The Role of Cesium-137 Chloride Irradiators in Transfusion Medicine

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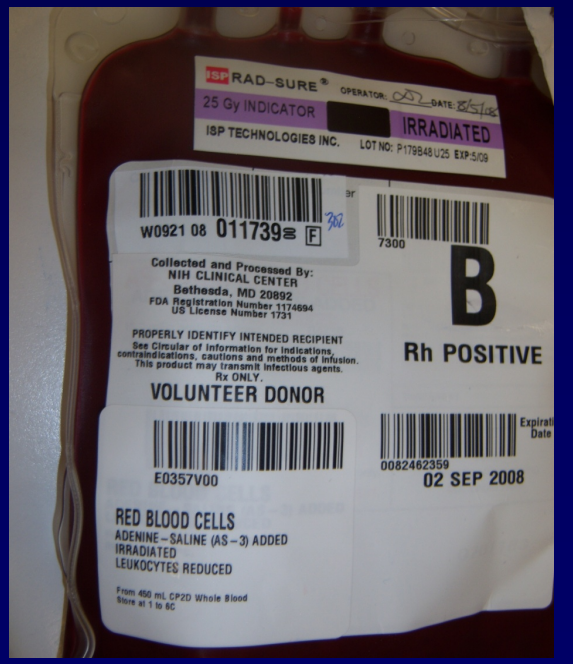
Blood components are irradiated for one reason:

To prevent transfusion-associated graft versus host disease (TA-GVHD).



Transfusion-Associated Graft versus Host Disease

- Rare but devastating complication of transfusion
- Mediated by immunocompetent transfused T-lymphocytes, which engraft, proliferate, and mount a severe immune reaction targeted against the HLA antigens of the host
- Host may be:
  (1) severely immunocompromised
  (2) may share an HLA haplotype with an HLA-homozygous donor

Patients at Risk of TA-GVHD

- Recipients of intrauterine transfusions (fetus)
- Recipients of postnatal exchange transfusions (neonates, HDN)
- Infants & children with severe congenital immunodeficiency states (SCID, WAS)
- Hematopoietic transplant recipients (allogeneic, autologous)
- Patients with hematologic malignancies (lymphoma, leukemia)
- Patients with solid tumors
  - Neuroblastoma, glioblastoma, rhabdomyosarcoma
- Patients receiving purine analogues
  - Fludarabine, cladribine, pentostatin
- Recipients of HLA-homozygous, haploidentical blood products
  - Related or HLA-matched
  - Unrelated or random donors

Frequency of Transfusion From HLA Homozygous Donor to Recipient Heterozygous for that Haplotype Among Different Populations

Population	Parent/Child	Sibling	Unrelated
US Whites	1:475	1:902	1:7174
Japanese	1:102	1:193	1:874
Canadian Whites	1:154	1:294	1:1664
Germans	1:220	1:424	1:3144
Koreans	1:183	1:356	1:3220
Spanish	1:226	1:438	1:3552
Italian	1:434	1:854	1:12870
French	1:762	1:2685	1:16835

Ohto, et al, Transfusion 1992.

Blood Components Implicated in Cases of TA-GVHD:

Any component that contains viable T-lymphocytes

- Red cells
- Platelets (apheresis or random)
- Granulocytes
- Plasma

TA-GVHD Clinical Manifestations

- Onset: 3-30 days post-transfusion
- Symptoms: fever, rash, liver function abnormalities, diarrhea, pancytopenia
- Diagnostic confirmation: skin biopsy, HLA typing
- Outcome: universally fatal (infectious death due to neutropenia)

Prevention of TA-GVHD

Goal: Elimination of viable lymphocytes in blood products

Methods available:

1. Washing
2. Freezing and thawing
3. Filtration
4. Irradiation

Prophylactic irradiation of blood products prior to transfusion is currently the most efficient way to eliminate the mitotic potential of lymphocytes and prevent TA-GVHD

Irradiation of Blood Components

- Dose: 2500 cGy (500 cGy enough)
- Storage:
  - RBCs lose viability with increasing storage time following irradiation
  - Irradiate immediate prior to issue
  - Irradiation performed in hospital Blood Banks rather than in Regional Blood Centers

How widely is Blood Irradiation Practiced? Is there a role for Universal Irradiation?

- Approximately 10-15% of red cell units are irradiated in U.S. (2009 NBCUS)
- Irradiation increases the average cost/unit by about $65
- Comprehensive cancer centers and pediatric cancer centers (20-25 hospitals) practice universal irradiation.

Techniques of Blood Irradiation

- **Ionizing Irradiation**
  - Free-standing blood irradiators
    1. G*amma rays:* cesium-137, cobalt-60
    2. *X-rays*
  - Radiation therapy devices
    1. Linear accelerators: *x-rays*
- **Ultraviolet irradiation**

Blood Irradiators – Gamma Emitters
(cesium-137, cobalt-60 sources)
90% of blood irradiated in US: CsCl source

Company	Device	Radiation source	Strength (Ci)	Chamber size (L)	Central dose rate (cGy/min)
CIS	**IBL-437C**	**Cs-137**	**5100**	**3.8**	**1200**
Best (Nordion)	**Gammacell 1000**	**Cs-137**	**2500**	**1.0**	**1800**
	Gammacell 3000	**Cs-137**	**2500**	**2.6**	**940**
Shepherd	**Model 143-45A**	**Cs-137**	**2200**	**1.4**	**1250**
	Model 143-68	**Cs-137**	**4000**	**3.7**	**1080**
	Model 109C	**Co-60**	**2000**	**3.2**	**3000**

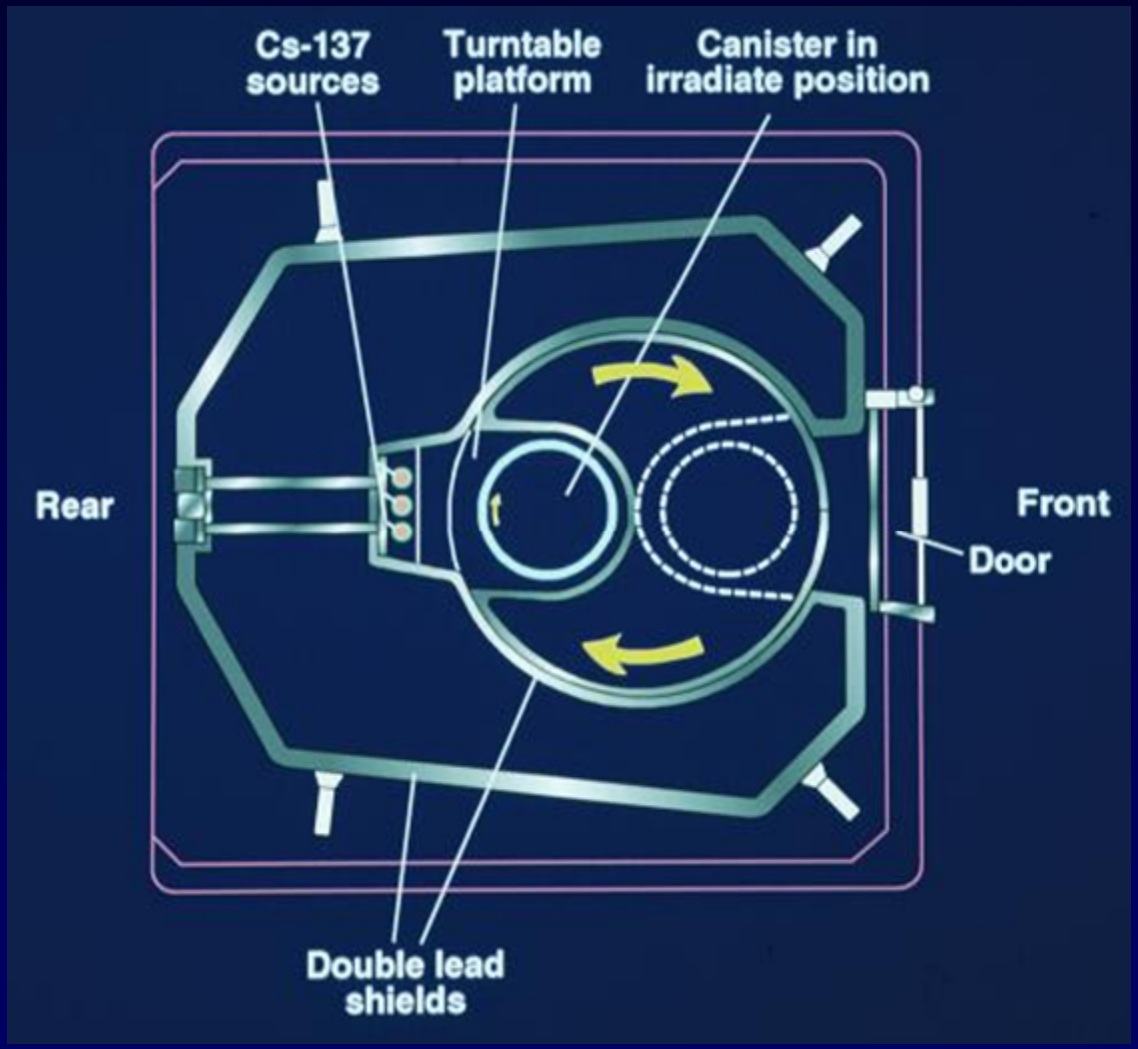
Cesium-137 source $t_{1/2}$= 30.2 yrs. Cobalt-60 source $t_{1/2}$= 5 yrs

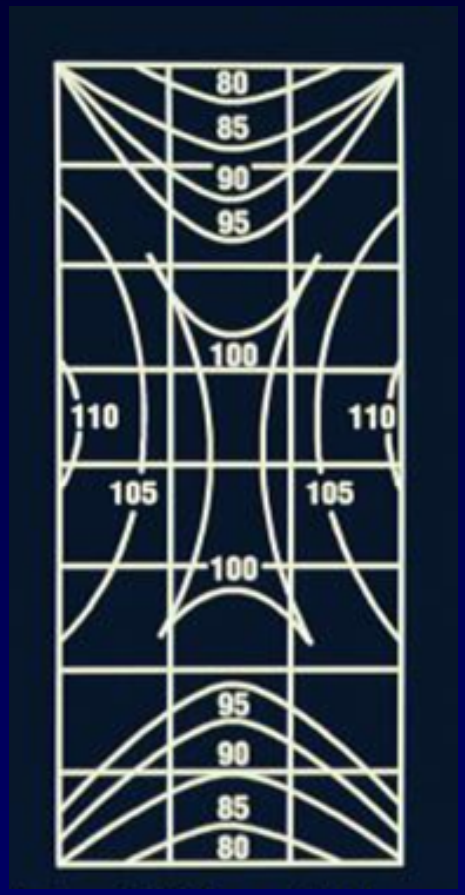
Delivery of 1500 – 3000 cGy requires 2-3 minutes.

CIS IBL 437C
Pharmalucence
CsCl

- 4400 lbs
- Floor loading
- Wgt distribution

- 3.8 L canister (6 bags)


Cs-137 sources
Turntable platform
Canister in irradiate position
Rear
Front
Door
Double lead shields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Dosimetry method: plastic phantom with rows of imbedded thermoluminescent dosimeter chips (TLDs) or MOSFETS

Gamma (CsCl) Irradiators
Advantages

- Rapid (2-3 mins), easy to use
- Efficient & convenient (next to sign-out station)
- Reliable – very rare mechanical issues
- Very low maintenance
- PM & dosimetry yearly
- Large capacity (3.8 L – 6 components at a time)
- Reasonably even dose distribution

X-ray Irradiator

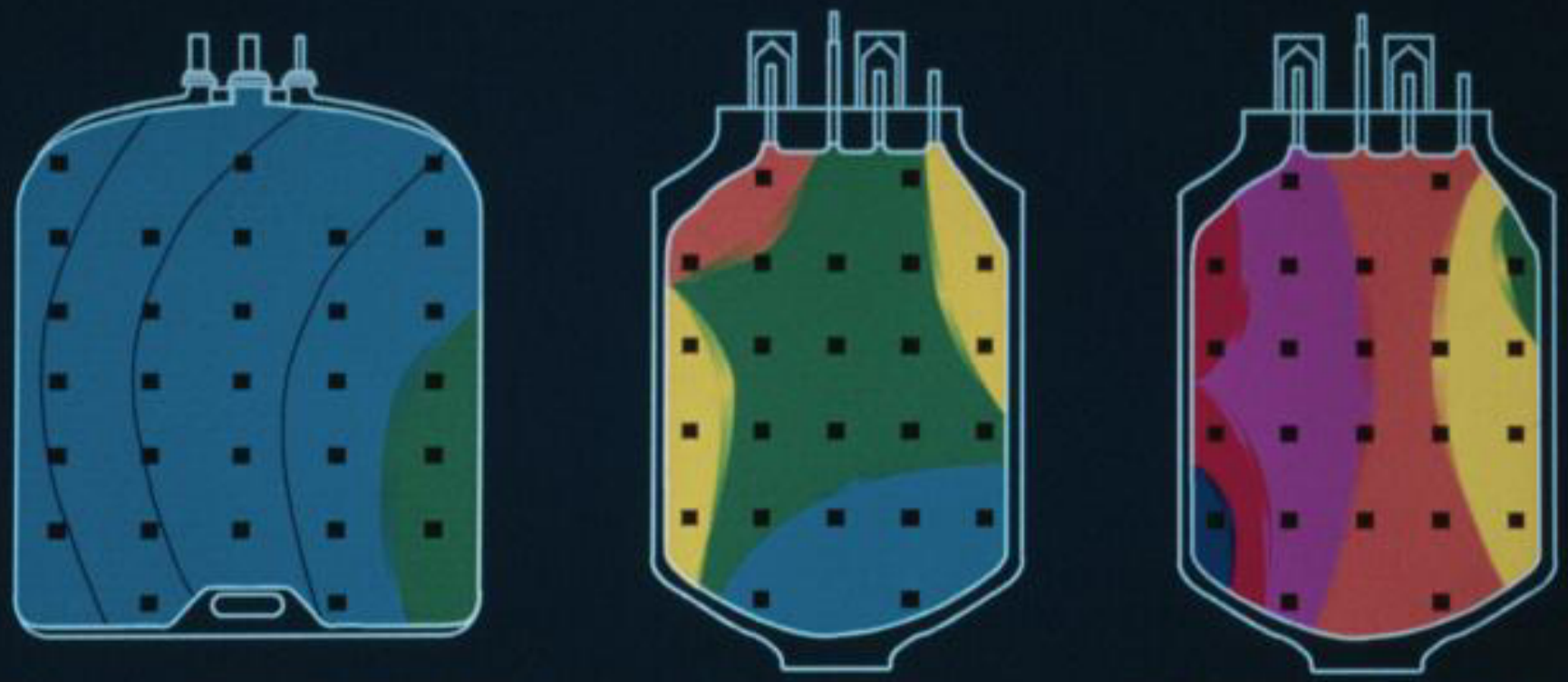
(Raycell, Best Theratronics)

- X-ray source
- No NRC license
- 1,566 lbs
- 5 minutes/ 25 Gy cycle
- 1.5 L (2 bags) canister

X-ray Irradiator

- Unreliable; frequent down-times
- Power source erratic, fails frequently
- High maintenance: X-ray tube replacement
- Need cool water supply: 10 L/minute, constant pressure, warm up time, wasted tech time
- Very expensive PM contract: $87K over 3 yrs (2 PM visits/yr, 2 power supplies, 1 tube)
- Door breaks easily, other mechanical problems
- Short device life-span: 6-10 yr life span

DOSE DISTRIBUTION IN SIMULATED COMPONENTS



Linear Accelerator
Unidirectional, Single Layer
Plateletpheresis PL-732 Bag

IBL 437C
Lucite Spacer
RBC PL-146 Bag

Gammacell 3000
Lucite Spacer
RBC PL-146 Bag

140 130 120 110 105 100 95

Linear Accelerator

Advantages

- Homogeneous dose distribution

Disadvantages

- Blood units must leave blood bank for uncertain length of time, uncertain temp control; difficult coordination, delays
- Cumbersome

Ultraviolet Irradiation

(UV-B 290-320 nm)

Favorable

- Abolishes lymphocyte mitotic activity
- Does not require NRC license, safe

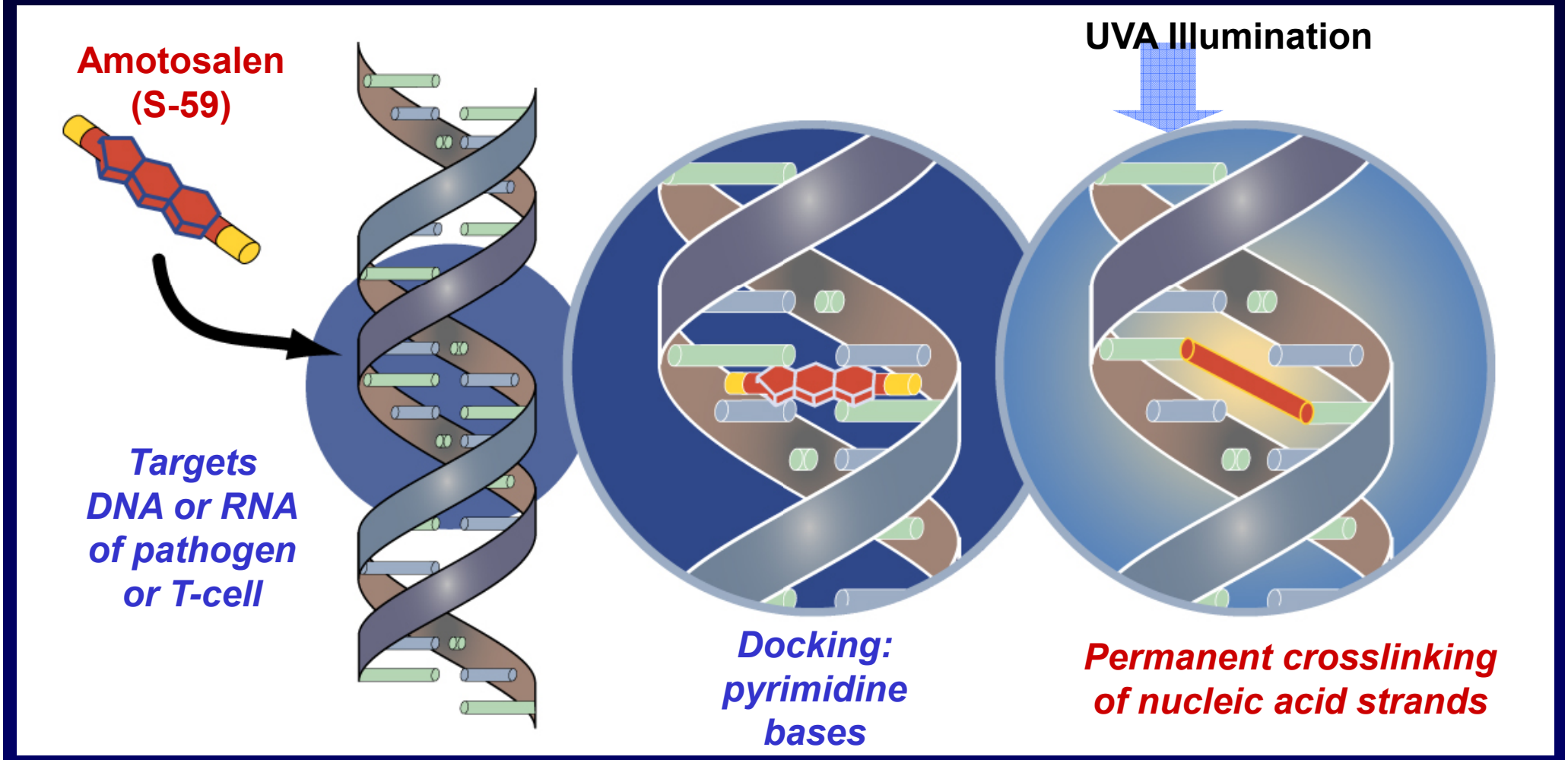
Problem

- UV light does not penetrate blood bag plastics, does not penetrate red cell solutions

Alternative Methods of T Cell Inactivation in Blood Products

Psoralen-Based Pathogen Inactivation Systems

Amotosalen HCl (S-59) (Intercept™)



Licensed in Europe, not in US.

Protection of CsCl Sources from Misuse

Irradiator "Hardening" Initiatives to Minimize Risk and Maximize Security and Safety of Sources

- Background security checks on all staff with unescorted access to irradiator
- Constant surveillance by security cameras to immediately detect & respond to unauthorized access
- Retrofit device with security enhancements (DOE); Permanent welded closure of rear of irradiator; access to isotopes extremely difficult
- Secure irradiator in locked cage or room

Miss Em!
SANYO

Surveillance cameras

Bolted cage

Conclusions

- CsCl irradiators remain the most reliable and efficient means to accomplish blood irradiation
- Other options (x-ray) improving
- Safety and security of CsCl sources markedly strengthened in past 2 yrs → initiatives by NRC
  - ✓ Physical security enhancements to all irradiators in US Blood Banks
  - ✓ Enhanced environment security (monitoring, locked access) in all US Blood Banks
  - ✓ Robust system for background security checks for personnel implemented