The efficacy and reliability of lung protection during total body irradiation of patients with disseminated malignancies*

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The main problem in total body irradiation (TBI) is obtaining a homogenous dose distribution inside the whole irradiated body and ensuring appropriate dose reduction in the lungs. The process of irradiation should be comfortable for the patients and repeatable despite the size and age diversity among patients.

The aim of this paper was 1) to check accuracy of the applied dose algorithm and reliability of the measurement technique used in the lung region during TBI taken alternatively on a Cobalt-60 unit and on 15 MV linear accelerators, and 2) to check if the described methodology made it possible to obtain reproducibly of the lowered level of the dose to the lungs for a diverse group of patients.

TBI was performed as a preparatory regiment in children and adults with disseminated malignancies undergoing bone marrow transplantation (a dose of 12.6 Gy in the midline/central beam axis). Two consecutive groups of patients were retrospectively included in the study: 15 irradiated with Cobalt-60 and 15 with 15 MV photons. The doses were evaluated for three sections passing through the middle of the lungs and at their upper and lower sides. Two types of detectors: semiconductor and thermoluminescent ones were used simultaneously. The measured doses were evaluated statistically to reveal agreement between readings of the two types of detectors and agreement between the measured doses and those previously calculated.

The results of measurements exhibited a not Gaussian-type distribution (dissymmetry). The Wilcoxon-type test revealed compliance between the doses measured with thermoluminescent (TL) and semiconductor (SEM) detectors for all sections passing through the lungs ($p>0.05$), excluding the lung exit (middle and lower sides) with the Cobalt therapy. The t-Student test used to compare the measured doses with those previously calculated revealed agreement ($p>0.05$) between the measured doses and those calculated for all lung sections for the 15 MV photon therapy, while for Cobalt therapy such an agreement was at some points doubtful.

The calculation algorithm and measurement techniques have proved to be correct, which was revealed by agreement between the doses measured and those calculated. The shielding of the lungs during both types of fields was effective and reproducible as indicated by agreement between the doses measured with the two types of detectors. Better agreement between the measured and calculated doses was found for 15 MV photons than for the Cobalt unit.

Key words: in-vivo dose measurements, TBI, dose accuracy, leukemia

Total body irradiation (TBI) is a widely used preparatory procedure in the treatment of a certain type of disseminated malignancies (i.e. in leukemia) [3, 4, 6, 7, 10, 14, 18, 30]. The main problem in TBI is to obtain a homogenous dose distribution inside the whole irradiated body and to ensure appropriate dose reduction in the lungs [3, 4, 6, 10, 22, 27, 28, 32–34]. The process of irradiation should be comfortable for patients and repeatable despite the size and age diversity among patients [1, 3, 10, 11, 29, 31]. Several modalities of such irradiation have been developed to meet individual and institutional conditions, e.g. the infrastructure (room size), type of therapeutic machine used, and the time which could be dedicated exclusively to this procedure [16, 17, 21, 26, 29–31]. Lung protection is the problem of the critical importance, because therapeutic doses lay above or close to the tolerance level of this organ. Therefore in this region an appro-

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priate protocol of *in-vivo* dosimetry is required, which involves usage of specifically calibrated detectors and the methodology of data interpretation [2, 5, 8, 9, 12, 13, 15, 19, 23, 24, 27].

The aim of this paper was 1) to check the accuracy of the applied dose algorithm and the reliability of the measurement technique in the lung region during TBI taken alternatively on a Cobalt-60 unit and on 15 MV linear accelerators, and 2) to check if the described methodology made it possible to obtain reproducibly lowered level of the dose in the lungs for a diverse group of patients.

Material and methods

Total body irradiation was performed as a preparatory regimen in children and adults with disseminated malignancies undergoing bone marrow transplantation. The total dose of 12.6 Gy was prescribed in the body midline on the central beam axis (CAX). The dose was specified in the section of coxa close to the mid-abdomen and umbilicus. The whole procedure was performed during four consecutive days, with two fractions per day.

The irradiation was performed between 1992 and 1997 using a Cobalt-60 unit, the details being reported by MALICKI et al [21, 23]. Since 1997 linear accelerators of various manufacturers (Saturne 43, Clinac 2300, Mevatron KD2) with the photon beam of 15 MV have been used. A combination of large lateral and antero-posterior (AP-PA) fields was used with the aim of delivering a homogenous dose to the body and of reducing the lung dose to a value below 10 Gy [21–23, 25, 26]. A dose of 8.2 Gy was delivered in 6 fractions (12 lateral fields) and a dose of 4.4 Gy in 2 fractions (4 AP-PA fields). The lungs were shielded only during AP-PA fields, when the patient was positioned on the floor. The distances from the source to the skin (SSD) were 307/206 cm at lateral/AP-PA fields for 15 MV, and 275/183 cm for Cobalt-60, respectively. The dose rates in the patient midline on CAX were approximately $(4.25/10.65)\text{x}10^{-2}$ Gy/min (lateral/AP-PA) for 15 MV, and $(6.67–9.01/17.75–27.90)\text{x}10^{-2}$ Gy/min for Cobalt-60, respectively [24, 26, 27].

A group of thirty consecutive patients was included in the study: fifteen patients were irradiated with Cobalt-60 and fifteen with 15 MV photons, respectively. The evaluation of the doses was made for the three sections passing through the middle of the lungs and near their upper and lower edges. The doses (D) were calculated before irradiation (formula 1) and then measured during irradiation.

$$D = D_{ref} * TPR * FP * (f_{ref}/f)^2 * K/K_{ref} * t \quad (1)$$

where D_{ref} is the dose measured at time unit in reference conditions; TPR – tissue-phantom ratio; FP – field profile; f_{ref} and f are distances from the source to dosimetrical point respectively at reference (ref) and present position; K, K_{ref} are temperature-pressure coefficients respectively at dosimetrical and reference (ref) conditions and t is a time of irradiation.

The size, shape and interior composition of these sections were taken from CT scans. The internal body inhomogeneity was accounted for in dose calculations using parameterisation of distance by density. The tissue-phantom ratios and field profiles were experimentally determined for the applied large distances and collimator angles in a long water phantom imitating the body size.

Two types of detectors, semiconductor p-Si type (SEM) and thermoluminescent Harshaw chips (TL), were used in-vivo and simultaneously. The dosimetrical points were located at the places where the beam entered and then exited the body. The measured doses were evaluated statistically to reveal agreement between the readings of the two types of detectors. Also agreement between the measured doses and those previously calculated was tested.

The evaluation was performed retrospectively, therefore the number of available data differed for various dosimetrical points due to the limited number of detectors, which could be used for this procedure. Consequently, only doses at the middle lung section were measured for each field and usually with two types of detectors. This situation, however, was taken into account during statistical analysis.

All the measured doses were normalized to those calculated. Consequently, if the value of the normalized dose was 1 then it was assumed to be in agreement with the value which was calculated for this dosimetrical point lying in the investigated region of the lungs. The doses calculated in the midline for the middle section of the lungs were 8.4–9.1 Gy (lateral fields considered) and 0.5–0.8 Gy (AP-PA fields) [22, 23, 25]. These dose ranges differed from those prescribed in the CAX/midline (8.2 Gy at lateral, 4.4 Gy at AP-PA). However, the obtained deviations reflected the diversity in individual body proportions in the whole group of patients and in the use of the lung shielding during AP-PA fields.

Consequently, the algorithm and measurement techniques were checked by comparing the readings of the detectors with the calculated doses, while the efficacy and reproducibility of the lungs protection was checked by evaluating the deviations between doses measured with the two types of detectors at the chosen lung sections.

Results

The results of measurements exhibited not Gaussian-type distribution (dissymmetry). Therefore, the Wilcoxon-type test (dependent samples) was used which revealed agreement between the doses measured with thermoluminescent and semiconductor detectors at the requested significance level of 0.05, for all sections passing through the lungs, excluding middle and lower sections of the lung at exit during the Cobalt therapy. The details of the statistical data are presented in Table 1 for the beam entry and exit, for lateral fields (a) and for antero-posterior fields (b), respectively.

Table 2 presents a number of collected data, mean, minimal and maximal values of the measured doses and their stan-

Table 1. The agreement (Wilcoxon test, dependent samples) between doses measured with two types of detectors with a Cobalt unit and with a 15 MV linear accelerator, for the beam entry and exit for (a) lateral fields, (b) antero-posterior fields

Section	Cobalt p	15 MV Linac p
Upper side of the lungs, entry: TL & SEM	0.4796	0.0665
Upper side of the lungs, exit: TL & SEM	0.2667	0.2506
Lungs (middle) entry: TL & SEM	0.1657	0.9695
Lungs (middle) exit: TL & SEM	0.0076	0.0583
Lower side of the lungs, entry: TL & SEM	0.1945	0.6857
Lower side of the lungs, exit: TL & SEM	0.0000	0.2913

Section	Cobalt p	15 MV Linac p
Upper side of the lungs, entry: TL & SEM	0.1095	0.6378
Upper side of the lungs, exit: TL & SEM	0.1394	0.1578
Lungs (middle) entry: TL & SEM	0.0918	0.6894
Lungs (middle) exit: TL & SEM	0.0019	0.1978

TL – thermoluminescent, SEM – semiconductor, N – number of measurements, p – significance level.

dard deviations (SD) for patients treated with a Cobalt-60 unit and with 15 MV photons, respectively.

The t-Student test was used to compare the measured doses with those previously calculated. The agreement between the measured and calculated doses at the requested level of confidence of 0.05 has been found for all sections passing through the lungs for the 15 MV photon therapy. The results of this analysis are given in Table 3.

Discussion

The lungs constitute the most critical region during total body irradiation. Some authors are doubtful about the need of lung shielding, however the doses in this region have to be checked. The doses in the middle of the lungs and near their upper and lower edges provide clinically important data related to the probability of early and late toxicity [6, 8, 10, 27].

All doses were collected for patients varying with in size and shape. Also in each field or fraction, the patient's position was slightly different, and consequently, the distances from the source to the measurement points were also different. This was taken into account in the calculations and affected both the calculated and measured doses. However, the

Table 2. Statistical data for a group of patients treated with a Co-60 unit and with a 15 MV linear accelerator for: (a) lateral fields, (b) antero-posterior fields

Section	N		Mean		Minimum		Maximum		SD	
	Co-60	15 MV	Co-60	15 MV	Co-60	15 MV	Co-60	15 MV	Co-60	15 MV
Upper side of the lungs, entry: TL	36	56	0.991	0.993	0.745	0.815	1.258	1.159	0.104	0.076
Upper side of the lungs, entry: SEM	36	56	1.007	1.017	0.918	0.859	1.294	1.182	0.059	0.067
Upper side of the lungs, exit: TL	24	49	1.128	0.982	0.924	0.769	1.780	1.196	0.195	0.104
Upper side of the lungs, exit: SEM	18	49	1.011	0.992	0.927	0.817	1.094	1.244	0.043	0.089
Lungs (middle) entry: TL	48	90	1.004	0.996	0.718	0.812	1.225	1.178	0.109	0.085
Lungs (middle) entry: SEM	203	90	1.010	0.995	0.442	0.844	1.183	1.125	0.081	0.066
Lungs (middle) exit: TL	36	70	1.002	0.989	0.615	0.748	1.357	1.203	0.151	0.110
Lungs (middle) exit: SEM	170	70	0.954	1.005	0.744	0.821	1.319	1.315	0.110	0.106
Lower side of the lungs, entry: TL	27	39	0.973	1.012	0.804	0.836	1.144	1.177	0.082	0.072
Lower side of the lungs, entry: SEM	32	39	0.997	1.019	0.937	0.912	1.066	1.165	0.034	0.064
Lower side of the lungs, exit: TL	32	45	0.837	0.992	0.777	0.779	0.906	1.307	0.034	0.110
Lower side of the lungs, exit: SEM	29	45	0.977	1.009	0.830	0.851	1.191	1.326	0.094	0.091

Section	N		Mean		Minimum		Maximum		SD	
	Co-60	15 MV	Co-60	15 MV	Co-60	15 MV	Co-60	15 MV	Co-60	15 MV
Upper side of the lungs, entry: TL	11	14	1.017	1.026	0.968	0.863	1.144	1.158	0.047	0.097
Upper side of the lungs, entry: SEM	11	14	0.983	1.041	0.859	0.873	1.035	1.160	0.051	0.078
Upper side of the lungs, exit: TL	10	14	1.003	1.025	0.865	0.859	1.258	1.127	0.117	0.090
Upper side of the lungs, exit: SEM	10	14	0.926	0.988	0.800	0.811	1.105	1.077	0.105	0.073
Lungs (middle) entry: TL	22	21	1.022	1.023	0.800	0.715	1.219	1.139	0.108	0.105
Lungs (middle) entry: SEM	52	21	0.996	1.021	0.929	0.874	1.138	1.145	0.041	0.081
Lungs (middle) exit: TL	17	19	1.035	0.995	0.898	0.895	1.201	1.120	0.091	0.072
Lungs (middle) exit: SEM	49	19	0.919	0.973	0.829	0.808	1.071	1.168	0.060	0.086

N – number of measurements, mean, minimal and maximal values of the doses measured, SD – standard deviations.

Table 3. The agreement between the measured and calculated doses (t-Student) for the lateral and antero-posterior fields.

Type of field ->	lateral		AP/PA	
Section/ type of therapeutic unit	Co-60	15 MV	Co-60	15 MV
	p	p	p	p
Upper side of the lungs, entry: TL	0.6145	0.4617	0.2593	0.3330
Upper side of the lungs, entry: SEM	0.4937	0.0552	0.3018	0.0674
xt180Upper side of the lungs, exit: TL	0.0039	0.2396	0.9464	0.3210
Upper side of the lungs, exit: SEM	0.2710	0.5322	0.0517	0.5495
Lungs (middle) entry: TL	0.7937	0.6300	0.3521	0.3310
Lungs (middle) entry: SEM	0.0753	0.4467	0.4948	0.2544
Lungs (middle) exit: TL	0.9388	0.4026	0.1273	0.7545
Lungs (middle) exit: SEM	0.0000	0.7019	0.0000	0.1972
Lower side of the lungs, entry: TL	0.0930	0.2842	no data	no data
Lower side of the lungs, entry: SEM	0.6603	0.0688	no data	no data
Lower side of the lungs, exit: TL	0.0000	0.6475	no data	no data
Lower side of the lungs, exit: SEM	0.1917	0.5222	no data	no data

TL – thermoluminescent, SEM – semiconductor, SD – standard deviation, N – number of measurements, p – significance level.

normalization procedure made this dependence avoidable and allowed to compare normalized doses for all fractions and patients, respectively.

The points at which doses were measured and calculated presented severe difficulties in determining and compensating for the dose algorithm (calculation) and in the measurement technique. The lungs represented region of physical complexity of both interior (low density) and outer contours, which differ in shape and size at each section.

The applied shielding made the determination of doses (both in the calculations and measurements) more complicated, which was noted during statistical analysis. Large standard deviations at certain points (Tab. 2) were probably caused by the attachment of detectors that was not reproducible rather than by the incorrect estimation of the lungs size and density. The shielded area during antero-posterior fields was small (in children), and there was sometimes not enough room to fix two types of detectors under the totally shielded region. A slight movement of the patient involved partial exposure and led to an increase in the reading. Consequently, the position of the detectors was not certain and deviations were larger. However, the lungs during AP-PA fields were shielded, and therefore they received only a fraction of the dose delivered to other parts of the body. In consequence, the larger standard deviations at AP-PA fields were not critical. During lateral fields the detectors had to be fastened to the thorax near the arm. Therefore, even slight movement of the arm (over 20 minutes of continuous irradiation) could shade the detector and thus increase the standard deviation. Also, during lateral fields boluses were used in the lung region, which made fastening of the detectors less reliable.

The results of the statistical analysis presented in Tables 1–3 show a better agreement between the measured and calculated doses for treatments performed with 15 MV photons than for those with Cobalt-60. This may only be explained by the constant improvement in quality assurance, which led to better accuracy in the measurements and in the dose delivery at the time when irradiations at the linac began.

The excessively low exit doses (mean: 0.954 and 0.837 – lateral; 0.919 and 0.926 – AP-PA, Tab. 2) during irradiation with a Cobalt unit need a more thorough analysis. The above deviations make it uncertain whether the results at these points are reliable. It seems however that the uncertainty involves the measurement technique rather than the real dose decrease. The readings of second type of detector at these points were in agreement with the calculations. Moreover, the above points lay in clinically different body parts during lateral (side under the arm), antero (thorax front) and posterior fields (back). The only common factor was that they were located always at the patient's side which was at a greater distance from the source and was partly hidden to the dosimetrist. Therefore, the position of the detector at that point was less accurate.

Conclusions

1. The calculation algorithm and measurement techniques have proved to be correct, as revealed by agreement between the doses measured and those calculated.

2. The shielding of the lungs during both types of fields and for all therapeutic units was effective and reproducible, as indicated by agreement between the doses measured with two types of the detectors.

3. Better agreement between doses measured and calculated was found for 15 MV photons (agreement for all dosimetrical points, both types of fields and detectors) than for the Cobalt unit (only few points without agreement).

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