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Review

Total skin electron beam (TSEB) therapy in pediatric patients: A review of the literature

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ABSTRACT

Aim: A literature review was undertaken to identify current TSEB therapy in pediatric patients.

Background: Total skin electron beam (TSEB) therapy is a method of irradiation with low energy electron beam dedicated to patients who have superficial skin lesions all over their body. Such skin malignancies are sparse among adults and even more uncommon with pediatric population.

Materials and methods: In this study, all reported case reports were summed up with a special emphasis on techniques used, doses prescribed and special shielding of critical organs. Moreover, potential problems that were encountered during TSEB irradiation of very young patients were depicted.

Results: The literature has described only seven case reports of children undergoing TSEB therapy. Most of them were infants; however, two adolescents were also treated. For all infants, general anesthesia was provided to allow safe and accurate TSEB irradiation. The prescribed dose varied from 16 Gy to 28 Gy depending on the irradiation schedule and patient condition. Usually, boost fields were applied to the scalp and perineum. Typical shields for fingernails, toenails and lenses were usually used.

Conclusion: This paper revealed that TSEB therapy may be considered as a palliative treatment for pediatric patients with leukemia cutis. However, its role is still unclear and should be further investigated.

1. Background

The idea of total skin electron beam (TSEB) therapy is to deliver a prescribed dose only to the patient's skin and to protect as much as possible healthy tissues inside the body. Electron beams of energy range 3–7 MeV are preferred for such task[1,2] due to their depth dose distribution which is characterized by a rapid fall off after reaching its "peak" at a shallow depth. This technique has been used for adults for many years to treat rare skin diseases such as mycosis fungoides, Sezary syndrome or Kaposi sarcoma[3–8]; however, it is uncommon in the

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pediatric population. Many various techniques of TSEB therapy for adults have been described in the literature[1,9–13] and lately two large reviews of all current techniques have been published by Diamantopoulos et al.[14] and Piotrowski et al.[15]

TSEB therapy is also used to treat pediatric patients with leukemia cutis (LC). LC, also called a cutaneous granulocytic sarcoma, is a term for an extramedullary leukemia where malignant leukocytes infiltrate into the skin[16]. The disease manifests with widespread bluish purple papules, nodules or plaques[17]. They may be different in size and appear on patient's face, legs, arms and trunk[18,19]. LC is a very rare disease and usually associated with poor prognosis[20]. It can occur before or after establishment of systemic leukemia and is more common in children than adults[16].

Literature on TSEB for pediatric patients is very limited and mostly described in brief case reports[20–24]. The first such description for a pediatric patient with LC was made by Rubin et al.[21] in 1985. Then in 1995, a detailed paper was published by Earley et al.[22] where the whole TSEB procedure for infants was depicted. In 2007, two more case reports were presented by Pepek et al.[23] Lately, Bao et al.[24] provided a report for a commissioning and quality assurance method of implementing TSEB therapy to a sedated infant, and Majd et al.[20] provided another case report on LC treated with TSEB therapy. Although new technologies have revolutionized the field of radiation oncology,[25–28] the TSEB irradiation of children has not changed so much since 1985.

1.1. *Aim*

The purpose of this study is to summarize the techniques applied in TSEB therapy for pediatric patients with LC and to report about common methods as well as potential problems of such therapy and how they have been solved in the literature.

2. Patients

To the best of my knowledge, only seven pediatric patients treated with TSEB have been reported in the literature. Most of them were infants (median age 14 months, range 12–17 months) and two patients were 13 and 18 years old. Among this group, there were three males and two females. The sex of two patients was not reported. The disease manifested with raised, violaceous nodules on the scalp, face, arms and back. Skin biopsy was done in all cases, LC was confirmed and TSEB treatment offered.

3. Techniques of irradiation

TSEB therapy has a long history in treating skin diseases. There are three main techniques of TSEB irradiation that have been well described in the literature.[29,30] Apart from them, there are many modified techniques that are combinations of the above mentioned ones. All modified techniques are well summarized in the paper by Diamantopoulos et al.[14]

For children, the most popular TSEB was a modified Stanford technique which was applied in four out of seven patients. In a paper presented by Pepek et al.,[23] a rotational TSEB technique was used, while Rubin et al.[21] used a multiple-field pendulum-arc technique. In the two cases described by Pepek et al.,[23] utilizing a rotational technique was possible as the patients were 13 and 18 years old. Thus, it was possible for them to stand on a spinning platform during irradiation with electrons. The rest of the patients were infants that were not able to stand on their own during the treatment. For this reason, some children[20,21,24] were placed in a custom-made harness which was attached to a special frame. Arm positions were secured with velcro strips and tape. Earley et al.[22] proposed infants to be irradiated in a lying position. The patient was positioned on a Plexiglas platform that was used for lifting and moving. For anterior and posterior fields, the child was irradiated lying on the floor with gantry angle set at 0°. For oblique fields it was lying on a table with gantry angle set at 60°. Arms and legs were adjusted appropriately for each field. The source-skin distance (SSD) was set to 200 cm. Fig. 1 provides a schematic picture of most popular TSEB techniques for children. To allow safe and accurate TSEB irradiation for all infants, general anesthesia was provided.

4. Dose prescription

TSEB therapy for children was planned mostly with 6 MeV; however, Rubin et al.[21] used 8 MeV degraded electron fields. The prescription doses varied from 16 Gy to 28 Gy. The irradiation schedule differed across radiotherapy centers and patient conditions (Table 1).

Additional boost fields were added to irradiate areas that received low doses from a normal TSEB treatment. Usually, boost fields were applied to the scalp and perineum. A boost dose can be assessed based on the underdosage of each region during a main TSEB treatment. Only in one case,[24] a bolus of 1 cm was used to boost the top of the head with 6 MeV electron beam energy. In the other case reports, no bolus was used during the treatment.

5. Shields

During TSEB therapy for children, some parts of the body should be shielded. This applies mostly to finger tips and toes since those areas are very thin and can experience much higher dose than the rest of the skin. Another organ that may be shielded during TSEB therapy are lenses since they are very sensitive to radiation dose. Depending on the degree of skin involvement, shields are included throughout or during part of the treatment course.

Pepek et al.[23] reported that eye shields were used for both patients throughout the treatment. Fingernails as well as toenails were also covered during the whole TSEB therapy for one of the patients (the younger one). The other patient received shielding of the nails after 12 Gy. Majd et al.[20] used only shields for fingernails. An interesting shielding was provided by Earley et al.[22] Beside external eye shields, special wax compensators around hands and feet were attached with lead shields for nail beds. Since the volume of infant's hand and foot is very small, the danger of overdosage to those areas is highly probable. For this reason, extra wax was added until the fist and foot had

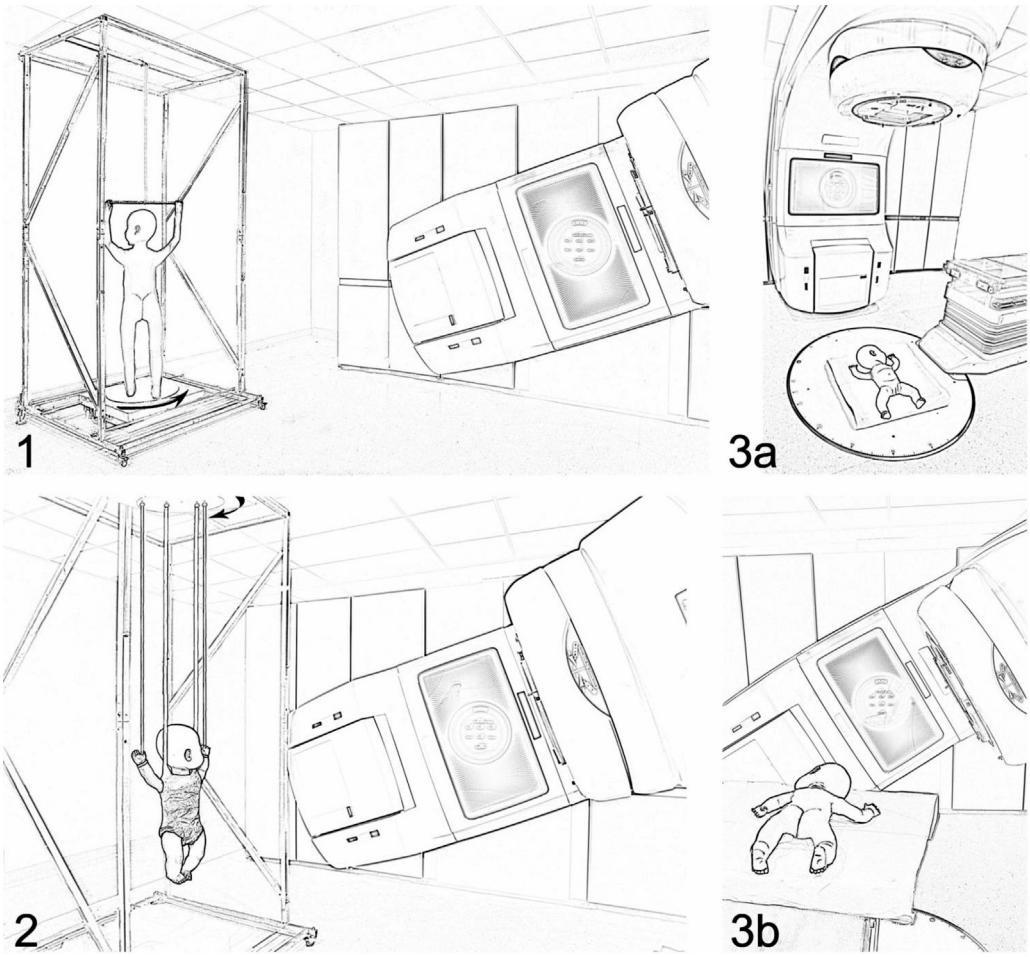

Fig. 1 – The most popular patient positioning for total skin electron beam therapy for children: (1) rotational technique – possible only for children who can stand on their own; (2) modified Stanford technique in vertical position – the infant was placed in a custom made harness attached to a special frame; (3) modified Stanford technique in horizontal position: (3a) treatment of the anterior and posterior fields – the gantry is set at 0° (3b) treatment of the oblique fields – the gantry is rotated 60° off vertical. For (2) and (3) arms were positioned to match the standard positioning.

Table 1 – Published case series of TSEB therapy for pediatric patients.

References	Age	Sex	Total dose [Gy]	Fractionation	Local boost
Rubin et al. [21]	13 months	Female	19	1.12 Gy/fx	12 Gy to perineun (3 Gy/fx)
Earley et al. [22]	14 months	Male	28	2 Gy/fx (2 treatments per week)	Not reported
Pepek et al. [23]	13 years	Male	16	2 Gy/fx (3 treatments per week)	6 Gy to scalp (2 Gy/fx)
	18 years	Male	18		None
Bao et al. [24]	17 months	Not reported	16	2 Gy/cycle[a] (2 days per cycle[a])	None
	12 months		16		To scalp (dose not reported)
Majd et al. [20]	15 months	Female	16		To perineum and plantar surfaces (dose not reported)

[a] Each cycle consists of 2 treatment days with 3 dual fields each.

diameters of at least 5 cm. The authors showed that this is the minimum thickness that should be provided to prevent high doses.

6. Potential problems

TSEB therapy for children can be administered without problems to adolescents as described by Pepek et al.,[23] because the patient can stand on their own and cooperate with the radiotherapy staff. The problem begins when a very young pediatric patient has to be irradiated. The most difficult part was to set up an infant for the time of treatment. In all cases where infants underwent TSEB therapy, the staff decided that anesthesia was necessary for proper immobilization. Due to this fact, the vital signs of the patient had to be monitored; however, the staff should always remember that such equipment should not shield the skin of the patient. To smear out the shielding effect of blood pressure cuff, it should be placed in different positions during the course of treatment.[24]

The infants were mostly irradiated in a custom made harness attached to a specially constructed frame.[20,21,24] As a result, the child was suspended above the floor and its trunk was rotated from above when necessary with arms positioned using velcro strips and tape as in the Stanford technique. In this setup, the harness covers the whole trunk and should be made from a fabric that does not attenuate the electron beam while being able to support the child. This problem does not exist when an infant is irradiated in a lying position as described by Earley et al.[22] In such case, the patient is naked, so, to maintain the body's temperature, a heat lamp should be present (outside the treatment field).

TSEB therapy in the case of infants brings also the problem of overdosage in very small volumes such as fingers and toes. Earley et al.[22] measured dose uniformity with thermoluminescent dosimeters (TLDs) and specially designed phantoms of different sizes, their diameters ranging from 1 cm to 7.5 cm. The results showed that the dose to the smallest phantom was approximately 4 times higher than that delivered to the skin of the trunk. The overdosage of small body parts can cause a bone growth disorder resulting in structural asymmetry. As a result, they suggested that any body part that is smaller than 5 cm in diameter should be compensated with wax.

7. Toxicity

TSEB therapy was always well tolerated by the patients. However, some mild skin toxicity appeared – it consisted of hyperpigmentation, dryness and minimal erythema. Only for one case, desquamation was reported.[21] Pepek et al.[23] noted that one of the patients developed grade 2 oral mucositis. Moreover, a mild fatigue could often be observed during the treatment.

8. Results of the treatment

In most publications regarding TSEB therapy for children, a significant improvement in skin lesions was noticed.[20–23] Rubin et al.[21] reported that all skin nodules disappeared and 12 months after the treatment the child remained in complete remission. Earley et al.[22] noted that 3 months after TSEB therapy the skin remained free of disease and healthy in appearance. However, the child relapsed of his initial disease so the prognosis was poor. Significant improvement of the skin lesions after TSEB treatment was also reported by Pepek et al.[23] Both patients did not develop any skin recurrence after 4 and 19.5 months after TSEB therapy, respectively, before dying due to complications of sepsis. A relapse of initial disease during the course of treatment was noted by Majd et al.[20] Although, radiation therapy improved skin lesions, the infant died due to leukemia progression.

9. Conclusions

All case reports mentioned that improvement of patient's skin lesions and nodules could be observed after TSEB therapy. Unfortunately, most of these patients died from sepsis after bone marrow transplant or due to the relapse of the initial disease in the bone marrow. However, based on the published case reports, one may assume that TSEB therapy might be used as a palliative treatment of young patients with LC.

Further data are needed to verify if TSEB therapy affects overall survival for pediatric patients. Moreover, before such treatment, one has to consider the long-term toxicity since tolerance for irradiation of total skin in very young patients is still unknown.

Conflict of interest

All authors have no actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three years of beginning the submitted work that could inappropriately influence, or be perceived to influence, their work.

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None declared.

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