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Total Body Irradiation Using a Modified Standing Technique: In Vivo Dosimetry with Semiconductor Diodes

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ABSTRACT

The aim of this study was to establish a fast and simple online dosimetric verification method for total body irradiation (TBI) using semiconductor diodes. Twenty one patients were treated with fractionated TBI (12 Gy, 2 Gy BID) using a modified standing technique between February 2010 and March 2012. The prescribed dose was administered to the patient's mid-plane at the level of the umbilicus. The lungs were shielded to allow only the absorption of an 8 Gy dose. To verify the dose administered during TBI, 12 semiconductor diodes were attached to the patient's skin to measure the entrance and exit doses at six anatomical reference points (umbilicus, lungs, neck, forehead, hand, and knee). An adapted version of the arithmetic method which uses a correction factor was used to calculate the mid-plane doses from the entrance and exit dose measurements. The mid-plane doses were then compared with the expected doses. The results of in vivo dosimetry showed that the mid-plane dose calculations conducted using the adapted arithmetic method were consistent with the expectations of the treatment plan. The average percentage dose differences and standard deviations were -0.5 ± 5.3 % for the neck, -2.1 ± 3.7 % for the umbilicus, 2.8 ± 5.2 % for the forehead, and -5.9 ± 11.1 % for the lungs. The extremity doses (hand and knee) were not calculated in the treatment planning program; however they were measured for documentary purposes. In vivo dose verification under TBI conditions was efficiently conducted through the use of semiconductor diodes. The measurement results were consistent with treatment plan dose calculations. The modified standing technique provides a practical method for TBI treatments. The observed heterogeneity is acceptable, the technique does not require additional shields or bolus material, the dosimetric verification is simple and fast, the set-up of the patient is easily reproducible, and the treatment time is within the acceptable limits for a non-dedicated treatment machine.

Keywords: Total body irradiation, In vivo dosimetry, Semiconductor diodes

ÖZET

Modifiye-Ayakta Tedavi Tekniği ile Tüm Vücut Işınlaması: Yarı-iletken Diyotlarla İn-vivo Dozimetri

Bu çalışmada amaç tüm vücut ışınlamasında (TVI) hızlı, kolay ve eşzamanlı bir dozimetrik doğrulama yöntemi olan yarı iletken diyotları klinik uygulamaya geçirmektir. Şubat 2010 ve Mart 2012 tarihleri arasında 21 hastaya modifiye-ayakta tedavi tekniği ile fraksiyone TVI uygulanmıştır (12 Gy, 2 Gy BID). Tanımlanan doz umbilikus hizasında orta-hatta olacak şekilde uygulandı. Akciğerler toplamda sadece 8 Gy doz soğurulacak şekilde korundu. TVI sırasında verilen dozu doğrulamak için 12 yarı iletken diyot cilt yüzeyine, giriş ve çıkış dozlarını ölçecek şekilde, altı farklı anatomik referans noktasına (umbilikus, akciğer, boyun, alın, el ve diz) yerleştirildi. Orta-hat dozları aritmetik metodun düzeltme faktörü içeren bir uyarlaması ile giriş ve çıkış doz ölçümleri kullanılarak hesaplandı. Daha sonra orta-hat dozları beklenen dozlar ile karşılaştırıldı. İn vivo ölçümler sonucu orta-hat dozu hesabında düzeltme faktörlü aritmetik metod kullanımı ile tedavi planları arasında uyum görülmüştür.

Ortalama yüzde farkları ve standart sapmaları boyunda %-0.5 ± 5.3, umbilikusta % -2.1 ± 3.7, alında %2.8 ± 5.2 ve akciğerde %-5.9 ± 11,1 olarak bulunmuştur. Ekstremite dozları (el ve diz) tedavi planlamasında hesaplanmamış, fakat kayıt amaçlı ölçülmüşlerdir. TVI koşullarında in vivo doz doğrulaması yarı iletken diyotlar kullanılarak etkin bir biçimde yapılabilmektedir. Tedavi planlamasından gelen hesaplarla ölçüm sonuçları birbirleriyle uyumludur. Modifiye-ayakta TVI pratik bir tedavi tekniğidir. Heterojenite ek koruma veya bolus gerektirmeden kabul edilebilir değerlerde kalmaktadır. Dozimetrik doğrulama ölçümleri kolay ve hızlı bir biçimde yapılabilmektedir. Tedavi kolayca tekrarlanabilmekte ve tedavi süresi TVI'a adanmamış tedavi cihazları için makul değerlerde kalabilmektedir.

Anahtar Kelimeler: Tüm vücut ışınlaması, In vivo dozimetri, Yarı-iletken diyot

INTRODUCTION

Total body irradiation (TBI) is used as a conditioning agent to kill acute leukemia (AL) or non-Hodgkin's lymphoma (NHL) tumor cells prior to autologous or allogenic bone marrow transplantation. TBI associated with chemotherapy eradicates tumor cells from sanctuary sites and causes severe immunosuppression, allowing for the engraftment of transplanted stem cells. However, TBI can be toxic to normal tissues. The acute side effects include mucositis, dysphagia, diarrhea, parotitis, erythema, pneumonitis and veno-occlusive disease. The long-term side effects include cataracts, increased risk of second malignancy, nephrotoxicity, hypothyroidism, sterility and pulmonary insufficiency.[1-4]

The total dose delivered to the patient has been predominantly limited by fatal pulmonary toxicity from interstitial pneumonitis, which is also influenced by the dose rate and fraction dose. Volpe et al. showed that a mean lung dose greater than 9.4 Gy causes lethal pulmonary complications.[5] Another study by Singh et al. showed that regimens with 9 and 6 Gy mean lung doses significantly improved survival compared to a 13.6 Gy regimen.[6] In addition, a dose of more than 12 Gy has no significant effect on long-term disease free survival.[7]

TBI was originally delivered as a single fraction, and for many years, 10 Gy single fraction TBI was the golden standard. However, it appeared that TBI fractionation could improve anti-leukemic effects without further increasing toxicity. A 12- to 13 Gy fractionated scheme can produce an anti-leukemic effect similar to that of the single dose 10 Gy scheme while causing less damage to the normal tissues.[8]

A variety of TBI treatment techniques has been developed. The choice of technique strongly depends on dose homogeneity, delivery accuracy, reproducibility, ease of dose verification and set-up. In addition to the delivery technique, there are many parameters that can influence the outcome of the treatment, including prescription dose, fractionation, dosimetric verification method, treatment planning, shielding of critical organs, treatment time and treatment equipment.[9]

Dosimetric verification must be performed before each TBI treatment. In vivo dosimetry is recommended as an independent final safety check not only for TBI patients but for the whole radiotherapy routine.[10] In the literature, several methods have been described for in vivo dosimetry, such as those involving semiconductor diodes, thermoluminescence dosimeters (TLDs), gafchromic films, and metal oxide semiconductor field effect transistor (MOSFET) detectors.[11-14] In our clinic, we established semiconductor diodes for in vivo dose verification because of their online readout and reuse advantages.[15]

MATERIALS AND METHODS

Patients

Twenty one consecutive patients were treated with fractionated TBI using the modified standing technique between February 2010 and March 2012. The patients received 2 Gy fractions twice a day, over three days, for a total dose of 12 Gy in six fractions. The treatment was administered with a minimum of six hours between fractions.

The patients were positioned lying on a computed tomography table with their knees bent and their hands at their sides. The CT was an 80 cm bore GE LightSpeed RT. The big bore allowed a whole body scan with bent knees. Knee and hand thicknesses and the tissue thicknesses of umbilicus, forehead, and neck levels were measured along with off-axis distances (origin at the umbilicus) for use in treatment planning. These regions were expected to affect the homogeneity of the delivered dose because of the different thicknesses with respect to the um-

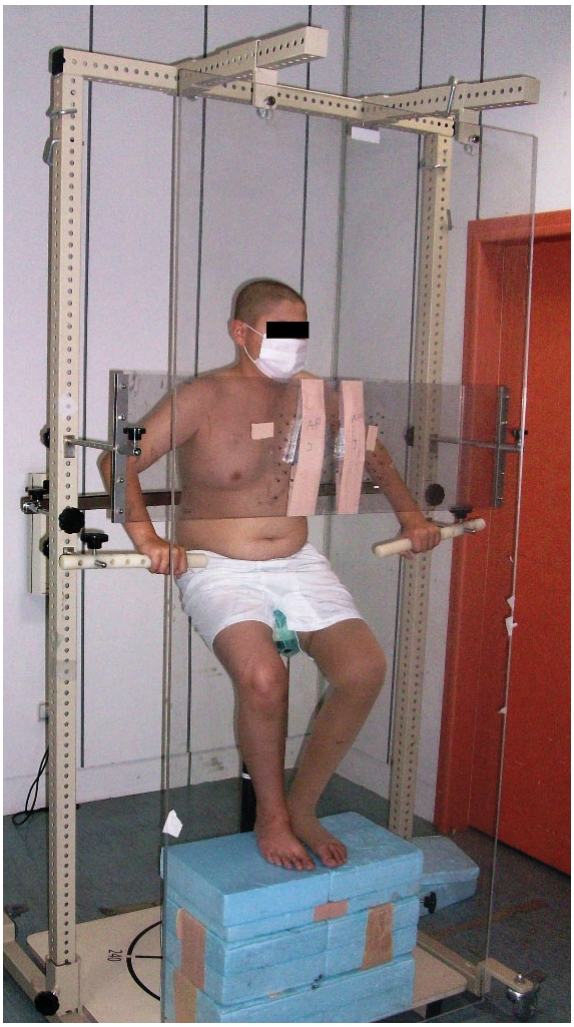

Figure 1. TBI treatment stand. The patient is facing the machine for the AP field.

bilicus level or because of the distance from the beam center. Lung contours were drawn based on computed tomography scans of the patients. Lung shields were virtually simulated in the Precise™ treatment planning system using these lung contours. The lung shields were molded from Cerrobend alloy and had a thickness of 1.6 cm to allow only two-thirds of the total dose, corresponding to 8 Gy, to be absorbed by the lungs.

Treatment Technique

The treatment was performed with an Elekta Synergy Platform™ Linear Accelerator using a 4 MV photon beam at a dose rate of 300 MU/min. A source axis distance (SAD) of 342 cm was necessary because of the limitations of the treatment room. At the isocenter (100 cm), the maximum field size of the linear accelerator was 40x40 cm^2, which extrapolates to 136.8 x 136.8 cm^2 at a SAD of 342 cm. With a gantry angle of 90^0 and a collimator angle of 45^0, the patients fit in this field with their knees bent, sitting on a saddle.

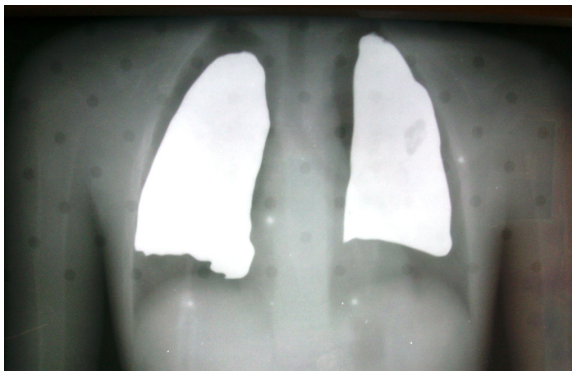

Figure 2. The placement of the lung shields was controlled for each fraction and each field using Kodak X-OMAT™ port films.

The patients were treated with anterior and posterior (AP/PA) fields using a modified standing position. The AP/PA TBI was preferred over other TBI delivery techniques because this arrangement provided sufficient dose homogeneity and effective lung shielding with easy patient set-up. A 1.5 cm Perspex™ [polymethyl methacrylate (PMMA)] screen was used as a spoiler to increase the skin doses. The use of the screen increased the skin dose up to 11% at 1 mm and 3% at 3 mm. Individualized Cerrobend lung shields were designed and supported behind the screen with a height-adjustable Perspex holder. The patients sat on a height-adjustable saddle facing the machine for the AP field and facing the wall for the PA field, with their arms at their sides holding adjustable handlebars (Figure 1).

A height-adjustable film cassette holder was fixed at the back of the TBI stand, which was positioned at the level of the lungs for each patient. At the beginning of each fraction, the positions of the lung shields were verified by AP and PA Kodak X-OMAT™ port films (Figure 2).

Treatment Planning

The isocenter was adjusted to the patient's mid-plane at the level of the umbilicus. A total of 200 cGy was administered to the isocenter with AP and PA

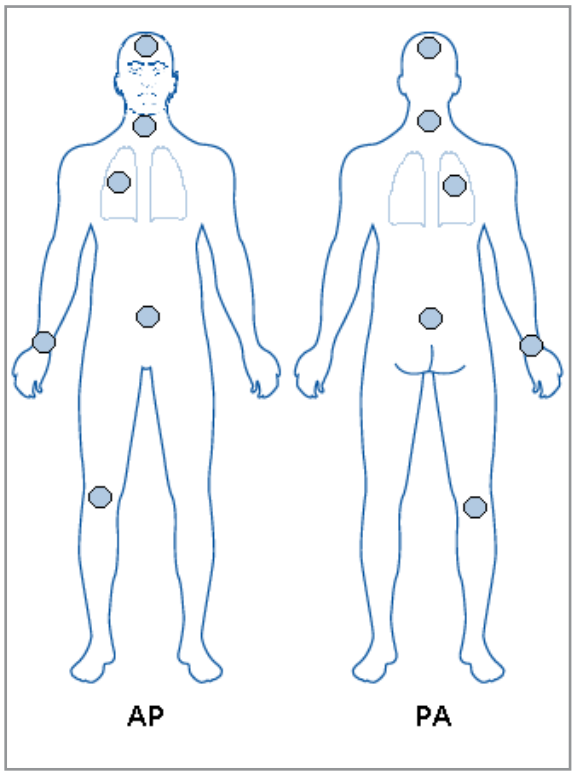

Figure 3. In vivo semiconductor probe positioning for six anatomical reference points to measure entrance and exit doses.

fields. Monitor units (MU) were calculated using an Excel™-based home-made treatment planning program (Created by Nina Tuncel). MU calculations for both the AP and PA fields were performed using pre-measured mid-plane dose tables under TBI conditions (4 MV, 40x40 cm^2 field, gantry 90^0, collimator 45^0, SAD 342 cm).

The dose heterogeneity at the forehead and the neck was calculated using both the pre-measured mid-plane dose tables and the pre-measured off-axis ratios. If the dose heterogeneity surpassed 10%, a bolus was wrapped round the neck to compensate for the decreased thickness of the tissue in this part of the body. Out of the twenty one treated patients, only one needed bolus material around the neck.

Dosimetry

Iba-Wellhofer™ semiconductor diodes were used with OmniPro-InViDos™ software for online dosimetric verification. The diodes were calibrated under TBI conditions.

At the beginning of the first fraction, 12 semiconductor diodes were attached to the patient's skin at six anatomical reference points (umbilicus, lungs, neck, forehead, hand, and knee) to measure the entrance and exit doses (Figure 3).

Three consecutive measurements were performed with 100 MUs for both the AP and PA fields. The entrance and exit doses were acquired using the semiconductor diodes. The mid-plane doses ($D_{Mid\text{-}Plane}$) at the six anatomical reference points were calculated from the average of the entrance and exit doses. An arithmetic correction factor (CF_a) was constructed as a function of the half-thickness. The corrected mid-plane doses were calculated using the mid-plane dose and the correction factor ($D_{C\text{-}Mid\text{-}Plane}=D_{Mid\text{-}Plane} \times CF_a$) and were compared with the expected doses.[16]

RESULTS

Treatment Planning

The prescribed dose was 200 cGy per fraction to the patient's mid-plane at the umbilicus level. All patients received a dose of 12 Gy in six fractions. The half-thicknesses of the patients at the level of umbilicus varied from 6.5 to 11.5 cm, resulting in MUs ranging from 1247 to 1413 per fraction for the AP and PA fields. The average and standard deviation of MU was 1320 ± 54. The dose to the lungs was predetermined to be two-thirds of the total dose, corresponding to 8 Gy total or 133 cGy per fraction. The doses to the forehead and neck regions were calculated from a home-made treatment planning program with the use of pre-measured dose tables for half-thicknesses and off-axis ratios. The average dose per fraction for the neck was calculated to be 211.6 ± 10.4 cGy. Treatment plan calculations for the forehead gave an average of 193.5 ± 7.0 cGy. A quantitative analysis of treatment plan calculations for the twenty one patients is provided in Table 1.

In vivo Dosimetry

The treatment plan calculations were consistent with the mid-plane dose measurements performed using the arithmetic correction factor, CF_a. The average mid-plane dose measurements for the twenty one patients conducted using the adapted

Table 1. Summary of treatment plan dose calculations and in vivo dose measurements per fraction for twenty one patients.

Anatomical reference point	Treatment plan Mean ± SD (cGy)	In vivo measurements Mean ± SD (cGy)	Average differences % ± SD %
Umbilicus	200	196.2 ± 7.2	-2.1 ± 3.7
Lungs	133	127.0 ± 14.9	-5.9 ± 11.1
Neck	211.6 ± 10.4	211.1 ± 11.3	-0.5 ± 5.3
Forehead	193.5 ± 7.0	199.5 ± 10.9	2.8 ± 5.2
Hand	Not calculated	241.5 ± 16.9	–
Knee	Not calculated	254.0 ± 14.2	–

The dose to the umbilicus mid-plane was taken to be 200 cGy, and the dose to the lungs was 133 cGy. Percent differences were calculated per patient, and the average percent difference was tabulated for each reference point.

arithmetic method were 196.2 ± 7.2 cGy for the umbilicus, 127.0 ± 14.9 cGy for the lungs, 211.1 ± 11.3 cGy for the neck, 199.5 ± 10.9 cGy for the forehead, 241.5 ± 16.9 cGy for the hand and 254.0 ± 14.2 cGy for the knee. A summary of the in vivo measurement results is presented as a box-whisker plot in Figure 4.

The treatment plan calculations and in vivo dosimetry measurements were compared for four anatomical reference points. The average percentage dose differences and standard deviations from smallest to largest in magnitude were -0.5 ± 5.3 % for the neck, -2.1 ± 3.7 % for the umbilicus, 2.8 ± 5.2 % for the forehead, and -5.9 ± 11.1 % for the lungs (Table 1).

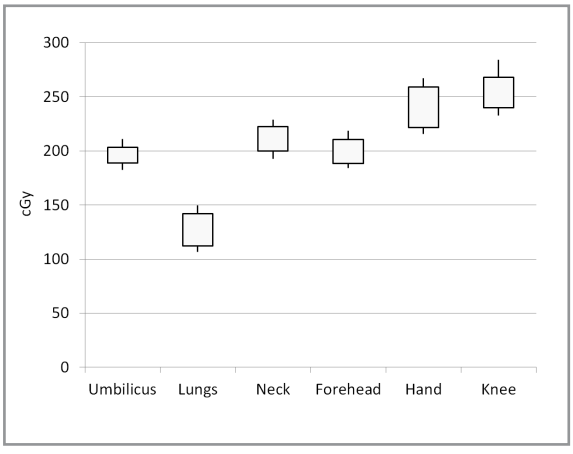

Figure 4. Summary of in vivo measurement results presented as a box-whisker plot. The box represents the standard deviation and the whiskers represent minimum and maximum values for twenty-one patients.

DISCUSSION

In this study, we treated twenty one patients with fractionated TBI using a modified standing technique. The use of AP and PA fields to deliver TBI allowed for a rapid and reproducible set-up of less than 10 minutes. For the first fraction only, the in vivo measurements took approximately 20 minutes. The total treatment time per fraction without measurements was 30 minutes, suggesting that the day-to-day treatment of routine radiotherapy patients would not be disrupted. The use of AP fields rather than lateral fields also improved the dose homogeneity. Apart from the lung region, which received a total dose of 8 Gy, there were no low-dose sanctuary sites. The doses to the hand, knee, and neck were higher than the prescribed dose. TBI protocols require a dose homogeneity along the body within ± 10%, except at the extremities.[17] Only one patient surpassed the 10% heterogeneity level at the neck reference point (229.6 cGy), which was compensated for by a 1 cm thick bolus material wrapped around the neck. In vivo measurements for the hand and knee reference points demonstrated high dose values of up to 30% with respect to the 200 cGy prescribed dose; this is to be expected, as extremities have small half-thicknesses with respect to the umbilicus.[14]

The calculations of the treatment plan were verified by in vivo dosimetric measurements to be within a 6% error range, which is consistent with values in the literature.[14-15,18-19]

The modified standing TBI technique is simple to use, is well tolerated by patients, can be easily and efficiently incorporated into the routine workload of a radiotherapy department, and allows for accurate and fast dose measurements.[20]

In vivo dose verification of TBI using the modified standing technique was successfully performed using semiconductor diodes. At the anatomical reference points, the measured dose was within acceptable limits with respect to the calculated dose. Semiconductor diodes are recommended for TBI dose verification not only because of their measurement efficiency but also because of their simple setup, online readout and reusability.

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