ORIGINAL ARTICLE

Dose optimization of total or partial skin electron irradiation by thermoluminescent dosimetry

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Abstract

Background   Due to the complex surface of the human body, total or partial skin irradiation using large electron fields is challenging. The aim of the present study was to quantify the magnitude of dose optimization required after the application of standard fields.

Methods   Total skin electron irradiation (TSEI) was applied using the Stanford technique with six dual-fields. Patients presenting with localized lesions were treated with partial skin electron irradiation (PSEI) using large electron fields, which were individually adapted. In order to verify and validate the dose distribution, in vivo dosimetry with thermoluminescent dosimeters (TLD) was performed during the first treatment fraction to detect potential dose heterogeneity and to allow for an individual dose optimization with adjustment of the monitor units (MU).

Results   Between 1984 and 2017, a total of 58 patients were treated: 31 patients received TSEI using 12 treatment fields, while 27 patients underwent PSEI and were treated with 4–8 treatment fields. After evaluation of the dosimetric results, an individual dose optimization was necessary in 21 patients. Of these, 7 patients received TSEI (7/31). Monitor units (MU) needed to be corrected by a mean value of 117 MU (±105, range 18–290) uniformly for all 12 treatment fields, corresponding to a mean relative change of 12% of the prescribed MU. In comparison, the other 14 patients received PSEI (14/27) and the mean adjustment of monitor units was 282 MU (±144, range 59–500) to single or multiple fields, corresponding to a mean relative change of 22% of the prescribed MU. A second dose optimization to obtain a satisfying dose at the prescription point was need in 5 patients.

Conclusions   Thermoluminescent dosimetry allows an individual dose optimization in TSEI and PSEI to enable a reliable adjustment of the MUs to obtain the prescription dose. Especially in PSEI in vivo dosimetry is of fundamental importance.

Keywords   Total skin electron irradiation · Partial skin electron irradiation · Thermoluminescent dosimetry · Mycosis fungoides · Cutaneous T-cell lymphoma · Skin metastases

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Dosisoptimierung bei Ganzhaut- und Teilhautelektronenbestrahlung mittels Thermolumineszenzdosimetrie

Zusammenfassung

Hintergrund Aufgrund der komplex geformten Oberfläche des menschlichen Körpers ist die Ganzhaut- oder Teilhautbestrahlung mit großen Elektronenfeldern eine Herausforderung. In dieser Studie quantifizieren wir die erforderliche Dosisoptimierung nach Anwendung von Standardfeldern zum Erreichen der Verschreibungsdosis.

Methoden Die Ganzhautelektronenbestrahlung (TSEI) wurde gemäß der Stanford-Technik unter Verwendung von sechs dualen Elektronenfeldern durchgeführt. Wenn die Läsionen auf eine Körperhälfte begrenzt waren, wurde eine Teilhautelektronenbestrahlung (PSEI) unter Verwendung individuell angepasster Elektronenfelder durchgeführt. Zur Verifizierung und Validierung der Dosisverteilung wurde eine In-vivo-Dosimetrie mittels Thermolumineszenzdosimetern (TLD) während der ersten Behandlungsfraktion durchgeführt, um potenzielle Dosisinhomogenitäten zu detektieren und eine individuelle Dosisoptimierung mit Anpassung der Monitoreinheiten (MU) zu ermöglichen.

Ergebnisse Zwischen 1984 und 2017 wurden insgesamt 58 Patienten behandelt: 31 Patienten erhielten eine TSEI mit jeweils 12 Behandlungsfeldern, während 27 Patienten mit einer PSEI mit 4–8 Behandlungsfeldern therapiert wurden. Nach Auswertung der In-vivo-Dosimetrie war bei 21 Patienten eine individuelle Dosisoptimierung erforderlich. Davon erhielten 7 Patienten (7/31) eine TSEI. Die MU mussten hierbei für alle 12 Behandlungsfelder um einen Mittelwert von 117 MU (±105, Spanne 18–290) gleichmäßig korrigiert werden, einer relativen Differenz von 12 % entsprechend. Im Vergleich dazu erhielten die anderen 14 Patienten (14/27) eine PSEI; die mittlere MU-Anpassung betrug 282 MU (±144, Spanne 59–500), auf einzelne oder mehrere Felder beschränkt und einer relativen Differenz von 22 % entsprechend. Bei 5 Patienten war außerdem eine zweite Dosisoptimierung notwendig, um eine befriedigende Abdeckung mit der Verschreibungsdosis zu erzielen.

Schlussfolgerung Die In-vivo-Dosimetrie mittels TLD ermöglicht eine individuelle Dosisoptimierung in TSEI und PSEI mit Anpassung der MU, um die Verschreibungsdosis zu erreichen. Besonders bei der PSEI ist die In-vivo-Dosimetrie unabdingbar.

Schlüsselwörter Ganzhautelektronenbestrahlung · Teilhautelektronenbestrahlung · Thermolumineszenzdosimetrie · Mycosis fungoides · Kutanes T-Zell-Lymphom · Hautmetastasen

Introduction

Total skin electron irradiation (TSEI) is a long-established treatment technique known since almost a century [1]. In cases of primary cutaneous T-cell lymphoma, including mycosis fungoides or Sézary syndrome, TSEI represents a very effective single modality treatment [2]. The technique is particularly suitable to deliver a uniform dose to the entire skin surface to treat the superficial pruritic patches and plaques, as it achieves therapeutic dose levels to the skin and a rapid fall-off in the tissue underneath [3]. For patients presenting with localized lesions to the upper or lower part of the body, partial skin electron irradiation (PSEI) was implemented at our department. PSEI was mainly used in a palliative setting for skin metastases (e. g. metastasized breast cancer).

Due to the complex surface of the human body, total skin irradiation is challenging. Different treatment approaches have been studied over the past decades: (1) large electron field techniques, (2) rotational techniques, and (3) techniques involving patient's shift during irradiation [4]. In the case of large electron field techniques, the patient is treated in a standing position. One major challenge is the avoidance of dose heterogeneity in the patients' skin. The optimal circumferential dose homogeneity was seen when the patient is rotated by 60° for every irradiation field or is standing on a permanently rotating platform during radiation treatment [5, 6]. Over the last few years, the techniques have been constantly optimized [7, 8].

In order to verify and validate the dose distribution, in vivo dosimetry is of essential importance. In the present study, thermoluminescent dosimetry was used to detect potential dose heterogeneity and to allow for an individual dose optimization. Thermoluminescent dosimetry is an extremely sensitive technique that allows the measurement of radiation doses to dose levels even below 1 mGy [9]. Due to their small size the thermoluminescent crystals are a perfect tool for in vivo dosimetry to detect over- or underdosage on different bodyparts. The aim of the present study was to quantify the magnitude of dose optimization required after the application of standard fields in partial or total skin electron therapy.

Materials and methods

Radiotherapy technique

For total skin electron therapy a modified Stanford technique with six dual-fields was used [5]. The method was introduced at our department in 1984. Within the first years, an acrylic glass plate was placed in front of the patient to provide additional electron scattering and to increase the electron incident energy at the patient's surface. In 2008, a custom-made platform with a 0.8 cm acrylic glass cylinder was built to obtain a more homogeneous distance of approximately 30 cm from the acrylic glass cylinder to the patient's skin surface. The cylinder was positioned at a distance of 209 cm from the isocenter in the treatment room (Fig. 1a). If necessary, an additional acrylic glass cuboid of 3 cm thickness, as well as custom-made glasses made with lead glass were available, to shield the head and/or the eyes. For cases of localized skin involvement, a partial skin irradiation technique using large electron fields was implemented. Therefore, additional curved acrylic glass plates of 2.4 cm thickness were used to shield the upper or lower part of the body. Moreover, tissue-equivalent flexible gel boluses with a thickness of >2 cm were used to shield individual body parts, if needed (see Fig. 2).

During treatment delivery the patient was standing in an upright position on the platform within the acrylic glass cylinder, with the hands elevated above the head. On top of the acrylic glass cylinder a rotating plate with handles for arm positioning was mounted, to facilitate patient rotation at 60° intervals for the 6 different treatment positions (0°, 60°, 120°, 180°, 240°, 300°, Fig. 1b). To improve patient compliance and collaboration during the treatment session, the treatment positions were indicated on the ground of the platform using different colors, to enable patients to easily rotate to the next treatment position. During the four oblique electron fields (60°, 120°, 240° and 300°) the patients were positioned in fencing stance to maximize unfolding of the skin and to prevent self-shielding (Fig. 3). To correct the longitudinal patient positioning in order to adjust the patient's height to the beam intersection, different polystyrol panels were available to be placed on the bottom of the acrylic glass cylinder in order to position the patient's umbilicus at about 1.25 m above the floor (Figs. 2 and 3).

For treatment delivery, a LINAC (Mevatron KD, later Oncor, Siemens Healthcare, Germany) with 6 MeV electron beams and a dose rate of 900 MU/min was used. To encompass the entire patient body surface with a single treatment field, a source to skin distance (SSD) of about 7 m would be required. As our treatment room did not allow such a long SSD to be obtained, we adopted the solution provided by Karzmark et al. [5] generally known as the "Stanford technique" by using two overlapping treatment fields. In the

original publication of 1960, the gantry was placed at +20° and –20° in relation to the horizontal axis, perpendicular to the patient plane [10]. We adjusted the gantry angles for the setup at our institution to 287° and 253°. Fig. 1a depicts the treatment setup. The prescribed dose for total skin irradiation for mycosis fungoides was 30 Gy in 20 fractions of 1.5 Gy, 5 fractions per week at the umbilicus.

Thermoluminescent dosimetry

For thermoluminescent dosimetry, rod-shaped thermoluminescent dosimeters TLD-100™ of 1 mm diameter and 6 mm length (Harshaw/Filtrol Partnership, Solon, OH, USA) made of lithium fluoride were used. When ionizing radiation interacts with the crystal structure of the TL dosimeter, it causes electrons in the crystal's atoms to jump to higher energy states, where they stay trapped in the crystal lattice due to intentionally introduced impurities (e. g. magnesium). By heating the TLDs, electrons drop back to their original ground state, releasing the captured energy from radiation as visible light. The intensity of light emitted is proportional to the absorbed radiation dose. Depending on age and material of the TLDs, loose electrons could also drop back to the ground state. This so-called fading effect can be balanced by preheating all TLDs prior to the readout [11].

Before dose exposure the TLDs were heated to 400 °C in a TLD oven for 1 h and cooled down afterwards. All electrons drop back to the ground state. The TLDs were placed in the area of interest before the first treatment fraction. A reference group of TLDs was irradiated by a caesium-137 source with exactly 1.00 Gy. After radiation exposure and before readout, all TLDs were stabilized in the TLD oven at 100 °C to remove electrons that are trapped in a loose state. In the TLD reader (Harshaw 2000D, Harshaw/Filtrol Partnership, Solon, OH, USA) the TLDs were heated one after another with hot nitrogen (340 °C) and light output from each crystal was read out separately. The applied dose to skin surface was calculated with an individual TLD correction factor. Differences due to minimal changes in time or temperature gradient during the preparation procedure or unknown environmental conditions were eliminated with a correction factor of the reference TLDs. In our TLD lab the physical deviation of dose measurement by TLDs is <1%.

Dose optimization

After readout, individual dose optimization with adjustment of monitor units (MU) was performed to obtain the prescribed dose at the prescription point. All TLD dose values within one treatment field were averaged and MUs were corrected correspondingly to achieve the prescribed dose.

Fig. 1 **a** Setup and geometrical arrangement for the total skin electron therapy technique with the custom-made acrylic glass cylinder and optimized gantry angles of 287° and 253°. **b** Angular orientation of the six dual-fields (0°, 60°, 120°, 180°, 240°, 300°) and the corresponding six treatment positions
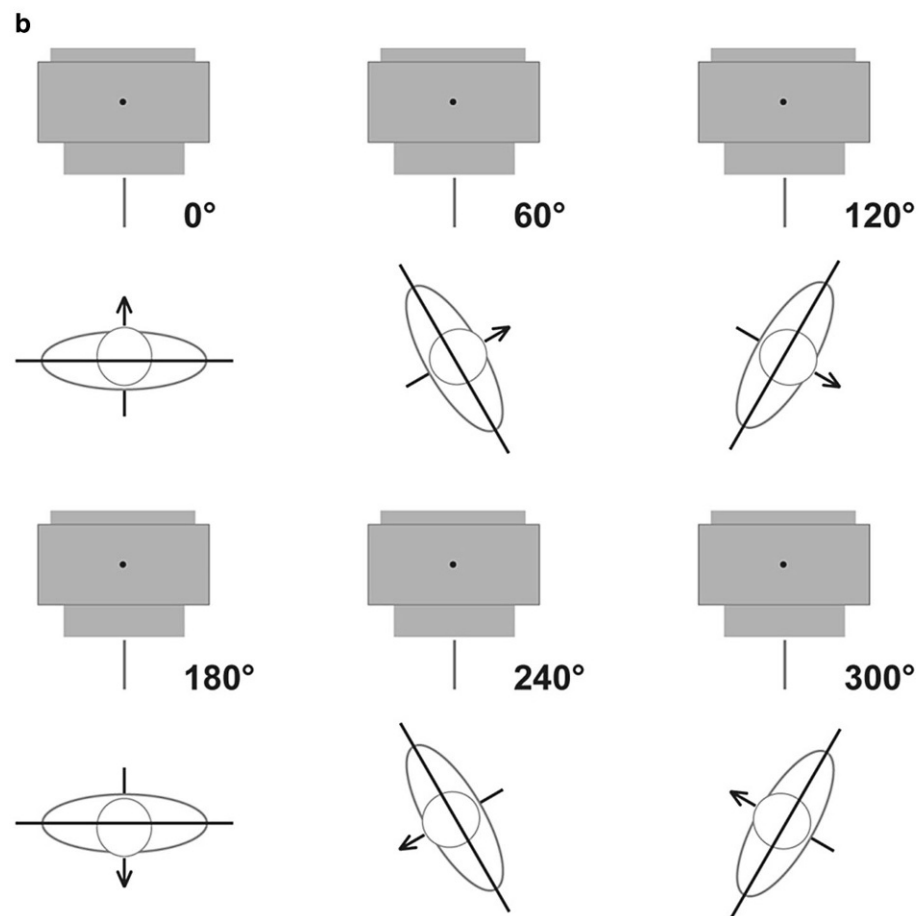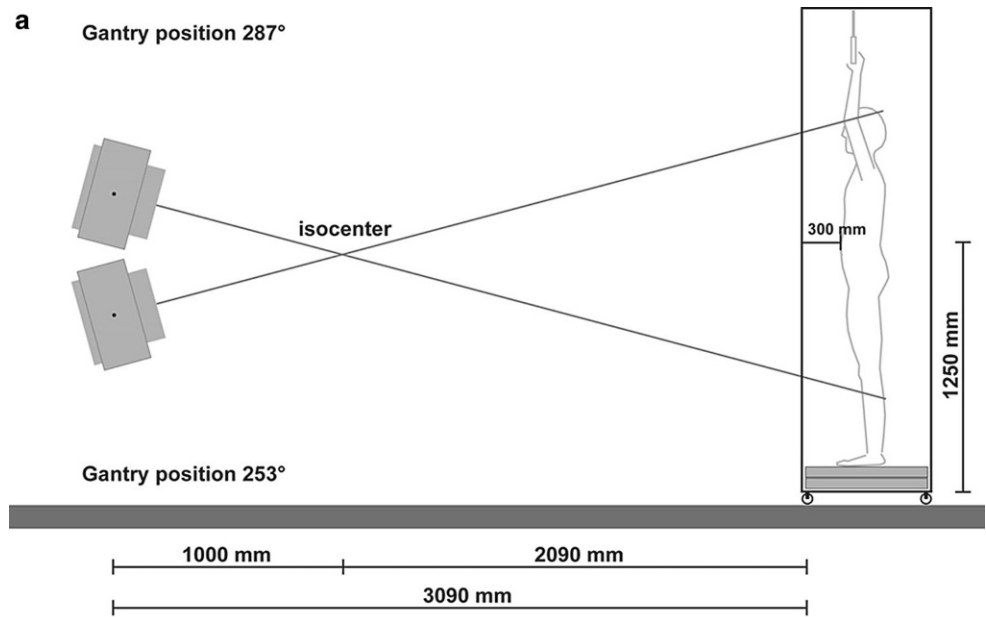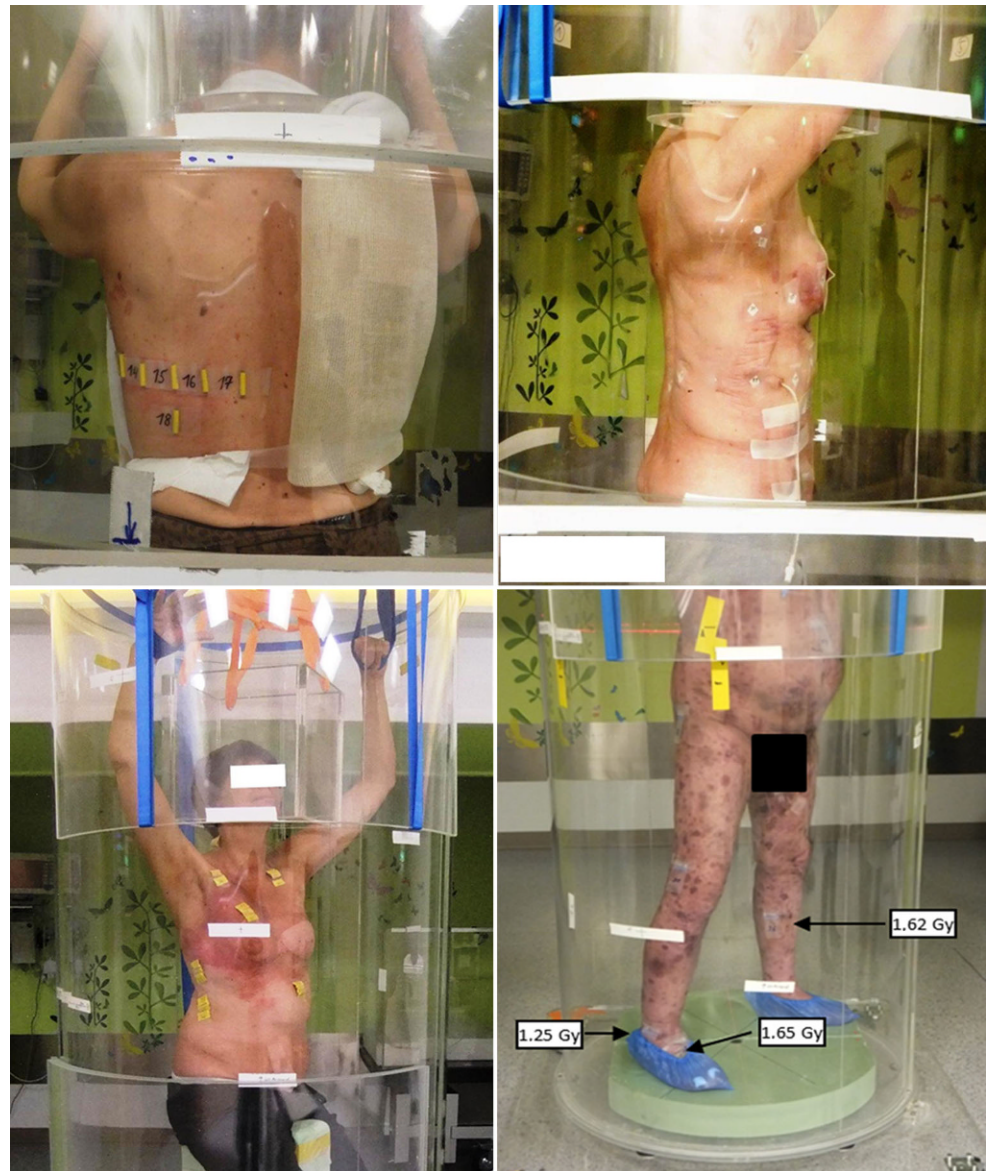
Fig. 2 Partial skin electron irradiation: Additional curved acrylic glass plates of 2.4 cm thickness were used to shield the upper or lower part of the body. Moreover, tissue-equivalent flexible gel boluses with a thickness of >2 cm were used to shield individual body parts, if needed

If single TLD measurements showed significantly deviated results from the mean value, this discrepancy was mostly related to patient positioning errors. All patients received an initial TLD measurement (20–30 TLDs per patient) as well as after the correction of MU during the next treatment session. If there were still discrepancies requiring further adjustments, once more a TLD measurement was performed to ensure dose delivery of the prescribed dose. For the present study, the magnitude of MU difference (addition or subtraction) was recorded and analysed.

Results

Since March 1984, a total of 58 patients were treated with total or partial skin irradiation using the described large

electron field technique. Thirty-one patients received total skin electron irradiation using 12 treatment fields, while 27 patients underwent partial skin irradiation and were treated with 4–8 treatment fields. During the first treatment fraction an extensive dosimetry using TLDs was performed for every single patient (see example in Figs. 3 and 4). The TLDs were attached to patients' surface at representative regions. After evaluation of the results, an individual dose optimization was necessary in 21 patients. Of these, 7 patients (33%) received a total skin electron irradiation for mycosis fungoides. Monitor units (MU) needed to be corrected by a net mean value of 117 MU (±105, range 18–290), corresponding to a mean relative change of 12% of the prescribed MU. In comparison, the other 14 patients (66%) received a partial skin electron irradiation and the mean adjustment of monitor units was 282 MU (±144,
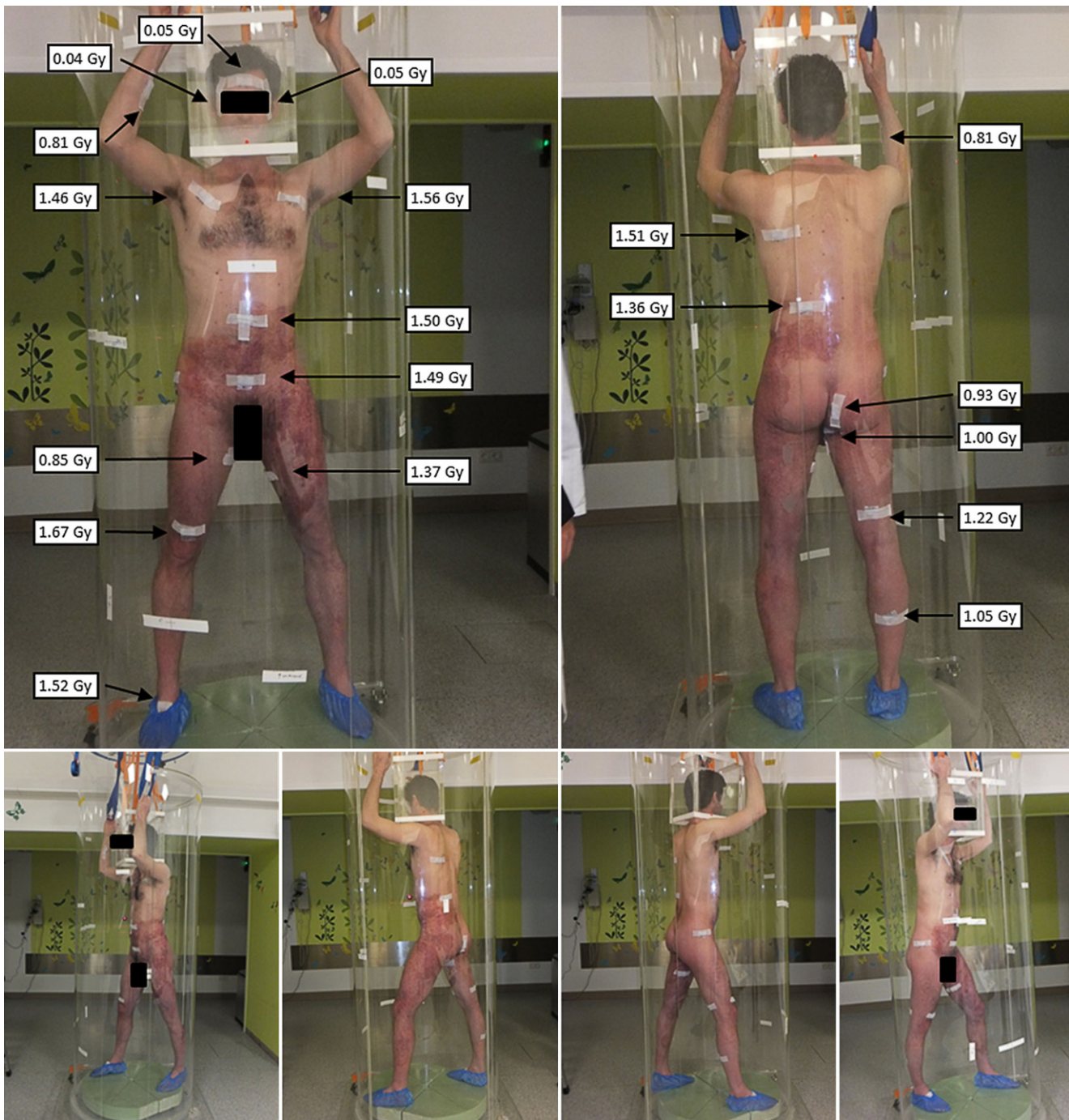
Fig. 3 Patient positioning in the acrylic glass cylinder in the six treatment positions. If there is no skin involvement, the head is shielded by an acrylic glass cuboid. Doses measured by thermoluminescent dosimeters (TLD) are shown

range 59–500), corresponding to a mean relative change of 22% of the prescribed MU. In all cases of TSEI the MUs were uniformly changed for all 12 treatment fields, while the partial skin irradiation technique required a more individualized dose optimization of single or multiple fields (overall 17 fields). Fig. 5 depicts the MU changes for all 21 patients. After adjustment of the MUs, all patients underwent a second TLD measurement to verify the results of

the dose optimization. A total of 5 patients needed a second dose optimization to obtain a satisfying dose distribution.

Despite the correction of the large electron fields, underdosage typically occurred at areas not directly exposed to the electron beam: axillae, perineum, medial upper arms and thighs, sole of feet. In cases of involvement of these areas, a sequential electron boost was performed, if required. If the head was not involved, it was shielded by an acrylic

Fig. 4 Total skin electron irradiation (TSEI) in two treatment cycles in cases of frail patients presenting with comorbidities: first the irradiation of the upper body part is performed, followed by irradiation of the lower body part. Thermoluminescent dosimetry at the region of rapid dose fall-off (penumbra region, see *green line*) at the umbilicus is fundamental. Several thermoluminescent dosimeters (TLDs) on a plastic catheter were used to monitor the dose fall-off in order to adjust the edge of the sequential caudal radiation field by moving the additional shielding acrylic glass plate to shield the area of first treatment series

Fig. 5 Required monitor unit (MU) changes to obtain the prescription dose after thermoluminescent in vivo dosimetry during the first treatment fraction for all treatment fields. *TSEI* total skin electron irradiation, *PSEI* partial skin electron irradiation
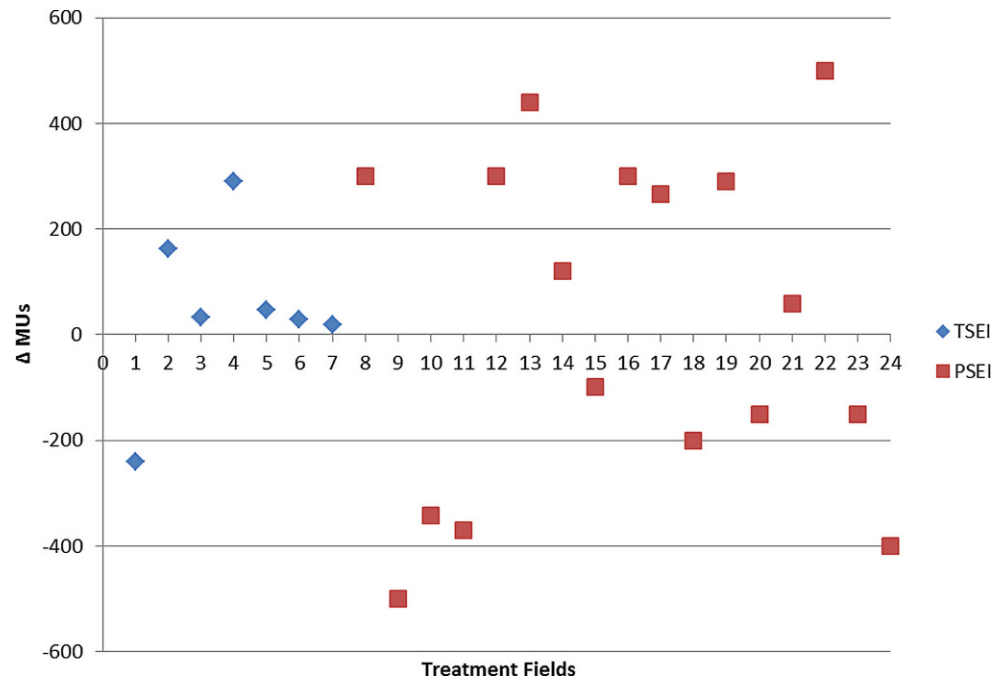
glass cuboid. TLD measurements close to the eyes documented a dose of 0.05 Gy per fraction (3% of prescribed dose).

For patients presenting with localized lesions to the upper or lower part of the body, a partial skin electron irradiation was implemented at our department. PSEI was mainly used in a palliative setting for skin metastases (e. g. metastasized breast cancer). Furthermore, this technique was also used to split the TSEI into two treatment cycles in cases of frail patients presenting with comorbidities. For the TSEI in two treatment cycles, dosimetry at the region of rapid dose fall-off (penumbra region) at the umbilicus was very important. We used several TLDs on a plastic catheter to monitor the dose fall-off in order to adjust the edge of the sequential caudal radiation field by moving the shielding acrylic glass plate (see Fig. 4). Moreover, in cases of partial skin electron irradiation, tissue-equivalent flexible gel boluses with a thickness of >2 cm were used to shield individual body parts, if needed (Fig. 2).

Discussion

Over the past decades, several other skin-directed local therapies, as well as systemic therapies have been investigated for the treatment of early stage cutaneous T-cell lymphoma, including corticosteroids, photochemotherapy (psoralen + UVA), UVB phototherapy, retinoids or immunotherapy [4]. Despite these new promising therapeutic approaches, radiotherapy still remains one of the most effective treatment options, with a complete response rate

of up to 97% in stage T1 disease [12]. As recently reported in a review of Elsayad et al. [2] even low-dose TSEI regimens appear to be an effective treatment alternative to conventional TSEI with 30–36 Gy. Low-dose regimens using 10–12 Gy have a significantly shorter treatment time and lower grade 2 adverse events as compared to conventional dose regimens [13, 14]. Even if standard-dose TSEI has higher local control rates, low-dose TSEI is a safe and well-tolerated treatment alternative to achieve rapid short-term palliation of cutaneous manifestations with minimal toxicity [15, 16].

The present study used TLD measurements to verify the in vivo dose distribution of standard fields using a modified Stanford technique. A dose uniformity of ±10% was the goal for all patients. While in vivo dosimetry is a routine procedure for many institutions, only few study groups focused on the evaluation and analysis of dose variations measured by TLD using a standing TSEI technique. Weaver et al. [17] showed a very good correlation of dose to flat surfaces of the body and the prescription dose. In contrast, tangentially irradiated regions of the body (e. g. lateral hip, inner thigh, lateral calf) were often found to have more variation. Also in thin areas of the body (e. g. hands, fingers and toes) or specific anatomic sites, as eyelid, top of head, axilla or perineum significant dose deviations on thermoluminescent dosimetry were measured. The authors conclude that patient positioning is of paramount importance especially during the treatment of the four oblique fields. Antolak et al. [18] reported the individual dosimetric results of 72 TSEI patients. The study similarly focused on dosimetric results of TLD measurements of specific anatomic sites and the

related problem of underdosage from self-shielding. Other study groups using a similar technique reported only limited data of small patient populations [19–21]. Overall, most reports presenting the results of dosimetric measurements confirm that uniformity of dose distribution using a modified Stanford technique varies from 90 to 110% [17, 18].

While the above-mentioned studies focused on a patient-to-patient variability of dosimetric inhomogeneity of specific anatomic sites, our study focused on the adjustment of monitor units of standard fields needed to obtain the prescribed dose. Thirty-one patients received total skin electron irradiation using 12 treatment fields. For these patients the application of the standard six dual fields showed good correlation to the prescription dose and only in 33% monitor units needed to be corrected. In contrast, 66% of patients receiving a partial skin electron irradiation needed an individualized dose optimization of single or multiple fields. Unfortunately, the correlation between required MU corrections and patients' characteristics, like height, weight or body shape, could not be adequately studied, as detailed information was not available.

Our TSEI technique is a modification of the Stanford technique [5] and slightly differs from other reported techniques. One of the unique modifications was the addition of a custom-made platform with a 0.8 cm acrylic glass cylinder that was built to obtain a more homogenous distance of approximately 30 cm from the acrylic glass cylinder to the patient's skin surface (Figs. 3 and 4). While other institutions [3, 17, 18] use a straight scatter plate, we found a more uniform dose distribution using this cylinder-shaped beam spoiler. Furthermore we adapted the large electron field technique to treat partial skin lesions of the upper or lower body part. This technique was used in palliative settings for skin metastases (e.g. metastasized breast cancer or lymphomas) or to split the TSEI treatment into two treatment cycles in cases of frail patients presenting with comorbidities, as the TSEI can be very time-consuming and involves the standing position of the patient of up to 60 min.

One unavoidable limitation of this retrospective study is the small sample size. Larger series are needed, to validate the observations of the present study. However, the present dosimetric results are a good source of information on in vivo thermoluminescent dosimetry in TSEI and PSEI and contribute to the small amount of existing data within this setting.

In conclusion, due to the data presented and discussed here, in vivo dosimetry is of essential importance for TSEI in clinical practice. A routine use of TLD measurements for TSEI should be strongly recommended. Although the method remains time-consuming, thermoluminescent dosimetry allows to identify areas of under/over-dosage in order to minimize dose heterogeneity through patient positioning errors. Furthermore, thermoluminescent in vivo dosimetry is a precise tool to optimize MUs of standard fields to obtain the prescription dose. Especially in cases of PSEI, TLD measurements enable a reliable dose optimization of individualized non-standard fields and should therefore be mandatory.

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