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Dosimetry of blood irradiation using an alanine/ESR dosimeter

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Abstract

A batch of 80 DL-alanine dosimeters was supplied to Hemocentro of the Hospital and Clinics of Faculdade de Medicina de Ribeirão Preto (HC-FMRP) SP, Brazil for the purpose of quality control of the radiation dose delivered to blood bags. The irradiation was made using two $(40 \times 40)\,cm^2$ parallel opposed radiation fields each with 80 cm of source to surface distance in the Radiotherapy Section of HC-FMRP with the ^{60}Co teletherapy unit. The calculated radiation absorbed dose at the center of the box was 20 Gy. The dosimeter readings were performed using a Varian E-4 ESR Spectrometer operating in X-band. For the 80 dosimeters and over the irradiation volume throughout a blood bag, the minimum and maximum doses were 14 and 23 Gy, respectively. The mean dose was (18 ± 2) Gy (1σ), and the coefficient of variability was 11.1%. Alanine dosimeters demonstrated easy handling, good precision and adequate sensitivity for this application.

Keywords: Blood products; Dosimetry; ESR; Alanine; Graft vs. host disease; Quality control

1. Introduction

Transfusion-associated graft-versus-host disease TA-GVHD is a possible complication of blood transfusion that occurs when viable donor T-lymphocytes proliferate and engraft in immunodeficient patients after transfusion. Presently, the only method accepted to prevent TA-GVHD is the irradiation of blood and its components before transfusion (Moroff and Luban, 1997). Ionizing irradiation eliminates the functional and proliferative capacities of T-lymphocytes leaving other blood components, especially erythrocytes, granulocytes and platelets, functional and viable. This is possible because T-lymphocytes are more radiosensitive than other blood components (Masterson and Febo, 1992). To carry out the irradiation of blood specially designed commercial irradiators exist, usually localized in blood banks, and dedicated exclusively to this task. These irradiators use radioactive isotopes such as ^{137}Cs or ^{60}Co. However, teletherapy machines, such as linear accelerators or ^{60}Co units already available at the hospital, may also be used for the same purpose (Moroff et al., 1997), improving the cost/benefit ratio of the process.

Independently of the methodology used for the irradiation, it is necessary to establish a quality control (QC) procedure to verify the radiation dose delivered to the blood bags (Blake and Pothiawala, 1992; McLaughlin and O'Hara, 1996). The radiation dose recommended by the Food and Drug Administration (FDA) is 25 Gy at the center of the canister or box and a minimum dose of 15 Gy elsewhere (FDA, 1993). The Brazilian Legislation requires that the minimum dose delivered to each bag should be 15 Gy (Norma Tecnica para Coleta-Ministerio da Saude, 1993). However, there are recent recommendations from the BCSH Blood Transfusion

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Task Force indicating that the minimum dose should be 25 Gy and no more than 50 Gy (BCSH, 1996) delivered to blood. There are several dosimetric systems already employed for the QC of radiation dose in the process of blood irradiation: TLD (Bogner et al., 1998; Kronholz et al., 1998; Masterson and Febo, 1992); Fricke dosimeter (Bogner et al., 1998); colorimetric dosimeter (Hillyer et al., 1993); and radiochromic film dosimeter (Butson et al., 1999). There the use of a MOSFET dosimeter (Moroff and Luban, 1997; Moroff et al., 1997), red perspex dosimeter (Masterson and Febo, 1992), and alanine dosimeter (Masterson and Febo, 1992; McLaughlin and O'Hara, 1996; Feinstein et al., 2000) for the same purpose has also been suggested.

Ionizing radiation produces stable alanine free radicals that can be quantified by the electron spin resonance (ESR) technique, by measuring the amplitude of the central line of its ESR spectrum. This amplitude is directly correlated with the radiation dose (Regulla and Deffner, 1982). Alanine has good characteristics as a dosimeter: Radiation response approximately equivalent to tissue, low fading ($<0.7\%$/y) (Alexandre et al., 1992; Juncheng, 1996), no energy dependence above 100 keV and linear response over a wide dose range. The alanine/ESR dosimetry technique has been used successfully for high-dose dosimetry applications (100 Gy–100 kGy), i.e., industrial applications of radiation, high-energy accelerators, etc (Wieser and Regulla, 1989; Coninckx et al., 1989; Bartolotta et al., 1989). More recently, this technique has been used in radiotherapy applications (Schaeken and Scalliet, 1996; Mehta and Girzikowsky, 1996). The objective of the present work is to employ the alanine/ESR dosimetry technique for quality control of the radiation dose in blood irradiation. The technique developed is capable of measuring a radiation dose as low as 1 Gy (Regulla and Deffner, 1982; Nette et al., 1993), making it suitable for the dose range used in blood irradiation.

2. Materials and methods

Dosimeters in cylindrical form are made with a uniform mixture of DL-alanine (No. A-7502, Sigma Chemical Company) plus pure paraffin. The procedure to prepare the dosimeters was taken from Alexandre and co-workers (Alexandre et al., 1992). Each dosimeter has a nominal mass of 240 mg with 80% DL-alanine and 20% paraffin. The paraffin was ground and sieved (mesh 32, particle diameter 500 μm), obtaining a fine powder before mixing it homogeneously with alanine. The compact cylindrical form was obtained by pressing the mixture into a cylindrical stainless-steel die. This die has a 3.5 cm diameter, 5.5 cm height and 0.47 cm inner diameter. The nominal height of the alanine/paraffin pellets is 1.2 and 0.47 cm diameter, resulting in a nominal volume and density of 0.21 cm^3 and 1.16 g/cm^3, respectively. To make handling of the pellets easy and to avoid gradual loss of mass, the pellets are covered with varnish and codified with pencil. For the present investigation, the dosimeters were attached to the blood bags inside an acrylic box with dimensions $(40 \times 40 \times 20)$ cm^3, the interspaces between the bags being filled with cold water, providing a homogeneous irradiation medium. There was no need to use a build-up cap around the dosimeters, because the acrylic box was about 5 mm thick providing the necessary electronic equilibrium, and the space between bags was filled with water.

The ESR measurements were performed using a VARIAN E-4 ESR spectrometer operating in the X-band (~9.5 GHz), equipped with a rectangular resonance cavity model E-231 operating in the TE_{102} mode. The spectrometer parameter settings were selected to optimize the recording of the ESR spectrum details. The modulation amplitude and frequency were 1 mT and 100 kHz, respectively. The microwave power was 50 mW, determined after the plotting of a saturation curve for our system. The central magnetic field H_0 was 325 mT and to record a complete spectrum a scan range ΔH of 20 mT was used. The scan time was 2 min and for each dosimeter, 10 scans were made for signal averaging. The sensitivity of the spectrometer was increased by the use of a digital lock-in amplifier (EG&G DSP lock-in amplifier, model 7260) with the following detection parameters: 500 μV gain and 500 ms time constant. A digital microwave frequency counter (HP model 5350B) allowed precise determination of g factors. All instruments were controlled through a GPIB card and the data acquisition was performed with a Pentium 100 microcomputer. The positioning of the sample in the resonance cavity is critical for recording variations in signal intensity of ESR spectra. For a precise positioning of the dosimeter into the cavity, the dosimeter was placed inside a double-walled quartz sample holder. All measurements were made at ambient temperature (~23°C).

A batch of 80 dosimeters was supplied to Hemocentro of the Hospital and Clinics of Faculdade de Medicina de Ribeirão Preto (HC-FMRP), São Paulo, Brazil. The dosimeters were attached to each of the blood bags and placed into the acrylic box. The irradiation of the box containing blood bags was made at the Radiotherapy Section of HC-FMRP with a Gammatron-S Siemens ^{60}Co teletherapy unit using two (40×40) cm^2 parallel-opposed fields each 80 cm source-to-surface distance (SSD). The irradiation time was enough to deliver a dose of 20 Gy approximately in the center of the box, with a $\pm 3\%$ precision. These 80 dosimeters were divided into eight groups of 10 dosimeters each and used in the QC of blood irradiation during a period of 2 months, approximately. A separate lot of dosimeters was used for calibration purposes. These dosimeters were placed inside a cylindrical piece of acrylic with a 5 mm wall. A $10 \times 10\,cm^2$ irradiation field was used in this case to produce the desired dose for calibration of signal intensity (**h**) versus dose.

3. Results and discussions

Fig. 1 shows a typical ESR spectrum of irradiated alanine showing its five characteristic lines, representing the hyperfine structure due to the interaction of the magnetic moments of four equivalent protons with the magnetic moment of an unpaired electron, which is the predominant free radical species at room temperature. For dosimetry purposes, the amplitude **h** of the central line of the spectrum is correlated with the radiation dose and interpreted as the dosimeter reading.

The calibration curve (Fig. 2) for a dose range of 1–20 Gy shows a linear behavior with a correlation coefficient $r = 0.9996$. Using this calibration curve, the uncertainty in the dose is better than $\pm 5\%$. Fig. 3 shows the frequency histogram for the measured dose of the 80 dosimeters irradiated together with the blood bags in a period of 2 months. The mean dose was (18 ± 2) Gy for 1σ and it is in the expected range of

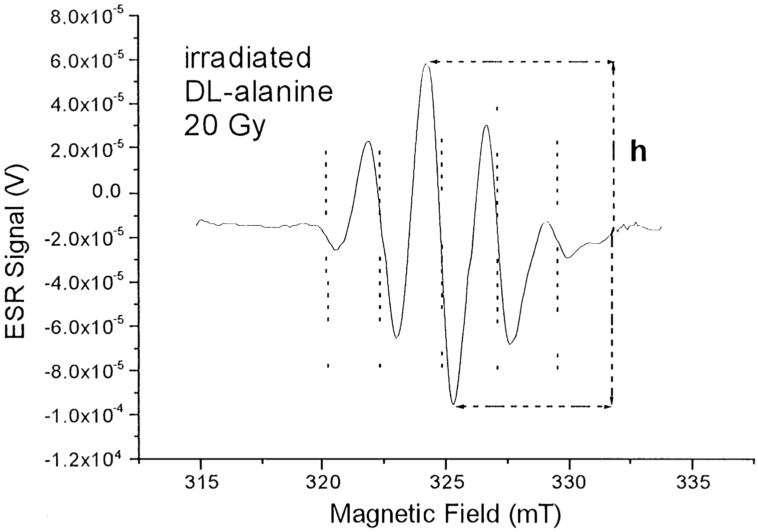

Fig. 1. ESR spectrum of the irradiated alanine, the intensity being given in volts detected at the lock-in amplifier. The five vertical dotted lines indicate the approximate position of the center of each line of the spectrum.

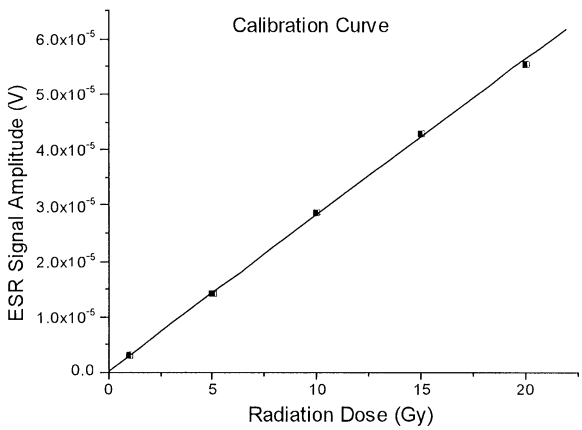

Fig. 2. Calibration curve of the intensity h as a function of dose. The intensity is given in volts detected at the lock-in amplifier.

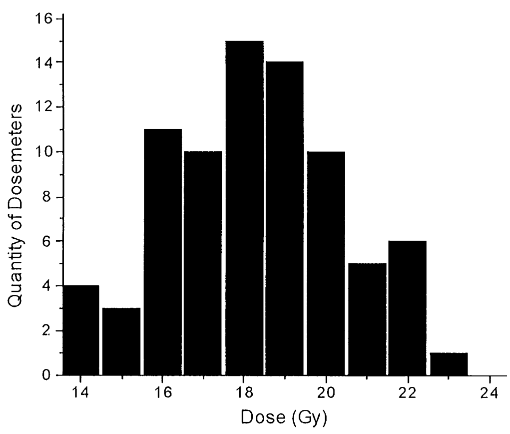

Fig. 3. Frequency histogram for the dosimeters used in QC of blood irradiation for TA-GVHD prevention.

values according to the calculated dose and its uncertainty. The minimum and maximum doses for the irradiated volume were 14 and 23 Gy, respectively.

The QC results indicated that a few percent of the bags irradiated in the period received a dose that were borderline from that recommended in Brazil, an increase of subsequent irradiation times guarantees a minimum dose to blood bags. It was shown that the alanine dosimeter could be used with good results for dose measurements of irradiated blood. At present, there are only a few suppliers of ESR equipment dedicated to ESR dosimetry and cost of this technique should decrease with its wider use in the future. An advantage of ESR is its non-destructiveness during reading, when compared with thermoluminiscence for instance. This characteristic, combined with the low fading of this dosimeter, could be advantageous when one is interested in keeping archival inventory of the dose delivered for reassessment of QC procedures.

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References

Alexandre, A.C., Baffa, O., Nascimento, O.R., 1992. The influence of measurements and storage conditions on alanine/ESR dosimeters. Appl. Radiat. Isot. 43, 1407.

Bartolotta, A., Onori, S., Pantaloni, M., 1989. Intercomparison of the dosimetric system used in industrial irradiation plants in Italy. Appl. Radiat. Isot. 40 (10–12), 1003–1007.

BCSH Blood Transfusion Task Force (Chairman: D. Voak), 1996. Guidelines on gamma irradiation of blood components for the prevention of transfusion-associated graft-versus-host disease. Transfus. Med. 6, 261–271.

Blake, M., Pothiawala, M., 1992. Blood irradiation: the need for true quality assurance. Transfusion 32 Suppl., 91S, abstract A52.

Bogner, L., Hartl, P., Scherer, J., Treutwein, M., Herbst, M., 1998. Dosimetry of blood irradiator. Strahlenther. Onkol. 174 (8), 431–436 (Abstract).

Butson, M.J., Yu, P.K.N., Cheung, T., Carolan, M.G., Quach, K.Y., Arnold, A., Metcalfe, P.E., 1999. Dosimetry of blood irradiation with radiochromic film. Transfus. Med. 9, 205–208.

Coninckx, F., Schönbacher, H., Bartolotta, A., Onori, S., Rosati, A., 1989. Alanine dosimetry as the reference dosimetric system in accelerator radiation environments. Appl. Radiat. Isot. 40 (10-12), 977–983.

Feinstein, C., Winkler, E., Saravi, M., 2000. ESR/alanine gamma dosimetry in the 10–30 Gy range. Appl. Radiat. Isot. 52 (5), 1195–1196.

Food and Drug Administration, 1993. Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products. Center for Biologics Evaluation and Research. Bethesda, MD, USA.

Hillyer, C.D., Hall, J.M., Lackey, D.A., Wazer, D.E., 1993. Development of colorimetric dosimeter for quality control of blood units and irradiators. Transfusion 33 (11), 898–901.

Juncheng, G., 1996. The NIM alanine-ESR dosimetric system for industrial radiation processing. Appl. Radiat. Isot. 47 (11/12), 1161–1163.

Kronholz, H.L., Moustakis, C., Wullenweber, J., 1998. Blood irradiators — Technique, dosimetry and suggestions to quality assurance. Infusionsther. Transfusionsmedizin. 25 (1), 56–61 (Abstract).

Masterson, M.E., Febo, R., 1992. Pretansfusion blood irradiation: clinical rationale and dosimetric considerations. Med. Phys. 19 (3), 649–657.

McLaughlin, W.L., O'Hara, K.P.J., 1996 The importance of reference standard and routine absorbed-dose measurements in blood irradiation. Transfusion 36, Supple. 82S, abstract A61.

Mehta, K., Girzikowsky, R., 1996. Alanine-ESR dosimetry for radiotherapy IAEA experience. Appl. Radiat. Isot. 47 (11–12), 1189–1191.

Moroff, G., Leitman, S.F., Luban, N.L.C., 1997. Principles of blood irradiation, dose validation, and quality control. Transfusion 37, 1084–1092.

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. Rev. 11 (1), 15–26.

Nette, H.P., Onori, S., Fattibene, P., Regulla, D., 1993. Wieser, A. Coordinated research efforts for establishing an international radiotherapy dose intercomparison service based on the alanine/ESR system. Appl. Radiat. Isot. 44 (1/2), 7–11.

Norma, Técnica para Coleta, Processamento e Transfusão de Sangue e Derivados No 1376, Ministério da Saúde, Brazil 1993 (Technical Norm for Harvesting, Processing and Transfusion of Blood and Its Derivatives, Brazilian Ministry of Health).

Regulla, D.F., Deffner, U., 1982. Dosimetry by ESR spectroscopy of alanine. Int. J. Appl. Radiat. Isot. 33, 1101–1114.

Schaeken, B., Scalliet, P., 1996. One year of experience with alanine dosimetry in radiotherapy. Appl. Radiat. Isot. 47 (11–12), 1177–1182.

Wieser, A., Regulla, D.F., 1989. ESR dosimetry in the "gigarad" range. Appl. Radiat. Isot. 40 (10–12), 911–913.