Mitigating Transition Challenges From Gamma Irradiators To X-ray Irradiators

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Council on Ionizing Radiation Measurement & Standard (CIRMS)

30th Annual CIRMS Meeting
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The Universities At Shady Grove
Rockville, MD

Topics Covered

- How to mitigate transition challenges
- Separate the Irradiators applications (research vs clinical)
- Institution efforts
- Manufacture efforts
- Government agencies efforts
- Share operational experiences
- Standardization
- BNL CIRPER 2023 report
- Two questions for the audience

Separate the Irradiators applications

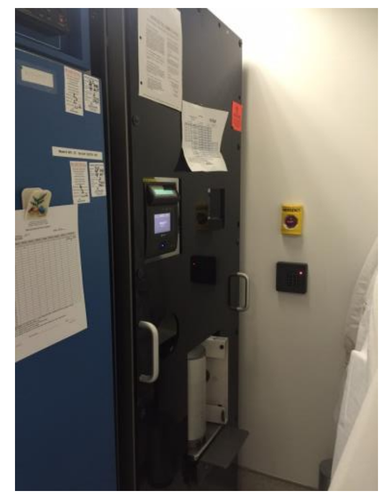
Research Irradiators

- It is used for mice or cells
- How many times a day is it used?
- They may need comparison studies

Blood Bank Irradiators

- FDA approved- No studies needed
- Is it reliable for major hospital operation?
- Do we need to have any back up plan?



All were considered to be category 2 radioactive sources.

Institutional Effort

- **Convince the leadership (risk vs benefit)**
- **Convince the researchers and blood bank staff- separately**
- **Explain the John McCain Act**
- **Get them involved in the process (selecting the vendor, etc.)**
- **Help them with comparison studies if needed**
- **Train personnel to operate the alternative technology.**
- **Walkthrough before gamma irradiator disposal.**
- **Weight of the Gamma Irradiator in the elevator**

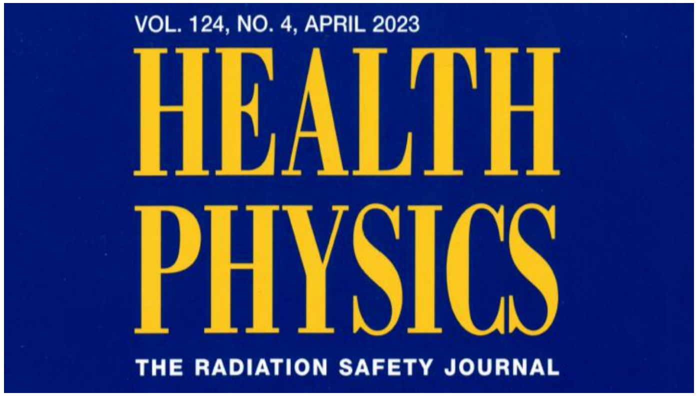
Manufacturer Support

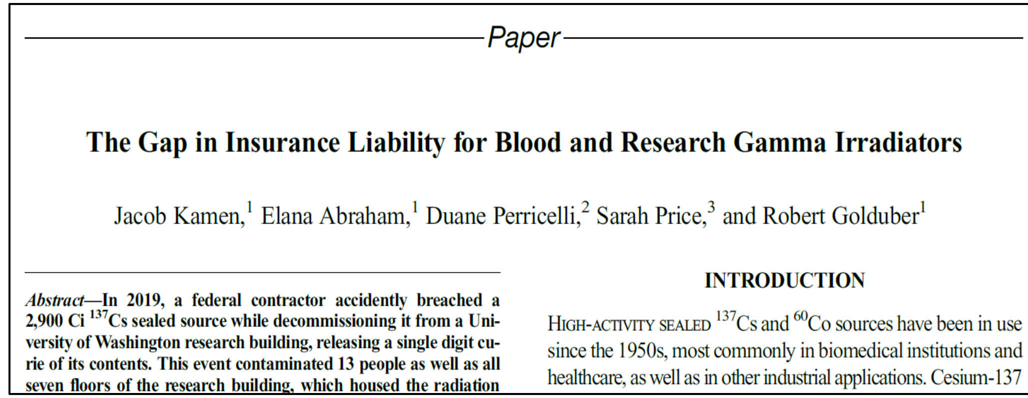
- **Removing the filter lead to the death of 42 mice.**
- **Set the machine to 448 sec instead of 4 min and 48 sec**
- **Require water filter for the irradiator**
- **House the X-ray Irradiator in an Air Conditioned room**
- **Hot summer and the need for the voltage stabilizer**
- **Share experiences learned during and after the transition for others to have a better transition**

Government agencies Effort

- Nuclear Regulatory Commission (NRC)'s role is central - their active participation and support is key!
- NRC and Financial Assurance
- DOE/NNSA/ORS effort- Good job
- Brookhaven National Laboratory (BNL) and Compatibility of Irradiation Research Protocols Expert Roundtable (CIRPER) report- Good work
- Government agencies (i.e. NIH) should require alternative technologies in their applications.

Convincing the leadership





Paper

The Gap in Insurance Liability for Blood and Research Gamma Irradiators

Jacob Kamen,[1] Elana Abraham,[1] Duane Perricelli,[2] Sarah Price,[3] and Robert Golduber[1]

Abstract—**In 2019, a federal contractor accidently breached a 2,900 Ci ^{137}Cs sealed source while decommissioning it from a University of Washington research building, releasing a single digit curie of its contents. This event contaminated 13 people as well as all seven floors of the research building, which housed the radiation**

INTRODUCTION

High-activity sealed ^{137}Cs and ^{60}Co sources have been in use since the 1950s, most commonly in biomedical institutions and healthcare, as well as in other industrial applications. Cesium-137

Owning a Gamma Irradiator is Risky

1 - Potential astronomical cost of radioactive mass decontamination
2 - High target value to terrorist
3 - The limited ability to shift risk to insurer or federal government.

SUGGESTIONS

1 - Ensure that correct coverage is endorsed onto your insurance policies.
2 - Ensure that there are no restrictions built into the policy coverage. These restrictions could excuse insurers from covering irradiator mass contamination event

Convincing the Users

Convincing The Users

- **Blood bank Management**
- **University of Washington**
- **Saving on security equipment, No more FBI background check, No more 10CFR part 37 inspection, OSRP and CIRP**
- **You could irradiate 6 bags of blood at one time**
- **Explain the John McCain Act**
- **Red Cross and a few other major institutions have already fully migrated**

- **Research Users**
- **Get them all in one room (with Pizza) with the dean of research**
- **Inform them a few major research institutions have already migrated. (Mount Sinai, NYU, UNSC, etc.)**
- **Show them the result of Mount Sinai comparison studies.**
- **Assure them they could have both technologies side by side for 6 months until they feel comfortable**
- **Assure them you will be with them until they totally migrated**

Explain the Possible Alternatives

Blood Irradiator

RS 3400, 150 kVp

Research Irradiator

X-RAD 320, 320 kVp

Get the users involved in the process of transition

Decision making on the Irradiators

Considerations

- FDA Approved (for Blood)
- Energy
- Irradiator chamber size
- Irradiator size (considering our space is limited)
- Self-cooling system
- The add-ons (collimators, adjustable shelves…etc.)
- Price of the machine and the warranty cost
- Renovation Cost
- Shorter downtime
- The review of other users

Process

Step 1. Collect information online to see what irradiators are available

Step 2. Narrow down to 2-3 desirable units

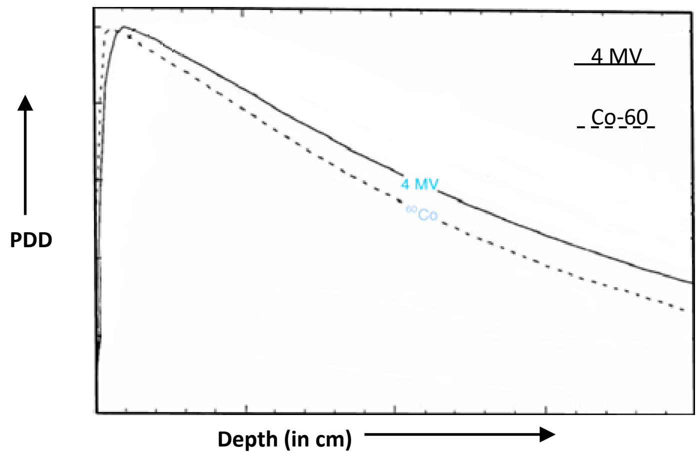
Step 3. Ask the vendors to introduce their units to the users (researchers, blood bank)

Step 4. Collect the opinions from the users and make a decision

Co-60 & LINAC (4MV)
Depth dose Comparison

LINAC

Co-60

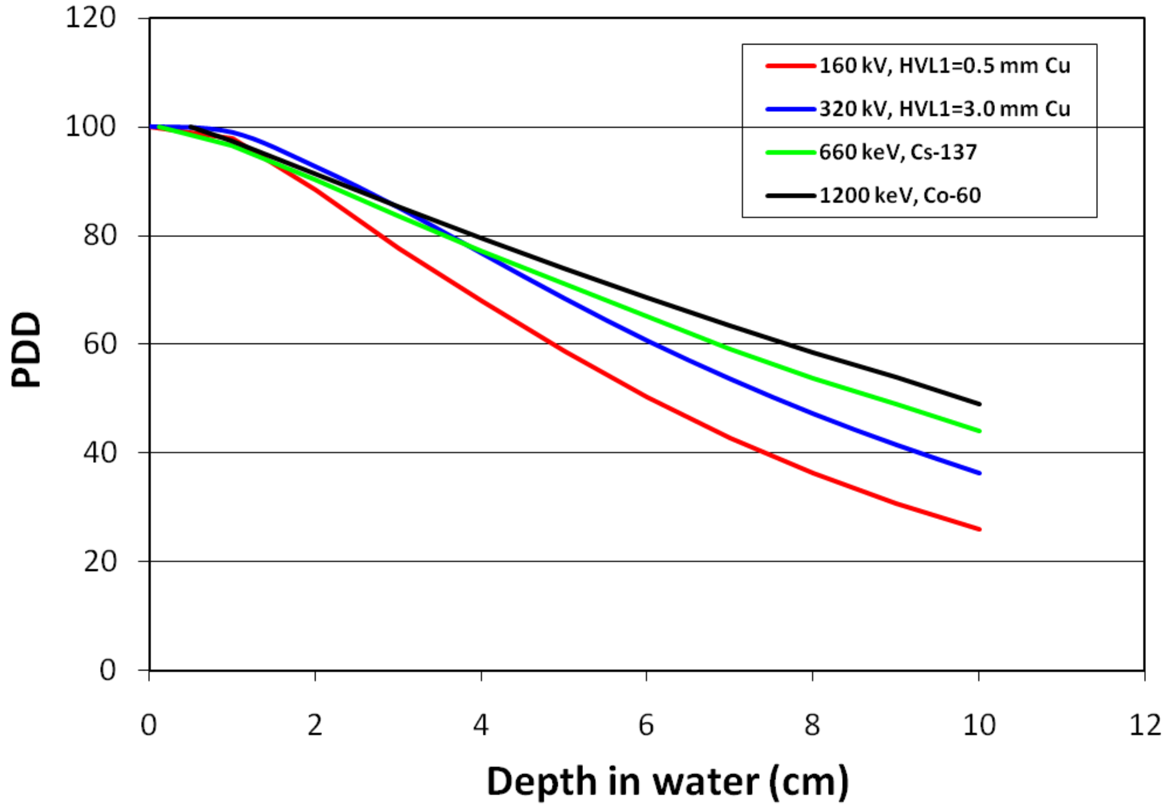


Percentage depth dose curves in water for a 10 × 10 cm2 field at 100 cm SSD for photon beams from cobalt-60 gamma rays and 4 MV X-rays.

10,000 Ci → @1ft → ~38R/sec

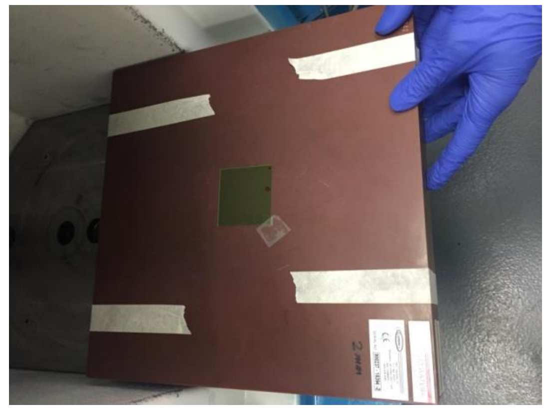
Explain similarity

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

Experimental Setup For Depth Dose Measurement

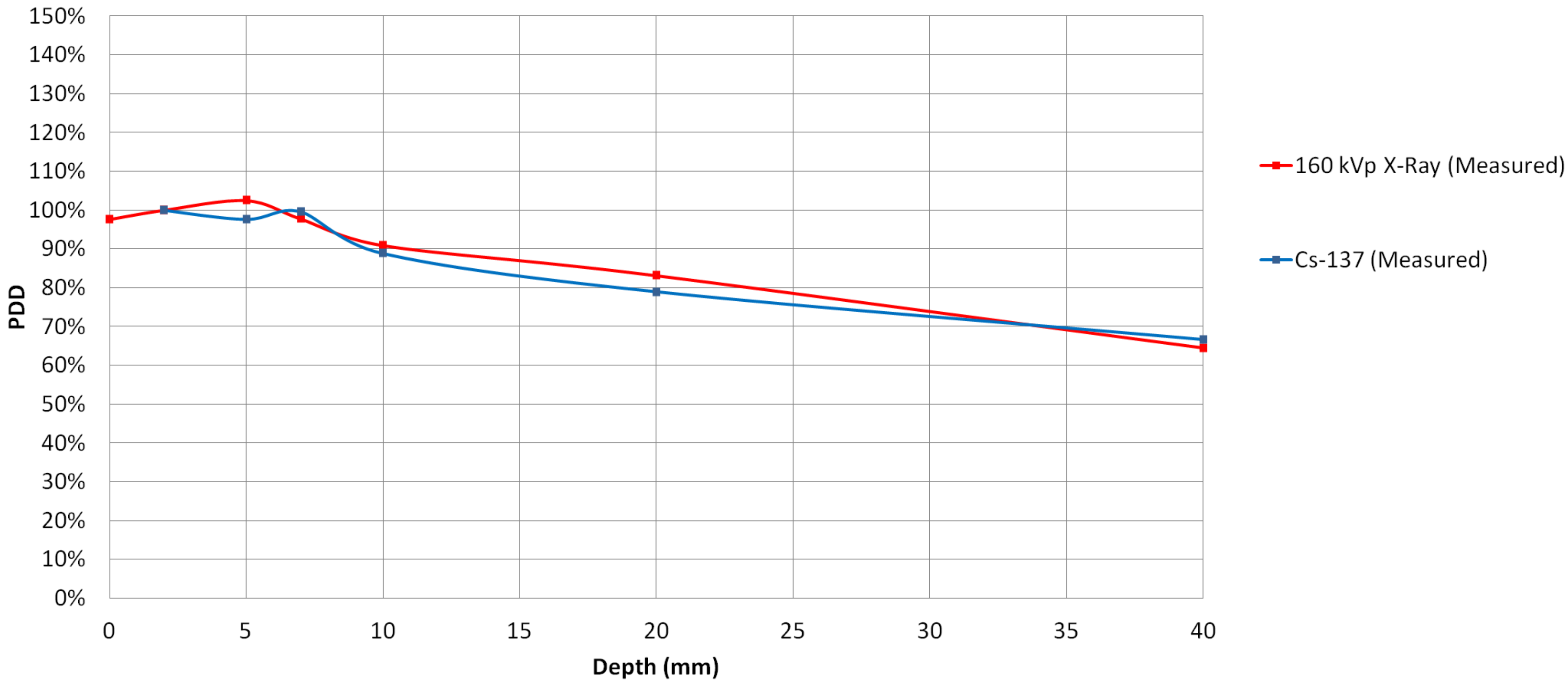


X-Ray Irradiator

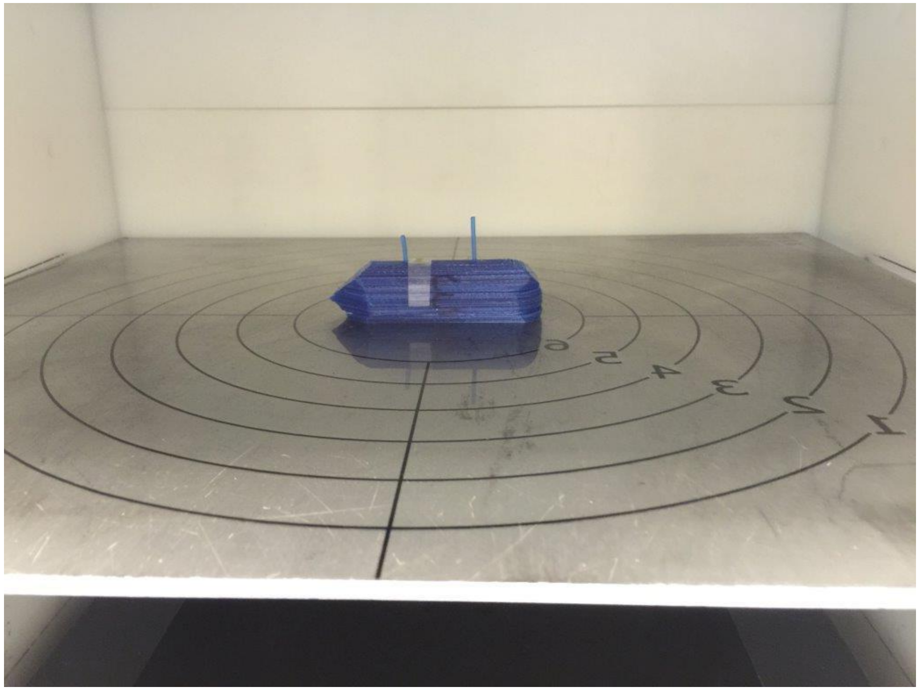
Cs-137 Irradiator

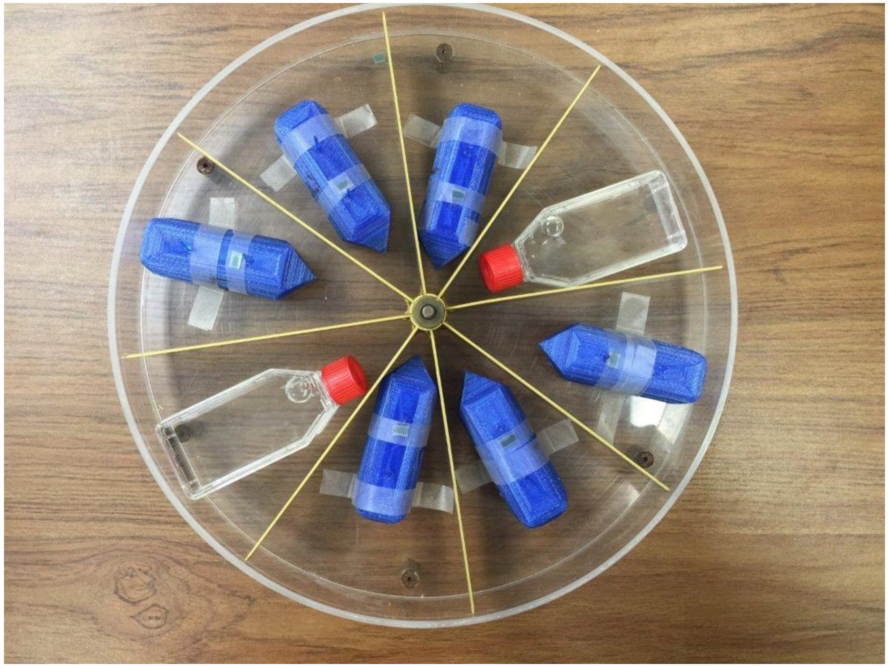
- **EBT2 film measurement in JL Shepherd Mark 1 Cs-137 irradiator, no lead attenuator was used, location 3, no turntable rotation, irradiated to the dose of 6 Gy; EBT2 film measurement in RS 2000 x-ray irradiator, 160 kVp, 25 mA, level 3.**
- **Solid water phantom was used. Films were sandwiched in different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

Comparing Measured Percent Depth Dose



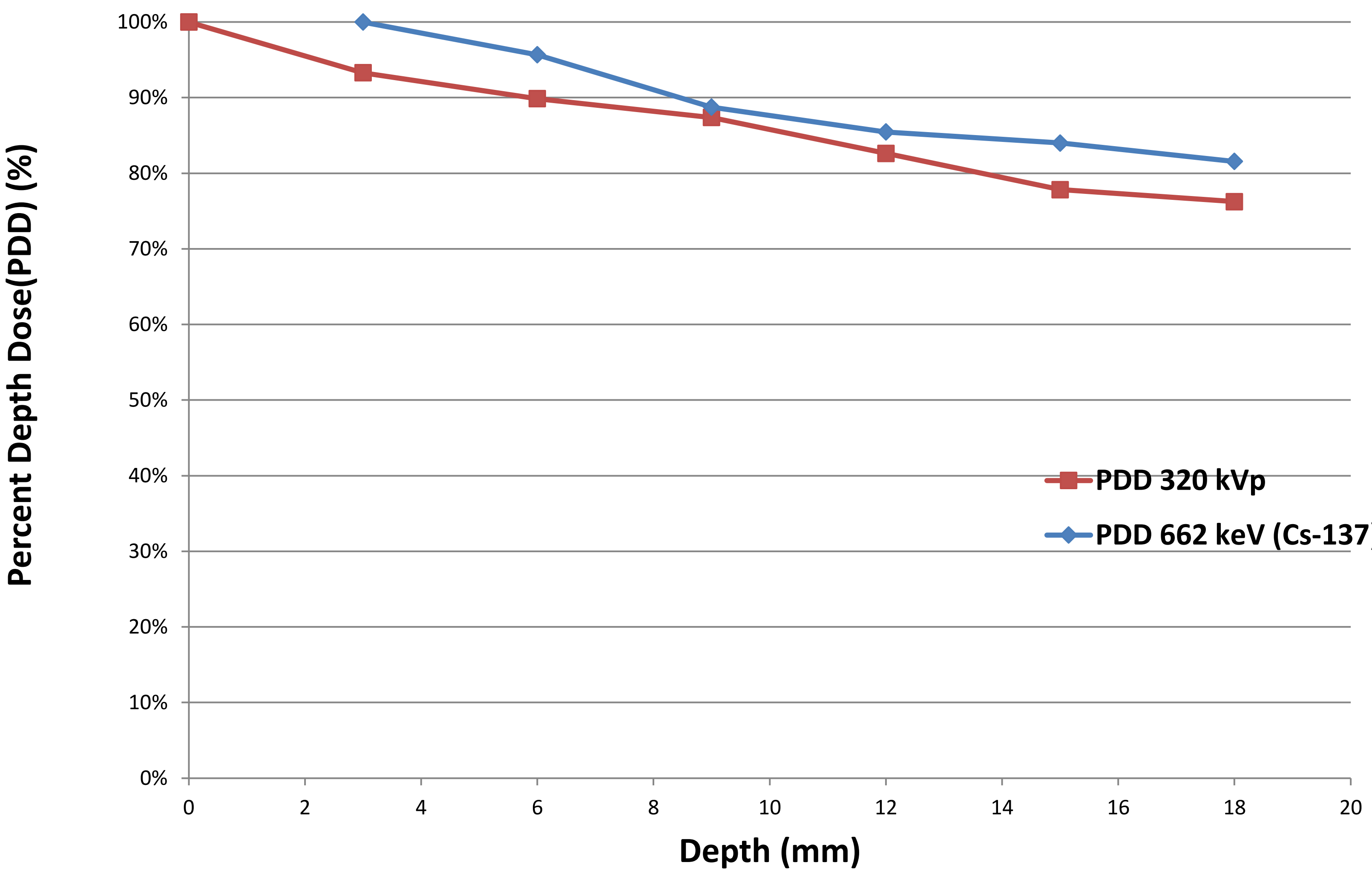
Mouse Phantom Measurement





MEASURMENT

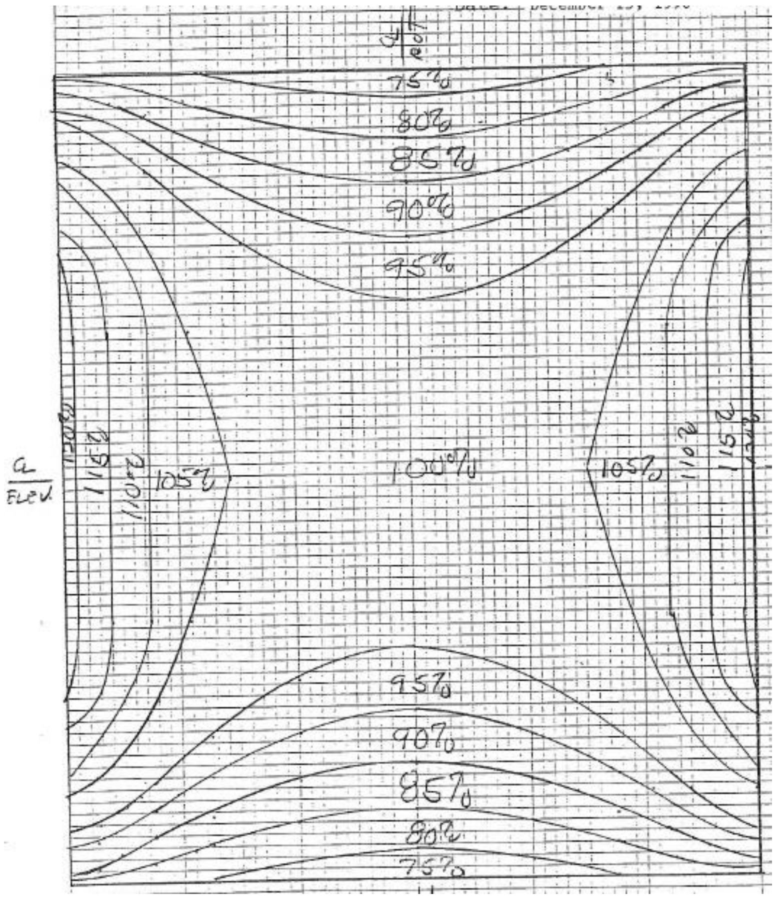
Percent Depth Dose (PDD) Curve of 320 kVp (Precision X-ray XRad 320) VS 662 keV (JL Shephard Mk-I-68) in Small Rodent Phantoms



X-ray irradiators advantages

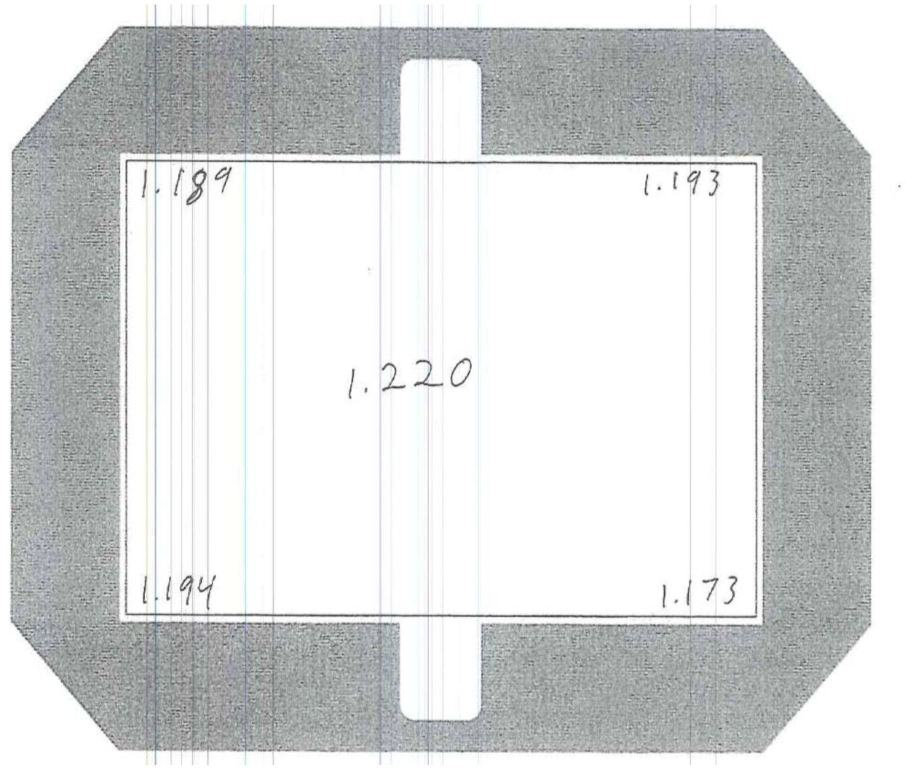
Dose Delivery Deviation

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

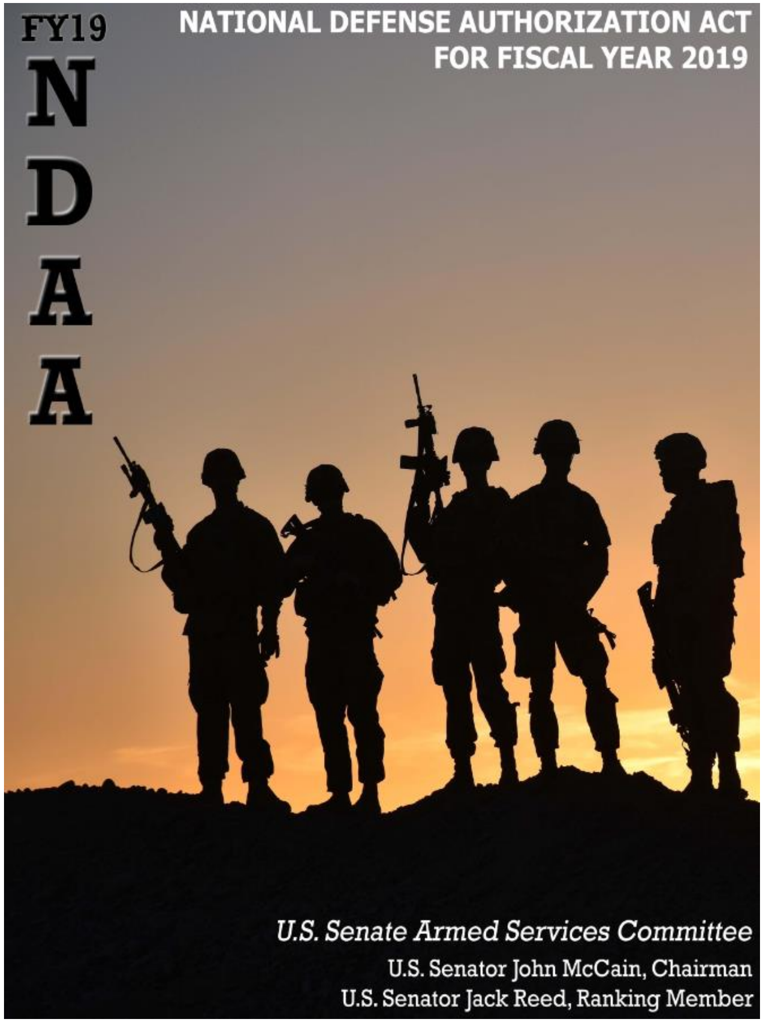
Cs-137 Decay Correction

- Cs-137 decays ~1% in 5 months or ~2.3% in a year. Need to correct every few months and recalibrate the 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

The John McCain Act

- Congress passed the John S. McCain National Defense Authorization Act for Fiscal Year 2019
  - One of the sections of the act involved accelerating blood irradiator replacement
- Goal: Eliminating the use of Cesium blood irradiation devices in the U.S. that rely on cesium chloride by Dec. 31, 2027
- Assessment: The program Administrator shall submit an assessment to the appropriate congressional committees by Sept. 20, 2023, of the results … under this section
- The programs tasked with implementing these goals are: CIRP and OSRP



https://www.congress.gov/bill/115th-congress/house-bill/5515/text

US government effort
Financial Resources Available

- **Off-site Source Recovery Program (OSRP)**
  - https://osrp.lanl.gov/

- **Office of Radiological Security (ORS) –**
- **Cesium Irradiator Replacement Project (CIRP)**
  - https://www.energy.gov/nnsa/office-radiological-security-ors

US government effort

- National Nuclear Security Administration's (NNSA), Office of Radiological Security's (ORS) Off-Site Source Recovery Program (OSRP) has removed > 500 Cs-137 and Co-60 devices since 2004.
- OSRP is managed out of Los Alamos National Laboratory (LANL) and Idaho National Laboratory (INL)
- >300 irradiators have been replaced to date through CIRP

COMPARISON STUDIES- IF NECESSARY

Successful X-ray Irradiation Experiments - 1*

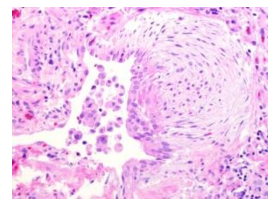
- **First experiment**:
  - Used 35 mice for bone marrow transplantation
  - Irradiation: 6 Gy each time (12 Gy total) (12-24 hrs interval)
  - Survival: 50 days. Only one mouse died out of 35 transplanted mice
  - Chimerism: All recipients were around 90% of donor origin. Similar result to using Cesium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

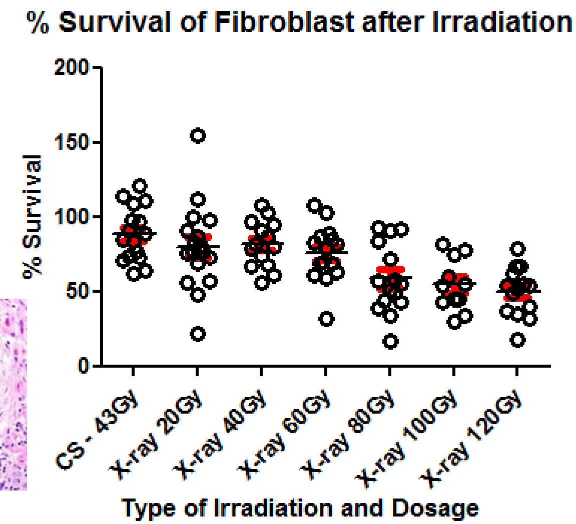
- **Second experiment:**
  - Irradiation: 6 Gy each time (12 Gy total) (12-24 hrs interval)
  - Survival: 30-50 days. This is a model disease and development of LCH is expected after transplantation
  - Chimerism: All recipients were around 100% of donor origin. Similar result to using Cesium source.

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

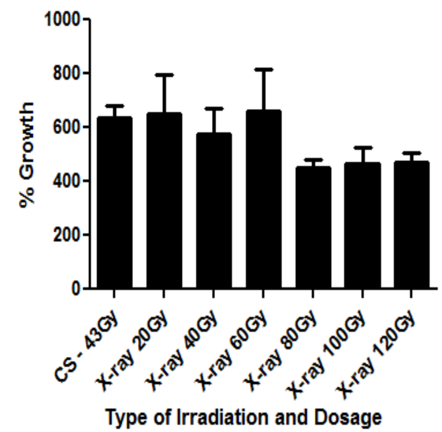
Successful X-ray Irradiation Experiments -2*

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



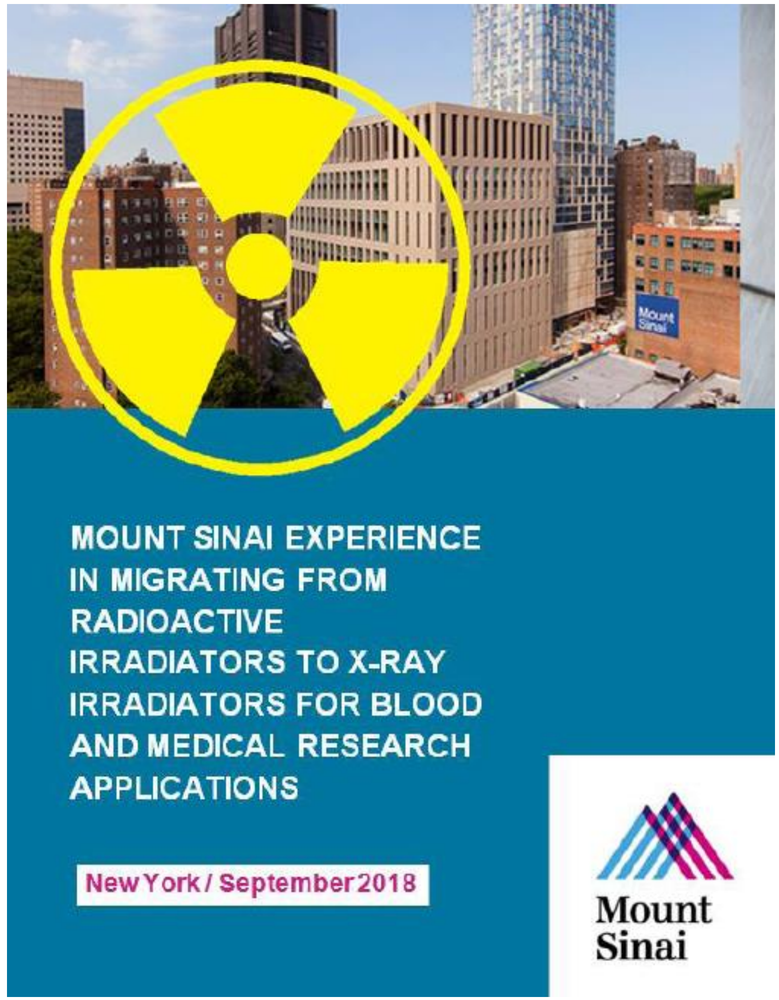


Comparison of % B Cell growth after being cultured in fibroblast exposed to various irradiation sources and dosages

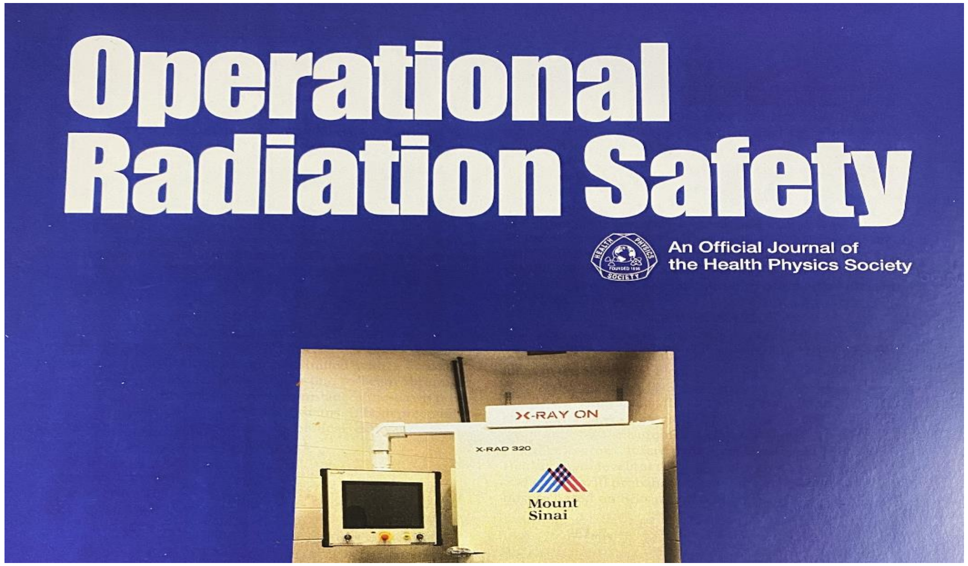


** Dr. Peter Heeger laboratory – Icahn School of Medicine at Mount Sinai*

Where can you find the report?



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



of radioactive materials permanently. Health Phys. 117(5):558–570; 2019

Operational Topic

OPEN

Close the gaps, minimize risks. If not now, when?

Successful Migration from Radioactive Irradiators to X-ray Irradiators in One of the Largest Medical Centers in the US

Jacob Kamen,[1] Wen-Ya Hsu,[1] Brandon Boswell,[1] and Colin Hill[2]

Abstract: *This paper summarizes about 9 years of effort by Mount Sinai to successfully migrate completely from radioactive irradiators*

24/7 video monitoring. In addition, a remote monitoring system with alarms was installed and connected to LLEA for constant monitoring

Key words: *operational topic; cesium; education, health physics; x rays*

Experience from other Alternative Technology Transition

30-45 minutes

60 years ago

1.2 minutes

2023

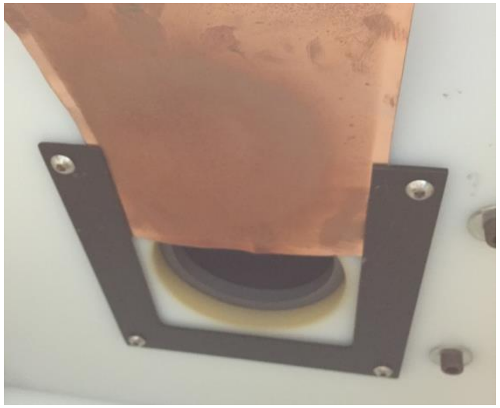
Operational Experiences

Operational experiences

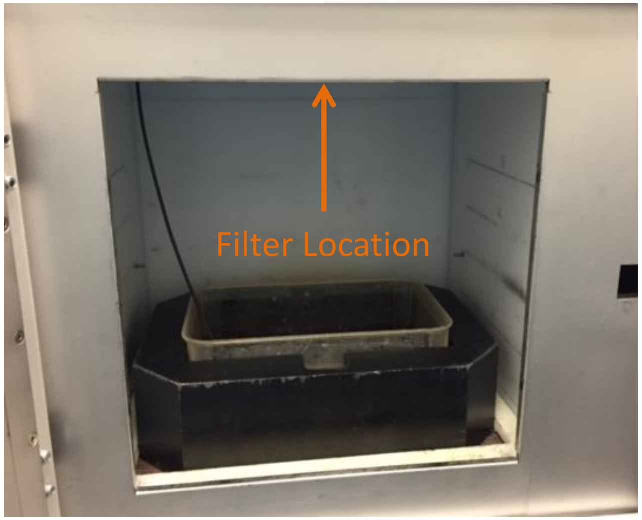
42 mice died- Copper Filter Issue

- The copper filter on the irradiator ceiling can be displaced inadvertently while moving cages or irradiator equipment
- If the copper filter gets dislodged it can result in a dose rate that is 10X higher
- Make sure the filter is completely covering the aperture before irradiation

Correct



Incorrect



Operational Experiences

Exposure Time Input Error

- The dose chart on the irradiator lists the time in **minutes and seconds**
- The irradiator accepts the time **only in seconds**
- If the time is inputted incorrectly it could result in an overdose
- Care must be taken to make sure the time is properly converted into seconds before starting the irradiation
- **A new time table shown in seconds is created to avoid the time input error.**

Intended Exposure Time	Actual Inputted Exposure Time
4 min 48 seconds (4 x 60 + 48 = 288 sec)	448 seconds
6 Gy dose delivered	9.33 Gy dose delivered
Correct dose delivered	Incorrect dose delivered (156% of intended)

RS 2000 Irradiation Time Tables

Machine Settings 160 kV 25 mA

LEVEL 1 (inside RAD+)
Dose rate: 1.25 Gy/min

Dose rad (cGy)	Dose Gy	Time (sec)
200	2	96
250	2.5	120
300	3	144
350	3.5	168
400	4	192
450	4.5	216
500	5	240
550	5.5	264
600	6	288
650	6.5	312
700	7	336
750	7.5	360
800	8	384
850	8.5	408
900	9	432
950	9.5	456
1000	10	480
1050	10.5	504
1100	11	528
1150	11.5	552
1200	12	576

LEVEL 3
Dose rate: 2.06 Gy/min

Dose rad (cGy)	Dose Gy	Time (sec)
200	2	58
250	2.5	73
300	3	87
350	3.5	102
400	4	117
450	4.5	131
500	5	146
550	5.5	160
600	6	175
700	7	204
800	8	233
900	9	262
1000	10	291
2000	20	583
2500	25	728
3000	30	874
3500	35	1019
4000	40	1165
4500	45	1311
5000	50	1456
6000	60	1748
7000	70	2039
8000	80	2330
9000	90	2621
10000	100	2913

LEVEL 5
Dose rate: 4.51 Gy/min

Dose rad (cGy)	Dose Gy	Time (sec)
2000	20	266
2500	25	333
3000	30	399
3500	35	466
4000	40	532
4500	45	599
5000	50	665
5500	55	732
6000	60	798
6500	65	865
7000	70	931
7500	75	998
8000	80	1064
8500	85	1131
9000	90	1197
9500	95	1264
10000	100	1330

Model: RS 2000
S/N: 3228
Mount Sinai Medical Center

Formula to calculate time based on Gy
Example: Target dose 45 Gy and sample placed on level 3 (2.06 Gy/min)

$$Time\ (sec) = \frac{45\ Gy}{2.06\ \frac{Gy}{min}} \times 60\ \frac{sec}{min} = 1311\ sec$$

Reliability Issue

- RS 3400 Blood Irradiator
- Installed in January 2017.
- It is FDA approved.
- Processes six 1-liter canisters in one cycle (25 Gy in less than 5 minutes).
- It was used to irradiate about 900 units of blood product in the first month.
- Stress tested to use it to irradiate more than 100 units of blood product in one day. It was successful
- During electricity outage the unit was back to work without any problem

Pros of X-ray Blood Irradiators

- FDA approved units
- No FBI finger printing and background check
- No security issues and quarterly testing of RMS
- No radioactive regulatory inspection
- Low initial transportation and disposal costs ($2,000 vs $200,000)
- Low insurance premium for possible sabotage and malicious use
- No decay correction
- Constant irradiation time throughout the lifetime
- Higher throughput (6 bags at once in x-ray irradiators vs 2 bags in CsCl irradiators)
- No annual reconciliation with NRC-NSTS website
- Self-shielded and self-cooled
- Discount on the annual warranty if the institution sends staff for training on trouble shooting.

Operational experience
Blood Irradiator

- September 2019: Rotator issue, needed new contract, new PO, ISODOSE curve, etc
- Summer 2022- Temperature in NYC reached 110 degrees, All AC for 14 million people were working at the same time. Input voltage was not stabilized, as a result the unit shut itself down.
- Voltage stabilizer installed and the unit went back to work.
- The company provides service on the same day.

Operational X-ray Irradiator Experience

External Mobile Air Conditioner

Voltage Stabilizer

Operational experience
Advance Walkthrough- Irradiator Disposal

Steps for Disposal of Radioactive Irradiator
From Source registration to source transferred

Preparation:

1- Register the source with NSTS and OSRP
2- Set up removal date with LLEA, regulatory agencies, etc.
3- Set up conference call and walkthrough
4- Make sure you have a back up date for rain or snow, etc.
5- Paperwork for ownership to be signed on the day of transfer
6- Organize security enclosure removal if it is needed
7- Make sure you are notified when the source delivered to final destination
8- Prepare NRC forms for license verification and source transfer
9- Obtain a copy of T&R before the day of removal

On the day of source removal:

1- Contact LLEA and disconnect RMS system
2- Truck arrives at the institution
3- The riggers unload the equipment- Riggers/Technician unbolt the irradiators
4- Irradiator moved from the room to loading dock then to the truck
5- Constantly survey the irradiator for any leakage
5- Must survey the truck & label the truck
6- LLEA make sure the route is cleared for the truck to pass
7- Police car escorts the truck to leave the institution

STANDARDIZATION

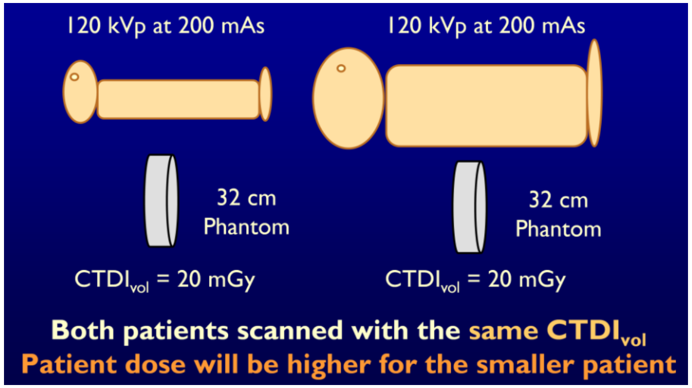
Rat- ~ 500 g

Mice – 20 g

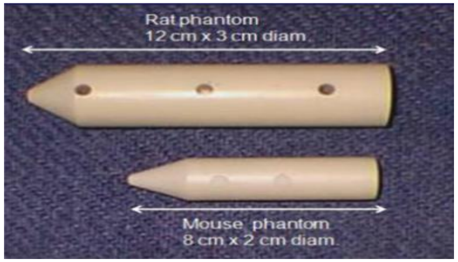
History of Standardization- Clinical CT

- **Standardization of protocols is not an issue unique to X-ray irradiators - Protocol optimization has been a concern for Computed Tomography (CT) users for decades**

- **AAPM developed a Working Group**
  - ***They compiled reference protocols for different machines and settings for everyone to use***
  - ***AAPM has been able to compile the ICRP's standard dose determinations to create a simple app for dose calculations***

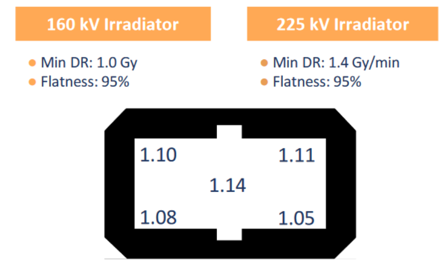


- **This is a good starting point. Medical/Health physicists should take inspiration from AAPM to develop a similar system for X-ray Irradiators**

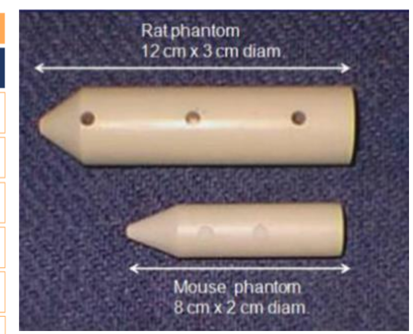


X-ray Irradiator calculating the dose

- Irradiator manufacturers calibrate their equipment
- Unit comes with a limited number of settings that the user can manipulate
  - Voltage, Current, Time, Position, and Filtration all affect the dose delivered
- However, the user must calculate the delivered dose themselves.
- Optimizing the dose for each target/application requires the skill and time of dosimetry experts, which are not available to all institutions



Plates and Rings	160 kV	225 kV
Chamber Plate Level	Dose Rate (Gy/Min @ Center)	Dose Rate (Gy/Min @ Center)
6	8.5	11.5
5	4.5	6.5
4	2.8	4.1
3	2.0	2.8
2	1.4	2.0
1	1.1	1.5



Brookhaven National Laboratory

February 2023- CIRPER

Warren Stern- Deputy Chair of Nonproliferation - BNL

Compatibility of Irradiation Research Protocols Experts Roundtable (CIRPER) Summary Report

CIRPER was held to understand what kinds of information should be published in literature and projects to involving alternative technologies.

Different types and energies of radiation cause different biological effects, which must be documented in order to properly compare outcomes.

The lack of standardized reporting has made it difficult for researchers to make informed decisions on whether they should transition from gamma irradiators to X-ray irradiators

CIRPER –Including Dosimetry in Publication

- The funding going toward researchers conducting experiments is wasted if all of the necessary radiation dosimetry details are not included in publications
- Therefore, NIH/NIAID has begun to increase awareness of this need to it's grant recipients
- Many standards have been published and workshops have been held to inform scientists how to conduct proper dosimetry measurements and document their parameters
- However, many institutions do not have dosimetry staff to support their research and regular quality assurance protocols may not be done

CIRPER – Spreading information

- Spreading information to researchers and establishing long-term incentives will be key to helping transition to alternative technologies

- Pathway
  - Agree on a set of standard parameters that should be reported
  - Obtain buy-in from key organizations to incentivize researchers to follow these standards
    - Funding agencies, federal programs, etc.
  - Ensure that information about irradiators and their protocols is easily accessible
    - Manufacturer support and public databases/forums

CRIPER – Challenges and Solutions

- Industry Engagement
  - Manufacturers publicize established reporting standards in their manuals and emphasize standards in trainings
  - Include CIRPER "Recommended Dosimetry Parameters" table as part of the vendor manual and placed as a decal on the machine
  - Spread information about common problems and protocols that researchers use and create more resources that provide additional information on tube voltage, filtration, HVL, etc.
- Journals
  - Enforce baseline reporting requirements for methodologies involving radiation, including descriptions of dosimetry and how to report uncertainty
    - Examples of methodological descriptions that meet the journal's expectations should be provided
  - Involve radiation biologists, medical physicists, and statisticians in the review process of related publications
  - A centralized database was proposed, where researchers would be able to submit the details of their protocols, which tend to be left out of their publications
  - A glossary could be created for the terminology that should be used to describe measurements and delivery of dosimetry, field geometry, as well as other aspects of experimental methods

CIRPER- parameters considered for standardized reporting

Device Parameters
*Manufacturer and Model
*Energy (kVp)
*Time (mAs) ***or*** Dose Rate
*Absorbed Dose to Water at midline ***or*** Device calibration details (air kerma)
*Filters (Materials and Thickness)

Experimental Setup
*Field Size
*Distance from source and orientation
*Sample description
*Sample Shielding
Sample Holder
Other Sources of Scatter

Calibration Details
*Frequency
Energy at which dosimeter was calibrated
Calibration Detector (Make and Model)

A Question for Audience
Dose Rate and Repair Mechanism

- 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

- **Threshold for repair is 1 Gy/min ??**
- A lower dose rate means longer irradiation time, which means more time for sub lethal damage repair
- **X-rays do not have this problem**

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

Another Question for the Audience

Total Dose given in a longer time

- If the Gamma irradiator is old and decayed to give 25 Gy to the bag of blood in 840 sec instead of 280 sec, would the graft disease be destroyed?

- **X-rays do not have this problem. It is always 280 sec.**

Cs-137 Irradiator	X-Ray Irradiator
25Gy	25 Gy
840 sec **irradiation time to give 25Gy**	**280 sec** **irradiation time to give 25 Gy**

THANK YOU

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