relapse. Those authors recommended a radiation schedule consisting of a total dose of 3060 cGy in fractions of 180-200 cGy. Wilson et al (7) similarly recommended a course of RT for minimal stage CTCL with curative intent; 21 patients were treated with a total of 32 lesions; 9 patients had previous non-radiation treatments; and none had previous RT. Wilson found a CR rate of 96.9%, with local relapse noted in 4 of 32 fields. They recommended a fractionation schedule with a minimum of 2000 cGy in 10 fractions to each lesion. Cotter et al (9) treated 110 lesions in 14 patients with palliative RT and recommended a total dose of 3000 cGy in 15 fractions. That study found a CR rate of 94.5%, and 30 of 100 lesions relapsed locally. Similarly, Heald et al (16) and Piccinno, et al (17) reported a CR rate of >90% in patients treated with localized multifractionated radiation schedule.

Although a multifractionated RT course has been the conventional treatment regimen for patients with CTCL, there are a paucity of data where 1 or 2 fractions are used to treat MF for palliation. Neelis et al (10) found that when 24 patients with either CTCL or cutaneous B cell lymphoma were treated to a total of 65 sites, a CR rate of 92.3% was seen, with local relapse in 5 of 65 sites. Patients in that study were treated to a total dose of 800 cGy in 2 fractions. The significant response rates for patients treated with low-fraction RT regimens support our data showing that single-fraction RT provides adequate palliation for patients with CTCL, especially in patients with MF.

We found a 208% increase in cost when we used Centers for Medicare and Medicaid Services carrier reimbursement rates to compare the current practice of a 10-fraction treatment vs that of a single-fraction treatment. In addition to the monetary savings of a single treatment, patients experienced less disruption in their lives with single vs multifractionated treatment.

Conclusions

Ours is the largest series of patients with CTCL treated with a single fraction of radiation that resulted in excellent palliation. We recommend a single fraction of 700-800 cGy, with higher doses for patients who have bulkier tumors. In future studies, patients should be stratified on the basis of location of lesions, LCT, tumor

Table 4 Studies in which patients were treated with localized RT for CTCL lesions

Study (ref)	No. of sites/no. patients	Previous therapy without RT (no. of patients)	Previous RT (no. of patients)	Response (no. of sites)			Relapse in RT field (no. of sites)	Recommended total dose/no. of fractions
				CR	PR	NR		
Cotter et al 1983 (9)	110/14	14/14	2/20*	94.5%	5.5%	0.0%	30/110	30 Gy/15 fractions
Micaily et al 1998 (5)	18/18	13/18	0/18	100.0%	0.0%	0.0%	2/18	30.6 Gy/1.8-2 fractions
Wilson et al 1998 (7)	32/21	9/21	0/21	96.9%	3.1%	0.0%	4/32	Minimum 20 Gy/10 fractions
Heald et al 2000 (16)	6/6	Not reported	Not reported	100.0%	0.0%	0.0%	1/6	30 Gy/10 fractions
Neelis et al 2009 (10)	65/24	24/24	15/31†	92.3%	6.2%	1.5%	5/65	8 Gy/2 fractions
Piccinno et al 2009 (17)	22†/15	7/15	0/15	95.5%	4.5%	0.0%	4/22‡	22 Gy/no. fractions not given
Our data	270/58	53/58	0/58	95.9%§	3.7%	0.4%	4/270	≥7 Gy/1 fraction

Abbreviations: CR = complete response; NR = no response; PR = partial response.

* Denominator includes patients who were eventually excluded due to lack of follow-up.

† Denominator also includes patients with CTCL histology and cutaneous B-cell lymphoma histology.

‡ Indicates number of fields instead of number of sites.

§ Initial CR of 94.4%, with second fraction overall CR of 95.9%.

morphology, tumor bulk, and immunophenotype to study the dose-response relationship. In addition, the modern era has brought molecular medicine with its new scope of understanding signaling pathways and targets important for this disease. Single-fraction treatment is cost-effective and convenient for patients.

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