Successful Migration From Radioactive Irradiators to X-Ray Irradiators in One of the Largest Medical Centers in the US

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Council on Ionizing Radiation Measurement and Standards- 2019 Annual Meeting

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Gaithersburg, MD

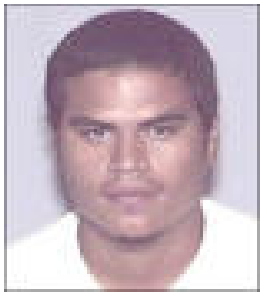
When was this started?

2010

One year before the 10th year 9/11 anniversary
RSC had some concerns about radiological terrorism

2010- Previous Attempts to Use Radioactive Materials as a Dirty Bomb

December 1998 -Chechnya- A container filled with RAM attached to an explosive device near a railway.



June 2002- Chicago- Jose Padilla, a US citizen with links to Al Qaeda was arrested in Chicago planning to build and detonate a dirty bomb. He underwent training in Pakistan to build dirty bomb.

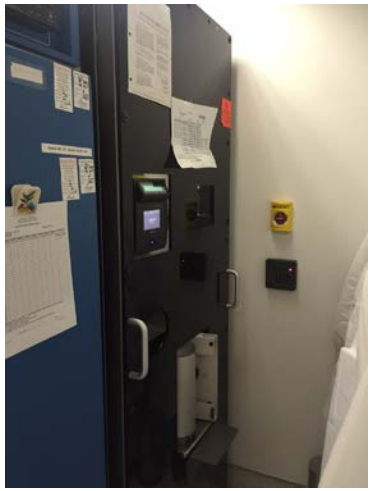
January 2003- Afghanistan-Based on evidence uncovered by the British intelligence, it was concluded that Al Qaeda has succeeded in constructing a small dirty bomb.

August 2004- London- Dhiren Barot was arrested for planning to blow up NY stock exchange with a dirty bomb.

2010- Irradiators at Mount Sinai

Research Irradiators

Blood Bank Irradiators



All were considered as category 2 radioactive sources.

Weapons of Mass Destructions (WMD)

Weapons of Mass Disruption (WMD)

Goiânia- Brazil Accident – 1987

- An old radiotherapy source was stolen from an abandoned hospital.
- 112,000 surveyed- 249 had significant contamination and 4 died.
- Small capsule contained about 93 grams (3.3 oz) of highly radioactive cesium chloride (Cs-137 CsCl).
- The IAEA states that the source contained 50.9 TBq (1,380 Ci) when it was taken away.
- 80 grams of CsCl powder resulted in more than 40 tons of radioactive waste.

Reference: The Radiological accident in Goiânia Vienna: International Atomic Energy Agency. 1988. ISBN 92-0-129088-8

2010- SPECIFIC TO MOUNT SINAI

- **Location in New York City**

  Since 9/11 there have been 20 terrorist attempts towards NYC. Mount Sinai is located in New York City with many subway entrances located within less than a mile.

. **Mount Sinai has 4 Radioactive Sources**

  These radioactive material sources could be used as dirty bombs (WMD)

- **Hospital Entity**

  Terrorist groups would target hospitals to delay the response to mass casualties - Mount Sinai is a major hospital.

- **Jewish Entity**

  Argentina bombing was chosen only because of its Jewish identity. Mount Sinai is a Jewish entity.

2010- ACTION PLAN

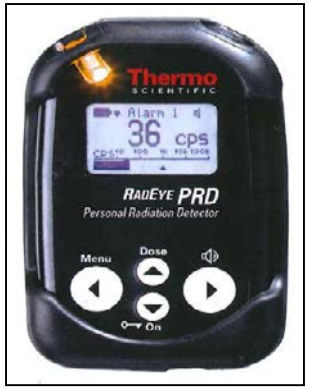
Phase 1- Get ready for the worst case scenario - Prepare to respond to Radiological Incidents.

Phase 2- Reduce the risk: Limit Access, Harden Security, FBI background check

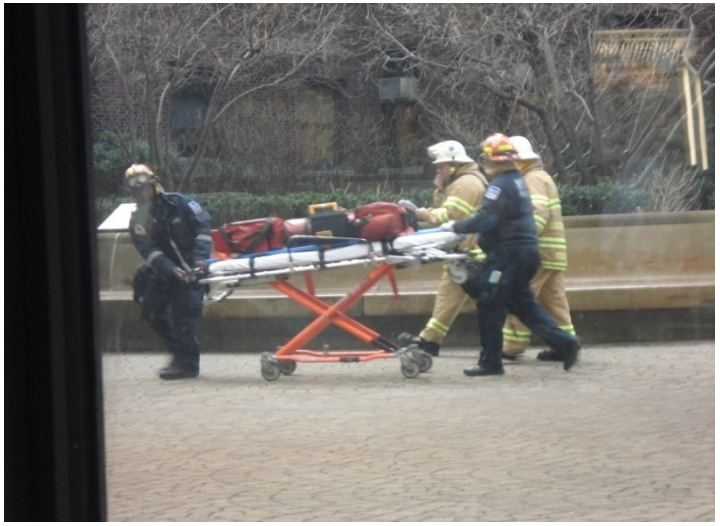
Phase 3- Remove the risk: Use Alternative Technology and dispose all radioactive irradiators.

Phase 1- Get Ready to Respond

Prepare for Radiological Incidents



Drills with Other Agencies



Phase 2- Steps Taken to Reduce Risk

- **Limit Access**
  - One person has unescorted access instead of many people.
- **Partnership with NNSA/GTRI**
  - Harden the irradiators.
- **Security Enhancement NNSA/GTRI**
  - Collaboration with DOE- NNSA and installing security enhancement. RMS unit, biometric access, intrusion detection, etc.
- **RMS was connected to police department**
  - Police department was connected to RMS unit for remote monitoring. Mount Sinai was the first to be connected to LMSI.
- **Background check**
  - FBI Background on those staff having unescorted access to the irradiators.
- **Pre-Arrange plan between police dept. and Mount Sinai**

2013-Crucial Decision

- **Needed to purchase a new irradiator for the bran new research building.**
- **Do we buy another Cesium Irradiator?**
- **Do we buy X-ray irradiator?**
- **We started investigating.**

Hess Center

Hess Center Research Building
10 stories, with one additional floor of mechanical space

Gaps in Insurance Coverage

- ✓ **Insurance policy usually excludes:**
- ✓ **Under our Property Damage Policy: loss or damage from nuclear radiation or radioactive contamination.**
- ✓ **Within the TRIPRA coverage, loss or damage from biological or chemical terrorism defined as the "dispersal, discharge or release of pathogenic toxic, poisonous or damaging biological or chemical agents in an act of terrorism."**
- ✓ **Exclusions Render Coverage for NBCR terrorism acts extremely limited with the exception of damage from fire.**
- ✓ **In order to add radioactive decontamination converge, it would cost about $1.5 Million**

Irradiator Comparisons*

	Cs-137 Irradiator	X-ray Irradiator
Purchase Price	$160.000-$325,000 Est. $242,500	$160.000-$240,000 Est. $220,000
Site Preparation	$7,500	$0 -3,600
Licensing Costs	$15,400	$2,500
FBI Background check	$3,800	None
Transportation+ Disposal	$20,000	$2,500
Life	the source needs to be replaced about every 30 years ($150,000)	The tube needs to be replaced about every 12 years ($20,000); The life span of x-ray machine is ~12 years
	After 10 year, the cost to keep is about the same (Cs blood irradiator and x-ray blood irradiator	
PM Cost per year	~$10,000 (RMS, PM, dose map)	$17,000 (warranty)
Regulatory Inspection	Yes, annually (NYPD + NYCDOH)	None
Insurance coverage for Decontamination	**$1.5 Million**	**None**

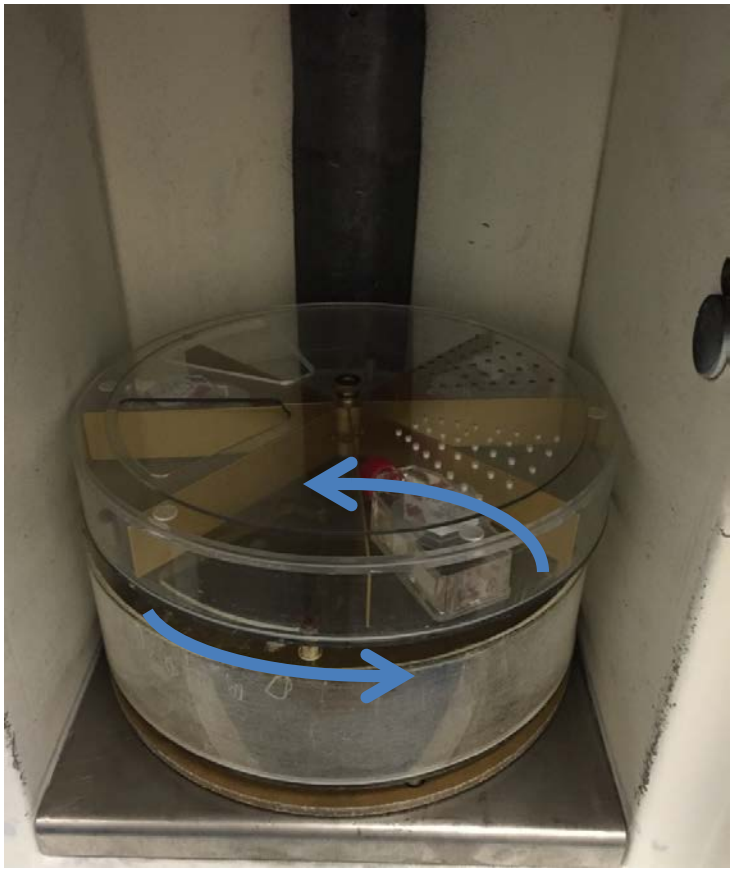
*Cost-Benefit Analysis of Switching from Cs to X-ray Irradiators – Erik Bakken, University of Wisconsin-Madison

Possible Sources of Error – Mechanical Source Lift

- The cesium irradiator irradiates mice by lifting the cesium source using a mechanical lift
- **This lifting time adds about 1 second of time to the total exposure**
- Example: A 60 second long exposure would be irradiated for about 61 seconds, which may increase the dose by **<1.7%**
- **X-rays do not have this issue**

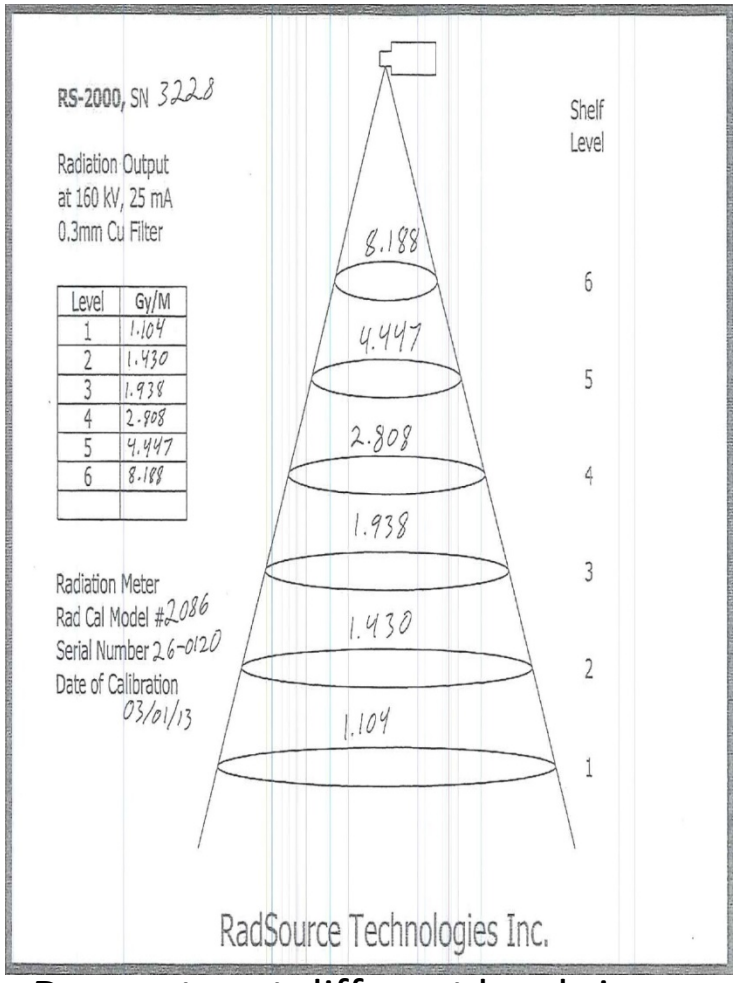
Possible Sources of Error - Rotation

- The rotation of the turntable causes changes in the dose rate over time as the mice get closer and further from the cesium source
- The **position of mice** the rotating table when the irradiation begins and ends could have an **impact on the total dose received**
- This possible source of error becomes more pronounced for shorter exposure times

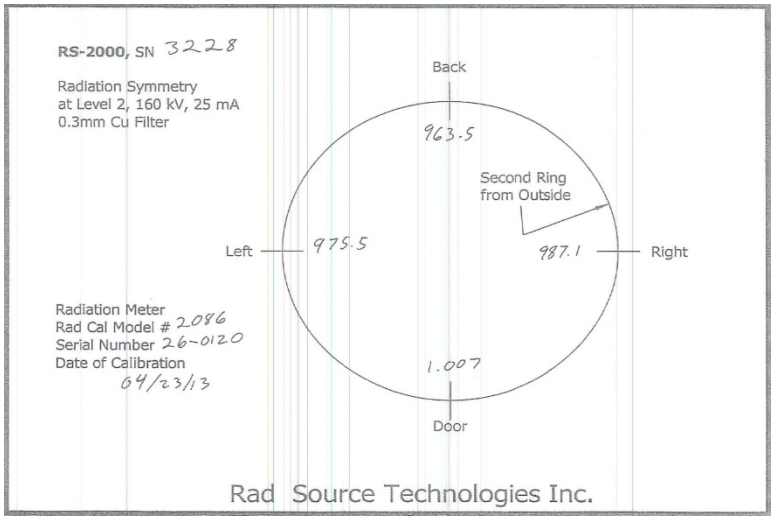


X-rays do not have this issue

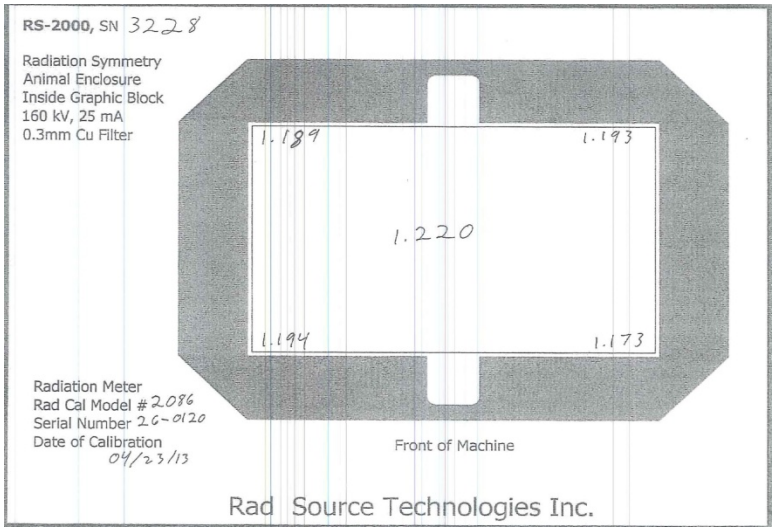
RS 2000 X-ray Irradiator Dose Distribution



Dose rates at different levels in the irradiator.

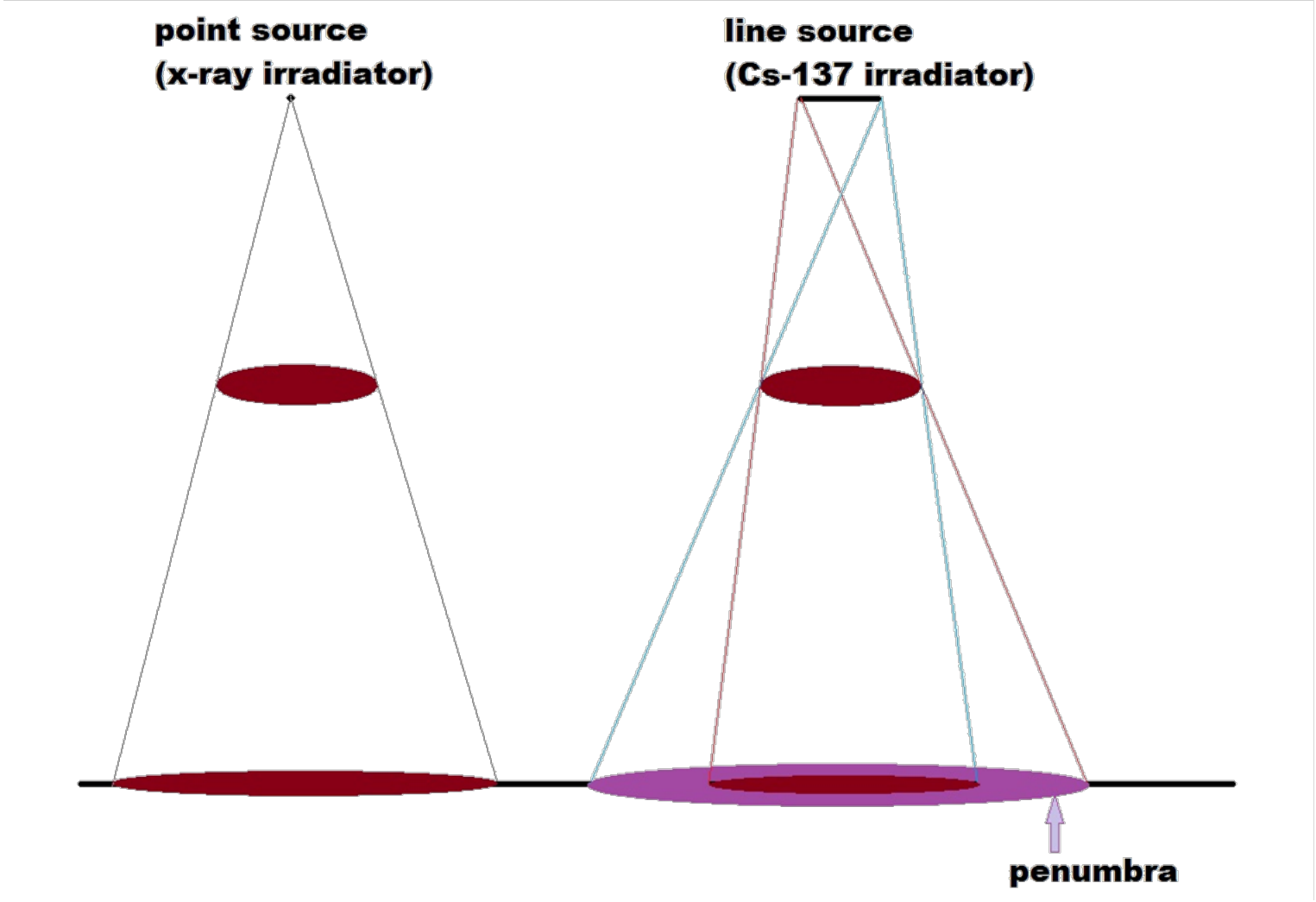


Homogeneity without the reflector at level 2 in the irradiator.



Homogeneity with the reflector at level 2 in the irradiator.

Penumbra

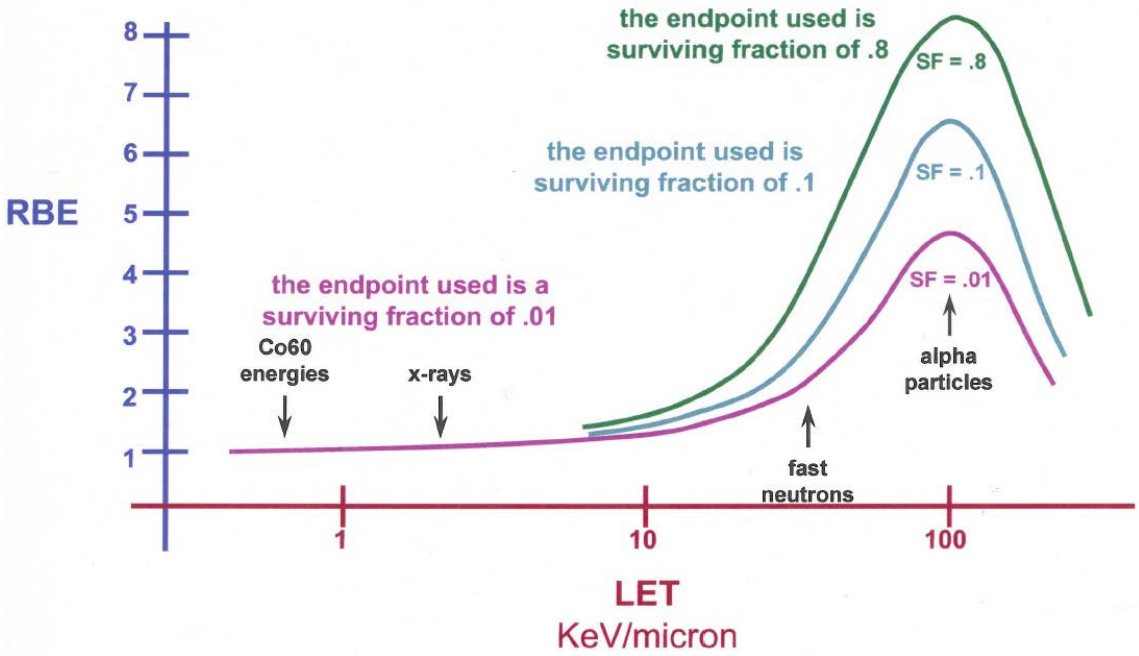

point source
(x-ray irradiator)
line source
(Cs-137 irradiator)
penumbra

Cs-137 Decay Correction

- Cs-137 decays ~1% in 5 months or ~2.3% in a year. Need to correct every a few months and recalibrate field once a year.
- After 10 years, the difference in calculated activities between a 30.17 year and 30.0 year half-life source is 0.13%
- **X-rays do not have this issue**

Reference	Half-life (yr)
NIST	30.17
IAEA	30.05
MIRD	30.0

Relative Biologic Effectiveness (RBE) & LET



Radiation	LET (keV/µm)	RBE
Co-60 γ-rays	0.2	**0.9**
250 kV x-rays	2.0	**1.0**

Variation of RBE with LET for survival of mammalian cells of human origin

(*from Radiobiology for the Radiologist, 6th Ed, Eric J. Hall; JB Lippincott Co., Philadelphia, 2005*)

Dose Rate Comparison and Repair

- The 4 R's of Radiobiology:
  - Repopulation
  - Redistribution
  - Re-oxygenation
  - **Repair**: Extending the period of time over which a dose is delivered allows for cells to repair sub lethal damage

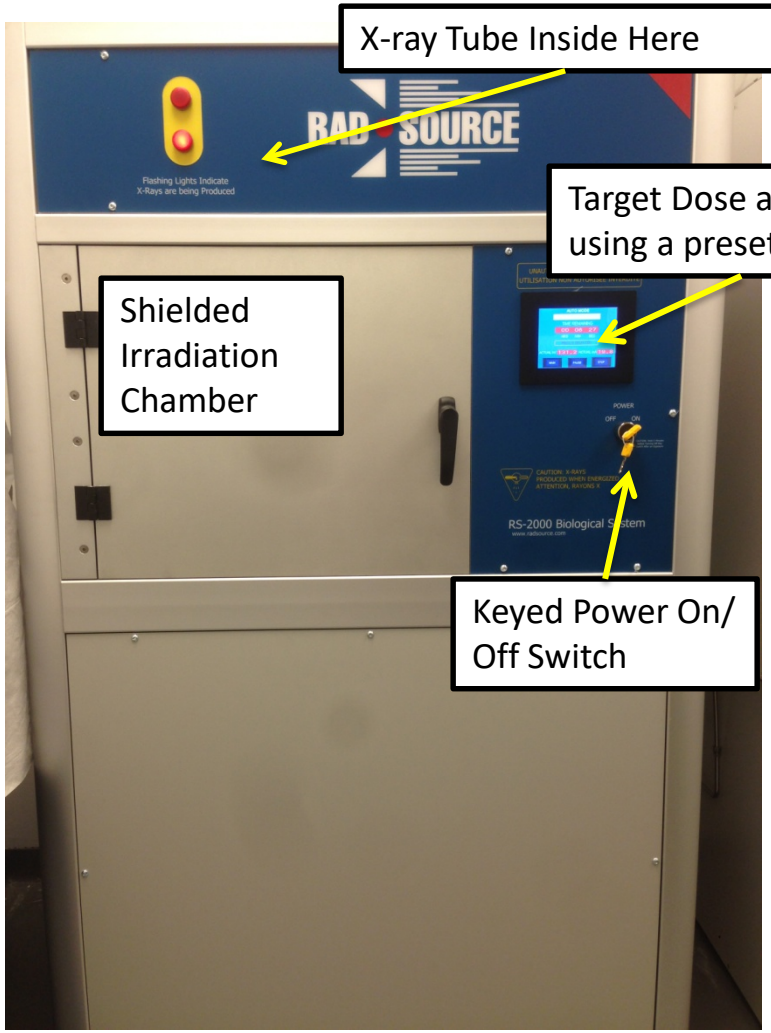
- A lower dose rate means longer irradiation time, which means more time for sub lethal damage repair
- This small difference in irradiation time will have a negligible impact on the amount of sub lethal damage repair and overall radiobiological effects

Cs-137 Irradiator	X-Ray Irradiator
0.5 Gy/min	1.25 Gy/min
~12 min irradiation time for 6 Gy	**~5 min** irradiation time for 6 Gy

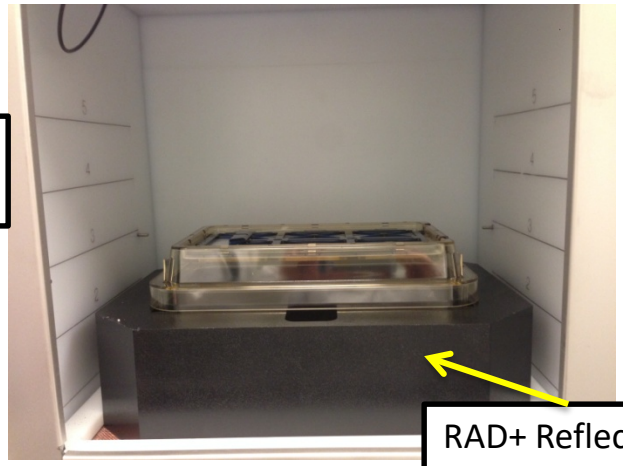
RadSource RS2000 X-ray Irradiator

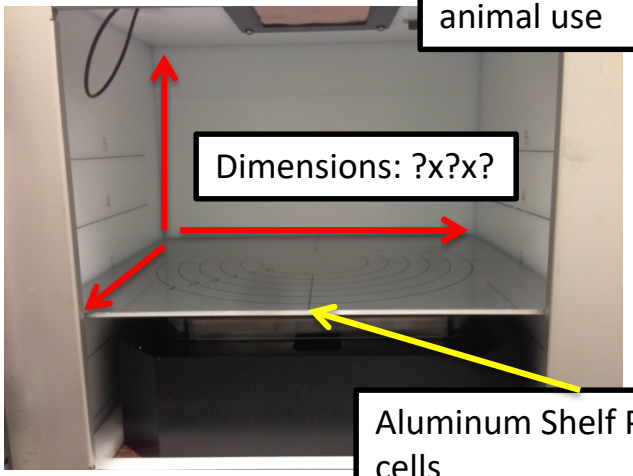
- Quick touch screen commanding and easy programming
- Comes with free smart phone app for dose mapping and irradiation time calculation
- Owned by Tisch Cancer Institute at Mount Sinai
- This unit requires annual preventive maintenance

Components of the RS2000 X-ray Irradiator



Inside the Irradiation Chamber:



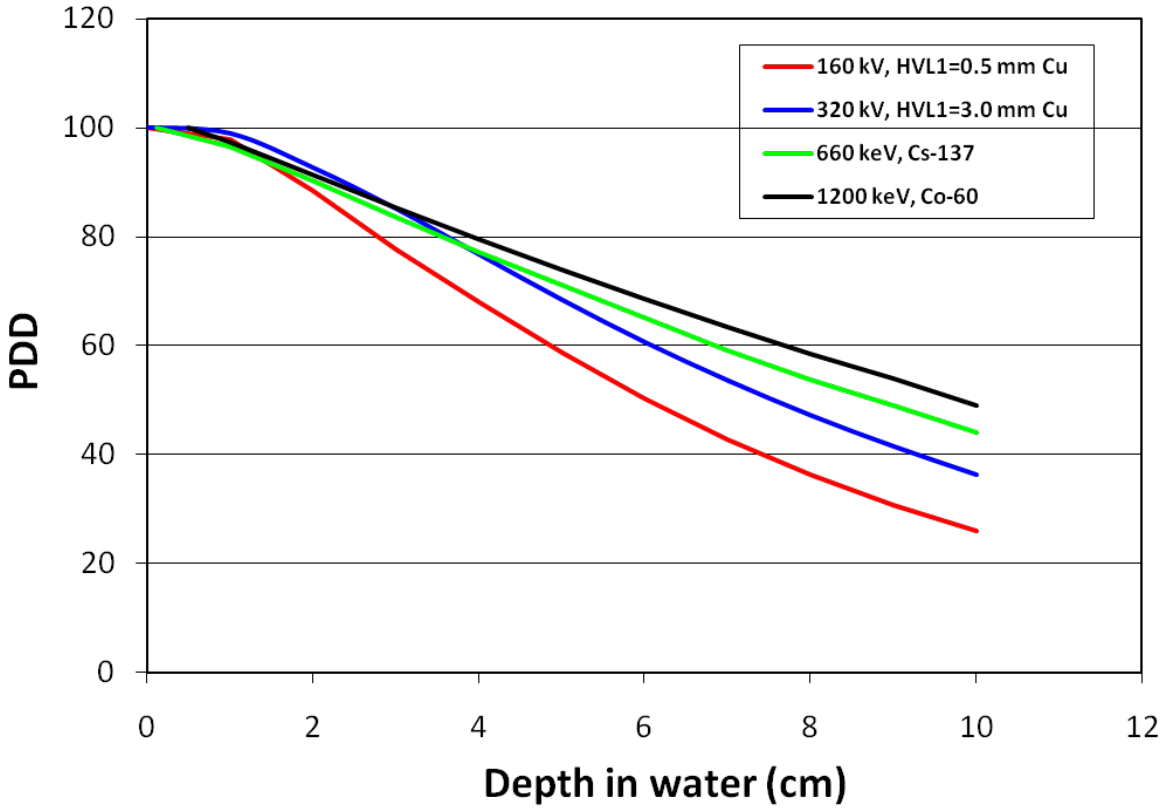


ALTERNATIVE TECHNOLOGY

- **Can we use X-ray (160 kVp) Irradiator instead of cesium irradiators (662 KeV) for research irradiation of mice and cells.**

- **Now we have tools to investigate.**

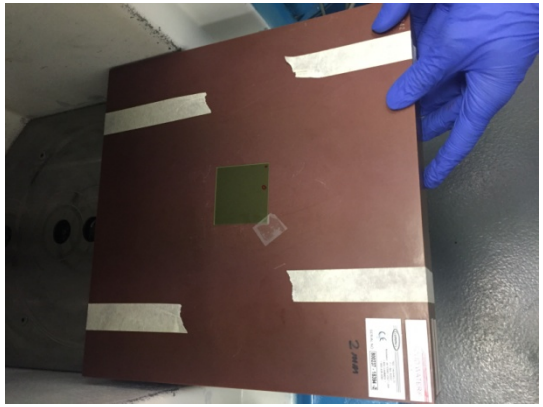
Penetration as a Function of Energy



PDD plotted from data in BJR Supplement 25, for Three X-ray Qualities and for Cs-137 and Co-60. For all the following parameters apply: W=10 cm, SSD=50 cm[11]

Experimental Setup For Depth Dose Measurement

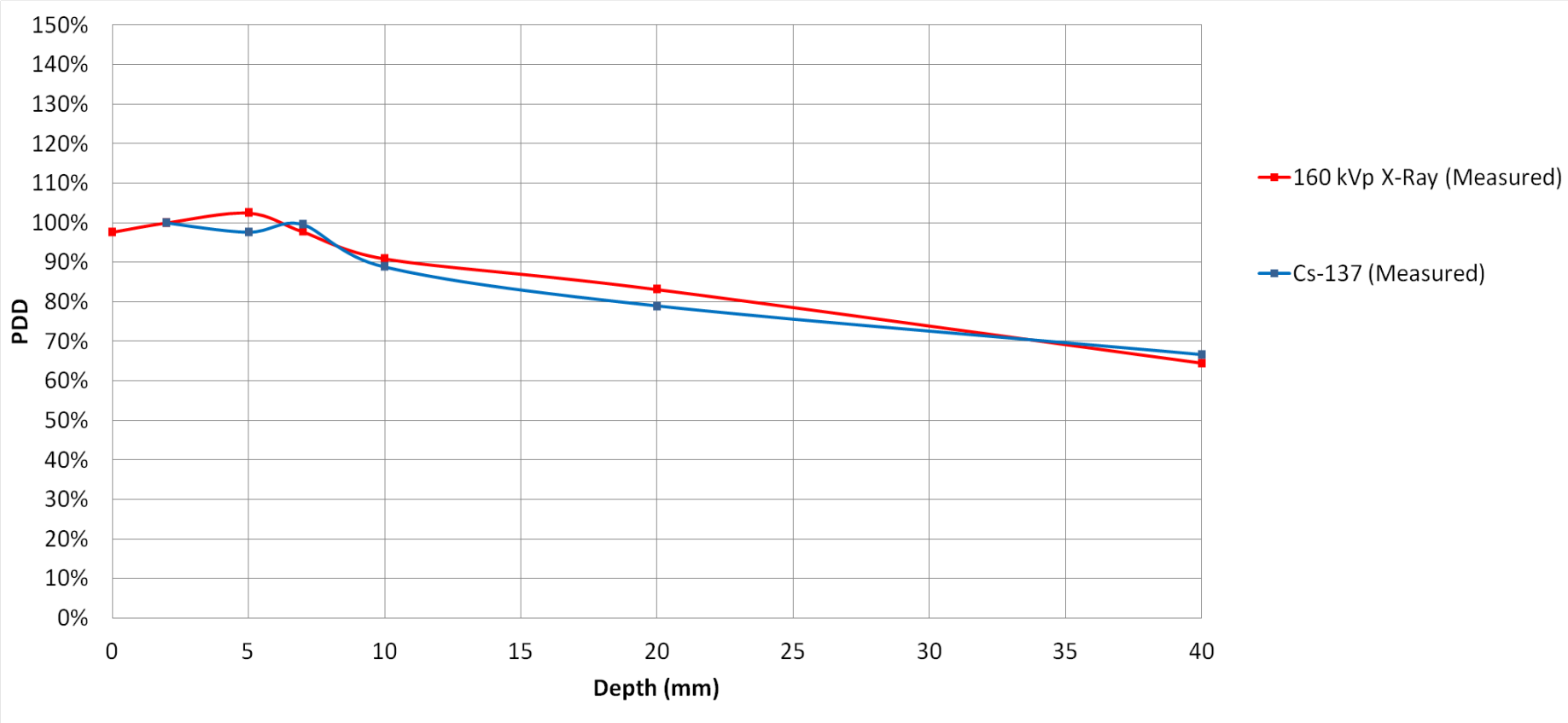
X-Ray Irradiator



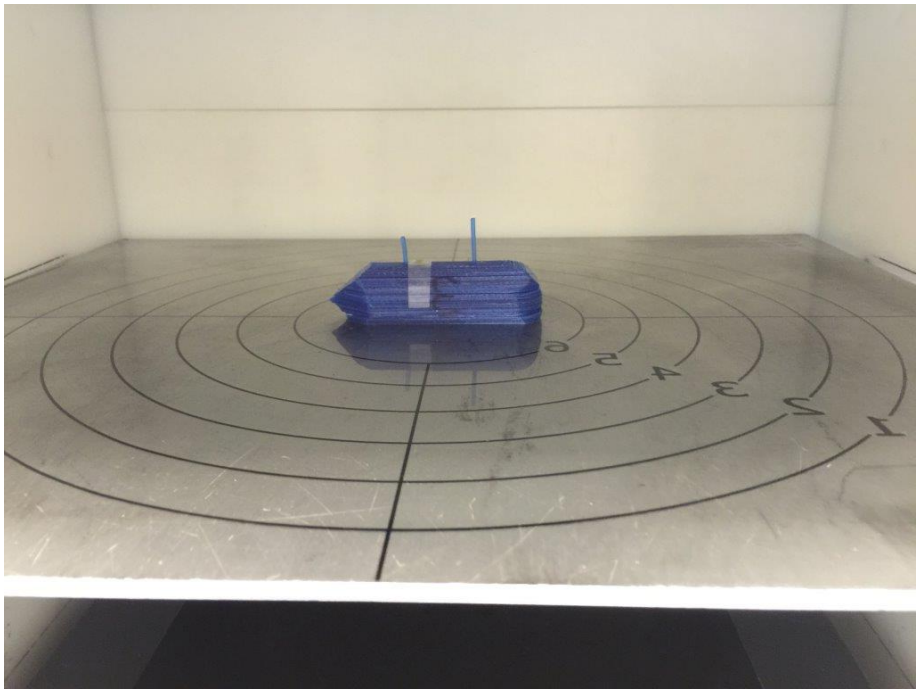
Cs-137 Irradiator

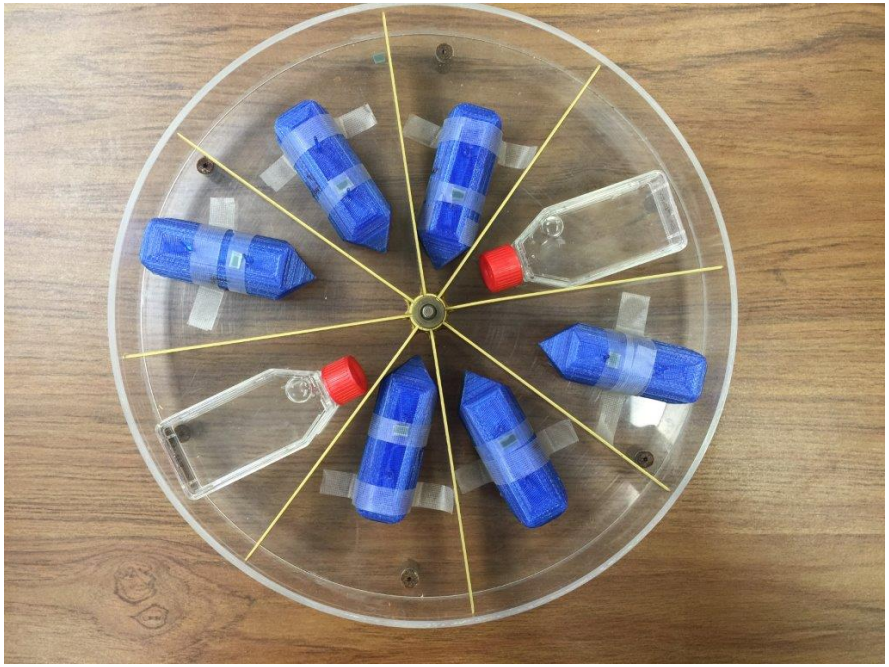
- EBT2 film measurement in JL Shepherd Mark 1 Cs-137 irradiator, no lead attenuator was used, location 3, no turntable rotation, irradiated to the dose of 6 Gy; EBT2 film measurement in RS 2000 x-ray irradiator, 160 kVp, 25 mA, level 3.
- Solid water phantom was used. Films were sandwiched in different thicknesses of solid water phantoms.

Measured PDD Comparison – Cs-137 and X-ray (160 kVp)



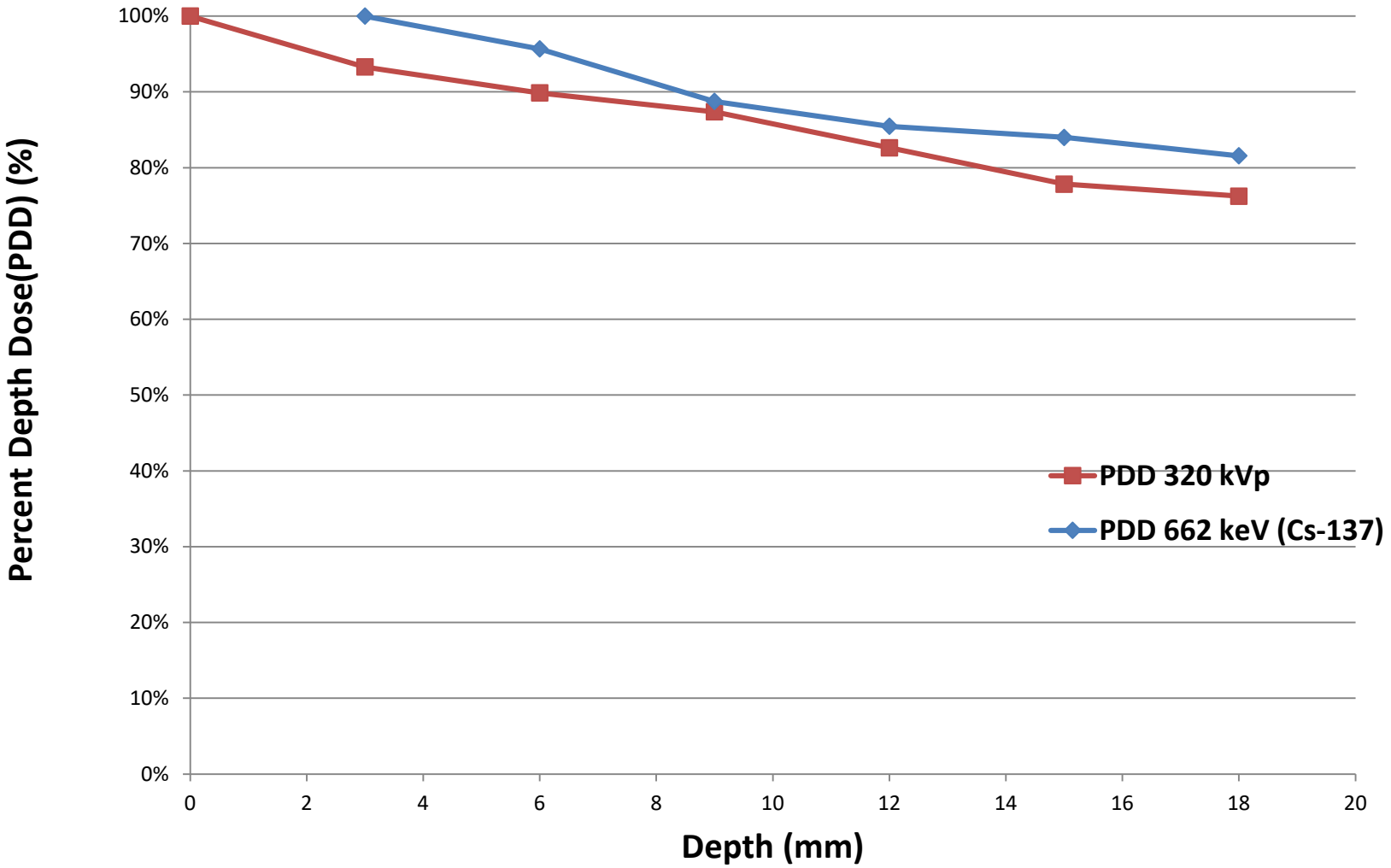
Mouse Phantom Measurement





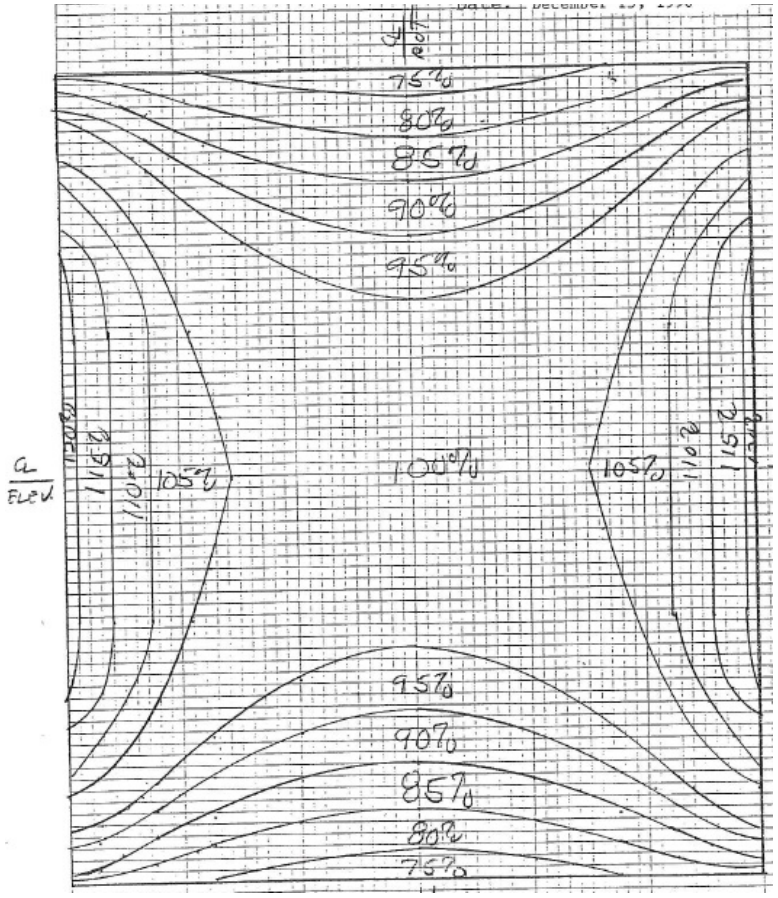
MEASURMENT

Percent Depth Dose (PDD) Curve of 320 kVp (Precision X-ray XRad 320) VS 662 keV (JL Shephard Mk-I-68) in Small Rodent Phantoms



Dose Delivery Deviation

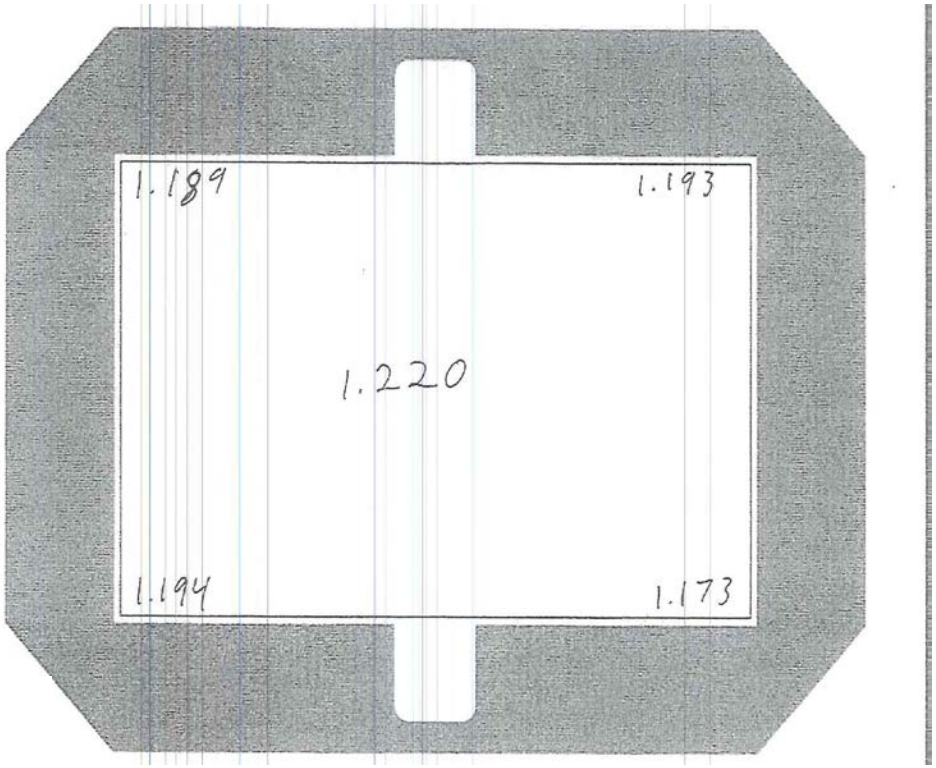
Cs-137



Isodose map of Cs-137 Irradiator at position 3

±20 % dose deviation while irradiating mice

X-ray



Dose rate measurement at RS2000 x-ray irradiator at level 1 with RAD+

±3.8 % dose deviation while irradiating mice

Successful X-ray Irradiation Experiments - 1*

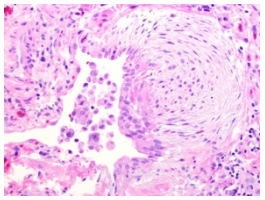
- **First experiment**:
  - Used 35 mice for bone marrow transplantation
  - Irradiation: 6 Gy each time (12 Gy total) (12-24 hrs interval)
  - Survival: 50 days. Only one mouse died out of 35 transplanted mice
  - Chimerism: All recipients were around 90% of donor origin. Similar result to using Cesium source.

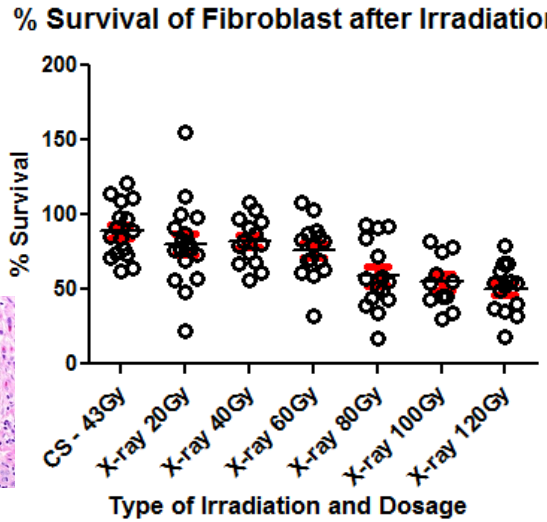
- **Second experiment:**
  - Irradiation: 6 Gy each time (12 Gy total) (12-24 hrs interval)
  - Survival: 30-50 days. This is a model disease and development of LCH is expected after transplantation
  - Chimerism: All recipients were around 100% of donor origin. Similar result to using Cesium source.

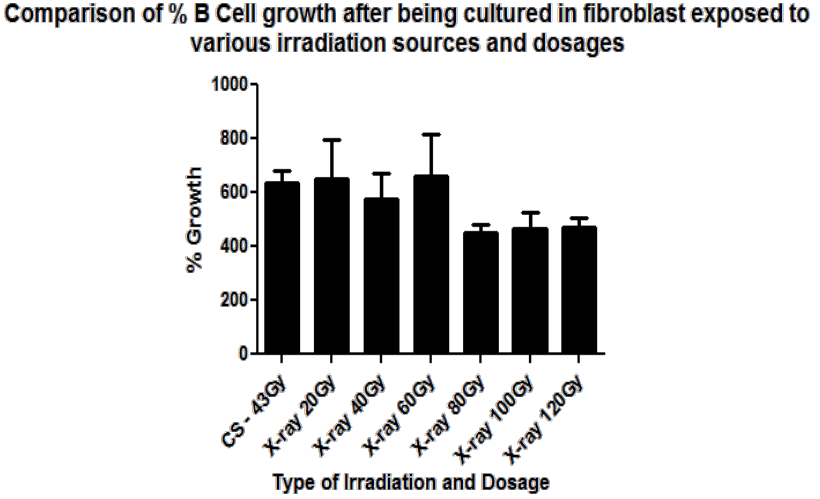
** Dr. Miriam Merad laboratory – Icahn School of Medicine at Mount Sinai*

Successful X-ray Irradiation Experiments -2*

- To grow human B cells on irradiated human fibroblasts
- To compare standard irradiation (43Gy) to various doses of x-ray (20-120Gy)
- Measured
  - fibroblast survival over 3 days
  - growth of B cells when plated on the fibroblasts
- Our data indicate that 20-60Gy x-ray has equivalent effects to standard 43 Gy cesium irradiation, and that Xray doses above 80Gy impair fibroblast and B cell growth compared to the standard 43 Gy cesium irradiation



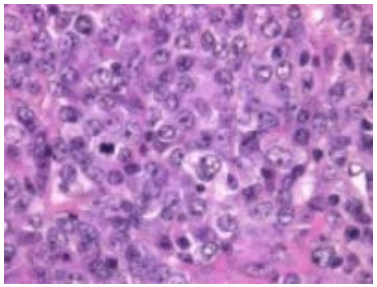




** Dr. Peter Heeger laboratory – Icahn School of Medicine at Mount Sinai*

Successful X-ray Irradiation Experiments -3*

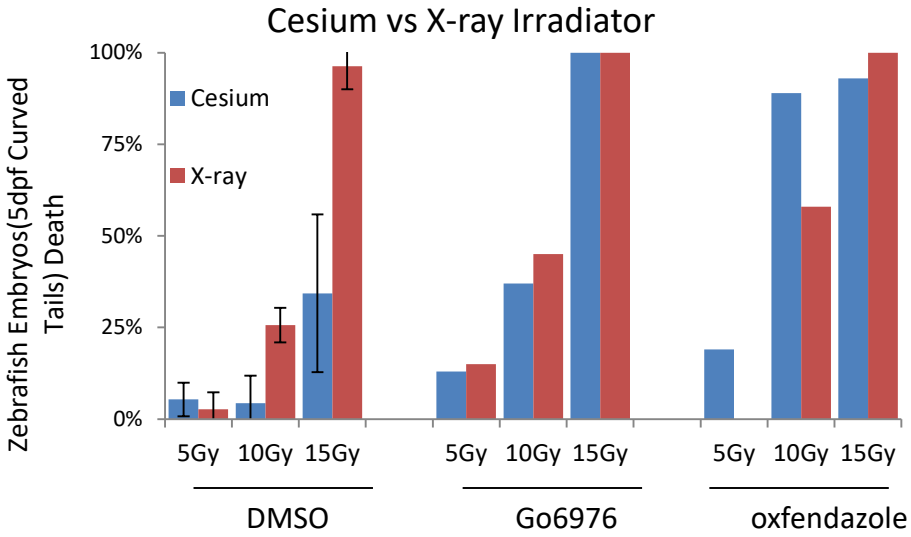
- Assess the effect of irradiation on survival of A20 lymphoma cell line
- Irradiation: various doses (9Gy-100Gy)
- Readout: Annexin V staining for apoptosis of A20 cells after 48h
- Apoptosis is induced in a dose dependent manner, increasing from 25% at 9Gy to 60% at 75Gy, doses over 75Gy did not show a further increase in apoptosis induction

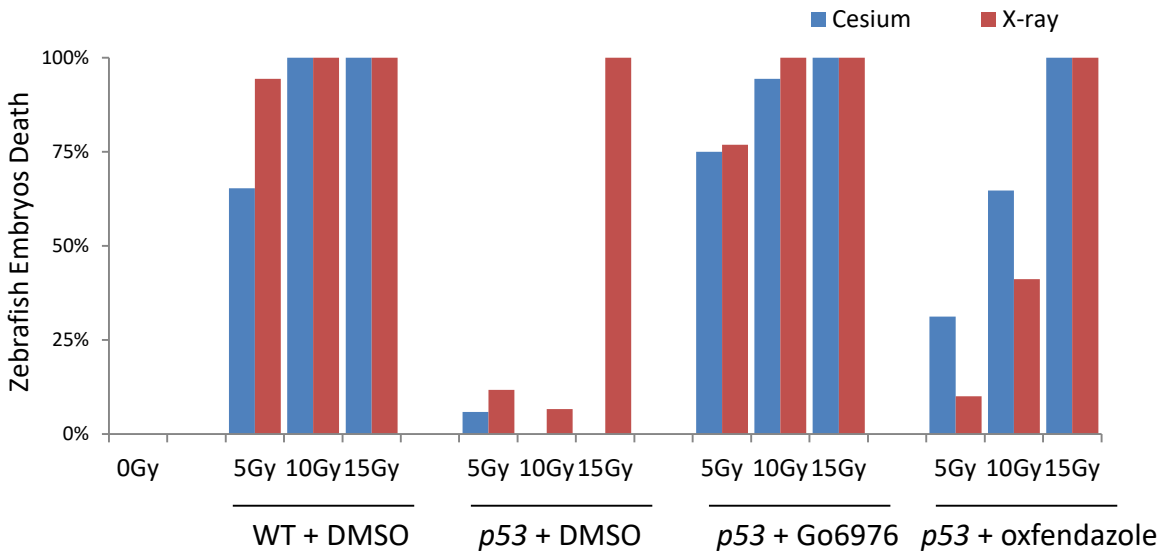


** Dr. Joshua Brody laboratory – Icahn School of Medicine at Mount Sinai*

Successful X-ray Irradiation Experiments – 4*

- X-ray is toxic at 10 and 15 Gy in embryos (5dpf curved tails) that normally tolerate these doses when delivered by Cesium with DMSO; otherwise, x-ray and cesium irradiation give very similar death rates under the condition that the same dose given to the zebrafish embyos.
- X-ray is toxic to the embryos of zebrafish when the embryos are irradiated to 15 Gy with p53+DMSO.





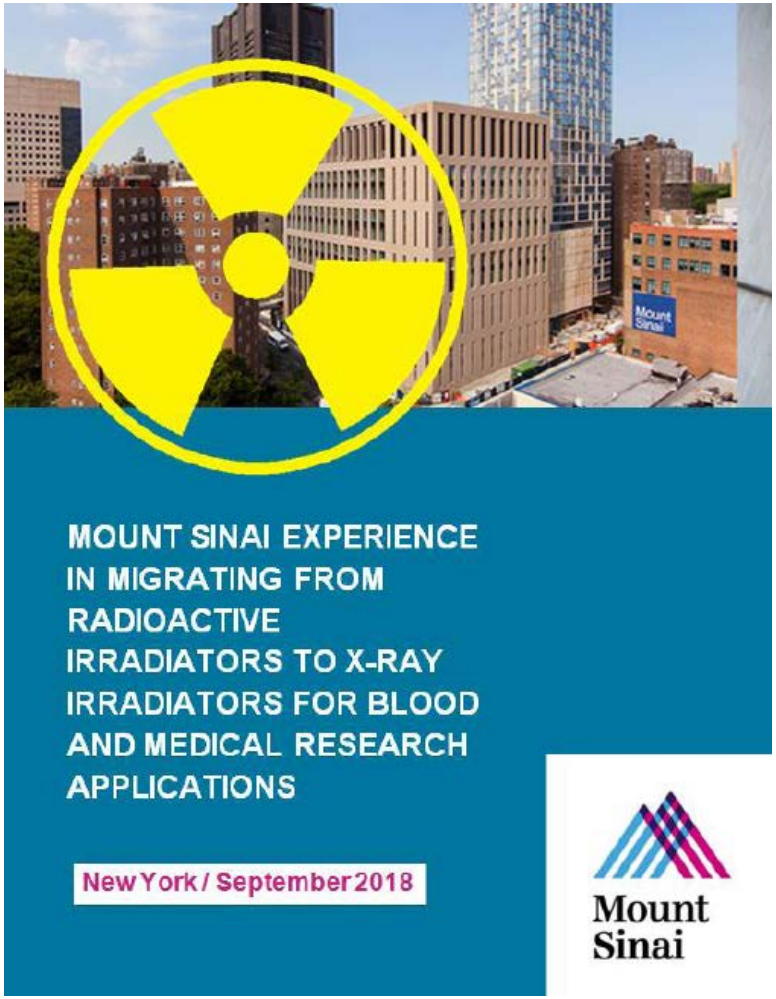
** Dr. Samuel Sidi laboratory – Icahn School of Medicine at Mount Sinai*

Successful X-ray Irradiation Experiment – 5*

- Experiment:
  - Used 12 mice for whole brain irradiation
  - Irradiation: 5 Gy x 2 (48 hour interval) [total: 10 Gy]
  - Survival: 30 days. No deaths.
  - X-Ray irradiator gives similar results to Cs-137 irradiator

** Dr. Costas Hadjipanayis laboratory – Icahn School of Medicine at Mount Sinai*

Where to find the report?



- https://www.nti.org/media/documents/Mt._Sinai_Final_Report.pdf

Phase 3- 2016 Irradiator Disposal

2017- New X-ray Irradiators in Mount Sinai

Blood Irradiator

RS 3400, 150 kVp

Research Irradiator

X-RAD 320, 320 kVp

FDA Radiological Devices Advisory Panel

April 12, 2012

Blood Irradiators Executive Summary

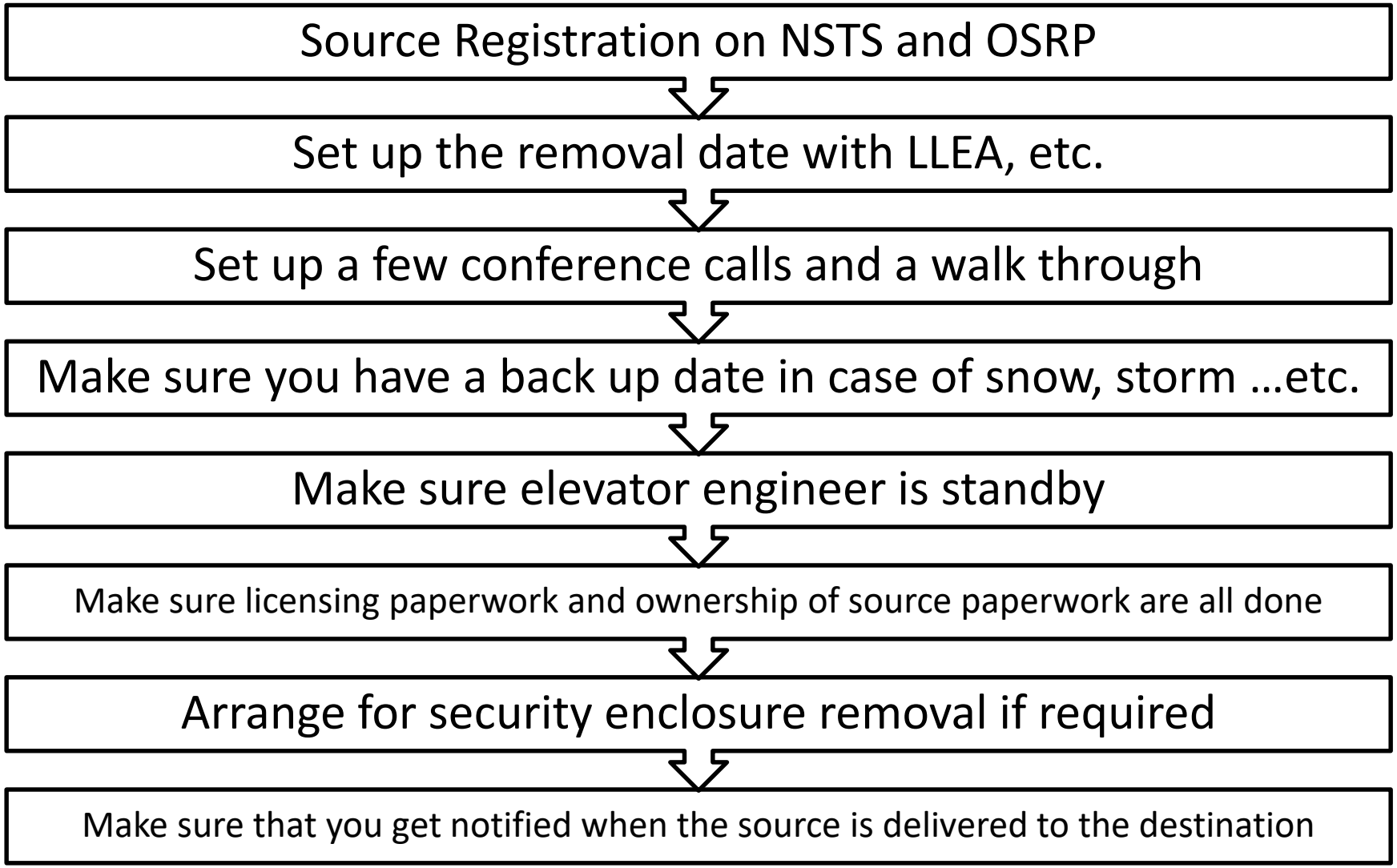
There are basically two types of radiation emitting devices (isotope-containing devices and x-ray tube containing devices) that pertain to the devices currently being regulated by CDRH under blood irradiator to prevent TA-GVHD. Both types are capable of delivering 2500 cGy of ionizing radiation to containers filled with blood or blood products.

2017-Reliability Issue with X-ray Irradiators – Mount Sinai's Experience

- **RS 2000 Research Irradiator**
  - Purchased in April 2013.
  - It is used on both mice and cells, including whole mouse irradiation, tumor targeting, and plates of cells irradiation.
  - 129 members of the Tisch Cancer Institute & 123 other labs have requested to use it. It is used daily ~ 3-4 times/day, everyday of the year.
  - **NO system failure has been reported since purchased.**
- **RS 3400 Blood Irradiator**
  - Installed in January 2017.
  - The RS 3400 is a registered medical device with a USFDA 510(k).
  - Processes six 1-liter canisters in one cycle (25 Gy in less than 5 minutes).
  - Dose uniformity.
  - It was used to irradiate about 900 units of blood product in the first month. We stress tested to use it to irradiate more than 100 units of blood product in one day . **No issues found.**

January 2018 - Final Irradiator Disposal

Preparation of Source Removal



Documents Required by Regulatory Agencies

- **The below documents were submitted to NYCDOH to be in compliance of 10CFR part 37:**
  - **T&R verification (from the contractors)**
  - **ATRO (signed by both Mount Sinai and OSRP)**
  - **License verification documents (NRC form 749)**
  - **Proof of source transfer on NSTS database (NRC form 748(b))**
  - **Preplanned truck route to the destination**
  - **A copy of the sign-in sheet during source removal**

GLOBAL EFFORT


France

Started in 2006 a 10 year plan- They had 30 Irradiators. Replaced them with x-rays. Completed successfully.


Norway

They had 13 irradiators. They replaced them gradually with X-rays . Completed in 2015 successfully.


Japan

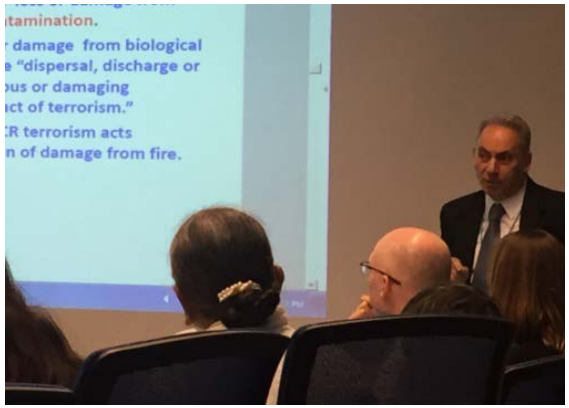
Started replacing about 20 years ago. 80% of blood irradiators have been replaced by X-ray

Snapshot of Mount Sinai Efforts

Organized a meeting with all irradiator users in NYC to answer their questions

Held a press conference-October 2017

Hosted a meeting with 20 VPs from all NYC area hospitals



Presented in National and International meetings


CAP TODAY

PATHOLOGY • LABORATORY MEDICINE • LABORATORY MANAGEMENT

MARCH 2017

New rays on blood safety

Cell-free DNA screening blooms in expansion to low-risk pregnancies

Published in CAP Today Journal

Our Experience

- **Separate applications**
  - **Blood- FDA approved- is it reliable?**
  - **Research – cells, mice, zebra fish, etc.**
- **Conduct side-by-side comparison to validate equivalency**
- **Self-cooled X-ray irradiator is preferred choice**
- **Water filter should be used if x-ray irradiator is not a self-cooled**
- **Keep X-ray irradiator in air conditioned room**
- **Get your staff trained by the manufacturer if possible**
- **Take advantage of remote assistance if provided by the manufacturers**
- **Encourage radiation physicists & researchers to work together**

THANK YOU