Principles of blood irradiation, dose validation, and quality control

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The use of irradiated blood components to prevent graft-versus-host disease in susceptible patients has increased dramatically in the past several years. Irradiation eliminates the proliferative capacity of lymphocytes present in red cell, platelet, and freshly collected plasma components.[1-3] After penetrating blood components, the photons delivered by a radiation beam cause the formation of electrically charged particles or secondary electrons. These electrons damage the DNA of lymphocytes, either by direct interaction or by reacting initially with cell water to form free radicals. The damaged lymphocytes are unable to proliferate in the host and therefore cannot mediate transfusion-associated graft-versus-host disease.

The photons used to irradiate blood components are generated by one of two methods, using either a gamma-ray beam or an x-ray beam. Gamma rays contain photons generated by the decay of radioactive isotopes such as cesium-137 (Cs-137) or cobalt-60 (Co-60). These isotopes can be positioned inside lead-enclosed chambers in dedicated irradiation instruments. X-rays are photon beams generated mechanically by teletherapy devices that accelerate electrons to very high speeds, directing them to a metallic target such as tungsten and generating a photon beam as a result of this collision. The linear accelerator is an example of the kind of instrument that generates x-rays as an irradiation source. There are no physical differences between gamma rays and x-rays; they exhibit the same radiation characteristics and damage lymphocytes in a similar manner.[4]

ABBREVIATIONS: LDA = limiting dilution analysis; MLC = mixed lymphocyte culture; Mosfet = metal-oxide silicon field effect transistors; TLD = thermoluminescent dosimeter.

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Recent investigations suggest that ultraviolet light may also be used to prevent graft-versus-host disease.[5,6] However, the wavelength of ultraviolet light that inactivates lymphocytes (ultraviolet B, 280-320 nm) cannot consistently penetrate currently licensed polyvinylchloride, polyolefin, and other plastic blood bags. Ultraviolet B exposure of blood components is thus not practical at present, although research to identify blood bag polymers that allow penetration and absorption of ultraviolet light are ongoing.

DESCRIPTION OF IRRADIATION INSTRUMENTATION

Dedicated blood irradiators generally use Cs-137 as the source of radiation because of its long half-life (30 years), high energy emission, and ease of shielding. Commercial irradiators contain one to four linear pencil-shaped sources, each filled with 600 to 1700 curies (Ci) of Cs-137. The strength of the radioactivity in the instrument may thus vary from 600 to 5100 Ci, depending on the number of pencil-shaped sources employed. The greater the strength of the source, the shorter the time necessary to deliver a given dose. The pencil-shaped sources are arranged vertically in the instruments, spaced so as to maximize homogeneity of dose distribution, and surrounded by stationary lead shielding. A canister containing the blood component(s) is placed on a turntable located at the front of the instrument. Irradiation is accomplished by moving the turntable in a 180° arc behind the lead shields so that the canister sits directly in front of the Cs-137 sources (Fig. 1). The turntable rotates while positioned in the field of radiation to improve the homogeneity of dose distribution inside the canister. Rotation speeds vary from 5 to 30 rpm; devices containing less cesium employ slower rotation frequencies. The length of exposure to the source determines the dose delivered. When the set exposure time is reached, the platform revolves to its original position to allow removal of the canister.

The size of the canister is one of several variables that distinguish different free-standing irradiators. Specific instruments currently available in North America include a device with a 1-L canister, which allows the irradiation of only 1 unit of red cells at a time (Gammacell 1000, Nordion In-

ternational, Kanata, ON, Canada), and a number of newer models with larger canisters, which allow 4 to 10 components to be irradiated concurrently (2.6-L canister; Gammacell 3000, Nordion; 1.44-L [Model 143-45A] and 3.7-L [Model 143-68] canisters, J.L. Shepherd and Associates, San Fernando, CA; and 3.8-L canister, Model IBL 437C, CIS-US, Bedford, MA).

Free-standing blood bank irradiators may also employ Co-60 as the source of gamma rays. In these models, 12 equidistant pencil-shaped sources of cobalt are configured in a circular arrangement along the perimeter of the radiation chamber. Blood unit(s) are placed into a canister that is moved vertically into the irradiation chamber by the use of an electropneumatic drive system. The circular arrangement of the radiation sources provides a highly homogenous delivery of gamma radiation, so that a turntable is not required. Co-60 sources require considerably more lead shielding than do Cs-137 sources, because cobalt has a greater emission strength than cesium. The half-life of Co-60 is only 5.3 years, so that the instrument must be calibrated frequently to ensure that the correct dose is administered as the energy of the source decays. Accordingly, timer corrections should be made on an annual basis with Cs-137 irradiators and on a quarterly basis with Co-60 instruments. It is advisable to replace cobalt sources when one or more half-lives have expired (5-10 years). Co-60 instruments are currently available with 1.44-L or 3.2-L canisters (Models 109-A and 109-C, J.L. Shepherd).

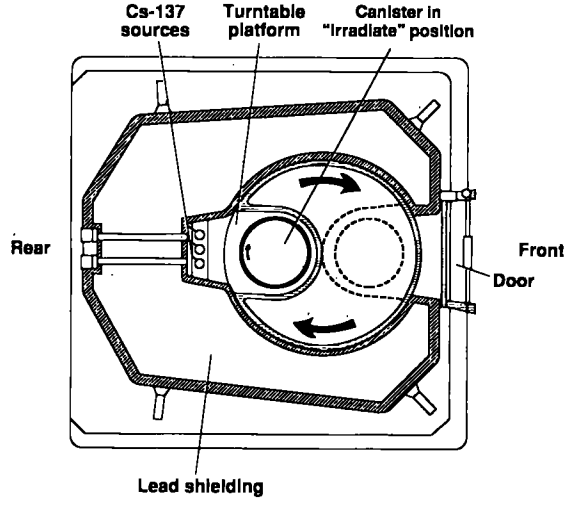

Fig. 1. Horizontal cross-sectional view of irradiation mechanism inside a typical Cs-137 irradiator (IBL 437C, CIS-US). Three vertically oriented, pencil-shaped sources of Cs-137 are enclosed in a chamber surrounded by a double layer of lead shielding. The chamber contains a turntable platform that opens to the front of the device when irradiation is not being performed. The canister containing blood components is placed on this turntable. Irradiation is accomplished by moving the turntable in a 180° arc (arrows) behind the lead shields so that the canister sits directly in front of the Cs-137 sources. The turntable rotates while in the field of radiation to improve dose homogeneity in the canister. After a set time has elapsed, the turntable platform is automatically returned to its original position in front of the lead shields. Adapted with permission from the operator's manual for the IBL 437C, CIS-US, Bedford, MA.

The manufacturers of cesium and cobalt blood bank irradiators provide a Calibration Certificate with all new instruments. The certificates contain information regarding the dose targeted to the central portion of the canister (central dose rate) and dose distribution at the time the source was initially installed. Monthly updates in the dose rate may also be included in these certificates to allow easy calculation of timer corrections that are necessary for longer exposure intervals as the strength of the source decays. Both Co-60 and Cs-137 blood irradiators are heavy, and structural analysis of the weight that the floor can bear (floor loading capacity) by a building engineer should be performed before installation. Cs-137 irradiators weigh between 2000 and 4400 lb; Co-60 instruments are heavier, weighing about 6000 lb. A major contributor to the variability in instrument weight is the amount of lead shielding around the radioisotope source.

Irradiation of blood components is also being performed with instruments used to treat patients with radiation. Linear accelerators are the predominant type of teletherapy instrument in current use. The accelerator enables electrons to be focused into a beam and altered to have a high energy state. When used to irradiate blood, the beam of electrons is converted into a beam of x-rays through contact with a metallic surface. Beam instruments employing Co-60 as the source of gamma rays are being utilized less and less, as greater reliance is placed on linear accelerators.

SELECTION OF DOSE

It is critically important to use a dose of irradiation that completely inactivates the T-lymphocytes in blood components. Data generated in the late 1970s using mixed lymphocyte culture (MLC) assays to assess the effect of irradiation on T-cell-mediated allogeneic reactivity led many blood banks to use a dose of 1500 cGy. For many years, little attention was paid to the configuration of blood bags in the irradiated field, to the homogeneity of dose distribution in the field, or to methods to confirm, ensure, and document that preset doses were actually administered. Furthermore, the 1500-cGy guideline was arrived at in experiments that used purified suspensions of lymphocytes irradiated in test tubes, a setting that may not be exactly applicable to blood bags. To date, three cases of transfusion associated-graft versus host disease have been reported in individuals who received components said to be irradiated with 1500 to 2000 cGy.[7-9] Because dose validation measurements (dosimetry) and qualitative radiation indicators (visual verification labels) were not utilized in these cases, it was unclear whether the stated doses actually were delivered to all parts of the blood

components, or even if the implicated components had been irradiated at all.

The optimal dose for irradiating blood components has been reevaluated in the last few years. The approach that we and other laboratories have taken is to irradiate blood components in a standard manner using either a blood bank irradiator or a linear accelerator. The degree of T-cell inactivation is analyzed in samples removed from the units after incremental radiation exposures. A sample taken from the bags before irradiation provides a baseline measurement.

To assess the effect of irradiation on the capacity for T-cell growth, we have used the limiting dilution analysis (LDA), which provides quantitative data on very low frequencies of proliferating T cells. The LDA is considerably more sensitive than the conventional MLC assay; it can detect a 5 $\log_{10}$ reduction in the ability of viable immunocompetent T cells to proliferate when exposed to stimuli, whereas the MLC assay can detect only a 1 to 2 $\log_{10}$ reduction.[1] To determine the radiation dose that caused complete abrogation of T-lymphocyte growth, red cells preserved in additive solution (ADSOL, Baxter Healthcare, Deerfield, IL) were exposed to increasing doses of gamma radiation in a Cs-137 irradiator.[10] Exposure to 1500 cGy resulted in a 2 to 3 $\log_{10}$ inactivation of T cells, but T-cell growth was still observed in all experiments. With 2000 cGy, more than 4.7 $\log_{10}$ T cells were inactivated and no T-cell growth was observed in seven of eight experiments. After delivery of 2500 cGy, no further T-cell growth could be detected in any LDA experiment, which represented a greater than 5 $\log_{10}$ inactivation in cells. These studies were performed using 1-day-old red cells preserved in ADSOL but were confirmed using 7- and 21-day-old units as well. Similar results were obtained using x-rays from a linear accelerator as the source. These data served as the basis for the Food and Drug Administration recommendation that the target dose for use in irradiating blood components should be 2500 cGy.[11] A dose of 2500 cGy targeted to the central portion of the irradiator canister used in these studies was associated with a dose range of 1800 to 2800 cGy throughout the volume of the blood bags, as documented by dose-mapping studies.[10]

In a related study, 1-day-old plateletpheresis components (collected with the CS-3000 apheresis device and in PL-732 containers, Baxter Healthcare) were initially irradiated with 1500 cGy and then with an additional 1000 cGy, for a total dose of 2500 cGy.[12] Platelet components were prepared in a way that allowed for the harvesting of sufficient lymphocytes so that the LDA could be utilized. After exposure to 1500 cGy, T-lymphocyte growth was still observed in all samples. However, no clonal growth could be detected in any experiments after exposure to 2500 cGy. These results reaffirmed 2500 cGy as an appropriate central target dose of radiation. Subsequent studies by other investigators on plateletpheresis components exposed to radiation doses ranging from 500 to 4500 cGy and analyzed with MLC and mitogen stimulation assays further supported these findings.[13]

It should be noted that long-term storage after exposure to 2500 cGy or more has been associated with impaired in vivo red cell recovery[14] but not with impaired platelet recovery.[15] For these reasons, the shelf life of irradiated red cells is limited to a maximum of 28 days, whereas the standard storage interval for platelet concentrates is not affected by prior irradiation.[11]

Cryopreservation of previously irradiated red cell units was shown to have no adverse effects on in vivo red cell recovery when the units were frozen within 6 days of collection and irradiation.[16] However, there are no published studies on the irradiation of red cell units in the frozen state. Gamma radiation affects blood components through the Compton effect, whereby the dose delivered is directly and linearly proportional to the density of the material being irradiated. Because ice is slightly less dense than water, the radiation absorbed by a frozen component would be slightly less than that absorbed by a liquid component at the same dose setting. However, the degree of this difference is minimal (<1%) and, on a practical level, trivial. Thus, the dose delivered to a frozen component is not significantly different than that delivered to a liquid component, and it is acceptable to irradiate frozen components at the same dose settings used for liquid components.

TABLE 1. Recommendations for quality assurance of free-standing irradiators and linear accelerators used to irradiate blood components

	Free-standing irradiators	Linear accelerators
Timer accuracy	Daily or monthly*	NA
Turntable operation (Cs-137)	Daily	NA
Qualitative indicator label	Every component	Every component
Dose mapping	Annually for Cs-137; semiannually for Co-60	Quarterly
Adjustment of timer for isotopic decay	Annually for Cs-137; quarterly for Co-60	NA
Preventive maintenance	Annually	Per instrument program
Personnel monitoring (TLD film badge)	Not necessary by Nuclear Regulatory Commission regulations	Monthly
Surface check for radioactive leak (wipe test)	Annually	NA
Consistency of beam quality	NA	Quarterly
Consistency in size of field	NA	Quarterly

* Daily if instrument has no back-up timer, monthly if instrument contains a back-up timer.

GUIDELINES FOR QUALITY CONTROL OF IRRADIATED BLOOD COMPONENTS

Free-standing blood irradiators provide the optimal mechanism for blood irradiation, in that the component remains in the blood bank and quality control is under the direct management of blood bank staff. Irradiation of blood by the use of teletherapy equipment may be inconvenient, because the component must leave the environment of the blood bank for an indefinite length of time and quality control of the irradiation process is out of the hands of blood bank staff. Most blood collection and/or transfusion services currently use designated blood irradiators located either within their own facility or at a nearby facility. There are approximately 500 such free-standing irradiators in use in the United States.

Appropriate quality control measures for blood irradiation (Table 1) include the routine use of qualitative indicators to confirm that radiation was performed as intended, daily confirmation of turntable operation (all Cs-137 models), yearly adjustment of the timer setting for Cs-137 devices and quarterly adjustment of the timer for Co-60 devices, yearly measurement of the delivered dose by appropriate dosimetric techniques, and yearly surveys to detect isotope leakage. In addition, timer accuracy should be confirmed monthly on irradiators containing back-up timers and daily on instruments not containing back-up timers. Monitoring with personal dosimeters (thermoluminescent dosimeter [TLD] film badges) of employees who perform irradiation of blood components is not required by the Nuclear Regulatory Commission (10 CFR 20), unless it is likely that an individual will receive more than 10 percent of the allowable annual dose limit. Monitoring thus does not need to be performed unless an annual exposure of at least 500 mrem to the whole body or 5000 mrem to the skin or extremity is expected. This level of exposure is extremely unlikely in users of free-standing irradiators, although the potential to exceed these thresholds does exist in operators of Co-60 teletherapy devices.

MEASUREMENT OF DELIVERED DOSE

As with other uses of radiation, it is vital to document the dose or quantity of radiation that is absorbed by blood components, to ensure that sufficient damage to lymphocytes has occurred. The absorbed dose, the critical determinant in this discussion, can be defined as the amount of radiation transferred to a blood component at a given point. The amount of radiation absorbed determines the extent of damage to the cell's DNA, which is expressed as the degree of lymphocyte inactivation. For many years, the unit of absorbed dose was the rad. Current nomenclature utilizes the terms gray (Gy) or centigray (cGy), with 1 Gy equal to 100 cGy, and 1 cGy equal to 1 rad.

It is also critical to document that the dose intended for delivery is actually delivered and that levels associated with an unacceptable degree of red cell, platelet, or granulocyte damage are not reached. Validation procedures must be in place to ensure that the technique of dose delivery is consistent and reproducible and that the mechanical systems involved in dose delivery, such as the turntable and the timer on gamma radiators, are operating correctly.[3] Periodic dosimetric assessment (documentation of dose distribution throughout the entire radiation field, also known as dose mapping) is the mechanism by which these objectives are met. Radiation dosimetry refers to the use of dosimeters to measure the absorbed dose of radiation throughout an irradiation field or to selected representative points in the field. Dosimeters are objects that convert the ionizing energy of radiation into another form, such as light, color, heat, or electrical output, which can be easily quantitated. Dosimetric assessments in gamma radiators are designed to evaluate whether turntable rotation, timer function, timer settings, and strength of source are correctly adjusted to yield the desired dose and to optimize dose homogeneity in the irradiation canister. Similarly, dosimetric assessments for linear accelerators or other teletherapy devices confirm that the configuration of the radiation field, the distance from the beam, the thickness of the plastic plates enclosing the blood components, and the duration of exposure—all calculated by radiation physicists using component simulation techniques—yield the required dose and maximize the uniformity of dose distribution.

DOSIMETRY WITH FREE-STANDING BLOOD BANK IRRADIATORS

Until recently, the procedures used to calibrate and validate the dose distribution in blood component irradiators varied greatly from facility to facility. In many cases, dosimetric measurements were not performed. In several case reports of transfusion-associated graft-versus-host disease after the administration of irradiated components, the absence of on-site programs for quality assurance of the irradiation process led to uncertainty as to the actual minimal dose delivered, and even to uncertainty as to whether the blood component had been irradiated at all.[7-9] Guidelines for blood component irradiation published by the Food and Drug Administration[11] highlighted the critical importance of standardization in irradiator dosimetry and made it mandatory to have mechanisms in place for validating the dose distribution throughout the irradiation field on at least a yearly basis. These guidelines stipulate that "the dose of irradiation delivered should be 2500 cGy targeted to the central portion of the container and 1500 cGy should be the minimum dose at any other point."[11(p11)] Several commercial firms, including manufacturers of blood bank irradiators, have responded to these concerns and developed standardized, reproducible, and convenient methods for irradiator dosimetry.

Dose mapping refers to the measurement of the absorbed dose over the entire area of an irradiation field, such as the canister of a free-standing irradiator. The dosimeter system used should be placed in a medium that closely mimics the radiation-interactive properties of blood. Both water and some types of plastic, such as clear polystyrene or polymethylmethacrylate, meet this requirement. The dose map is usually given as a two-dimensional diagram of absorbed dose at various locations in the canister. Particular emphasis is given to the dose targeted to the central portion of the irradiation canister, to the dose at the periphery of the canister where the amount of radiation is greatest (maximal dose), and to the dose at the top and bottom of the canister where the amount of radiation is lowest (minimal dose). These central and minimum dose measurements are utilized in the United States to evaluate compliance with regulatory standards.

Dose mapping should always be conducted in a fully loaded canister. This configuration causes maximum attenuation in the strength of gamma rays, thus yielding the lowest possible absorbed-dose values. As stated above, dosimetric measurements are generally performed using a phantom substance or solution with an adsorption coefficient equivalent to a canister full of blood components. If all points in the canister are documented to exceed minimum standards for absorbed dose in this test, then it is impossible to overfill an irradiation canister during daily operations of the irradiator. Thus, blood centers or transfusion services do not need to limit the loading of irradiators in standard daily practice. On the other hand, because canisters may not always be fully loaded with blood components, the dose absorbed by the blood component when a significant amount of air fills the canister will be higher than that predicted by the dose map of the fully loaded canister. This means that many components may receive slightly more than the targeted dose, to avoid a circumstance in which an underdose of a component might be given. In a recent study, increasing numbers of saline-filled blood bags were placed in the canister of a Cs-137 irradiator and film-based dosimetry was used to demonstrate that, as canister volume was filled incrementally from 0 to 100 percent with blood bags, the absorbed dose fell correspondingly.[18] The minimum absorbed dose in a completely filled canister was 500 cGy less than that in an empty canister. As reviewed below, the location of a component in the canister is responsible for a much greater degree of dose variation than is the degree of canister filling.

USE OF SPACERS IN IRRADIATOR CANISTERS

With all models of free-standing Cs-137 irradiators, blood components or portions of blood components at the bottom of the canisters receive somewhat less radiation than components or portions of components in the central section. To remedy this situation and elevate components above the area of minimum absorbed dose, spacers may be placed in the bottom of the canisters. One study has documented the quantitative influence of using such spacers.[19] Saline-filled red cell and plateletpheresis bags were manufactured to contain an immobilized grid of TLD chips. Lucite and styrofoam spacers were constructed so that they occupied the bottom 2.7 to 6.0 cm of the canisters of two instruments (Gammacell 3000 and IBL 437C, respectively). The mean minimum radiation dose absorbed by a pair of simulated red cell units increased from 2054 to 2454 cGy in the Gammacell 3000 and from 1892 to 2265 cGy in the IBL 437C when either of the two types of spacers was added and the canister was irradiated to 2500 cGy.[19]

COMPARISON OF DOSIMETRY SYSTEMS

A variety of dosimetry systems can be used to perform dose mapping. Of the currently available commercial systems, one uses TLD chips, two use radiation-sensitive film material, and one uses metal-oxide silicon field effect transistors (Mosfet).

The system involving TLD chips is based on a technique originally described by Masterson and Febo.[20] A cylindrical polystyrene phantom, or mold, is created that fully occupies the internal volume of the irradiator canister. TLDs are immobilized along two parallel axes within the phantom, the centerline axis and a peripheral axis, with sites sampled at the top, bottom, and midpoint of each axis. The TLD-containing phantom is sent to the irradiating facility, where it is placed in the irradiator and exposed to a conventional irradiation cycle. The phantom is then sent back to the manufacturer for analysis. This system has been validated by assessing its performance in 20 dosimetric measurements taken at eight centers over a 6-month period (IBL 437C). The distribution of the measured dose in the canister showed a very tight correlation with the theoretical isodose-distribution curves supplied by the manufacturer for each instrument.[21] TLDs such as lithium fluoride or calcium fluoride manganese are particularly applicable for the dose ranges used in blood irradiators. They are packaged as small plastic chips of approximately 3 × 3 × 1 mm. Exposure to ionizing radiation produces free electrons and holes that are trapped in the crystalline structure of the TLD. Heating the chip releases this excitation energy as light, with the amount of light generated being proportional to the energy of the radiation absorbed.[22]

Two systems employing film dosimeters have been developed.[23] In one system, a sheet of radiation-sensitive film is sandwiched between the walls of a flat, watertight plastic cassette. The cassette is customized by the manufacturer to fit inside almost any irradiator canister and is sent by the manufacturer to the irradiating facility. When the canister is filled with water and the cassette is placed along the inner diameter (central plane) of the canister, turntable rota-

tion during exposure causes the cassette to trace the three-dimensional volume of the canister. After exposure, the film cassette is sent back to the company for analysis. A readout of the change in film density after irradiation provides a continuous dosimetry map of the irradiation field (DOSE-MAP Dosimetry System, International Specialty Products, Wayne, NJ).

In the other film dosimetry system, film (Gafchromic, International Specialty Products) is sandwiched between two halves of a cylindrical polystyrene phantom, along the long axis of the phantom (Nordion). A series of three films are irradiated at different timer settings, and the resulting data are used to generate an isodose-distribution map, normalized to the desired central midplane (centerline axis) dose (Fig. 2). The central dose rate is determined separately by use of a Fricke dosimeter, in which absorbed radiation causes a change in the state of an iron salt that is quantitated spectrophotometrically. Small vials of the iron salt are placed in the center of the plastic phantom for this analysis. Dosimetry using this latter film-based system is performed by the manufacturer's staff, generally at the time of preventive maintenance visits.

Mosfet dosimeters were recently developed as a way of mapping the canister dose. These dosimeters store absorbed dose as a change in electronic charge. A series of Mosfet dosimeters is arranged on an electronic circuit board and the board is placed between the two halves of a cylindrical polystyrene phantom. Before and after irradiation, the circuit board is connected to a measurement system (Irradiator Dosimeter System, Thomson and Nielsen Electronics, Ottawa, ON, Canada). The electronic charge stored by a specific dosimeter after exposure is displayed as a dose of radiation. A Mosfet dosimeter can be used repeatedly until the total radiation-absorbed dose equals its electronic charge capacity. In contrast to the TLD, film, and Fricke dosimetry systems described above, the availability in this system of a portable, countertop measurement unit allows Mosfet-based dose maps to be generated on-site, immediately after the dosimetry test.

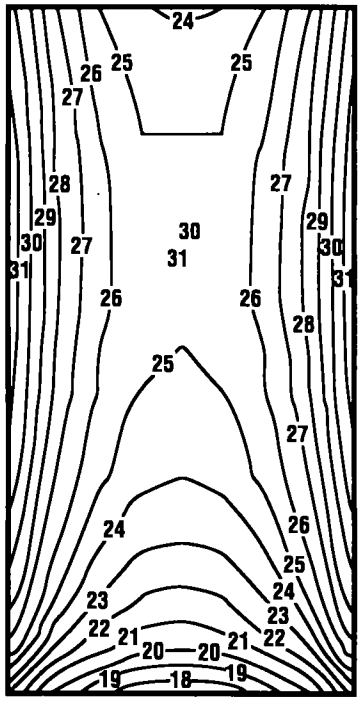

Fig. 2. Dose-distribution map for the 2.6-L canister of the Gammacell 3000. Isodose curves were determined by using sheets of radiochromic film sandwiched between two halves of a cylindrical polystyrene phantom and exposed to radiation cycles of varied lengths. The graphic representation of dose distribution is normalized to 25 Gy (2500 cGy) at the center of the canister. Minimum and maximum absorbed doses on this graph are calculated, not measured, from the isodose distribution curves and from a separate, Fricke-based measurement of the central dose rate in the same canister (Dose-Mapping Service, Gammacell 1000/3000, Nordion).

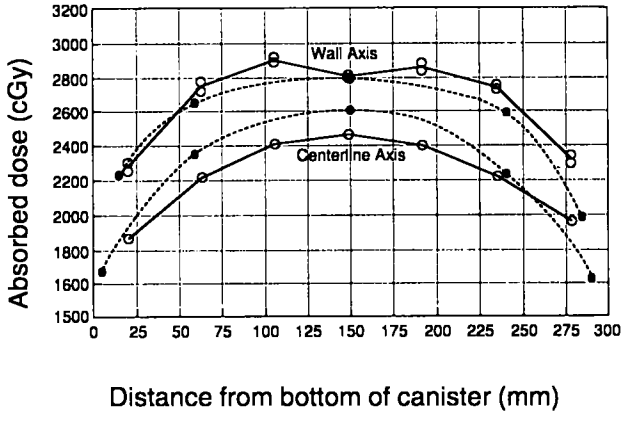

Fig. 3. Dosimetry validation reports on the IBL 437C set to deliver a central dose of 2500 cGy, as performed by two commercially available techniques. In the first technique, a plastic cassette containing radiochromic film was placed along the axis of rotation of a water-filled 3.8-L canister and exposed to a standard irradiation cycle; it yielded a continuous readout of absorbed dose throughout the canister. The straight lines display absorbed dose readings at selected points along the centerline axis and the wall or peripheral axis (International Specialty Products) O—O. With the second technique, a 3.8-L cylindrical polystyrene phantom containing 10 sets of triplicate TLD chips, five along the centerline axis and five along the canister wall, was exposed to a standard irradiation cycle, yielding 10 discrete measurements of absorbed dose at designated points in the canister. The dashed lines represent polynomial regression fits of these data points, as computed by the manufacturer (CIS-US) ●- - -●. Central and peripheral dose rates were found to agree within 5 percent using the two techniques, which is within the range of ± 5- to 10-percent accuracy of each method.

A comparison of dosimetric measurements taken on the same blood irradiator using both the phantom-imbedded TLD technique and one of the film-based dose-mapping techniques is shown in Fig. 3. The values obtained were identical using the two techniques (± 5% for points assessed at equivalent locations) which is within the range of ± 5- to 10-percent accuracy of each technique. Delivery of lower doses was noted along the central axis of the canister, with the very lowest doses delivered at the extreme top and bottom of the central axis; delivery of higher doses was noted along the canister wall. Using a programmed target dose of 2500 cGy, the measured mean central dose was 2510 cGy, with a range of 1560 to 2920 cGy (± 38% of the target dose).[24]

It is thus clear that a number of standardized, convenient, and accurate techniques to measure irradiator dosimetry currently exist. In deciding which of these to use, or in designing in-house systems using TLDs, liquid dosimeters, films, or customized phantoms, consultation with a medical physicist or radiation biologist is very helpful. The Calibration Certificate and source decay tables provided by the manufacturer with each new irradiator should be the basis upon which times of exposure are set, so as to deliver a targeted midplane dose, but dose distribution must be validated yearly and dosimetric validation repeated whenever repairs are made to the irradiator or when the irradiator is moved.[11]

DOSIMETRY WITH LINEAR ACCELERATORS

When blood components are irradiated using linear accelerator or Co-60 beam instruments, they must be placed between "tissue-equivalent" plastic slabs of defined thickness, in a sandwich configuration. The plastic slab closest to the source of the beam causes the radiation to be at electronic equilibrium and therefore at maximum energy when it traverses and is absorbed by the blood component. The plastic slab farthest from the beam source maintains the uniformity of the radiation field by providing a source of back-scattered radiation. Studies using TLD chips imbedded in simulated blood components (water-filled blood bags) have shown that the range between the maximum and minimum absorbed dose in each component was twofold greater with a Cs-137 irradiator than with a linear accelerator.[19] Overall, radiation using beam instruments results in highly uniform and reproducible dose distribution in the blood component.

The ionization chamber is the dosimetric device currently used by radiation physicists to determine the output of beam instruments. A typical ionization chamber is a cylindrical structure containing air. With continuous radiation, ions are formed in the air, and the magnitude of the current generated is proportional to the absorbed dose, as measured by an electrometer. The ionization chamber should be immersed in a water-filled phantom resembling a fish tank, with the water serving as an acceptable tissue or blood substitute. For the actual measurement, the ionization chamber is surrounded by a protective sheath and placed at a given depth in the water. The absorbed dose of radiation can be assessed at a specific distance from the source, mimicking the position of a blood component. The data generated are used to calculate the time needed to deliver a specific dose. Procedures to validate the delivered dose of beam-type instruments should be performed on at least an annual basis. Ionization chambers should have a calibration traceable to the National Institute of Standards and Technology.

Because blood components will be irradiated in most cases with beam instruments used to provide radiation therapy to patients, dosimetry will generally be performed more frequently than yearly. Dosimetric assessment on a quarterly basis is recommended as a monitoring tool by many blood centers and hospitals that utilize beam instruments. The procedures in these instances do not require a water medium. Tissue-equivalent plastic phantoms that are designed for use with ionization chambers are adequate. Here too, the ionization chamber is placed at a given depth in the phantom. Two recent publications by the Radiation Therapy Committee of the American Association of Physicists in Medicine provide guidelines and recommendations for performing quality control assessments of radiotherapy accelerators.[25,26] These guidelines should be utilized to ensure that the conditions used to irradiate blood components provide for the prescribed dose.

Although ionization chambers are currently the primary tool for assessing dosimetry in beam instruments, it is also possible to document absorbed dose in a manner that mimics the actual physical geometry of the irradiation field, as is being done for blood bank irradiators. Both TLD chips and dosimetric films could be placed in tissue-equivalent plastic phantoms or inside water-containing blood component bags. This would eliminate the ambiguity of the fact that ionization chambers provide a direct measurement of ionization, while TLDs and other systems are relative measuring devices. Such dosimetry systems are not currently available on a commercial basis for use with beam instruments.

QUALITATIVE INDICATORS

Quality assurance of blood component irradiation also involves a system to ensure that components intended and assumed to be irradiated have, in fact, been exposed to ionizing radiation before release. Several visual verification labels for blood irradiation have recently been developed. One label contains a radiation-sensitive film chip that blackens with increasing exposure to ionizing irradiation, which obliterates the writing beneath the chip and alters the printed message from "Not Irradiated" to "Irradiated" (RADSURE, International Specialty Products). Labels that are sensitive to either 1500 or 2500 cGy are available. These labels were shown to be 100-percent accurate as indicators of ex-

posure to ionizing radiation.[27] It should be emphasized that the labels, called indicators to make the point more clear, are neither intended nor licensed for use as dosimeters. They cannot reliably distinguish between full and suboptimal doses of irradiation and were only 80-percent accurate in detecting components that were purposefully exposed to 1200 rather than 1500 cGy.[27] Thus, they cannot be used to ensure that a certain minimum dose of radiation has been given; they are simply meant to indicate that a component has actually been exposed to ionizing radiation (i.e., undergone a completed radiation cycle in a blood bank irradiator). Their use does not supplant or obviate the need for yearly dosimetric mapping of the irradiation field. In fact, it would be expected that an occasional indicator that is sensitive to 2500 cGy would not turn completely opaque if positioned at the very bottom of a canister, where the dose delivered might be as low as 1600 to 1700 cGy, and would still be within the acceptable performance limits of the irradiator device. In contrast, if an indicator that is sensitive to 1500 cGy darkens, but does not turn completely opaque after irradiation, an immediate dosimetric map of the irradiation field should be obtained. It thus makes most sense to use indicators that are sensitive to the lowest acceptable limits of radiation absorbed dose (1500 cGy) rather than the central targeted dose (2500 cGy). The use of such qualitative indicators completes the processes critical to the assurance of a correctly irradiated component.

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