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Very low-dose versus standard dose radiation therapy for indolent primary cutaneous B-cell lymphomas: A retrospective study

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To the Editor

Primary cutaneous follicle center lymphoma and primary cutaneous marginal zone lymphoma are the most common types of indolent primary cutaneous B-cell lymphoma (pcBCL). Although pcBCLs are skin-limited and rarely demonstrate extracutaneous spread, [1] they can be distressing to patients and disfiguring. Common local therapies include intralesional steroid injection, topical steroids,[2] and excision.[3] Steroid injections induce a durable complete remission in only 44% of patients and may require multiple rounds of injections; topical steroids are typically ineffective.[2] Excision can be definitive, but these lymphomas have a strong propensity for local recurrence, making field therapy preferable. Locoregional radiation therapy (RT) is an alluring option with significantly higher complete remission rates.[4,5]

Current barriers to referral for RT include the number of treatments needed (12–20) and side effects of standard dose RT (SD-RT). The National Comprehensive Cancer Network recommends 24 to 40 Gy for the treatment of pcBCL (www.nccn.org/about/nhl.pdf). Although effective, SD-RT is associated with dose-dependent cutaneous side effects,

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including erythema, desquamation, ulceration, and alopecia. While the latter grade 3 toxicities are quite rare even at the highest recommended radiation doses, very low-dose RT (VLD-RT; 2 Gy × 2 treatments) is an attractive alternative currently used in the treatment of indolent nodal non-Hodgkin's lymphoma that can also be applied to cutaneous disease.

In this retrospective study, we compared the efficacy of VLD-RT to SD-RT for treatment of pcBCLs. A total of 54 patients with 98 lesions of pcBCL were identified (31 with primary cutaneous marginal zone lymphoma, 27 with primary cutaneous follicle center lymphoma, and 1 patient with low grade B-cell lymphoma not otherwise specified) (Table I). Lesions were treated with either VLD-RT (4–8 Gy in 2 treatments) or SD-RT (24–40 Gy in 12–20 treatments). Some patients had SD-RT to an initial lesion but then received VLD-RT to sites of distant relapse; the subsequent lesions were excluded, leaving 88 lesions for analysis. To account for correlation within-person, repeated measures models were used. The median lesion follow-up was 4.8 years.

Of lesions treated with VLD-RT, 94.1% achieved an initial complete response (CR); 97.3% of lesions treated with SD-RT achieved an initial CR ($P = .49$). Of those achieving a CR, there was no significant difference for time to local failure ($P = .07$), with 1-year Kaplan–Meier failure rates of 6.7% for VLD-RT and 5.6% for SD-RT (Fig 1). Location of lesion (leg vs. nonleg) did not impact the response rate.

SD-RT was associated with a significant increase in acute toxicities ($P < .0001$), most commonly erythema, but none greater than grade 2. Patients receiving SD-RT were more likely ($P = .004$) to experience long-term side effects (lasting >6 months), such as postinflammatory hyper/hypopigmentation or alopecia.

In this study, we found no difference in CR rates between VLD-RT and SD-RT. In addition, the shorter course of therapy is associated with fewer toxicities, including skin dyspigmentation. We recommend that VLD-RT be considered a preferred initial strategy for treatment of pcBCL because of the minimal time commitment (2 treatments), excellent toxicity profile, and improved efficacy over other treatment modalities, such as repeated intralesional steroid injections. The limitations of this study include its retrospective nature and limited sample size.

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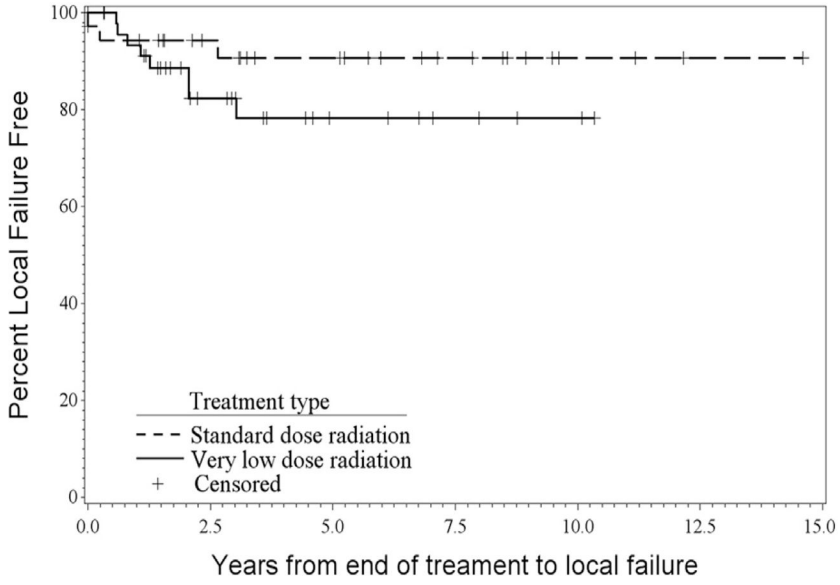

Fig. 1.

Kaplan–Meier curve showing the freedom from local failure for very low-dose radiation therapy and standard dose radiation therapy. Although they initially have similar response rates, lesions treated with very low-dose radiation therapy are more likely to have recurrences or in-field relapses than those treated with standard dose radiation therapy. This difference is not statistically significant, with a log-rank *P* value for the comparison of 0.07.

Table I

Characteristics of lesions treated with very low-dose radiation therapy and standard dose radiation therapy and side effects of treatment

Lesion information	VLD-RT (n = 51)		SD-RT (n = 37)		*P* value*
Lesion diagnosis, n (%)					.1912
pcMZL	34 (66.7)		17 (48.6)		
pcFCL	17 (33.3)		18 (51.4)		
NOS	0		2 (0.05)		
Location, n (%)					.5184
Head	15 (29.4)		17 (46.0)		
Trunk	21 (41.2)		8 (21.6)		
Extremities	15 (29.4)		12 (32.4)		
Lesion size (cm)					.0145
N	33		27		
Range	0.2–6.0		0.2–14.0		
Median	1.0		3.0		
Duration of follow-up (years)					.0271
Range	0.02–12.6		0.2–18.8		
Median	3.9		7.0		
Immediate side effects, n (%)					<.0001
No	43 (84.3)		8 (21.6)		
Yes					
Erythema	8 (15.7)	5	29 (78.4)	22	
Itch		1		2	
Fatigue		1		2	
PIH		1		0	
Erythema and fatigue		0		1	
Itch and fatigue		0		1	
Pain and fatigue		0		1	
Long-term side effects (>6 months), n (%)					.0036
None	47 (92.2)		22 (59.5)		
Yes					

Lesion information	VLD-RT (n = 51)		SD-RT (n = 37)		*P* value*
PIH	4 (7.8)	2	15 (40.5)	9	
Hair loss		2		4	
Pain		0		1	
PIH and hair loss		0		1	
CR, n (%)					.4937
No					
No response	3 (5.9)	0	1 (2.7)	1	
PR		2		0	
PR with recurrence		1		0	
Yes					
CR	48 (94.1)	39	36 (97.3)	25	
CR with in-field occurrence of new lesions		5		2	
CR with out-of-field occurrence of new lesions		0		8	
CR with relapse of same lesions		4		1	

CR, Complete response; NOS, not otherwise specified; pcFCL, primary cutaneous follicle center lymphoma; pcMZL, primary cutaneous marginal zone lymphoma; PIH, postinflammatory hyperpigmentation; PR, partial response; SD-RT, standard dose radiation therapy; VLD-RT, very low-dose radiation therapy.

*Obtained from generalized repeated measures linear models with the appropriate link function based on the distribution of the lesion characteristic. Continuous measures were transformed when their distributions were skewed.

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