# Acute toxicity and risk of infection during total skin electron beam therapy for mycosis fungoides

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***Background:*** Detailed rates of acute toxicity and skin infection during total skin electron beam therapy (TSEBT) for mycosis fungoides have not been reported in a large, modern series.

***Objective:*** We sought to demonstrate the rates of acute toxicity and skin infection during TSEBT.

***Methods:*** We retrospectively reviewed 89 consecutive courses of TSEBT. In all, 82 courses were prescribed a dose of 30 to 36 Gy and were included in the toxicity analysis. We recorded the types and grades of acute treatment toxicities and the incidence of infection during TSEBT for comparison with the previously documented baseline incidence of infection in mycosis fungoides.

***Results:*** The most common toxicities included erythema/desquamation (76%), blisters (52%), hyperpigmentation (50%), and skin pain (48%). The worst reported toxicity grade per patient was grade 1 in 21%, grade 2 in 67%, and grade 3 in 10%, with no grade 4 or 5 toxicities. According to the previously reported rate, a total of 2.4 infections were expected for our cohort at baseline. The number with skin infection was 26 (32%) (relative risk 10.8, $P < .01$), and of these, 12 (15%) were culture confirmed (relative risk 5.0, $P < .01$).

***Limitations:*** This was a retrospective study design.

***Conclusion:*** The risk of cutaneous infection is significant during TSEBT. (J Am Acad Dermatol 2013;69:537-43.)

***Key words:*** extracorporeal photopheresis; infection; mycosis fungoides; race; radiation therapy; toxicity.

Mycosis fungoides (MF) is a low-grade, non-Hodgkin lymphoma caused by skin-homing $CD4^+$ cells that form cutaneous patches, plaques, and tumors, and that have the potential for systemic involvement. It is the most common subtype of cutaneous T-cell lymphoma.[1] MF is highly radiosensitive and radiation is a very effective treatment option leading to at least partial clinical response in close to 100% of patients.[2] Total skin electron beam therapy (TSEBT) is best thought of as a palliative therapy as most if not all patients recur[3] but it may delay the time to systemic spread.[4] Although multiple treatment techniques exist, the Stanford technique is the most well developed and widely reported. It incorporates the basic principles of a broad beam at an extended source skin distance and multiple patient positions to improve skin dose around the circumference of the patient.

*Abbreviations used:*

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| AJCC: | American Joint Committee on Cancer |
| ECP: | extracorporeal photopheresis |
| MF: | mycosis fungoides |
| OR: | odds ratio |
| RT: | radiation therapy |
| TSEBT: | total skin electron beam therapy |

Specific information about the rates and grades of acute toxicity from TSEBT has been reported only qualitatively or in older series with limited numbers

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of patients.[5-7] Infection has been shown to be a significant cause of death in MF[8] and an elevated baseline incidence of cutaneous infection is documented.[9] A predisposition to skin infection results from disruption of the skin barrier and potential immunosuppression from lymphoma.[10] Both skin breakdown and decreased cutaneous immunity can also be exacerbated or caused by TSEBT, yet the incidence of cutaneous infection during TSEBT has not been delineated.

More detailed information about adverse treatment effects is needed so providers know what is to be expected during TSEBT and patients can make decisions regarding consent for treatment. The aims of this analysis were to determine the rates and degrees of acute toxicity, cutaneous infection, and treatment modifications as a result of acute toxicity from TSEBT in patients with MF.

**CAPSULE SUMMARY**

- The rates of acute toxicity and infection during total skin electron beam therapy for mycosis fungoides are poorly delineated.
- This large, modern series provides detailed toxicity information and demonstrates that the risk of cutaneous infection is higher than previously supposed.
- Knowledge of these risks can help guide treatment of mycosis fungoides.

## METHODS

### Study population

This study was exempted by an institutional human investigation committee. We retrospectively reviewed patients treated for MF using TSEBT from 2001 to 2012 in our department, which serves as a referral center for MF. Initial evaluation included a physical examination, appropriate imaging, complete blood cell count, and assessment for blood involvement when appropriate. Patients with suspicious lymph nodes underwent lymph node biopsy. Patients were staged according to the American Joint Committee on Cancer (AJCC).[11]

### Treatment

A 6-field overlapping treatment technique with dual gantry angles (Stanford technique) was used with a 6-MeV linear accelerator. The patients stood 3.8 m from the radiation source. On treatment day 1, the anteroposterior, right posterior oblique, and left posterior oblique positions were treated, and on treatment day 2, the posteroanterior, right anterior oblique, and left anterior oblique positions were treated with the same dose, the 2 treatments making up 1 cycle. For 9 weeks, 4 Gy were given per week in patients receiving 36 Gy. Using this technique, the dose maximum is at approximately 1-mm depth and the 80% isodose line is 6-mm deep to the skin surface.[12,13] An orthovoltage boost was provided to the soles of the feet to 14 Gy with 120-kV photons and the perineum to 18 Gy with 120-kV photons. The scalp was boosted with an electron deflector.

Interval blocking to the hands, feet, eyes, and nails was provided. External eye shields were worn on the first 22 treatments and internal eye shields are worn on the last 14 treatments. A testicular shield was used for male patients with the perineal boost only. In addition, spot radiation treatment was added concurrently for areas of tumor or significant disease burden using 120- to 250-kV photons from 6 to 10 Gy in 13 patients. Concomitant extracorporeal photopheresis was given in monthly cycles of 2 to 14 days.[14] Seven patients (7.8%) had received prior TSEBT, and all 7 of them were initially treated to doses of 30 to 36 Gy with a good initial response and an extended interval before retreatment. Of these, the second treatment with TSEBT consisted of 36 Gy in 1, 34 Gy in 1, 30 Gy in 3, 20 Gy in 1, and 16 Gy in 1.

### Assessment of infection and toxicity

Treatment toxicities were assessed and reviewed on a weekly basis during treatment and at a 3-week follow-up appointment by a single radiation oncologist with extensive experience using TSEBT. Patients were also in contact with a member of the clinical treatment team including nurses, radiation therapists, and residents on a daily basis. Toxicities assessed included alopecia, blisters, edema, epistaxis, erythema/desquamation, eye irritation, fatigue, hyperpigmentation, nail changes and/or loss, pain/discomfort, and any other symptoms the patients were experiencing. Acute treatment toxicity was graded using the Common Terminology Criteria for Adverse Events.[15]

Cutaneous infection was suspected when findings consistent with cellulitis, folliculitis, impetigo, or abscess occurred: (1) in areas surrounding skin breakdown from tumor or ulceration, (2) in areas not usually prone to radiation dermatitis using our technique, (3) in patients who were previously prone to infection, (4) when the dose received was lower than the dose typically necessary to cause radiation dermatitis, or (5) in the presence of fever. Patients were generally evaluated by a radiation oncologist and a dermatologist, medical oncologist,