X-ray irradiation of blood components

1 Background

The risk of development of Transfusion-Associated Graft versus Host Disease (TA-GVHD) following transfusion of blood components containing viable lymphocytes to susceptible individuals has been well documented (1). It is routinely prevented by irradiation of components, and British Committee for Standards in Haematology (BCSH) Guidelines outline the use of gamma irradiation for the prevention of TA-GVHD (1).

Gamma irradiation, although effective in preventing TA-GVHD, has some drawbacks. It involves the use of a radioactive source, which is subject to stringent health and safety regulations. The machines are also very expensive to buy and decommission when no longer required. In addition, due to decay of the source, regular recalibration is required and irradiation time is increased.

X-ray irradiation is a possible alternative to gamma irradiation. This has been delivered in some areas using linear accelerators, though dose mapping these machines for this purpose may be difficult. However, a shielded cabinet X-ray radiation source is now available - the Raycell, manufactured by Nordion. SACBC have reviewed data on the use of this machine.

2 Raycell x-ray irradiator

In 1998, this machine (then the 'RS 3000 shielded cabinet X-ray source', manufactured by Rad-Source and later sold to Nordion) was granted a marketing license by the FDA to market the device as 'substantially equivalent' to a gamma irradiator. It is CE marked (for conformance to electrical specifications - CE mark does not deal with the effects of ionising radiation on blood components).

It is in use in several European and US sites, including Puget Sound in Seattle, Sweden, Italy, France and Germany. In France, EFS and AFSAPS approval has been granted based on published data (2).

It is dose-mapped prior to release from the factory and at installation, and the manufacturers recommend routine dosimetry at 6-monthly intervals. They also manufacture a radiation sensitive label specifically for use with X-radiation.

3 Blood component data

3.1 Efficacy for prevention of TA-GVHD

Several publications state that X-ray irradiation is equivalent to gamma irradiation (2-4). Moroff and Luban state that "Two types of ionising radiation, ? rays and X-rays, inactivate T lymphocytes. Both can be used to irradiate blood and blood components. At a given absorbed dose, both ? and X-rays are equivalent in their ability to inactivate T lymphocytes" (5).

Janatpour et al (2) compared X-ray with gamma irradiation using the Raycell irradiator. They performed a small study on lymphocyte function as part of this work. They reported as follows: "Lymphocytes isolated from both gamma- and X-ray-irradiated (25 Gy) portions of one unit showed an identical lack of proliferation when stimulated with mitogen or with allogeneic leucocytes. One cell division was observed in the cultures with PHA, no cell division was observed in the MLC cultures. Lymphocytes from the control portion showed expected proliferation in both assays".

Herva and Kiviniity in an earlier study found no difference between the effects of X-ray irradiation, cobalt and 45 MeV electron irradiation on lymphocyte response when equivalent doses were given (6).

During Process Qualification prior to implementation, Dinwiddie et al from the Puget Sound Blood Centre in Seattle compared lymphocyte viability following irradiation of red cells in the x-ray irradiator with gamma irradiation (7). Compared to control cells, those irradiated in the X-ray irradiator showed a 6 – 30 fold decrease in viability and were not significantly different from those irradiated in the gamma irradiator.

On personal communication with a senior radiation physicist, we are advised that in general, X-rays should have very similar effects to gamma rays on blood components as the energy disposition mechanisms are similar, provided the doses delivered are equivalent. X-rays however are attenuated more rapidly therefore dose distributions can be variable – dosimetry therefore needs to be checked carefully.

Use of X-irradiation is already established in Centres in Europe and the US. Communication from a large transplant unit in Seattle confirmed that X-irradiated components were being transfused to stem cell transplant patients without problems. In addition, it is licensed as equivalent to gamma irradiation with the FDA.

3.2 Component quality

Irradiation can be applied to all cellular components: red cells, platelets and granulocytes. Below are summaries of 1) published data; 2) data provided by the Karolinska Institute; and 3) data generated by the NHSBT Component Development Laboratory.

3.2.1 Published data

3.2.1.a Red cells

Janatpour and co-workers compared red cell quality after irradiation with gamma and X-rays at 2 doses (25 Gy and 35 Gy). The recommended dose in the UK is a minimum of 25 Gy and maximum of 50 Gy. They looked specifically at free plasma haemoglobin (Hb), and extracellular potassium levels, as these have previously been shown to be parameters affected by irradiation. They found that at 25 Gy, X-ray irradiated units had slightly higher levels of free plasma Hb, whereas at 35 Gy, gamma irradiated units showed higher levels of extracellular potassium. They concluded that small differences in red cell membrane permeability were found between ? irradiated and X-irradiated units, but that these differences were not likely to be clinically important. This study however was conducted using non-leucodepleted red cells in CPDA-1. Leucodepletion may increase free Hb levels further. Most red cell units in the UK are resuspended in SAG-M additive solution, and one report has suggested that the presence of mannitol after irradiation may increase extracellular potassium (4).

3.2.1.b Granulocytes

One study has shown that neutrophil chemotaxis and chemiluminescence is unaltered by exposing buffy coats to 1500 rads (15 Gy) of x-irradiation (8). A further study has shown that neutrophil function is only marginally affected by exposure to 10,000-20,000 rads (100-200 Gy) of x-irradiation (9). Therefore exposure to 25-50 Gy is unlikely to have an impact on neutrophil function in granulocyte concentrates.

It is unlikely that red cell haemolysis or potassium leakage would be an issue in granulocyte components due to the lower red cell content and shorter shelf life than red cell concentrates. Puget Sound Blood Center is a centre of excellence for granulocyte studies, and routinely uses X-irradition for its components.

3.2.2 Data provided by Dr Hans Gulliksson, Karolinska Institute, Sweden

The Raycell is in routine use in Dr Gulliksson's facility and he has provided data on component quality of leucocyte depleted x-irradiated components. A summary is given below, the original data is available on request.

3.2.2.a Platelets

Platelets can be irradiated at any point during their normal shelf life and irradiation does not reduce platelet shelf life. Data from a pooled and split study on leucocyte depleted apheresis platelets stored in plasma is shown in Table 1. Platelets were irradiated on day 1 and stored for 7 days (n = 3 controls, n = 3 x-irradiated). The data shows that there is negligible effect of X-irradiation on platelet quality in vitro.

Table 1. The effect of x-irradiation on platelet quality (Karolinska Institute)

Validering av bestrålade trombocytkoncentrat från aferes. Start 20040928									
Test	units	Day 1		Day 3		Day 5		Day 7	
		x-ray	control	x-ray	control	x-ray	control	x-ray	control
Volume	mL	401±5	402±9						
platelets	10^9/unit	329±35	326±36	325±41	320±40	314±37	312±36	312±41	308±38
MPV	fl	7,8±1,0	7,7±0,8	7,6±0,7	7,7±0,9	7,8±0,8	7,8±0,8	7,9±0,8	8,1±0,8
pH	37°C	7,086±0,050	7,090±0,046	7,161±0,042	7,164±0,039	7,195±0,046	7,193±0,050	7,192±0,067	7,186±0,072
pCO_2	kPa 37°C	3,76±0,23	3,75±0,24	3,24±0,11	3,18±0,12	3,05±0,13	3,03±0,15	2,89±0,14	2,92±0,15
pO_2	kPa 37°C	17,5±1,3	16,8±1,6	17,5±1,3	17,5±1,3	19,5±1,7	19,3±1,1	20,1±1,7	20,3±1,4
Bicarbonate	mmol/L	8,1±0,7	8,1±0,6	8,3±0,6	8,3±0,5	8,6±0,9	8,5±1,0	8,1±1,5	8,1±1,5
Glucose	mmol/L	6,5±0,3	6,5±0,4	6,0±0,5	6,0±0,5	5,2±0,5	5,2±0,6	4,3±0,7	4,2±0,7
Lactate	mmol/L	1,3±0,2	1,3±0,2	2,7±0,4	2,7±0,5	4,1±0,6	4,1±0,8	5,8±1,0	5,7±1,0
ATP	umol/10^{11} plt	6,87±0,61	7,13±0,72	6,41±,75	6,52±0,75	6,02±0,59	6,15±0,60	5,59±0,53	5,74±0,70
LDH	%	4,2±0,8	4,1±0,7	4,6±0,7	4,3±0,9	4,7±0,6	4,9±0,8	5,3±0,7	5,4±0,7
PF 4	IU/10^{6}plt	17,4±7,6	18,4±8,3			48,7±13,1	53,8±14,7	58,1±15,9	58,5±16,4
RANTES	IU/10^{6}plt	100,7±28,2	94,5±24,6	223,1±73,5	226,0±73,0	317,0±105,1	301,2±85,5	380,9±99,6	353,9±89,3
HSR	IU/10^{6}plt	80,4±11,6	78,7±8,8	68,3±12,8	66,6±13,9	56,9±13,0	61,0±11,4	58,5±7,8	55,9±8,4
ESC	IU/10^{6}plt	39,5±9,7	38,2±7,7	28,7±5,5	28,2±5,5	29,0±1,7	28,4±3,7	21,7±5,9	20,6±5,0
Swirling		yes	yes	yes	yes	yes	yes	yes	yes

3.2.2.b Red cells

The following red cell components may be gamma-irradiated for clinical use:

- Red cells produced for intra-uterine transfusion (IUT)
- Red cells for exchange transfusion to neonates
- Red cells in additive for neonates following IUT or for adults for certain clinical indications

Red cells produced for IUT or exchange transfusion must be irradiated no later than 5 days following donation, and must be transfused within 24 hours of irradiation and no longer than 5 days following donation. Red cells in additive can be irradiated up to 14 days following donation, and must be transfused within 14 days of irradiation.

The main result of irradiation of red cells is an increase in haemolysis of red cells and potassium leakage into the supernatant. Both of these parameters increase during red cell storage and following irradiation. Data provided by the Karolinska Institute on x-irradiated red cells is given in Tables 2 - 4, alongside historic data from NHSBT.

Table 2. X-irradiation of LD red cells in SAG-M irradiated day 1 (mean ± SD, n=6)

	Day 1	Day 7	Day 14	Day 21	Day 28
Haemolysis (%)	0.06 ± 0.00	0.14 ± 0.05	0.24 ± 0.08	0.37 ± 0.15	0.44 ± 0.07
ATP (?g/gHb)	5.00 ± 0.57	5.30 ± 0.88	5.18 ± 0.54	4.47 ± 0.48	4.04 ± 0.60
Supernatant Potassium (mmol/l)	6 ± 1	39 ± 4	48 ± 3	53 ± 3	56 ± 3

Table 3. X-irradiation and gamma-irradiation of LD red cells in SAG-M irradiated day 14

	Day 14/15	Day 21	Day 28
Haemolysis (%) – x-irradiated	0.20 ± 0.25	0.24 ± 0.13	0.40 ± 0.20
Haemolysis (%) – gamma-irradiated	0.07 (0.05-0.10)	0.16 (0.13-0.24)	0.31 (0.24-0.40)
ATP (?g/gHb) –x-irradiated	5.27 ± 0.46	5.09 ± 0.41	4.25 ± 0.42
Supernatant Potassium (mmol/l) – x-irradiated	23 ± 5	44 ± 5	50 ± 5
Supernatant Potassium (mmol/l) – gamma-irradiated	42 (38-45)	60 (52-64)	66 (63-69)

x-irradiated unit data from Karolinska (mean ± SD, n=6), gamma-irradiated data from NHSBT (mean with range, n=10)

Table 4. X-irradiation and gamma-irradiation of LD red cells in plasma irradiated day 4/5 (for neonatal exchange transfusion)

	Day 4/5	Day 6/7	Day 7/8
Haemolysis (%) – x-irradiated	0.21 ± 0.13	0.29 ± 0.12	0.28 ± 0.10
Haemolysis (%) – gamma-irradiated	0.04 (0.02-0.12)		0.05 (0.03-0.19)
ATP (?g/gHb) –x-irradiated	4.90 ± 0.22	5.18 ± 0.04	5.63 ± 0.03
Supernatant Potassium (mmol/l) – x-irradiated	6 ± 1	10 ± 1	12 ± 1
Supernatant Potassium (mmol/l) – gamma-irradiated	13 (11-19)		21 (19-25)

x-irradiated unit data from Karolinska (mean ± SD, n=3), gamma-irradiated units from NHSBT (mean with range, n=10)

The data in Tables 2 - 4 suggest that the quality of red cells in SAG-M are suitable up to 14 days following x-irradiation and for red cells for exchange up to 24 hours after irradiation. However, the levels of haemolysis appear to be higher than in historical data from the NHSBT on gamma-irradiated units and no data are available on IUT units. Therefore it was decided that haemolysis and potassium levels should be further assessed during validation studies as follows:

Component	Day of irradiation	Time points following irradiation to assess
Red cells for IUT	4	0, 24 hours
Red cells for exchange	4	0, 24 hours
Red cells in additive	14	0, 7 days, 14 days

This work was undertaken by the NHSBT Component Development Laboratory (CDL), in collaboration with NHSBT Oxford (X-irradiated units), and NHSBT Brentwood (gamma-irradiated units).

3.2.3 Data from NHSBT Component Development Laboratory (EVAL/CD/2007/57)

3.2.3.a Study design

Study 1: Effect of X-ray irradiation on red cell units in SAG-M

10 units of whole blood were processed into RCC-SAGM. 6 units were prepared by TAT processing and other 4 units were prepared by BAT processing. All the units were X-irradiated (central dose 35.9 Gy) using the Raycell X-ray irradiator on day 14. Samples were taken pre-irradiation, post-irradiation (0 hrs), post-irradiation (7 days) and post-irradiation (14 days). Supernatant samples were achieved by double centrifugation at 2000 rpm for 30 and 15 minutes. All samples were stored at -40°C. All the frozen samples were couriered to CDL on dry ice for analysis of supernatant potassium and haemoglobin.

Study 2: Effect of X-ray irradiation on red cell units for Exchange

10 units of whole blood units were prepared by TAT processing into red cell units for Exchange. All the units were X-irradiated (35.9 Gy) using the Raycell X-ray irradiator on day 4. Samples were taken pre-irradiation, post-irradiation (0 hrs) and post-irradiation (24 hrs). Samples were processed as for study 1.

Study 3: Effect of X-ray irradiation on red cell units for IUT- Intrauterine Transfusions

10 units of whole blood units were prepared by TAT processing into red cell units for IUT. All the units were X-irradiated (35.9 Gy) using the Raycell X-ray irradiator on day 4. Samples were taken pre-irradiation, post-irradiation (0 hrs) and post-irradiation (24 hrs). Samples were processed as for study 1

3.2.3.b Results

Please note that for clarity the figures show only the results of statistical tests for difference (p value) between the irradiation treatment (X-ray v gamma) at the end of shelf life.

Study 1 Effect of X-ray irradiation on RCC in SAG-M

a) Supernatant Potassium

No difference was seen between pre and post-X-ray irradiation (0 hrs). Although supernatant potassium levels increased by Days 7 and 14 post X-ray irradiation.

There was no significant difference in Supernatant Potassium levels in X-ray and Gamma irradiated RCC in SAG-M at the end of shelf life, as shown in Figure 1.

Figure 1A **Figure 1B**

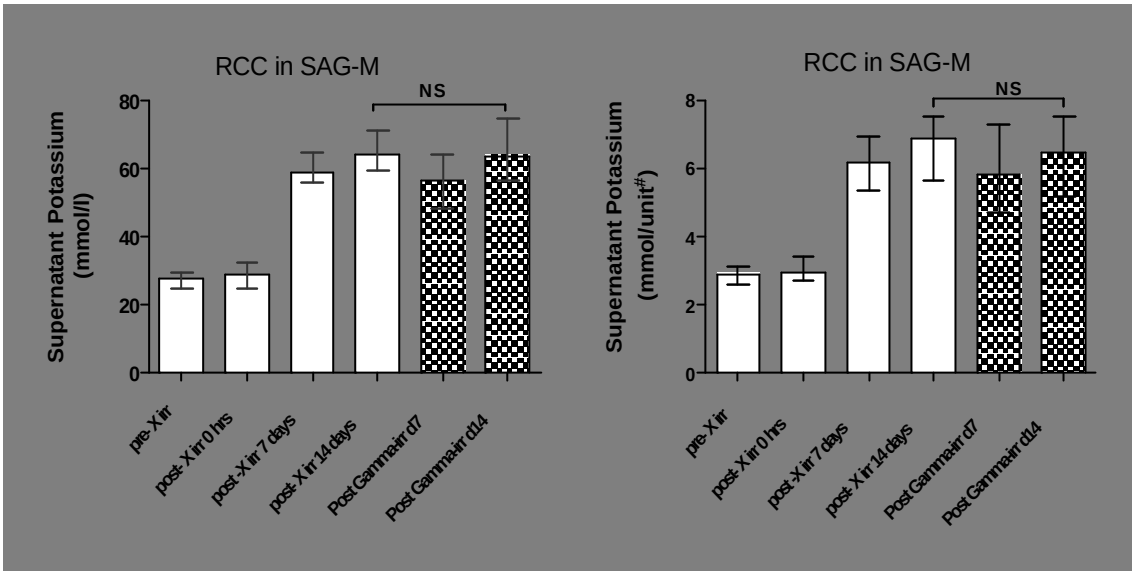

Figure 1 Potassium levels in X-ray irradiated (at Day 14) and CDL data from gamma irradiated RCC in SAG-M. K^+ expressed as mmol/l in figure 1A and mmol/unit in figure 1B.

NS – p value is Non Significant
Potassium levels calculated using unit volume corrected to account for sampling.
Data plotted as median with range
n=10 for X-ray irradiated units
n=20 for gamma reference data

b) Haemolysis

No difference was seen between pre and post-X-irradiation (0 hrs). Although haemolysis increased by Days 7 and 14 post X-irradiation, all were all below the UK limit of 0.8%.

There was no significant difference in haemolysis in X-ray and Gamma irradiated RCC in SAG-M at the end of shelf life, as shown in Figure 1c

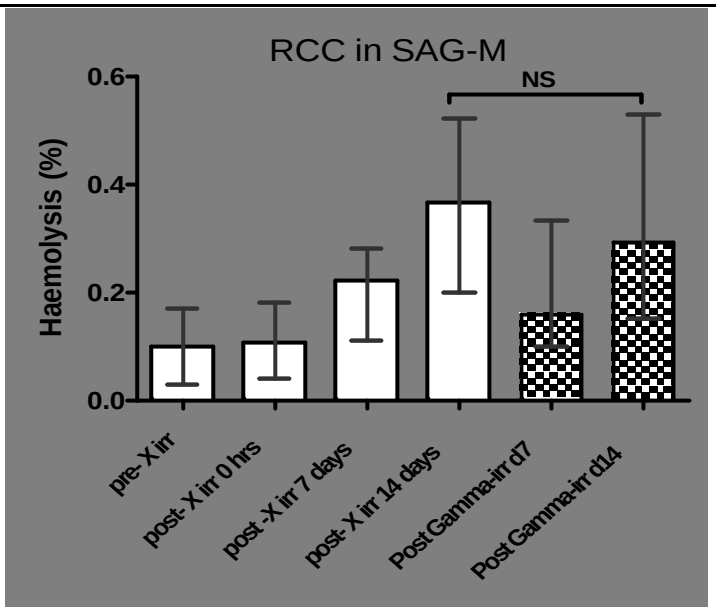

Figure 1c Haemolysis in X-ray irradiated at Day 14 and CDL data from gamma irradiated RCC in SAG-M.

NS – p value is NonSignificant
Data plotted as median with range
n=10 for X-ray irradiated units
n=20 for gamma reference data

Study 2 Effect of X-ray irradiation on red cell units for exchange transfusion

a) Supernatant Potassium
No difference was seen between pre and post-X-irradiation (0 hrs).

Units were X-irradiated on day 4, and tested at 24 hours post X-irradiation (end of shelf life). Units showed significantly higher levels of supernatant potassium, and free potassium per ml of RCC than CDL reference data for Gamma irradiated Red cell units (Figure 2).

Figure 2A **Figure 2B**

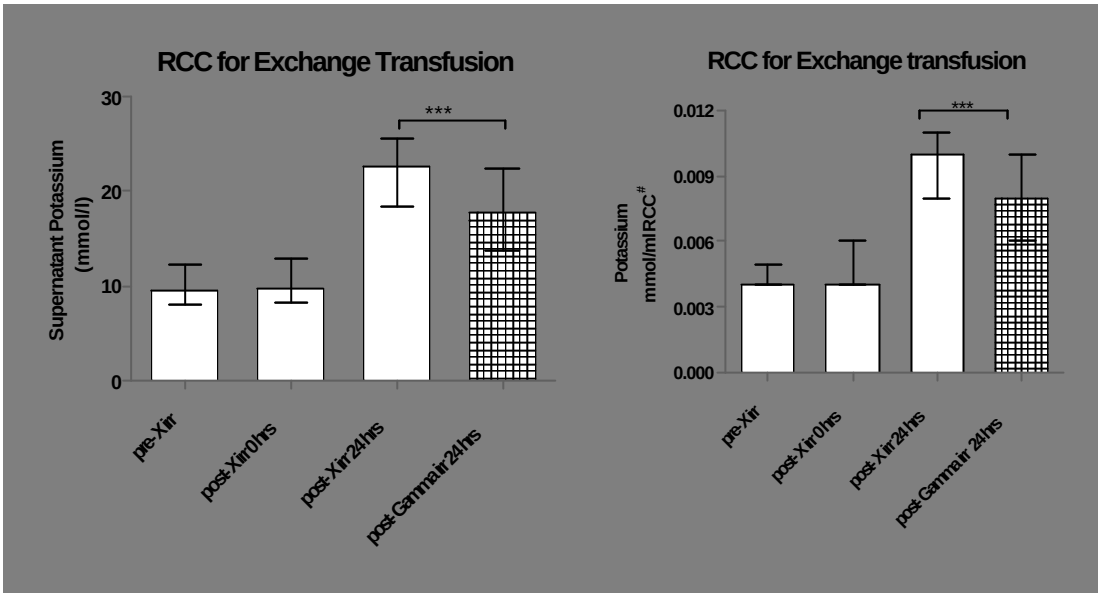

Figure 2A & 2B Potassium levels in X-irradiated (at Day 4) and CDL data from gamma irradiated RCC for Exchange. K^+ expressed as mmol/l of supernatant in figure 2A and mmol/ml of RCC in figure 2B.

*** $p < 0.001$
# Potassium levels calculated as mmol/ml of RCC.
Data plotted as median with range
n=10 for X-irradiated units
n=20 for gamma-irradiated reference data

b) Haemolysis

There was no difference in haemolysis pre and post-X-irradiation (0 hrs) of RCC for exchange transfusion.

There was no difference in haemolysis between X-ray and Gamma irradiated RCC for exchange at the end of shelf life (24 hours post-irradiation), and all were below the European limit of 0.8% (Figure 4).

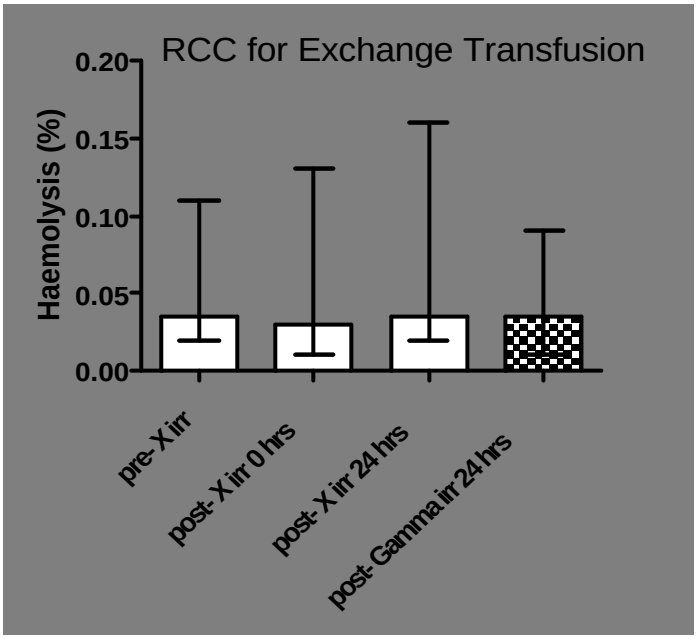

Figure 2C Haemolysis in X-ray irradiated (at Day 4) and historic data from gamma irradiated Red cell units for exchange.

Data plotted as median with range
n=10 for X-irradiated units
n=20 for gamma-irradiated reference data

Study 3 Effect of X-ray irradiation on red cell units for IntrauterineTransfusion

There was no difference in supernatant potassium pre and post-X-irradiation (0 hrs) of RCC-IUT.

Although supernatant potassium levels increased in RCC-IUT units 24 hrs post X-irradiation, there was no significant difference in supernatant potassium levels in X-ray and Gamma irradiated RCC for IUT with 90% Hct at the end of shelf life (24 hours post-irradiation; Figure 3A). This was also the case for the total amount of potassium per ml of RCC (Figure 3B).

At 24 hours (end of shelf life) post X-ray irradiation RCC for IUT with 90 % Hct had significantly lower levels of supernatant potassium than Gamma irradiated RCC for IUT with 80% Hct, as shown in Figure 3.

Figure 3A **Figure 3B**

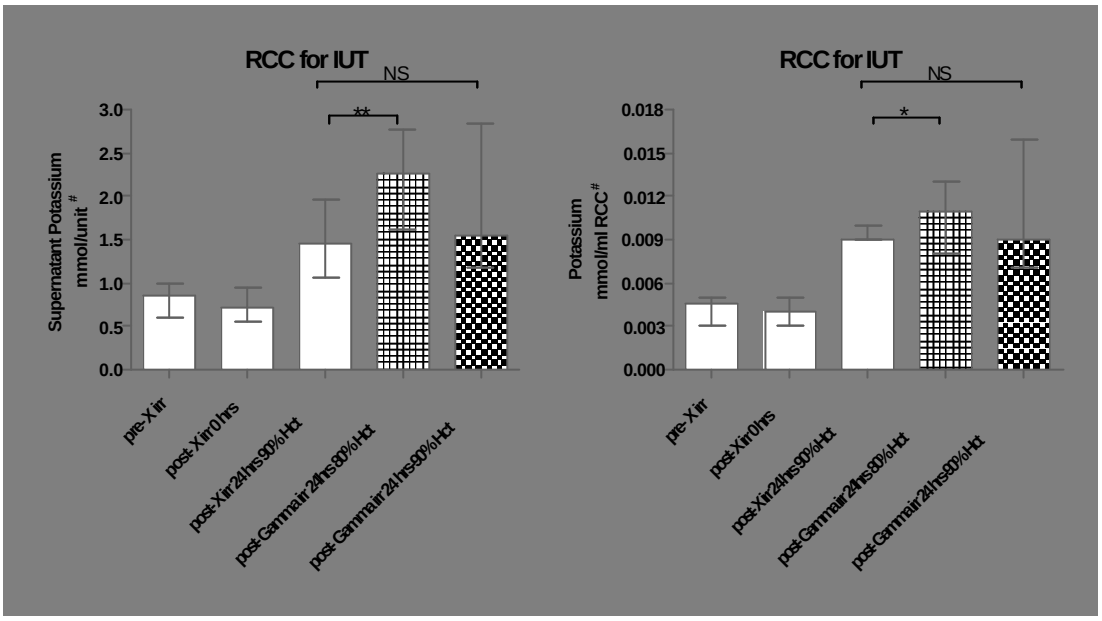

Figure 3A & 3B Supernatant Potassium levels in X-ray irradiated (on Day 4) Red Cell units for IUT. K^+ expressed as mmol/L of supernatant in figure 3A and mmol/mL of RCC in figure 3B.

Potassium levels calculated using corrected unit volume to calculate K^+ in mmol/ml of RCC.
NS –p value is not significant
** $p < 0.01$
Data plotted as median with range.
n = 10 for X-ray irradiated units with 90% Hct (Eval/CD/2007/57)
n = 10 for gamma irradiated units with 80% Hct (Eval/CD/2007/57b)
n = 9 for gamma irradiated units with 90% Hct (Eval/CD/2007/57b)

b) Haemolysis

There were no significant differences in haemolysis pre and post-X-ray irradiation (0 hrs) of RCC for IUT.

There was no increase in haemolysis in X-irradiated RCC for IUT at 24 hrs (end of shelf life), as shown in figure 3C.

All gamma irradiated RCC-IUT with 80 % Hct were below the European limit of 0.8% haemolysis at 24 hrs (end of shelf life), but one of ten gamma irradiated RCC-IUT with 90 % Hct showed high haemolysis. However, there was no statistically significant difference between X-irradiated or gamma-irradiated units.

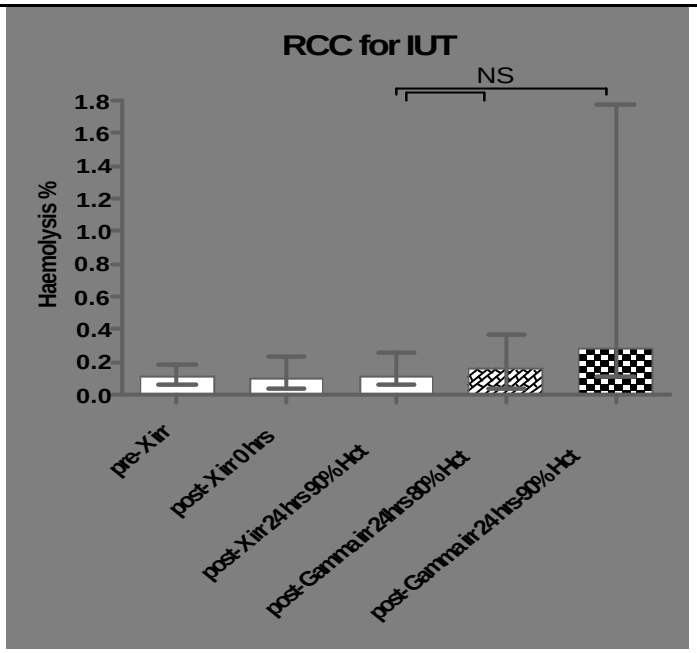

Figure 3C Haemolysis in X-ray irradiated (on Day 4) Red cell units for IUT.

NS – p value is Not Significant
Data plotted as median with range
n = 10 for X-ray irradiated units with 90% Hct (Eval/CD/2007/57)
n = 10 for gamma irradiated units with 80% Hct (Eval/CD/2007/57b)
n = 9 for gamma irradiated units with 90% Hct (Eval/CD/2007/57b)

3.2.3.c Discussion

Irradiation causes damage to the RBC membrane, increasing the membrane permeability(1,2) and leading to potassium leakage from red cells. Supernatant potassium levels post–gamma irradiation are reported to be elevated to clinically significant levels (3,4,5) and have been associated with foetal and neonatal arrhythmia and hyperkalemic cardiac arrest. Several publications have shown that X-irradiation is equivalent to gamma–irradiation (6,7,8,9) for inactivation of leucocytes. This study investigated the effect of X-irradiation on red cell concentrates. Components Development Laboratory Gamma-irradiated RCC reference data from EVAL/CD/2006/43 and EVAL/CD/2006/35 were used for comparison to determine whether X-irradiation has a significant impact on two markers of red cell quality - haemolysis and potassium leakage.

X-irradiated red cells in SAG-M or for exchange or IUT did not exceed the current European limit of 0.8% haemolysis at the end of shelf life in any units studied.

When X-irradiation of RCC in SAGM or RCC for exchange transfusion were compared with reference data from gamma-irradiated units, no significant differences were seen in haemolysis levels at the end of shelf life. Furthermore, the haemolysis data was also comparable to the Karolinska Institute's data.

The supernatant potassium levels of RCC in SAG-M doubled 7 days after X-ray irradiation, but no significant difference was seen between X-ray and gamma irradation up to day 14 of storage post-irradiation (end of shelf life). Supernatant potassium levels seen after X-irradiation in this study are similar to those reported in gamma–irradiated red cell units by other workers (10), but slightly higher than in X-irradiated RCC in SAG-M in the data from the Karolinska Institute.

However, irradiation did lead to higher supernatant potassium concentrations in RCC for Exchange transfusion. At 24 hours post X-irradiation RCC for Exchange transfusion (haematocrit 53 - 58%) had significantly higher supernatant potassium than gamma irradiated RCC. Although these levels were markedly higher than the Karolinska data, similar values have been reported in other studies using gamma radiation (11;12), and higher levels than those seen in NHSBT studies have been reported in non-leucodepleted X-irradiated RCC in CPDA-1 with haematocrit of 70 - 80% (2). The data generated from NHSBT studies was discussed with Dr Helen New, Consultant Haematologist at St Mary's who has specialist expertise in transfusion to neonates. Her conclusion, following discussion with other colleagues, was that the magnitude of the differences seen in potassium levels in red cells for exchange transfusion was not likely to be clinically significant.

X-ray and gamma-irradiation of RCC for IUT with 90% Hct led to comparable potassium leakage, which was lower than that seen following gamma-irradiation of RCC for IUT with haematocrit of 80 %. In addition, when the potassium concentration was calculated per mL of RCC the results were very similar (around 0.01 mmol/mL RCC) to gamma-irradiated RCC for IUT safely used for IUT by Win et al (13).

4 Overall conclusions

X-irradiation has considerable logistical advantages over the use of gamma irradiation. There is now a CE marked, FDA approved, machine available to deliver X-irradiation, which has already been implemented in some Centres outside the UK.

Published data on the efficacy of X-irradiation for leucocyte inactivation are sufficient.

Internal data on red cells that were X-irradiated do not show any clinically significant differences to those irradiated with gamma irradiation.

Data from the Karolinska Institute indicate that X-irradiated platelet components are of acceptable quality for clinical use.

Published data on granulocyte components indicate adequate neutrophil function after X-irradiation.

5 Recommendation

The use of X-irradiation using the Raycell device is approved for irradiation of red cells, platelets and granulocytes.

If approved, the Red Book Guidelines will require limited review, as in several entries irradiation is specified as gamma-irradiation.

Stephen Thomas & Rebecca Cardigan for SACBC
29 October 2008

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APPENDIX 1

RAD-SOURCE

K974210

MAR 30 1998

510(k) Summary
as required by 807.92(c)
for the RS 3000 Shielded Cabinet X-ray Radiation Source
Prepared November 6, 1997

Submitted by: Rad-Source, Inc..
475 Ramblewood Dr. #207
Coral Springs, Florida 33071
Tel. 954 755-0328

Contact Person: Randol E. Kirk
President

Device Trade Name: **RS 3000 Shielded Cabinet X-ray Radiation Source.**

Common Name: blood irradiator.

Classification: not classified.

Predicate Device: **IBL 437C** (K865027) manufactured by
CIS-US, Inc.
10 DeAngelo Drive
Bedford, Massachusetts 01730

Description of Device:

The **RS 3000 Shielded Cabinet X-ray Radiation Source** consists of A shielded enclosure containing 2 vertically opposed x-ray tubes with provision for a sample holder (canister) between them, a power supply and a controller. (Brief physical description of the device and its function)

Intended Use of Device:

The **RS 3000 Shielded Cabinet X-ray Radiation Source** is intended for the irradiation of blood or blood products packaged in transfusion bags in accordance with "Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products" (22 July 1993 memorandum from Acting Director Office of Blood Research and Review, Center for Biologics Evaluation and Research, FDA to all registered blood establishments) when irradiation to reduce the risk of Graft Versus Host Disease is indicated.

475 Ramblewood Dr #207 Coral Springs Fl 33071
(954) 755 0328

RAD SOURCE

Substantial Equivalence to Predicate Device:

The **RS 3000 Shielded Cabinet X-ray Radiation Source** is substantially equivalent to the **IBL 437C Blood Irradiator** (K865027). Both are indicated for the irradiation of blood and blood products to reduce the risk of transfusion-associated graft-versus-host disease in recipients at risk of this complication. The significant clinical characteristics of the two devices are compared below.

	RS 3000	**IBL 437C**
Source:	160 kVdc x-rays .38 mm Cu filter hvl app. 4 cm H_2O	Cs-137, 662 keV
Dose rate:	3 Gy min^{-1}	> 4 Gy min^{-1}
Max/min dose ratio:	< 1.3	< 1.67
Sample holder:	fixed, presents maximum width, minimum depth	rotates in beam
Radiation safety:	Pb shielding, interlocks	Pb shielding, interlocks
Federal Regulatory Environment:	Requires 510(k). Must comply with 21 CFR 1020.40	Requires 510(k), user must have NRC license and radiation safety officer, operators must be film-badged.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

MAR 30 1998

Ronald E. Kirk
Rad-Source, Inc.
475 Ramblewood Drive, Suite 207
Coral Spring, FL 33071

Re: K974210
RS 3000 Shielded Cabinet X-Ray Radiation Source
(Blood Irradiator)
Dated: February 18, 1998
Received: February 20, 1998
Unclassified
Procode: 90 MOT

Dear Mr. Kirk:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4613. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Lillian Yin, Ph.D.
Director, Division of Reproductive,
Abdominal, Ear, Nose and Throat
and Radiological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Indications for Use

(For Indications for Use Statement and
Section 8 of Premarket Submission Cover Letter)

The RS 3000 Shielded Cabinet X-ray Radiation Source is intended for the irradiation of blood or blood products packaged in transfusion bags in accordance with "Recommendations Regarding License Amendments and Procedures for Gamma Irradiation of Blood Products" (22 July 1993 memorandum from Acting Director, Office of Blood Research and Review, Center for Biologics Evaluation and Research, FDA to all registered blood establishments) when irradiation to reduce the risk of Graft Versus Host Disease is indicated.

(Division Sign-Off)
Division of Reproductive, Abdominal, ENT,
and Radiological Devices
510(k) Number K974210

Prescription Use ✓
(Per 21 CFR 801.109)

Return to Search

Device Classification Name	IRRADIATOR, BLOOD TO PREVENT GRAFT VERSUS HOST DISEASE
510(k) Number	K974210
Device Name	SHIELDED CABINET X-RAY RADIATION SOURCE DEVICE MO
Applicant	RAD-SOURCE, INC. 475 RAMBLEWOOD DR., SUITE 207 CORAL SPRINGS, FL 33071
Contact	RANDOL E KIRK
Product Code	MOT
Date Received	11/10/1997
Decision Date	03/30/1998
Decision	SUBSTANTIALLY EQUIVALENT (SE)
Classification Advisory Committee	Radiology
Review Advisory Committee	Radiology
Statement/Summary/Purged Status	Summary only
SUMMARY/Approval Letter	SUMMARY
Type	Traditional
Reviewed by Third Party	No
Expedited Review	No

(Database Updated August 5, 2002)

Accessibility