Operational Topic

Prior to making the switch from gamma to x-ray research irradiators, it is essential to establish consensus among the researchers.

Establishing Consensus with Users of Research Irradiator Devices to Facilitate Source Type Replacement

Danette R. Fennesy,[1] Janet M. Gutiérrez,[1,2] Scott J. Patlovich,[1] and Robert J. Emery[1]

Abstract: *The ability to irradiate cells, tissues, and other biological materials with high-energy photons has been an essential tool in the discovery of numerous biomedical research advancements. Historically, such irradiation was accomplished using sealed sources of radioactive materials in the form of ^{137}Cs or ^{60}Co. After the tragic events of 11 September 2001, a particular focus was placed on the vulnerability that irradiators represented due to the potential malicious acts that might lead to the creation of a radiological exposure or dispersal device. To mitigate this risk exposure, the United States Department of Energy National Nuclear Security Administration (NNSA) developed programs to both enhance the security associated with these devices and to incentivize the replacement of the units with x-ray-based technology. However, a significant barrier to engagement with the exchange program is the hesitancy on the part of the research community that does not wish to disrupt existing and established research protocols. This hesitancy stems from an inherent desire to adhere to the scientific process with the strict control of variables so that a single aspect can be isolated and then determined to result in an effect. A change from a gamma source to an x-ray source introduces a variable that warrants careful consideration and could have significant scientific and data-related impacts. Described here is the process undertaken by the radiation safety program for a major academic biomedical research institution to successfully transition from the use of gamma irradiators to x-ray devices without disrupting or negatively impacting critical research activities. The key to this successful transition was the establishment of consensus amongst the scientific and administrative communities prior to any formal commitment to the NNSA for the replacement endeavor. Ultimately, the researchers have found success in the transition and use of the x-ray irradiator replacements. Health Phys. 128:222–226; 2025*

Key words: *operational topics; gamma radiation; radiation safety; weapons*

INTRODUCTION

After the tragic events of 11 September 2001, a particular focus was placed on the vulnerabilities associated with irradiators due to potential malicious acts that might lead to the creation of a radiological exposure or dispersal device. Many of these irradiators contain Category 1 or Category 2 quantities of radioactive material, as defined by the International Atomic Energy Agency (IAEA), indicating a security risk and potential for harm should these radioactive sources be misused by nefarious parties. The National Defense Authorization Act mandates the replacement of cesium-based blood irradiators by 2027 (H.R. 5515 2018) due to security concerns and the general advancement of x-ray-based irradiation technology in recent years has enticed many entities to participate in the federally sponsored replacement program. To mitigate this risk exposure, the United States Department of Energy National Nuclear Security Administration (NNSA) developed programs to both enhance the security associated with these devices and to incentivize the replacement of the units with x-ray based technology.

Launched in 2014, the Cesium Irradiator Replacement Program (CIRP) offered through the United States Department of Energy has been widely advertised to licensees who possess irradiators. The CIRP pays for the disposal of irradiator sealed source(s) and approximately half of the cost to procure a replacement x-ray device, further incentivizing participation. The benefits of participation include the ability to stand down personnel security screening programs, significantly reduce physical security requirements, and, in many cases, experience a reduction of insurance premiums due to reduced risk, reduced fees associated with radioactive material licensure, and reduced overall labor hours and costs associated with the maintenance of secure status.

While cesium self-shielded irradiators have been used for many years for both blood processing and biomedical research, the total number of cesium irradiator sources has diminished across the United States. In 2009, Dodd and Vetter

[1]*The University of Texas Health Science Center at Houston, Environmental Health & Safety, 6431 Fannin St, CYF G.102, Houston, TX, 77030;* [2]*Corresponding author.*

Danette Fennesy is a licensed Medical Physicist currently working at UT Health Houston in the Radiation Safety Program which oversees the use of radioactive material and all radiation producing machines within the six health care school's teaching, research and clinical practices. Her previous experience includes 20+ years of Nuclear Medicine and Radiation Oncology work with Harris Health. She participates in Radiological Emergency Response with the State of Texas serving as a ROSS and is a huge proponent of the ORS CIRP program. Her email is ***Danette.Fennesy@uth.tmc.edu****.*

noted the era of the cesium irradiator may be drawing to a close and the renaissance of its currently most feasible alternative, the x-ray irradiator, is beginning (Dodd and Vetter 2009). The data they present concludes that it is possible to replace cesium blood, biomedical, and small animal irradiators with cabinet x-ray machines with little or no reported loss of performance (Dodd and Vetter 2009). Therefore, a transition to x-ray irradiators should be considered.

Two institutions have published data regarding recent experiences in replacing cesium irradiators with alternate technologies. The University of California System established a faculty-led system-wide working group that was charged to make technical recommendations regarding the conversion from cesium sources to x-ray irradiators, which included comparison studies between the two approaches (MacKenzie et al. 2020). Both faculty involvement and campus leadership support were credited as important factors in the success of the replacement project with minimal impacts on research outcomes. This endeavor included the removal of 37 cesium irradiators and the purchase of 25 x-ray irradiator replacements across the University of California System institutions (MacKenzie et al. 2020). They concluded that the removal of cesium irradiators from both university research and medical facilities was a sound investment when it was determined that equivalent data could be obtained using x-ray irradiators (MacKenzie et al. 2020). Kamen et al. described the process at Mount Sinai Health System which obtained dose distribution data and depth dose comparisons for both cesium and x-ray irradiators (Kamen et al. 2019).

For some institutions, the replacement of radioactive material source irradiators with an x-ray alternative may not be needed. For example, Vernig described the disposal of a Veteran's Affairs Health Care System's ^{60}Co self-shielded irradiator through the Department of Energy's Off-Site Source Recovery Project (Vernig 2009). Institutions taking advantage of these financial resources to support appropriate disposal, security during transport and potential alternative replacement may prove to be wise investments.

Users of cesium irradiators should also consider possible gaps in insurance liability as described by Kamen et. al. (Kamen et al. 2023). Kamen et. al. notes potential insurance exclusions in coverage for radioactive material and terrorist events, therefore, there is limited ability to shift risk to insurers and would not protect from significant financial lost in the event of a release (Kamen et al. 2023). In 2019, an incident at the University of Washington Harborview Medical Center during a source removal operation resulted in a cesium source breach that caused an estimated total loss of greater than $150 million (Joint NNSA/TNS 2020). Thus, even accidental radiation contamination from these irradiators can be extremely costly.

X-RAY IRRADIATOR TECHNOLOGY

In 2009, the US Food and Drug Administration (US FDA) granted approval for an x-ray blood irradiator from Rad Source Technologies (4907 Golden Parkway, Suite 400, Buford, Georgia, 30518) and more recently lists at least four manufacturers approved for x-ray irradiation of blood (NASEM 2023). Additionally, manufacturers have developed x-ray irradiators specifically marketed as suitable alternatives to the cesium research irradiators. As more institutions make the transition to x-ray irradiators, x-ray irradiator manufacturers have been able to offer enhanced technology options. A recent comparison study concluded replacing their cesium irradiator with an x-ray based system allowed them to perform experiments using equivalent radiation dose while maintaining the ability to directly compare previous data with future data (Andersen et al. 2020). Additionally, existing publications provides data to support successful transition from gamma to x-ray irradiation (Eng et al. 2020; Gibson et al. 2015; Kamen et al. 2019; Murphy and Kamen 2019; Wittenborn et al. 2021). These studies have demonstrated the x-ray irradiator could successfully replace the cesium irradiator.

TRANSITION PROCESS

The University of Texas Health Science Center at Houston (UTHealth Houston) began investigating the process of transitioning from ^{137}Cs irradiators to x-ray irradiators in late 2019. At the time, the institution possessed two cesium irradiators that were primarily used for cell and small animal research. Due to previously existing hesitancy among the research community that utilized these devices at the institution, the Radiation Safety Program started by initiating discussions with the principle investigators who used the gamma irradiators to determine their concerns about a possible transition to x-ray technology. Many of the researchers were concerned about animal skin doses and others were concerned that there might not be correlating dose exposures. It was necessary to provide evidence that the same results could be achieved using x-ray radiation rather than gamma irradiation.

It was first important to understand how the current irradiators were being used for research purposes so that the opportunity for possible x-ray alternatives could be explored. The initial results of these discussions, coupled with the presentation of data from existing publications providing data to support successful transition (Andersen et al. 2020; Eng et al. 2020; Gibson et al. 2015; Kamen et al. 2019; Murphy and Kamen 2019; Wittenborn et al. 2021), were provided to the UTHealth Houston institutional Radiation Safety Committee and key institutional leadership (e.g., Vice President for Research) for review and deliberation. Comparisons were presented to the Radiation Safety

Committee regarding the physical protection, access authorization, inventory tracking, installation, and removal and disposal costs for cesium irradiators vs. x-ray irradiators. In addition, research considerations were also discussed to minimize the impact to research, especially in our vivarium facilities, which includes immune-compromised animals.

As part of this process, multiple stakeholder meetings were held to identify and address any potential concerns for the transition to x-ray irradiation. Additionally, x-ray irradiator manufacturers were invited to provide product overview presentations to these same key stakeholders, inclusive of the Radiation Safety Program staff. Science advisors were able to demonstrate results that were more than satisfactory by employing various filters to the x-ray beams during x-ray irradiation. This shared governance approach and decision-making process proved to be helpful in facilitating a thorough review of the risks and benefits of transition and ultimately garnered sufficient support to allow the institution to engage with the exchange program.

One device, a JL Shepherd Model 6810 from JL Shepherd & Associates (1010 Arroyo St, San Fernando, California, 91340) was used for cell irradiation. Due to the physical security measures required for this device in a densely populated research facility, an offsite location was required to safely and securely house this device. The location was administratively managed by the institution's Radiation Safety Program staff. This arrangement required researchers to call ahead to the Radiation Safety to schedule a time for cell irradiation to occur. Research staff must then walk to an adjacent building in order deliver their cells, and approximately 1 to 2 hours later return to the facility to collect their irradiated cells. Prior to participation in the CIRP program, the institution already possessed a Rad Source RS 2000 x-ray irradiator from Rad Source Technologies (4907 Golden Parkway, Suite 400, Buford, Georgia 30518). This allowed the researchers to potentially perform their own side-by-side evaluations with the x-ray irradiation technology prior to accepting participation and embarking upon removal of the cesium device. For the cell irradiation, the transition was seamless for the cell irradiator users. In the current configuration, researchers need only walk a short distance within the building and can irradiate at any time they choose without an appointment.

The second device, a Best Theratronics Gammacell 40 by Best Theratronics (413 March Road, Ottawa, Ontario, K2K 0E4 Canada), was within in a barrier facility housing immunocompromised mice. At the time, no x-ray alternative device was available within this facility and therefore in-house comparison studies could not be performed initially. When the transitioning concept was first presented, there apparently was a lack of positive data regarding mouse irradiation protocols and some of the researchers were quite dubious about making the transition. At the time, equipment from Precision X-ray Irradiation (14 New Road, Madison, Connecticut, 06443, United States) was being considered as an option and their science advisor was excellent at providing resources and answers to all the questions the researchers had. It appeared that the MultiRad 350 by Precision X-ray Irradiation might be a good fit for the existing research needs. Features such as motorized shelves and a filter wheel with four beam conditioning filters were described and the researchers became intrigued with the opportunity. Researchers within the Radiation Safety Committee and existing cesium irradiator users provided input on x-ray irradiator features to select to accommodate research needs.

While in the midst of these discussions, the Gammacell 40 was scheduled for routine preventive maintenance and, unfortunately, the system's computer failed. The repair cost was estimated to be $20,000. This event prompted the collective decision to move forth with the replacement rather than repair the cesium irradiator. Unfortunately, the researchers were not able to do side-by-side comparisons with the Gammacell 40 and the MultiRad 350 since Gammacell 40 was no longer operational. The Gammacell 40 was replaced with the Precision X-ray MultiRad 350 and the researchers, to date, have been very pleased with the results and the selection options.

After the installation of the MultiRad 350 X-ray irradiator, the safe and secure removal of both the JL Shepherd and the Best Theratronics irradiators was scheduled and performed as part of the CIRP program. One cesium device was transferred in 2022 and the remaining cesium device was transferred in 2023. The CIRP program includes the disposal of the sealed sources within these devices, the transportation container and the security during transport resulting in significant cost savings to the University.

DISCUSSION

Shifting from ^{137}Cs irradiation to x-ray irradiation affords benefits to both users and licensees. The primary benefit is the elimination of both physical security measures for the device and personnel trustworthy and reliability processes for unescorted irradiator access. Users and service providers did not enjoy the multiple security checks made on a regular basis to ensure that all cameras and alarms were functioning properly. The entire process of fingerprinting and background checks was costly and time-consuming. The enhanced security aspects associated with the radioactive material devices were viewed by the researchers as extremely burdensome, so losing these restrictions is a significant advantage when transitioning to x-ray irradiation.

Our users have indicated their satisfaction with the x-ray irradiation option and are very pleased with the aspect of accessibility. Irradiator use logs for the x-ray irradiator unit (after the transition) has exceeded the frequency of use for the cesium irradiator. For cell irradiation, the cesium irradiator was used 44 times in 2020, 10 times in 2021, and once in 2022. In contrast, for cell irradiation, the existing x-ray irradiator was used 30 times in 2020, 67 times in 2021, and 78 times in 2022. In two years, the cell x-ray irradiation research use has almost doubled from the 2020 cesium use levels. Our observations and communications with colleagues note, irradiation use has increased due to the ease of access to the user. For blood bank applications, it has become beneficial to use the x-ray irradiators because there is a high throughput and very little concern about filters and shielding. Those using irradiation for research purposes have been slower to change. Earlier models of x-ray irradiators did not offer the amenities that the current units offer. Newer amenity examples include programmable motorized shelf, adjustable filters and adjustable collimator as well as recording specific program parameters for later use.

While cell irradiation has been easy to achieve, irradiation of animals has been a greater challenge. However, by filtering out the low energy rays with optimal metal filters and employing other key factors, the x-ray irradiator can allow researchers much more flexibility. A researcher utilizing animals noted the new x-ray irradiator has multiple preset programs and availability for diverse purposes. This researcher also noted no difference was seen regarding engraftment efficiency and no-hematopoietic damage between the two irradiators. While the benefits are offered by NNSA CIRP, it is highly advisable to consider making the switch. Not only does an x-ray irradiator have more to offer, the users seem to be pleased with easy access and the elimination of the enhanced security controls. Additionally, avoided cesium transport and disposal costs may be significant savings to the institution.

SUMMARY

X-ray irradiators allow researchers the ability to irradiate cells, tissues, and other biological materials with high energy photons as an essential tool in the discovery of numerous biomedical research advancements. With the involvement of the researchers early and throughout the transition process, they have been pleased with the x-ray irradiator transition. The early hesitancies from the research irradiator users were openly addressed at the start of the process and a joint governance approach ensued and resulted in concurrence. Overall, the CIRP program was implemented successfully at UTHealth Houston without disrupting or negatively impacting critical research activities. The key to this successful transition was the establishment of consensus amongst the scientific and administrative communities prior to any formal commitment to the NNSA for the replacement endeavor. Feedback from the researchers utilizing these devices has been primarily positive and has resulted in increased x-ray irradiator use.

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