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Scientific Article

Recumbent Total Skin Electron Beam Therapy

Bradley G. Ackerson, MD,[a,*] Qiuwen Wu, PhD,[a] Oana Craciunescu, PhD,[a] Taofik Oyekunle, MS,[b] Donna Niedzwiecki, PhD,[b] Jennie Gupton, RT,[a] Patrick Laug, RT,[a] Karibee Brumfield, RT,[a] Erin Crain, RT,[a] Colin E. Champ, MD,[a] and Chris R. Kelsey, MD[a]

[a]*Departments of Radiation Oncology;* [b]*Biostatistics and Bioinformatics, Duke University Medical Center, Durham, North Carolina*

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Abstract

Purpose: Our purpose was to describe preliminary dosimetric and clinical results of a recumbent total skin electron beam therapy (TSEBT) technique and compare this to a conventional standing TSEBT technique.

Methods and Materials: A customized treatment platform with recessed side wheels was constructed and commissioned for patients to be treated in a recumbent position. Dosimetric and clinical information was collected for patients treated with this new recumbent technique in addition to that of a cohort of patients treated contemporaneously using the conventional standing method. Dose delivery and clinical outcomes were compared for patients treated with the recumbent and standing techniques.

Results: Between 2017 and 2019, 27 patients were treated with TSEBT with the recumbent (n = 13) or conventional standing technique (n = 14) at our institution. Measured dose at 15 body sites could be directly compared. Of these, 10 showed no significant difference between the two techniques while five sites showed significant differences in median measured dose, including the top of left shoulder, right biceps, bend of left elbow, upper back, and medial right thigh ($P < .003$). Measured dose was significantly higher with the standing technique at these sites with the exception of the upper back. Rates of complete response (25% vs 23%), partial response (50% vs 69%), and stable disease (17% vs 8%) were similar between the standing and recumbent cohorts, respectively ($P = .78$).

Conclusions: We have developed, commissioned, and implemented a floor-based, recumbent technique that allows for treatment of patients who would otherwise not be eligible for TSEBT. Dosimetric and clinical measurements suggest that this technique is a viable alternative to the standing method.

Introduction

Mycosis fungoides (MF) is the most common lymphoma that originates in the skin.[1] The disease presentation is variable but it typically begins with pruritic patches and plaques on nonsun exposed areas that can slowly evolve to tumors. Radiation therapy (RT) plays an integral role in all stages of the disease and can be used in different ways depending on disease extent and responsiveness to other modalities. Localized RT can be

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*Corresponding author: Bradley G. Ackerson, MD; E-mail: bradley.ackerson@duke.edu

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employed to control discrete plaques or tumors. Total skin electron beam therapy (TSEBT) is appropriate in cases of widespread disease, especially in the setting of thick plaques, multiple tumors, or disease refractory to other interventions.[2]

The standard technique for TSEBT requires patients to stand for an extended period of time, typically an hour, and often on an elevated platform to provide optimal dosimetry.[3,4] Most patients will have their eyes and mouth protected with either external or internal shields compromising the ability to maintain balance and communicate. For these reasons, TSEBT can be difficult for elderly patients and those debilitated from their disease or other severe comorbidities. Some patients who would benefit from TSEBT are simply not candidates due to the physical requirements of the treatment. Additionally, patients are at risk of falling and sustaining significant injury during treatment delivery.

To provide TSEBT to a larger patient population and optimize safety for patients at risk of falling, we elected to commission a recumbent TSEBT technique. Several prior reports have described recumbent TSEBT techniques.[5-8] These were invaluable and taken into consideration as we designed an innovative method to optimize ease of patient positioning, minimize duration of treatment, and optimize dosimetric homogeneity. Herein we report our technique, dosimetric results, and preliminary clinical experience.

Methods and Materials

Platform design and technique

A treatment platform measuring 180 × 80 cm^2 of 1.25 cm polycarbonate with recessed side wheels was constructed to place a patient as close to the floor as possible (body-to-floor distance is 5 cm) (Fig 1). A customized scattering filter made of 0.025 cm copper was fabricated and placed in the interface mount of the linear accelerator (Varian TrueBeam STX; Varian Medical Systems, Palo Alto, CA) to further broaden the beam.[7]

A 10-field beam arrangement, using 6 MeV beams with a 2500 MU/min dose rate, was designed with the patient supine and prone for five fields each (Fig 2). During treatment, the patient is first positioned supine on the platform with the arms alongside the body. The platform is placed under the linear accelerator with an approximate source-skin distance (SSD) of 195 cm. Three overlapping fields with gantry angles 60° apart (300, 0, and 60) are used with the weights of each field optimized to produce the flattest profile at D_{max}. The platform is then wheeled out 191 cm and rotated 90° to an SSD of 305 cm and gantry angle of 300°. After the left anterior oblique (LAO) field is treated, the platform is rotated 180° and the right anteior oblique (RAO) field is subsequently treated. Next, the patient is

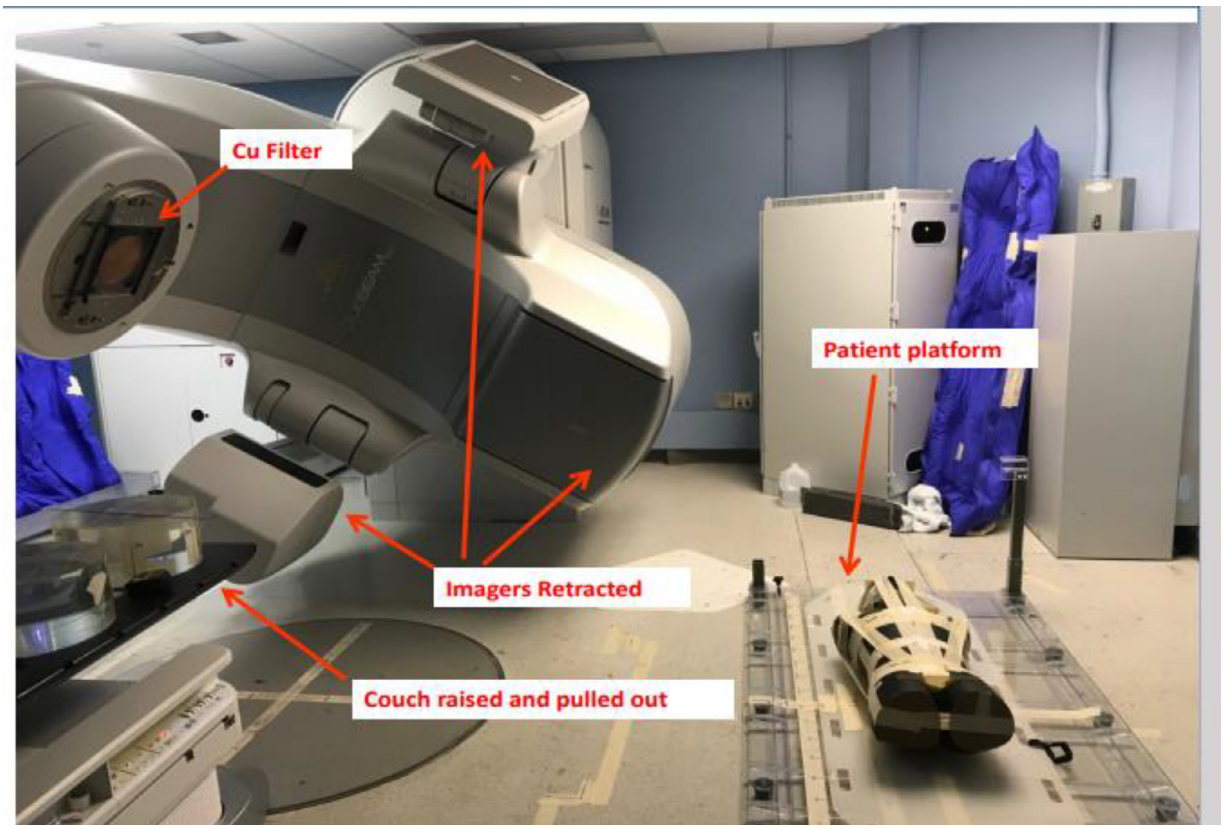

Figure 1 Recumbent total skin electron beam therapy setup (oblique field). Cu filter at interface mount; imagers retracted; couch raised and pulled out; phantom patient on platform; gantry at 300°; source-skin distance (SSD) = 305 cm.

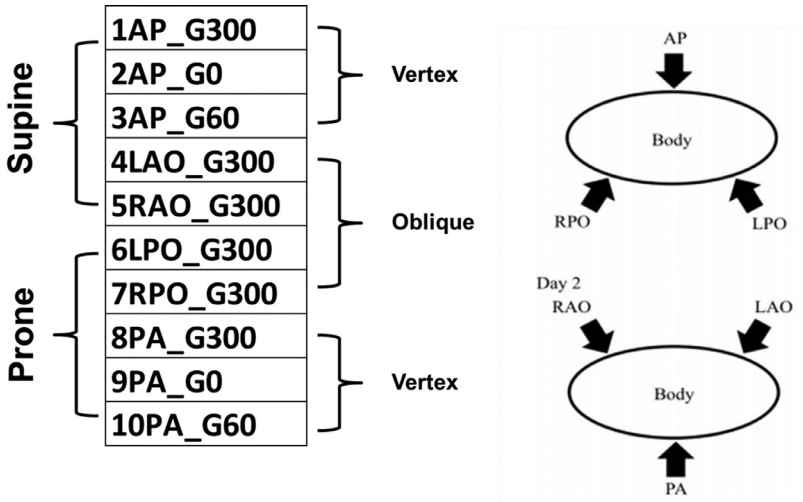

Figure 2 Beams for recumbent total skin electron beam therapy. Patient positioned supine and placed under gantry for three anteroposterior fields. Platform is rolled out and rotated 90° for 4 left anterior oblique and then rotated 180° for 5 right anterior oblique. Patient is then positioned prone and two oblique fields treated. Final three posteroanterior fields then treated.

placed prone and the final five fields are treated in the reverse order. All 10 fields have the same jaw setting of 30×40 cm^2 and collimator angle of 0.

Dosimetric analysis (phantom and patient measurements)

During the commissioning process, a plane-parallel chamber was used to measure the output at these extended SSDs. External beam therapy-3 (EBT3) films were sandwiched in the 30-cm diameter cylindrical phantoms to measure the percentage depth doses of composite dose. Additionally, optically stimulated luminescent dosimeters and thermoluminescent dosimeters were placed in representative points on the anthropomorphic phantom to verify dose distribution. Further details validating the commissioning process have been previously published.[9,10]

During treatment of the initial patient cohort with the recumbent technique, optically stimulated luminescent dosimeters were placed in 30 representative points on each patient with the first fraction to verify dose distributions, 15 of which corresponded with measurement points used routinely on patients treated with the conventional standing technique. At our institution, the hands and feet are shielded with the standing TSEBT method and treated separately with photons. Therefore, dosimetric comparisons of the hands and feet were not practical with this analysis.

Clinical outcomes

Clinical information was collected for 13 patients treated with the recumbent technique and 14 patients treated contemporaneously with the conventional standing technique. This included age, gender, race, body mass index, underlying disease, mycosis fungoides details (eg, folliculotropic, large cell transformation, etc), prior treatment regimens received, T-stage at time of TSEBT, date of start and end of TSEBT, dose per fraction, total prescription dose, the need for RT boost, acute and long-term toxicity, best response to TSEBT, date of best response, adjuvant therapies administered after TSEBT, date of skin progression, date of last follow-up, date of death, and cause of death.

Best response to therapy was classified per the Consensus Statement of the International Society for Cutaneous Lymphomas, the United States Cutaneous Lymphoma Consortium, and the Cutaneous Lymphoma Task Force of the European Organization for Research and the Treatment of Cancer.[11] Complete response was defined as a 100% clearance of skin lesions, partial response a 50% to 99% clearance of skin disease without new tumors, stable disease a <25% increase to <50% clearance in skin disease without new tumors, and progressive disease a ≥25% increase in skin disease or the development of any new tumors. In the event that patients completed only part of the prescribed radiation course, they were included in the dosimetric analysis but were excluded from the clinical data analysis.

Statistical considerations

Detailed dosimetric, demographic, and clinical characteristics were summarized for all patients and separately for recumbent and standing groups using numbers and frequencies for categorical variables and medians and interquartile estimates for continuous variables. After excluding one patient treated for leukemia cutis, treatment and disease characteristics were summarized.

We sought to compare delivered dose (dosimetry) between the recumbent and standing techniques measured at 15 standard points on the skin. A Bonferroni adjusted Wilcoxon rank sum test was used with statistical significance considered at < 0.003 level. The 15 sites compared were vertex of the head, forehead, top of left shoulder, right biceps, anterior chest wall, bend of left elbow, umbilicus, upper back, lower back, left shoulder blade, left midriff, left and right hip, and medial right and left thigh. Dosimetric measurements from five patients (three in the recumbent and two in the standing cohort) who had the head shielded during TSEBT were excluded from the analysis for three sites: vertex of the head, forehead, and top of left shoulder. Toxicity and response rates were also compared. The Kaplan-Meier method was used to estimate progression-free survival and the log-rank test was used to compare treatment arms. Progression-free survival was defined as time from last radiation treatment to skin progression or death.

Statistical analyses were conducted using SAS Version 9.4 (SAS Institute, Cary, NC) and Stata 14.2 (Stata Corp, College Station, TX).

Results

Demographics

Between 2017 and 2019, 27 patients were treated with TSEBT using the recumbent (n = 13) or conventional standing technique (n = 14). Patient characteristics can be found in Table 1. Median age was 64 years (65 for the recumbent group vs 59 for the standing group, $P = .53$). Time from diagnosis to TSEBT was 25 months for the recumbent group versus 45 months for the standing group.

All patients had MF, with the exception of one patient treated for leukemia cutis. This patient was included in the dosimetric analyses but not the response analyses. The majority of patients with MF had T3 disease (n = 14, 54%). The median number of therapies used before the initiation of TSEBT was 4 (range, 2-8) (Table 1). The most common included topical steroids (n = 23), chemotherapy (n = 17), systemic retinoids (n = 14), psoralen and ultraviolet A (n = 11), interferon (n = 11), and localized RT (n = 7). One patient in the standing group had received 36 Gy in 1.5 Gy fractions TSEBT in 2015 before a planned second course in 2017.

Treatment and dosimetry

Median prescribed TSEBT dose was 15 Gy for both cohorts. The following TSEBT doses were prescribed: 15 Gy (n = 16), 36 Gy (n = 6), 34.5 Gy (n = 2), 30 Gy (n = 1), 24 Gy (n = 1), and 23.4 Gy (n = 1). All but one patient was treated with 1.5 Gy fractions. The patient with leukemia cutis, treated using the recumbent technique, was treated with 1.8 Gy fractions. To facilitate comparisons, the dose measurements for this patient were normalized to 1.5 Gy.

Table 1 Patient characteristics

Characteristic	All	Standing	Recumbent	*P* value
Disease				
Mycosis fungoides	26			
Folliculotropic	1		1	
Large cell transformation	6	4	2	
Sezary syndrome	3	3		
Leukemia cutis	1		1	
Age (median)	64	59	65	0.53
Sex				0.30
Female	6	2	4	
Male	21	12	9	
Race				0.70
White	12	7	5	
Black or African American	14	6	8	
Other	1	1		
Body mass index (median)	27.4	28.4	25.9	0.42
Prescribed dose				
15 Gy	16	8	8	
24 Gy	2		2	
30 Gy	1		1	
34.5 Gy	2	1	1	
36 Gy	6	5	1	

For the patients treated with the recumbent technique, 30 dosimetric values were obtained for all patients (Table 2). Measured dose at 15 body sites could be directly compared between the recumbent and standing techniques. Of these, 10 showed no significant difference between the two techniques: vertex of the head, forehead, anterior chest wall, umbilicus, lower back, left shoulder blade, left midriff, left hip, right hip, and left anterior inner thigh. Five sites showed significant differences in median measured dose: top of left shoulder, right biceps, bend of left elbow, upper back, and medial right thigh ($P < .003$). Measured dose was significantly higher with the standing technique at these sites with the exception of the upper back.

There were an additional 15 points measured only in the recumbent group, which included the palms, dorsal hands, soles of the feet, right elbow, left eye, right cheek, chin, right outer thigh, inner and outer left lower leg, posterior left thigh, and top of the right foot, with results found in Table 2.

Outcomes/toxicity

Two patients with MF that were included in the dosimetric analysis were excluded from the clinical comparisons. This included one patient who completed only one full fraction in the standing group but was unable to tolerate further RT and one patient in the recumbent group who never returned for follow-up after TSEBT. One patient started treatment in the standing group and was transitioned to the recumbent technique after experiencing a fall on the first day of treatment. They were included in the clinical outcomes analysis for the recumbent group. Considering the 24 patients with MF who completed TSEBT and returned for follow-up, rates of complete response (25% vs 23%), partial response (50% vs 69%), and stable disease (17% vs 8%) were similar between the standing and recumbent cohorts, respectively ($P = .78$). Patients in both groups tolerated TSEBT reasonably well, with no grade 3 to 5 toxicities. The most

Table 2 Median measured dose with standing and recumbent TSEBT techniques

Site	Standing (IQR), cGy	Recumbent (IQR), cGy	*P* value
Standing and recumbent			
Vertex of the head	66 (54-78)	36 (18-72)	.11
Forehead	150 (141-156)	156 (150-175)	.10
Top of left shoulder	104 (78-122)	34 (19-46)	< .001*
Right biceps	142 (136-151)	117 (90-127)	< .001*
Anterior chest wall	154 (150, 161)	171 (158-174)	.009
Bend of left elbow	148 129, 181)	88 (87-111)	< .001*
Umbilicus	152 (148-158)	162 (159-168)	.003
Lower back	159 (152-161)	161 (159-168)	.077
Left shoulder blade	157 (148-161)	143 (139-154)	.035
Left midriff	159 (147-165)	141 (134-149)	.005
Left hip	144 (136-151)	128 (119-140)	.013
Right hip	148 (140-162)	123 (115-130)	.0036
Upper back	160 (154-163)	175 (172-183)	< .001*
Right medial thigh	149 (145-158)	106 (84-136)	< .001*
Left medial thigh	151 (144-155)	149 (140-153)	.92
Recumbent only			
Right palm		95 (93, 100)	
Right dorsal hand		105 (97-116)	
Left palm		96 (93-98)	
Left dorsal hand		99 (95-113)	
Left sole of foot		76 (67-78)	
Right sole of foot		72 (56-86)	
Right outer elbow		136 (127-159)	
Left eye		128 (121-150)	
Right cheek		163 (159-167)	
Chin		173 (168-181)	
Right outer thigh		143 (126-153)	
Left inner calf		155 (144-179)	
Left outer calf		152 (145-159)	
Right top of foot		170 (164-179)	

Abbreviations: IQR = interquartile range; TSEBT = total skin electron beam therapy.
* Significant differences (< .003)

commonly reported grade 1 to 2 toxicities were dermatitis (n = 9), eye irritation (n = 6), extremity pain (n = 6), and mucositis (n = 5).

Adjuvant systemic therapy after TSEBT was administered to 17 patients with MF. This included interferon (n = 6), interferon and systemic retinoids (n = 3), gemcitabine (n = 3), systemic retinoids (n = 2), romedepsin (n = 1), pralatrexate (n = 1), and brentuximab (n = 1). Topical steroids were used in 10 patients, eight of whom also received adjuvant systemic therapy. During the follow-up period, 19 patients experienced disease progression, four had stable disease at their last follow-up, and one died. Median progression-free survival of patients in the standing group was 4.6 (95% confidence interval, 1.3, 9.6) months versus 2.6 (95% confidence interval, 0.9, 7.3) months in the recumbent group ($P = .51$) (Fig 3).

Discussion

We were prompted to commission an efficient recumbent technique for TSEBT after numerous patients were unable to initiate or complete therapy using the conventional standing method. The primary difference between our technique and other recumbent techniques is our wheeled platform that facilitates efficient and safe treatments. Patients with MF are often older with comorbidities that make standing in one position for prolonged periods challenging. Furthermore, with the vault closed these patients are not easily or quickly assisted should they experience difficulties. Communication with staff is hampered by mouth shields while the patients' ability to maintain balance is compromised by eye shields. The risk of serious injury can be high. The recumbent technique we commissioned is safer, allows for treatment of almost all patients, and provides similar dosimetric and clinical outcomes. To our knowledge, this is the largest cohort of patients in the literature evaluating the use of a recumbent technique and provides valuable data on the differences between the two treatment techniques.

The recumbent technique has many logistical advantages but also some limitations. Our experienced therapists have found that after an initial learning curve, the recumbent technique is quicker and easier to set up correctly. It eliminates many of the movements and patient instructions that are required when using the standing technique. Therefore, less time is spent instructing and coaching patients through daily treatments. Aside from lying down on the table, turning once from supine to prone, and standing at the conclusion of treatment, the patient is only required to lie still. The novel wheeled platform allows the therapists to execute all movements. This decreases setup uncertainty and treatment pauses due to inevitable movements that are observed as patients attempt to stand for prolonged lengths of time.

There are two major limitations of this technique. First, some patients with mobility issues can have difficulty transitioning from a standing to recumbent position on the floor and vice versa at the conclusion of treatment. This has been rare but does put stress on staff when significant assistance is required. Second, maneuvering the wheeled platform requires physical exertion on the part

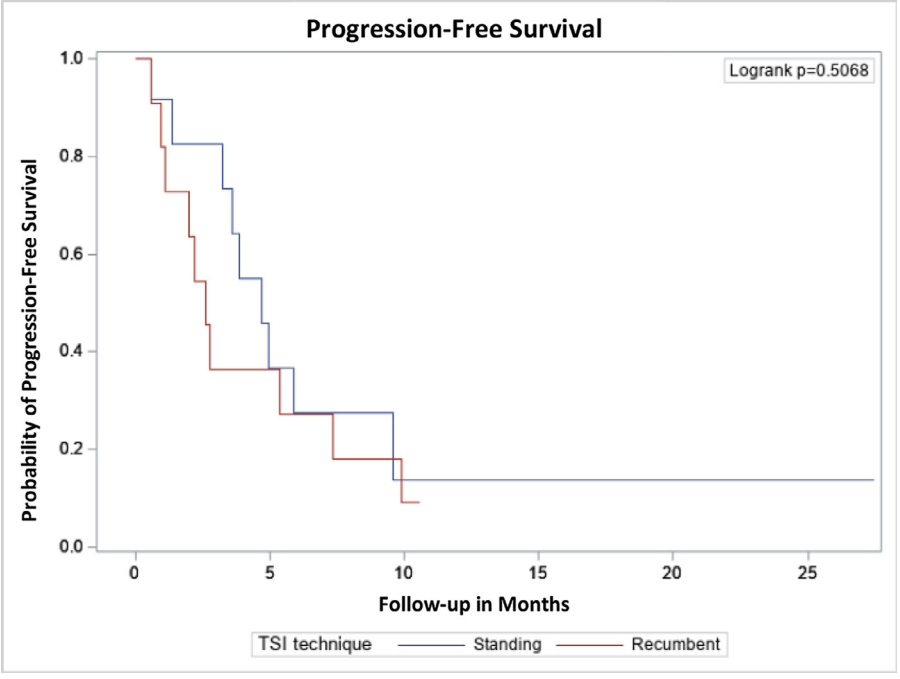

Figure 3 Progression-free survival by total skin electron beam technique (recumbent vs standing).

of the therapists who have worked closely with the Duke University Safety and Ergonomic Team to implement protocols to ensure staff safety.

Although dosimetric measurements were reasonably comparable between the two techniques, we did observe significant differences in measured dose at some skin sites, with the recumbent technique generally providing less reliable prescription dose delivery. As with all TSEBT techniques, there is wide patient variability, including differences in dosimeter position at any single body site, variation in body habitus, patient motion, and so forth. Previously published experiences with recumbent techniques used radiochromic film to measure dose and found a 28% difference between the dose that was expected and what was measured in vivo.[5] Part of this discrepancy was thought to be due to the patient-specific body factor and partly due to setup variation. With the recumbent technique, the left and right medial thighs received a relatively large difference in delivered dose. Possible explanations include subtle differences in placement of dosimeters, patient positioning, or limitations of the recumbent technique in this body area. As detailed previously, the recumbent technique may underdose certain key areas that often require a separate boost, especially the hands and feet. We were unable to compare dosimetry with the hands and feet as we universally shield both during the standing TSEBT technique and treat them separately with photons.

Despite differences in prescribed dose (low-dose vs conventional dose) and dosimetry between the two techniques, clinical response rates were comparable. Overall response rates after conventional TSEBT vary widely in the literature, ranging from 8% to 98% depending on stage, RT dose, and use of adjuvant therapies after TSEBT.[12-16] It is challenging to compare outcomes in small patient cohorts treated with such diverse management plans, and larger patient cohorts would be required to assess this.

In conclusion, the recumbent technique described herein appears to provide a safe and reliable method of TSEBT delivery, particularly for frail patients who would otherwise be put at risk with the standing technique. It can be implemented quickly, is preferred by therapists, and is associated with comparable clinical outcomes. Although this analysis represents the largest comparison between these two techniques, more data are required to better understand the clinical and dosimetric outcomes.

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