Vox Sanguinis (2004) **86**, 105–110

ORIGINAL PAPER

Quality control system for blood irradiation using a teletherapy unit

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Vox Sanguinis

Background and Objectives Irradiation of whole blood and blood components before transfusion is currently the only accepted methodology to prevent transfusion-associated graft-vs.-host disease. In the present work, we developed an automated system for blood bag storage during irradiation, using a teletherapy unit.

Materials and Methods A device with two thermal compartments was constructed in acrylic and foam, for the storage of blood bags during irradiation. An automatic acquisition system, coupled with an amplifier and a thermal-sensitive probe, were developed to check blood temperature during irradiation. A polystyrene phantom was constructed to simulate the volume of blood routinely irradiated. The dose distribution was measured in the phantom using thermoluminescent dosimeters and represented in terms of isodose curves.

Results The thermal device kept the blood temperature below 6 °C for more than 2 h. Our system allowed the simultaneous irradiation of two different blood components while maintaining a constant temperature. The temperature monitoring system remained invariant (0·2 °C) over the whole irradiation interval. Phantom dosimetric results showed a homogeneous dose distribution when the phantom was irradiated, using rotational fields with a 2 r.p.m. frequency.

Conclusions The methodology developed in the present work provides appropriate storage conditions during irradiation of both red blood cells and platelet blood components using a teletherapy unit.

Received: 28 February 2003, revised 5 December 2003, accepted 4 January 2004

Key words: blood, graft-vs.-host disease, irradiation, quality control.

Introduction

Graft-vs.-host disease (GvHD) is commonly observed after allogeneic bone marrow transplantation, but rarely recognized after transfusion or solid-organ transplantation. Transfusion-associated graft-vs.-host disease (TA-GvHD) is a rare, but fatal, potential complication that occurs when viable donor T lymphocytes proliferate and engraft in susceptible patients after transfusion of whole blood and cellular components [1,2]. TA-GvHD can occur in severely immunocompromised patients, including patients with congenital immunodeficiencies, and in bone marrow transplantation recipients, as well as in patients with cancer treated using chemotherapy or radiotherapy [3–9]. TA-GvHD has also been reported in immunocompetent patients who have received blood from donors homozygous for shared human leucocyte antigen (HLA) haplotypes [10]. At least three factors appear to be directly related to the risk of TA-GvHD [11]:

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(1) The susceptibility of the patient's immune system to the engraftment.

(2) The degree of HLA similarity between donor and recipient.

(3) The number of viable donor lymphocytes present in the transfused components.

There is no effective treatment for TA-GvHD, and the irradiation of cellular blood components prior to transfusion has been the only proven method of preventing this reaction [12]. Gamma and X-rays, both representing ionizing radiation, damage DNA T lymphocytes and arrest responses to allogeneic cells [13]. Thus, these lymphocytes are unable to proliferate in the host and therefore cannot mediate TA-GvHD. A study carried out to evaluate the efficacy of irradiation by assessment of functional T cells using a limiting-dilution analysis that provides quantitative data on very low frequencies of proliferating T cells, showed that 2500 cGy may be required to completely inactivate T cells [13,14]. For patients at risk for GvHD, all components that might contain viable T lymphocytes should be irradiated, including red blood cells (RBC) and platelet components [15].

Blood irradiation can be performed using commercial irradiators designed specifically for blood irradiation, usually located in blood banks. Commercial irradiators incorporate one to four gamma ray sources, generally caesium-137 (0·662 MeV), of 22–89 TBq (600–2400 Ci) each, and typical initial dose rates range from 300 to 1000 cGy/min. In this case, a 2500 cGy minimum dose, necessary for TA-GvHD prevention, is delivered in few minutes. However, if a dedicated blood irradiator is not available, teletherapy units, such as linear accelerators or cobalt teletherapy machines, already available at many hospitals, can be used for this task [16–18], thus improving the cost/benefit ratio of the process. The use of cobalt teletherapy machines for blood irradiation may be inconvenient owing to the long time needed to deliver the minimum dose necessary for TA-GvHD prevention. Depending on the activity of the cobalt-60 source, irradiation can last for longer than 60 min. When blood irradiation is performed using a linear accelerator, the time necessary to liberate the minimum dose is reduced and the entire irradiation process is completed in 30 min [18]. In such cases, the blood components remain at room temperature (≈ 23 °C) during the irradiation process. RBC units should be stored at 2–4 °C, while platelets should be shaken gently during storage and maintained at 20–24 °C. Therefore, environmental conditions can degrade the quality of the blood components when irradiation is performed using a teletherapy unit. Despite the important role of teletherapy as an alternative means for blood irradiation, little attention has been paid to the quality of the blood irradiated using this equipment. We propose a system that allows controlled conditions during blood irradiation with a teletherapy unit. This system includes: a device with two thermal compartments; a data-acquisition system for temperature measurements; and a phantom, built with polystyrene plastic, used to simulate dose distributions in blood bags.

Materials and methods

The mechanical system used to store blood bags

A mechanical system was built to store blood bags during irradiation with teletherapy equipment. The system is composed of a cylindrical device, 20 cm in diameter and 20 cm in height, constructed of acrylic plates and foam, each 5 mm thick (Fig. 1). The thermal device was built with two compartments to allow simultaneous irradiation of approximately 13 platelet bags and six RBC bags. A thermal isolation system between the compartments was built to maintain storage temperatures of 2–4 °C for RBC and 20–24 °C for platelets, during irradiation. The simultaneous irradiation of these blood components is very important to optimize the time of use of the teletherapy unit. The thermal compartments were sealed and the temperature monitored using a thermometric probe. In order to assess the performance of each compartment, we drilled an opening on the cover and another in the divisory of the device which, when aligned, allowed the passage of a thermometric probe.

A platform with two columns was used to support the axis of the device (Fig. 2). A stepping motor fixed on the platform was coupled to the axis of the device by a chain belt system. The platform, made of wood and formica, was fixed on a table with four adjustable screws. This system facilitates the alignment of the device with the radiation field, using the luminous field and laser ray of the teletherapy machine (Fig. 3).

A computer-controlled stepping motor provided control of the rotation rate of the device. In addition, a sensor/alarm monitored rotation during irradiation (Fig. 4).

Automatic system for temperature monitoring

The thermal performance of the device was evaluated at an environmental temperature (23 °C) using an automated data-acquisition system built for this purpose. A PT-100 sensor (cromel-alumel junction) with an aluminium mini-head and stainless sheath (6-mm diameter and 200-mm long) and a linear amplifier (2000×) were used. The output signal was calibrated for a temperature range of 0–40 °C, with an uncertainty of 0·2 °C. Values at the output of the amplifier were fed to a 12-bits analogical/digital converter (1/2 LSB error). Stored data from the thermal probe were averaged using a 10-point temporal window for the entire irradiation time. This automated system monitored the temperatures of six RBC bags and 13 platelets bags stored separately in the two compartments. Normally, irradiation is performed with

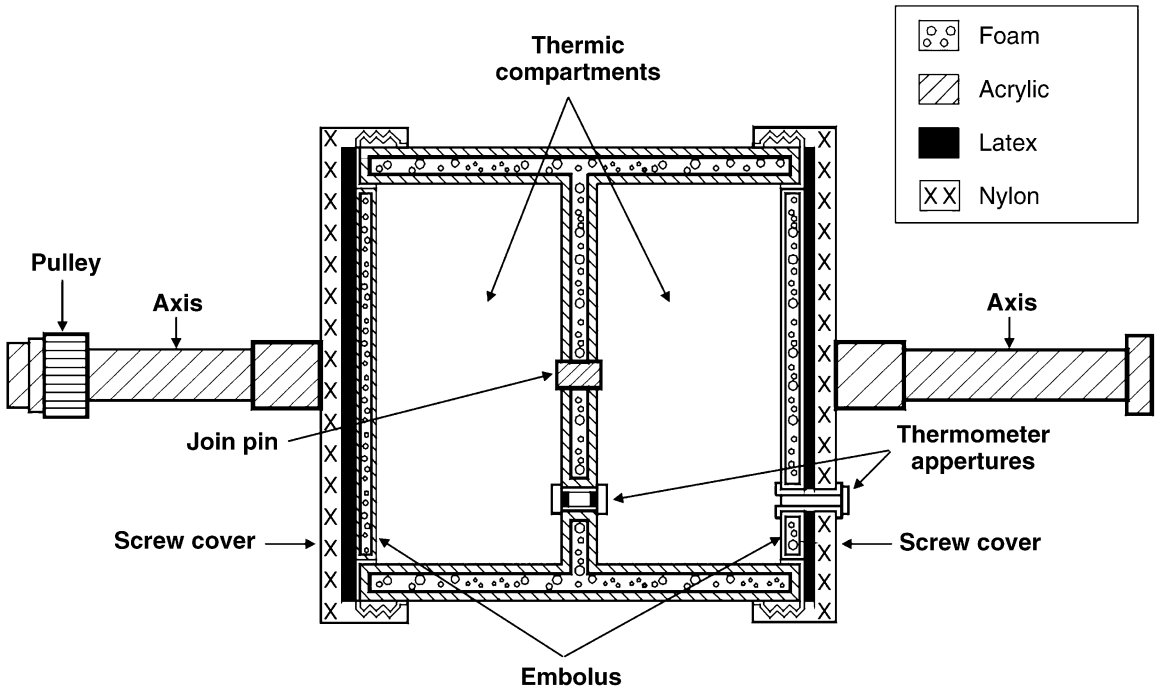

Fig. 1 Scheme of the device.

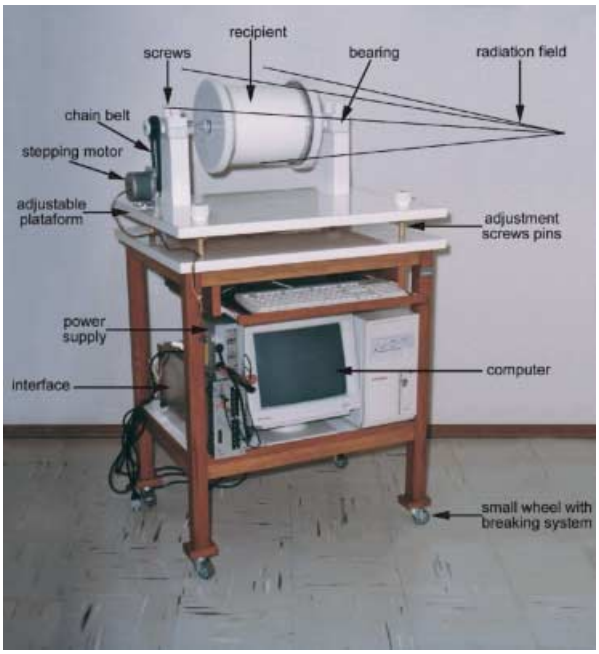

Fig. 2 The automated system for blood bag storage.

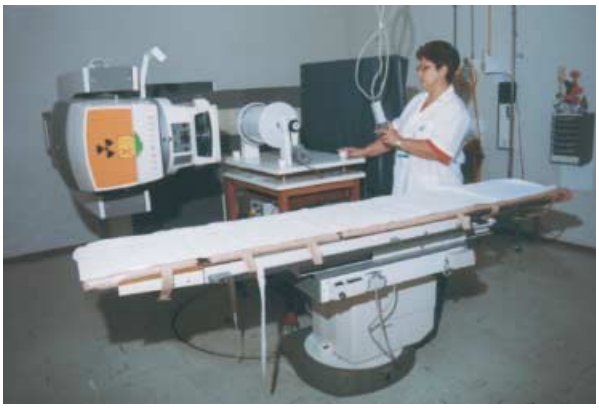

Fig. 3 The automated system for blood bag storage at irradiation position in a cobalt-60 therapy machine.

spaces between blood bags filled with water, to obtain a better homogeneity in dose distribution. Thus, the performance of the thermal device was evaluated with the RBC and platelets compartments filled with water at initial temperatures of 2 °C and 22 °C, respectively. For each compartment evaluated, the sensitive region of the thermometer probe was positioned between blood bags and 20 cm away from the compartment wall. For comparison, the temperature of a single blood bag was monitored at the centre of the volume (250 ml) exposed to room temperature.

Dose distribution in blood bags

The dose distribution in a blood bag was simulated using a cylindrical homogenous clear polystyrene phantom with

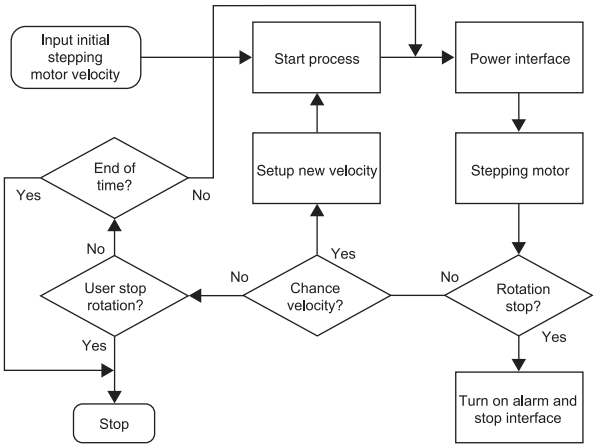

Fig. 4 Diagram of the routine to control the stepping motor and alarm activation.

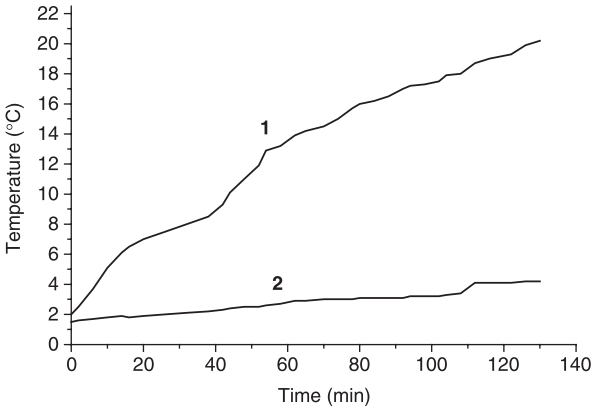

Fig. 6 Blood temperature during irradiation. 1, Bags exposed to environmental conditions; 2, bags stored inside the thermal device.

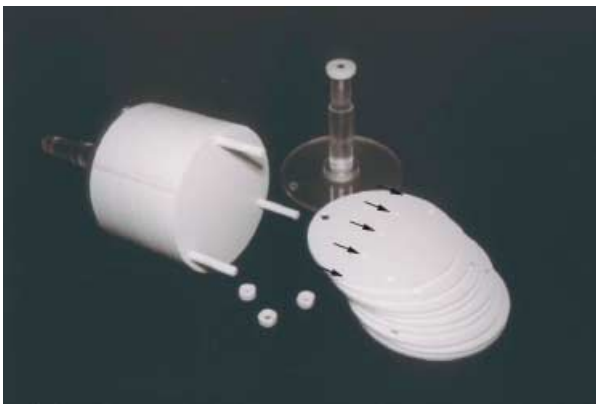

Fig. 5 Phantom plates assembled by three connecting screws. Note the two rotating acrylic axes. Arrows indicate cavities (a total of 25 was distributed in five plates) used to locate thermoluminescent dosimeter (TLD) chips.

dimensions matching those of the irradiation device. As the difference in linear attenuation coefficients of clear polystyrene plastic and whole blood for energy, normally used for blood irradiation, is lower than 5%, this type of material is recommended to represent blood for dosimetric purposes [19]. Plaques of clear polystyrene were cut according to the phantom dimensions and attached face-to-face with screws of the same material (Fig. 5). Thermoluminescent dosimeters (TLDs) were used to measure the absorbed dose. A total of 25 cavities ($9 \times 3 \times 1$ mm) containing three TLDs (TLD-100; Harshaw Chemical Co., Solon, OH, USA) were used to measure the dose along the central plane of the phantom. The plaques were aligned and, according to the arrangement presented in Fig. 3, the phantom was placed in the irradiation device and irradiated with a cobalt teletherapy unit (Gammatron 80S; Siemens, Munich, Germany) using a 30×30-cm^2 field at the surface of the phantom and a 80-cm source to phantom surface distance. The dose rate was determined by an international protocol formalism [20]. The irradiation time was selected to obtain a dose of 200 cGy at the phantom volume centre, with ±3% uncertainty. A total of 85 TLDs were individually calibrated for each dose and separated in two groups, one for the phantom dosimetry and the other for the control. The TLD response was analysed by using a Harshaw reader, model 2000-B/2000-C. The TLDs were annealed according to the manufacturer's recommendations (1 h at 400 °C followed by 2 h at 100 °C). Three field configurations were used – single, parallel and opposed – and a 2 r.p.m. rotational field. For both rotational and parallel-opposed fields, the dose in each cavity was measured using three TLD readings that were averaged and normalized to the maximum dose value obtained at the phantom centre. For the single field, these doses were normalized to the maximum entrance value. For these three irradiation geometries, dose distributions in the phantom were represented in terms of isodose curves, using a cubic spline interpolation technique [21].

Results and discussion

Performance of the thermal device

Evaluation of the performance of the thermal device showed that, over an interval of 120 min, the temperature of the water in which the RBC bags were immersed increased from 2 to 4 °C (Fig. 6). For platelet bags, the temperature remained between 22 °C and 23 °C during this 120-min time interval, showing that there was good thermal isolation between the two compartments of the device. Temperature monitoring of an RBC bag at room temperature showed a blood temperature range from 2 to 13 °C, in the first 60 min, reaching 19 °C by 120 min (Fig. 6). Kathleen & Davey [22] recommended that RBC units should be maintained between 2 and 4 °C and not be kept above 6 °C for more than 30 min. Thus, Fig. 6 demonstrates that the device provides an optimum thermal

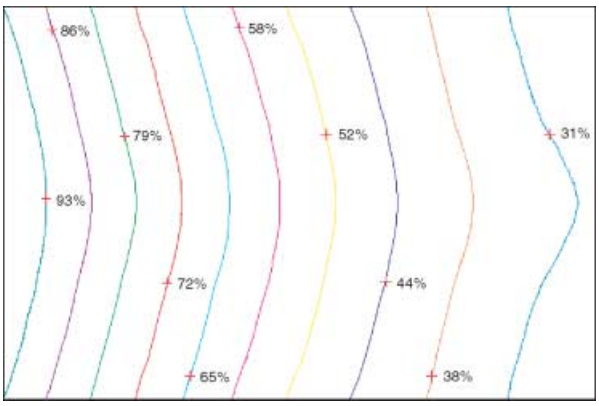

Fig. 7 Isodose curves obtained at the central plane when the phantom was irradiated with a single field.

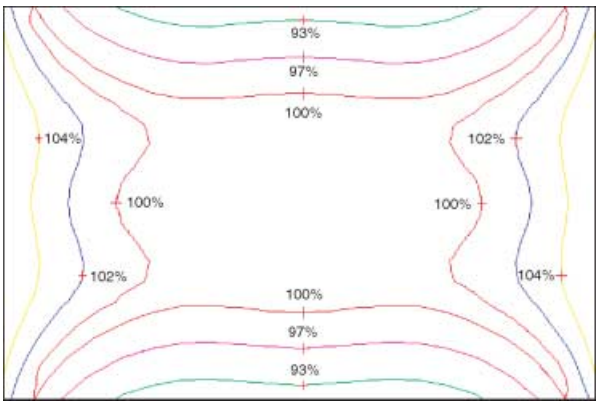

Fig. 9 Isodose curves obtained at the central plane when the phantom was irradiated using a 2 r.p.m. rotational field.

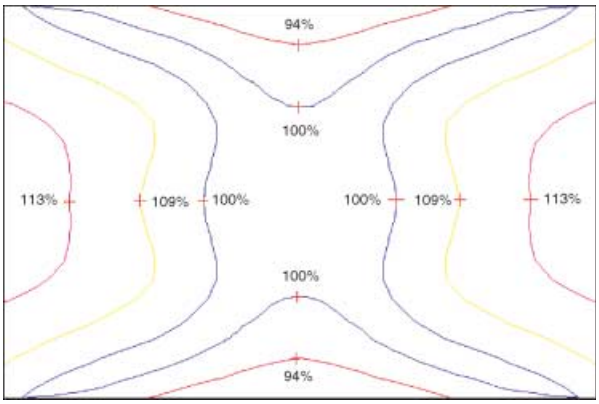

Fig. 8 Isodose curves obtained at the central plane when the phantom was irradiated using parallel-opposed fields.

environment during teletherapy irradiation of blood and platelets.

Dose distributions in blood bags

Determination of dose distributions (isodose curves) within the irradiation volume is a relevant physical aspect in the process of blood irradiation. These dose distributions depend on the radiation source energy, the volume to be irradiated and the choice of irradiation geometry. Knowledge of these curves is important in order to guarantee that no point in the volume receives less than 2500 cGy. A study of dose distribution in the irradiated volume, with various blood irradiators (from one to four sources of caesium-137 and blood recipients with volumes from 749 to 3674 cm^3), showed a large range of dose distributions, from a minimum of 70% to a maximum of 135% [23]. Compared to caesium-137 irradiators, cobalt teletherapy machines provide higher effective energy (1·25 MeV) and improved dose homogeneity in the irradiated volume. A minimization of dose-distribution heterogeneity is important in order to avoid overdosage of some of the blood cells. In this work, results of dosimetry performed with a phantom specially developed to represent the volume of the thermal device, showed significant heterogeneity in dose distributions (from 31 to 93%) when the phantom was irradiated with a single field (Fig. 7). For parallel-opposed fields, a minimum of 94% and a maximum of 113% were observed (Fig. 8). For a 2 r.p.m. rotational field, a minimum of 93% and a maximum of 104% was observed (Fig. 9). Therefore, rotational fields provide the most homogeneous dose distribution in the target volume, minimizing the effects of hot spots.

Conclusion

The methodology developed in this work provides appropriate storage for blood irradiated with teletherapy machines, representing a suitable alternative for the prevention of TA-GvHD at blood banks which have only this type of equipment.

Acknowledgements

The authors would like to thank Prof. Dr Thomaz Ghillardi Netto, Elisa A. Reis, Maria H. da Silva, Renato Glauco, and José Luiz Aziani, for their technical assistance. This research was partially supported by FAPESP and FUNDHERP.

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