**Symposium on Globalization of Nuclear Activities**

June 15-18, 1997, Rio de Janeiro, BRAZIL

-

# IRRADIATION OF BLOOD PRODUCTS: DEVELOPMENT OF SPECIFICAL IRRADIATORS

**Nélida L. DEL MASTRO & Paulo R. RELA**

Instituto de Pesquisas Energéticas e Nucleares, IPEN-CNEN/SP

Caixa Postal 11049, 05422-970 São Paulo, SP Brasil

email: *nlmastro@net.ipen.br*

## ABSTRACT

Leukocytes present in blood components are responsable for the so-called transfusion-associated graft-versus-host disease (GVHD). To avoid the occurrence of GVHD enterely, one would have to deplete blood components of all measurable lymphocytes physically. Irradiation of blood components, a method that completely eliminates lymphocyte mitotic potential, appears as the only practical way to avoid the disorder. This work aims at the discussion of the convenience of the development of specifical irradiators in our community for irradiation of blood products. The proposed irradiators will have a feature design that permit to be furnished with radiotherapy or industrial spent sealed sources, when their activities have decayed to the extent that are no longer suitable for their original purpose, but are still available at current active level for blood products irradiation.

## INTRODUCTION

Leukocytes present in blood components are responsable for the so-called transfusion-associated graft-versus-host disease (GVHD). Transfusion of labile blood product (whole blood, packed red cells, platelets or granulocytes concentrates) provides, along with therapeutically active cells, dangerous lymphocytes called immunocompetent cells, which are normally rejected in recipients with unimpaired immunity.

To avoid the occurrence of GVHD enterely, one would have to deplete blood components of all measurable lymphocytes physically. There are currently no methods available to accomplish this degree of leukoreduction. Prolonged storage at 4° C, glycerolization, freezing at -70° C and subsequent deglycerolization, washing or filtration may all effect up to a 1-4 $\log_{10}$ -fold reduction in leukocyte content but do not eliminate leukocytes enterely, and the remaining cells have been shown

to be mitotically active.

As physical depletion has not resulted in the degree of leukocyte reduction necessary to prevent GVHD, irradiation of blood components, a method that completely eliminates lymphocyte mitotic potential, appears the only practical way to avoid the disorder. This choice is supported by the large difference in radiosensitivity fortunately present between lymphocytes and therapeutically active cells. On the other hand, it is worthy to keep in mind that platelets, granulocytes and red cells begin to lose their functional properties beyond 50Gy. Installations as diverse as X-rays generators, telecobalt devices and electron accelerators may be used, more or less easily, to irradiate one bag of blood products. The low delivery of X-rays generators implies irradiation times which are too long to make them convenient. Telecobalt equipment may deliver a dose of 40 Gy in 15 to 55 minutes according to the charge. Particle accelerators may deliver the same dose in only 4 to 5 minutes. The adaptation of such various equipments to the use for which they are not intended rises the need of highly specialized personnel in order to determine, for each device and each shape of blood bag, the dose rate delivery, the depth efficiency and the homogeneity of the irradiation field.

## TECNHIQUES OF BLOOD COMPONENT IRRADIATION

There are two methods currently available to irradiate blood components [1]. One uses γ ray-emitting radioisotopes such as $^{137}Cs$ or $^{60}Co$, which are encased in free-standing commercially available devices designed specially for use in blood banks. The other approach uses radiation therapy equipment such as linear accelerators, which emit high-energy photons in the form of X-rays [2]. They are both ionizing radiations that damage cells directly or by interacting with other molecules, particularly water. A third method of irradiating blood components involves exposure to ultraviolet (UV) light. Nevertheless, a practical and effective method of exposing blood components to UV is not currently available.

Optimal irradiation doses for the prevention of post-transfusion GVHD are selected according to two criteria [3]:

i. The inhibition of proliferative capacity of dangerous lymphocytes called immunocompetent cells is abolished at 5Gy and DNA synthesis is blocked at 9Gy;

ii. The first significant functional disorders occur from 5Gy for granulocytes and platelets and from 200Gy for red cells.

Preparers of blood products have therefore a range between 10 and 50 Gy that they may use with preservation of the functional qualities and the therapeutic effectiveness of blood cells.

In the United States, the American Association of Blood Banks mentions doses between 15 and 50Gy [4]. Most American teams use 15 or 25Gy.

In France, the regulations define "the qualification *irradiated* as applaying to all therapeutic blood products, cellular or possibly containing cells, when these products have been exposed to a dose of ionizing radiations between 25 and 45Gy" [5]. French teams use normally 25 or 30Gy.

In order to have acces to a flux of gamma radiation intense enough to deliver doses of a few dozen grays, users have two alternatives:

a. have the Radiotherapy Department use $^{60}Co$ sources or particle accelerators adapted to the irradiation of blood products;

b. acquire a self-contained commercial irradiator.

## PRESENT STATUS OF BLOOD IRRADIATION IN BRAZIL

The international market for blood irradiators is booming. Only in Japan, within the first 5 months of 1997, 22 units of blood irradiators were sold by an important local distributor. In Brazil, blood products irradiation started to be performed under medical demand for mainly packed red cells and platelets. Some successful attemps have been made to use radiotherapy equipment for blood components and cell cultures irradiation in this country [6]. At the Department of Radiotherapy of the Fundação Antonio Prudente in Sao Paulo, irradiations of blood components have been performed during the last 5 years in a small scale. For the few cases of bone marrow transplantation at that institution, all the transplanted blood components were irradiated.

At the main blood bank in Sao Paulo, located at the Hospital das Clinicas of the Sao Paulo University, about 200 hospitals are attended using a commercial $^{137}Cs$ irradiator. Platelet and red blood cells concentrates and leukocyte mixture cultures are the main irradiated products in about 3,000 irradiations a month. An annual demand increase of 30% is expected for the next years. Also, some big hospitals are planning to have its own equipment for blood component irradiation.

So, at present, it is extremely opportune to discuss the convenience of the development of specifical irradiators in our community for irradiation of blood products in order to prevent the risks of post-transfusion graft-versus-host disease in immune-depressed patients.

## THE PROPOSED IRRADIATOR FEATURE DESIGN

The irradiators will have a design that permit to be furnished with radiotherapy or industrial spent sealed sources, whose activities have decayed to extent that they are no longer suitable for the original purpose, but are still available at current active level for blood products irradiation.

The design of this irradiation device will be similar to the self-shielded "gammacell" used for currently for research works. The sources will be positioned vertically in four positions at different heights around the irradiation chamber. The products to be treated will be placed inside a 3.5 liter cylindrical metal canister, when moved down inside the irradiation chamber it rotates at 2 to 45 rpm, in order to maximize the dose uniformity. The Figure 1 illustrates the proposed irradiation device.

The used sealed sources before be fixed inside the irradiators will be submitted to a leakage test to attend the performance and safety established by the international standards ISO 2919 and ISO 9978. The total activities of the sealed sources will be from 2000 to 6000 Ci.

As the range of doses to be delivered to the blood components is quite narrow, it is important to determine the isodose curves inside the irradiation chamber. The implementation of a radiation dosimetry, dosimetric validation and a good manufacturing practice (GMP), all of this procedure are necessary to assure:

- the proposed irradiation technique delivers the required doses and it must be consistent, reproducible and easily certificated by the dosimetric assessment;
- the proposed methodology prevents human errors, such as under or over doses, absence of irradiation or double exposure of a product;
- Identification with special labeling and recording of irradiated units;
- Verification of mechanical components and instruments of control and exposure time.

## CONCLUSION

Presently, exposure of blood products to certain doses of ionizing radiations is the most efficient way to prevent post-transfusion GVHD. In this paper, a self-contained irradiator, especially designed for blood products irradiation using spent sources is presented as an alternative of commercial irradiators. The recycle of spent sources will reduce the cost of irradiators. From the point of view of radioactive waste management the reuse of spent sources is highly desirable to minimize mainly the number of $^{137}Cs$ sources stored pending disposal.

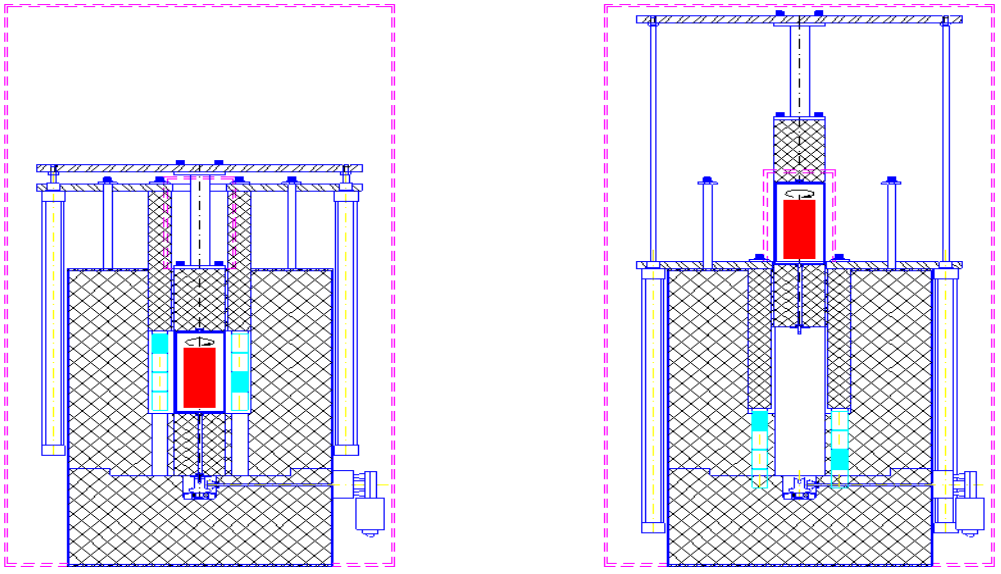

FIGURE 1- Proposed irradiation device

## REFERENCES

[1] Leitman, S. Leukocyte Inactivation by Blood Irradiation. In: "**Clinical Practice of Transfusion Medicine"**, Petz, Swisher, Kleinman, Spence and Strauss. Churchill Livingstone, New York, 1996.

[2] Tanata, S.;Sugimoto, A.; Fukumori, Y.; Ohnoki, S. & Yamaguchi, H. Inactivation of lymphocytes by irradiating blood products with X-ray to prevent post-transfusion GVHD. **Nippon-Yuketsu-Gakkai-Zasshi, 36**(6):687-694, 1990.

[3] Reviron, J. & Gerota, J. Produits sanguins irradiés. Mormes françaises. Problemes posés par les contrôles de qualité. **Rapport Ministère de la Santé**, projet n$^{o}$ 1, Paris, 1984.

[4] **Technical Manual, AABB**, 1985, 276 and 341, USA, 1985]

[5] **Decree of Ministere de la Santé** 15.09.1983, art. 21, France, 1983]

[6] Fernandes, M.A.R., Pereira, A.J. and Novaes, P.E.R.S. Irradiação de sangue, hemoderivados e culturas celulares em equipamentos de radioterapia de uso clínico. Estudo sobre volume e doses ideais. **III Brazilian Meeting on Nuclear Applications, 2:**.969-974, 1995.

Return Techical Posters

Return Index of Authors

Return Index of Works