



Study of the spatial distribution of the absorbed dose in blood volumes irradiated using a teletherapy unit

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ABSTRACT

Blood irradiation can be performed using a dedicated blood irradiator or a teletherapy unit. A thermal device providing appropriate storage conditions during blood components irradiation with a teletherapy unit has been recently proposed. However, the most appropriated volume of the thermal device was not indicated. The goal of this study was to indicate the most appropriated blood volume for irradiation using a teletherapy unit in order to minimize both the dose heterogeneity in the volume and the blood irradiation time using these equipments. Theoretical and experimental methods were used to study the dose distribution in the blood volume irradiated using a linear accelerator and a cobalt-60 therapy machine. The calculation of absorbed doses in the middle plane of cylindrical acrylic volumes was accomplished by a treatment planning system. Experimentally, we also used cylindrical acrylic phantoms and thermoluminescent dosimeters to confirm the calculated doses. The data obtained were represented by isodose curves. We observed that an irradiation volume should have a height of 28 cm and a diameter of 28 cm and a height of 35 cm and a diameter of 35 cm, when the irradiation is to be performed by a linear accelerator and a cobalt-60 teletherapy unit, respectively. Calculated values of relative doses varied from 93% to 100% in the smaller volume, and from 66% to 100% in the largest one. A difference of 5.0%, approximately, was observed between calculated and experimental data. The size of these volumes permits the irradiation of blood bags in only one bath without compromising the homogeneity of the absorbed dose over the irradiated volume. Thus, these irradiation volumes can be recommend to minimize the irradiation time when a teletherapy unit is used to irradiate blood.

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1. Introduction

Blood and blood components containing viable T cells are recommended to be irradiated prior to transfusion to immunocompromised patients to reduce the risk of transfusion-associated graft-versus-host disease (TA-GVHD) (Chapman et al., 1996). Ionizing radiation breaks the DNA molecules of T lymphocytes, the cells causing TA-GVHD, and prevents the latter from setting up an immunological response against the recipient (Pelszynski et al., 1994). Blood irradiation can be performed using commercial irradiators specifically designed for this purpose, usually located in blood banks. These irradiators incorporate 1–4 gamma ray sources, usually cesium-137 (¹³⁷Cs), of 22–89 TBq (600–2400 Ci)

each. However, in the absence of a blood irradiator, other alternatives such as X-rays produced by a linear accelerator or gamma rays derived from cobalt-60 (⁶⁰Co) source of a cobalt teletherapy machine can be used for this purpose, improving the cost/benefit ratio of the process (Anderson et al., 1991; Moroff and Luban, 1997; Patton and Skowronski, 2001; Chen et al., 2001).

Studies on the radiosensitivity of T cells to X-rays (generated by a linear accelerator) and to gamma rays (generated by ¹³⁷Cs sources of a specific irradiator and by ⁶⁰Co of a teletherapy unit) have shown that a minimum dose of 2500 cGy is necessary to prevent TA-GVHD (Pelszynski et al., 1994; Luban et al., 2000; Góes et al., 2006). These studies were conducted on T cells isolated from irradiated red blood cells (RBCs) units (Pelszynski et al., 1994; Góes et al., 2006) and from platelet concentrates obtained by apheresis (Luban et al., 2000). On the other hand, in addition to damaging T lymphocytes, irradiation also damages other blood cells such as platelets, granulocytes, and RBCs (Moroff and Luban, 1997). The American Food and Drug Administration (FDA, 1993), the American Association of Blood Banks (AABB, 2005), and the

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Guidelines for Blood Transfusion Services in the UK (UK Red Book, 2002) require a minimum dose of 2500 cGy at the middle plane of the irradiated volume. The Council of Europe Guidelines (European Guidelines, 2005) states that irradiation must deliver at least 2500 cGy but no more than 5000 cGy.

One difficulty in using teletherapy units for blood irradiation is the long time necessary to deliver the minimal dose of 2500 cGy. The time necessary to complete this process is less than 10 min when an irradiator is used and approximately 30–60 min when a linear accelerator or a telecobalt therapy unit are used to this task. Thus, the environmental conditions can degrade the quality of the blood components when blood irradiation is performed using a teletherapy unit. To standardize the process of blood irradiation by teletherapy units, our group has proposed an electro-mechanical system for the storage of blood bags during irradiation (Góes et al., 2004). The system, equipped with two thermal compartments, allows the simultaneous irradiation of platelets, granulocytes and RBC units while maintaining a constant temperature for each of these blood components (2–4 °C for RBCs and 20–24 °C for platelets or granulocytes). To homogenize the dose distribution in the volume, the thermal device is rotated in the radiation field at a rate of 2 r.p.m. by means of a computer-controlled stepping motor. Recently, we have shown that this rotation rate does not cause injuries to the RBC membrane (Góes et al., 2008). However, it is necessary to select the irradiation volume in a way that minimize both the spatial heterogeneity of the absorbed dose in the irradiated volume and the time necessary to complete the irradiation process using a teletherapy unit. Thus, using treatment planning system and phantoms consisting of acrylic plastic, we decided to study the spatial distribution of the absorbed dose in the blood volume irradiated with a linear accelerator and a ^{60}Co unit to indicate the size of the thermal device in order to minimize both the time of use of the teletherapy equipments for blood irradiation and the heterogeneity of the dose in the irradiated volume.

2. Materials and methods

2.1. Selection of the irradiation volume

For the minimization of irradiation time it would be interesting to maximize the irradiation volume in order to irradiate the blood bags in a single bath. On this basis, irradiation time was established by considering the best combination between volume and source–surface distance (SSD) that would guarantee sufficient dose homogeneity in the irradiated blood volume. This volume was selected using a treatment planning system developed by the National Institute of Health, USA, (InterSoft), which calculated the spatial dose distribution in the volume and represented it by means of isodose curves. Cylindrical acrylic volumes were chosen as the interaction medium and rotational fields with a rotation rate of 2 r.p.m. were used for both gamma and X-rays. The teletherapy units used in the present study were a linear accelerator (Mevatron XII; Siemens, Munich, Germany) with X-ray photons of 10 MV and a ^{60}Co teletherapy unit (Gammatron S-80; Siemens). The absorbed doses in the irradiated volumes were planned to each irradiation field, which were established according to each SSD and energy used. The dose rate was determined using a calibrated clinical dosimeter consisting of an electrometer (DI4, PTW, Freiburg, Germany) and ionization chambers (M23332, PTW; 2571, Nuclear Enterprise, Edinburgh, Scotland), based on the use of an internationally recommended protocol (IAEA, 2001).

2.2. Measurement of the absorbed dose in the phantoms

Cylindrical acrylic homogeneous phantoms were constructed to confirm the dose distribution calculated by the treatment planning system. The phantom dimensions match the volumes previously selected using the treatment planning system. Two centimeter thick acrylic plates were cut according to the phantoms' dimensions and were attached face-to-face with screws of the same material (Fig. 1). TLDs were used to determine the spatial distribution of the absorbed dose in the irradiated volume. Cavities ($10 \times 3 \times 2 \text{ mm}^3$) were constructed in some of the plates of both phantoms (Fig. 1) to allocate at least three TLDs (TLDs-100; Harshaw Chemical Co., Solon, OH, US), in order to measure the dose along the middle plane of the phantom. The plaques of each phantom were aligned according to the arrangement presented in Fig. 1. Two different phantoms were constructed for irradiations using the linear accelerator and the ^{60}Co teletherapy unit according to the theoretical results previously obtained. Both phantoms were positioned and rotated in the radiation fields using an electro-mechanical system constructed for this task (Fig. 2). A platform with two columns was used to support the axis of the phantom. The distance between these columns was selected in order to permit the use of the same platform for both phantoms. A stepping motor fixed to the platform was coupled to the axis of the phantom by a chain belt. The platform, made of wood, was fixed on a table with four adjustable screws in order to facilitate the vertical and horizontal alignments of the phantom with the irradiation field. A computer-controlled stepping motor provided control of the rotation rate of the phantom at 2 r.p.m., as described in the literature (Góes et al., 2004).

One phantom was irradiated using a $40 \times 40 \text{ cm}^2$ field size at 80 cm ^{60}Co source-to-phantom surface distance. The other phantom was irradiated using a $35 \times 35 \text{ cm}^2$ field size at 100 cm X-ray source-to-phantom surface distance. These irradiation parameters were selected according to the dose distribution results obtained previously by the treatment planning system. The irradiation time was selected in order to obtain a dose of 500 cGy at the phantom surface entrance. A total of 120 TLDs were individually calibrated and annealed for each phantom according to manufacturer recommendations (1 h at 400 °C followed by 2 h at 100 °C). The TLD response was analyzed using

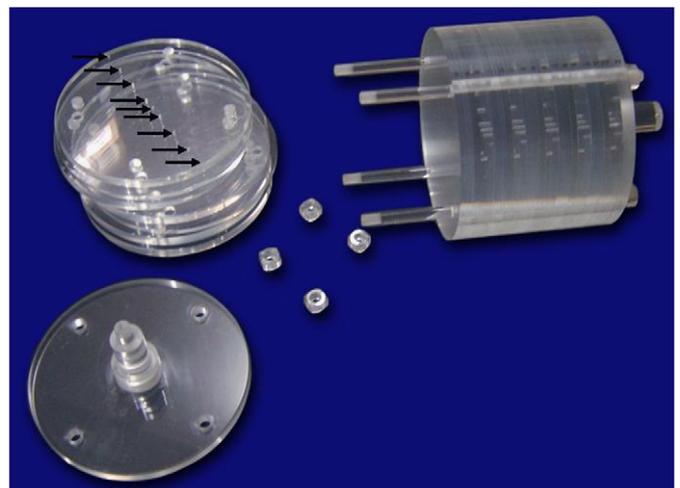


Fig. 1. Phantom plates assembled by four connecting screws and two rotating axes. Arrows indicate cavities used to locate thermoluminescent dosimeters.



Fig. 2. Automatic system used to support and align the phantoms in the fields of gamma and X-rays.

a Harshaw reader, model 2000-B/2000-C. The dose in each cavity was measured using 3 TLDs readings that were averaged and normalized to the maximum dose value obtained at the phantom surface entrance. The dose distribution on the middle plane of the phantom was represented by isodose curves according to the methodology described in the literature (Góes et al., 2004).

3. Results and discussion

The results obtained in this study have demonstrated that a volume measuring 35 cm in height and 35 cm in diameter is necessary, when a cobalt teletherapy unit is used to irradiate blood, and a volume measuring 28 cm in height and 28 cm in diameter is necessary when a 10 MV linear accelerator is used to this task, to minimize both the irradiation time and heterogeneity of the absorbed dose in irradiated volume.

In this study, we have considered the relation between the dose rates at different SSDs and the maximum blood volume that could be irradiated at these distances in order to choose the size of the thermal device that would minimize the irradiation time. The maximum volumes of the thermal device correspond to the volume of a cylinder of height and diameter equal to the maximum field size obtained at the corresponding distance. Since

the volume of the thermal device differed for each distance, for comparison purposes, the irradiation times were calculated in order to irradiate the same blood volume obtained at 120 cm. Two factors contribute to the heterogeneity of the dose in the irradiation volume: the phantom dimensions and the contamination of the primary beam with photons and electrons of lower energy produced by the interaction of the primary beam with the materials that compose the collimation system of the equipment. The latter factor is more relevant since lower energy photons are absorbed by the outermost layers of the irradiated volume, thus contributing to an increased value of the absorbed dose in these regions of the volume. On this basis, giving priority to the homogeneity of absorbed dose in the irradiated volume and to the minimization of the occurrence of errors of alignment of the thermal device in the irradiation field, we selected as optimum geometry of irradiation the one that uses the standard SSD value of each equipment (100 cm for linear accelerators and 80 cm for cobalt therapy units). This choice can also be justified by a small difference in the irradiation times used and by taking as a base the mean blood volume irradiated by blood centers, of the order of 16,000 cm³ and therefore lower than the volume of more than 17,000 cm³ obtained at 100 cm.

Thus, we recommend the use of a thermal devices with cylindrical shape measuring 35 cm in height and 35 cm in diameter for an SSD of 80 cm and a field size of 40 × 40 cm², to store the blood bags when the blood irradiation is performed by a cobalt therapy unit, and a thermal device measuring 28 cm in height and 28 cm in diameter for an SSD of 100 cm and a field size of 35 × 35 cm², when the blood irradiation is performed by a linear accelerator.

Fig. 1 shows one of the cylindrical acrylic homogeneous phantoms constructed to confirm the dose distribution calculated by the treatment planning system. The automatic system used to support and align the phantoms in the irradiation fields is showed in Fig. 2. Fig. 3, parts A and B, and Fig. 4, parts C and D, show the spatial distribution of the absorbed doses (represented by isodose curves) on acrylic phantoms simulating these devices. Fig. 3A shows theoretical isodose curves obtained at the middle plane of the phantom with size of 28 cm in height and 28 cm in diameter, using rotational fields at 2 r.p.m., SSD of 100 cm, field size of 35 × 35 cm², and 10 MV X-rays. According to the data showed in this figure, the absorbed doses in this volume ranged from 93% to 100%. Fig. 3B shows the isodose curves obtained experimentally at the middle plane of the same phantom using the same photon beam and geometric conditions cited above. According to the data showed in this figure, the absorbed doses in this volume ranged from 88% to 100%. Fig. 4C shows theoretical isodose curves obtained at the middle plane of the phantom with size of 35 cm in height and 35 cm in diameter, using rotational fields at 2 r.p.m., SSD of 80 cm, field size of 40 cm × 40 cm, and ⁶⁰Co gamma rays. According to the data showed in this figure, the absorbed doses in this volume ranged from 66% to 100%. Fig. 4D shows the isodose curves obtained experimentally at the middle plane of the same phantom using the same photon beam and geometric conditions cited above. According to the data showed in this figure, the absorbed doses in this volume ranged from 63% to 100%. Thus, according to these data, the difference between the relative values of absorbed dose calculated by the treatment planning system and those obtained experimentally are 5%, approximately, for both beams used. This difference may be attributed to the uncertainty associated with both the response of TLDs and the method used to interpolate the data. However, this difference can be considered small when compared to the great heterogeneity of the absorbed dose in the blood volume irradiated with specific irradiators, which ranges from 70% to 135% (Masterson and Febo, 1992).

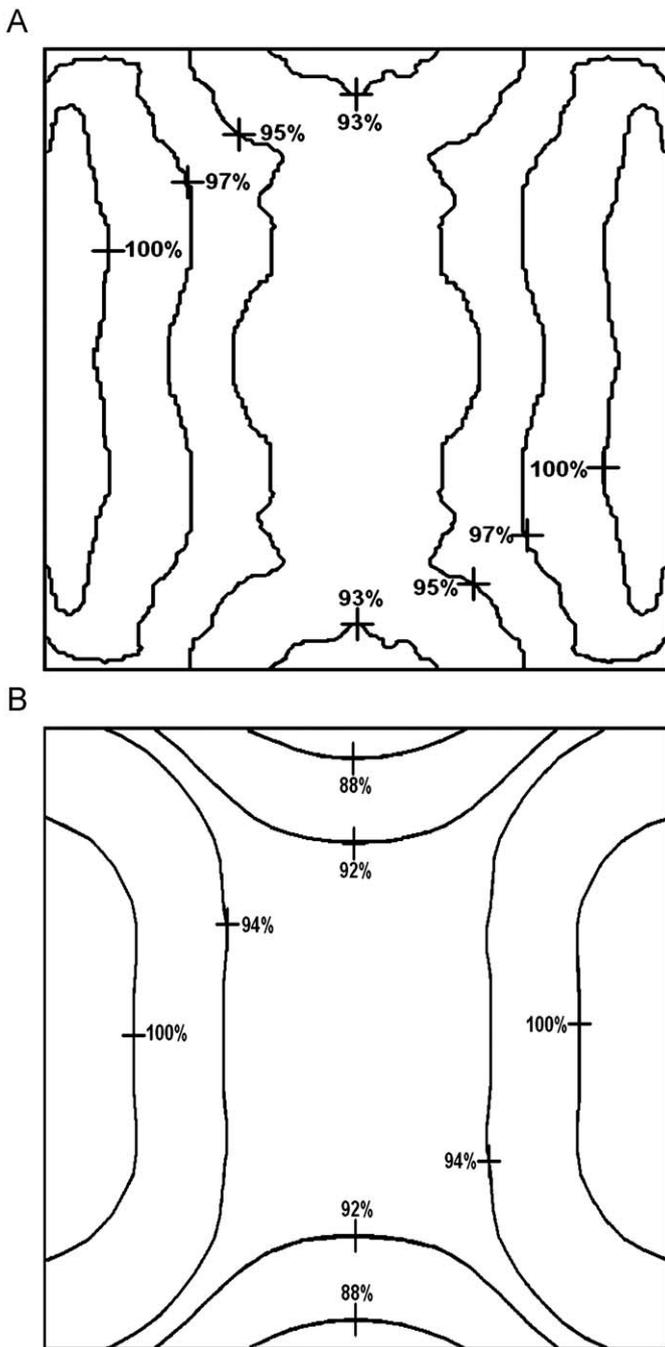


Fig. 3. Isodose curves obtained at the middle plane of the minor phantom irradiated with X-rays: (A) theoretical data and (B) experimental data.

The technology associated with LiF-100 detector is available and well-established. This detector provides good spatial resolution (approximately $3 \times 3 \times 1 \text{ mm}^3$) for mapping out dose distribution in blood irradiation, and its response practically does not depend on the dose rate or energy range used to irradiate blood (Masterson and Febo, 1992). Acrylic matches the attenuation coefficient of blood within 9% in this energy range (White et al., 1989), and this material can be used for blood irradiation measurement purposes (Moroff and Luban, 1997). Thus, we have determined in this study one suitable methodology to be carried out in blood irradiation in order to minimize the time of the irradiation when a teletherapy unit is used for this task without, however, compromising the dose homogeneity in the irradiated volume.

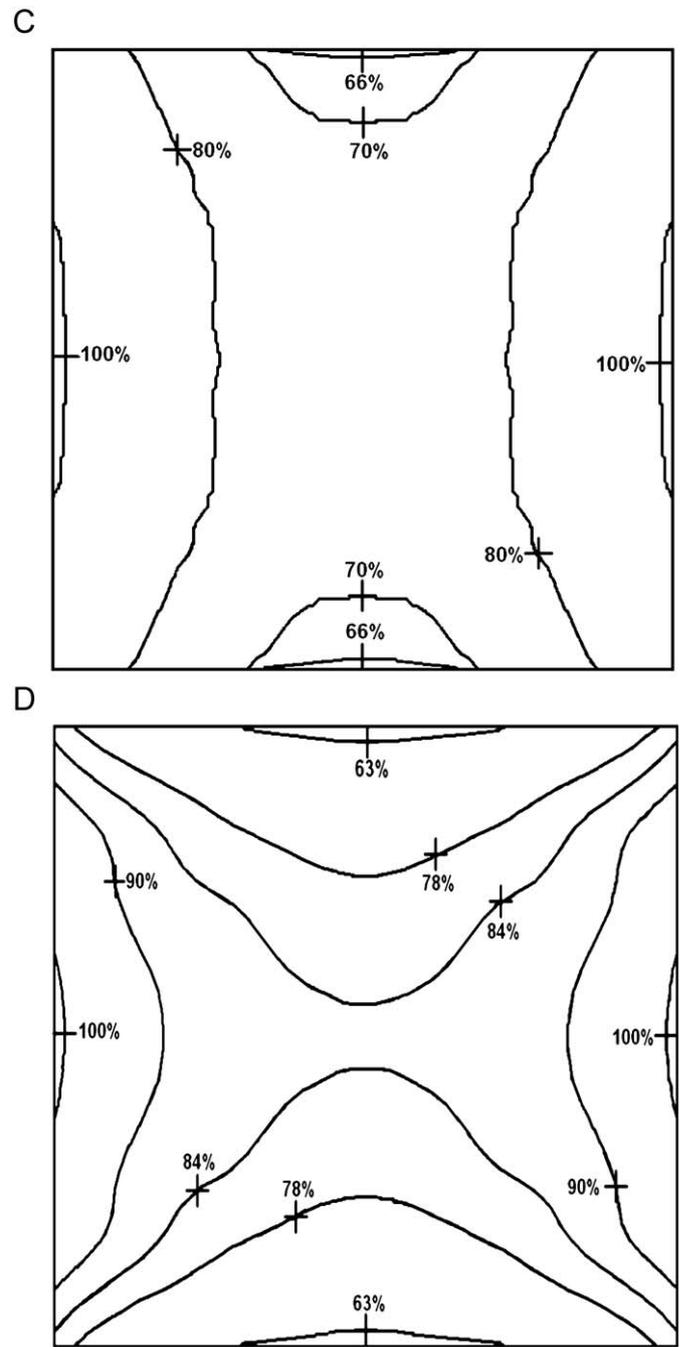


Fig. 4. Isodose curves obtained at the middle plane of the major phantom irradiated with gamma rays: (C) theoretical data and (D) experimental data.

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References

- American Association of Blood Banks 2005: Standards for Blood Banks and Transfusion Services, 23rd edn. Bethesda, American Association of Blood Banks, 26p.

- Anderson, K.C., Goodnough, L.T., Sayers, M., et al., 1991. Variation in blood component irradiation practice: implication for prevention of transfusion-associated graft-versus-host disease. *Blood* 77, 2096–2102.
- Center for Biologics Evaluation and Research 1993. License amendments and procedures for gamma irradiation of blood products. MD: Food and Drug Administration. Bethesda, July 22.
- Chapman, J., Finney, R.D., Forman, K., 1996. Guide on gamma irradiation of blood components for prevention of transfusion-associated graft-versus-host disease. *Transfusion* 6, 261–271.
- Chen, F., Covas, D.T., Baffa, O., 2001. Dosimetry of blood irradiation using an alanine/ESR dosimeter. *Appl. Radiat. Isot.* 55, 13–16.
- Góes, E.G., Covas, D.T., Haddad, R., et al., 2004. Quality control system for blood irradiation using a teletherapy unit. *Vox. Sang.* 86, 105–110.
- Góes, E.G., Borges, J.C., Covas, D.T., et al., 2006. Quality control of blood irradiation: determination T cells radiosensitivity to cobalt-60 gamma rays. *Transfusion* 46, 34–40.
- Góes, E.G., Ottoboni, M.A., Palma, P.V.B., et al., 2008. Quality control of blood irradiation with a teletherapy unit: damage to stored red blood cells after cobalt-60 gamma irradiation. *Transfusion* 48, 332–340.
- Guidelines for Blood Transfusion Services in the UK, 2002. 6th edn. TSO, London 98p.
- Guide to the Preparation Use and Quality Assurance of Blood Components, 2005. 11th edn. Council of Europe Publishing, Strasbourg, France.
- International Atomic Energy Agency, 2001. Absorbed dose determination in external beam radiotherapy: an international code of practice for dosimetry based on standards of absorbed dose to water. Technical reports Series 398. Vienna, Austria.
- Luban, N.L.C., Drothler, D., Moroff, G., et al., 2000. Irradiation of platelet components: inhibition of lymphocyte proliferation assessed by limiting-dilution analysis. *Transfusion* 40, 348–352.
- Masterson, M.E., Febo, R., 1992. Pretransfusion blood irradiation: Clinical rationale and dosimetric considerations. *Med Phys* 19, 649–657.
- Moroff, G., Luban, N.L.C., 1997. The irradiation of blood and blood components to prevent graft-versus-host disease: technical issues and guidelines. *Transfus Med* 11, 15–26.
- Patton, G.A., Skowronski, M.G., 2001. Implementation of a blood irradiation program at a community center. *Transfusion* 41, 1610–1614.
- Pelszynski, M.M., Moroff, G., Luban, N.L.C., et al., 1994. Effect of gamma irradiation of red blood cell units on T-cell inactivation as assessed by limiting dilution analysis: implication for preventing transfusion-associated graft-versus-host disease. *Blood* 83, 1683–1689.
- White D.R., Booz J., Griffith R.V., et al., 1989. Tissue substitute in radiation dosimetry and measurement. Report 44. International Commission on Radiation Units and Measurement, Bethesda, Maryland.