INDIANA UNIVERSITY
OFFICE OF THE EXECUTIVE VICE PRESIDENT
FOR UNIVERSITY ACADEMIC AFFAIRS
University Environmental Health and Safety

IUPUI/IUMC Radiation Safety Office

11 December 2020 (Resubmitted 12 February 2021 with redacted names)

Mrs. Deborah A. Piskura
Senior Health Physicist
U.S. Nuclear Regulatory Commission – Region III
2443 Warrenville Road, Suite 210
Lisle, IL 60532-4352

Re: Follow Up of Inspection on 10/19/2020

NRC License No. 13-02752-03
Notification No. 54946

Dear Mrs. Piskura,

This letter is to follow up with requested items from your inspection on 10/19/2020, in which you reviewed a reportable event from a Y-90 TheraSphere misadministration (Notification No. 54946). As part of our exit interview you requested several items, which I have included with this letter as follows:

1) Review of IR/Y-90 AU personnel dosimetry over the previous several years, including retroactive dose assessments for times the physicians were not apparently wearing their dosimetry badges. Data and methodologies are detailed below.

2) Excerpts from our policies regarding Personnel Monitoring and our ALARA program. I have included the IU Health Policy "Radiation Safety: Personnel Monitoring", as well as excerpts from our "Nuclear Medicine/PET Radiation Safety Procedures Manual".

3) The most recent IRB approval of Humanitarian Use Device (HUD) for TheraSphere use.

4) Report on TheraSphere device forensics: Our internal assessment of the delivery device did not provide any conclusive evidence. Visual inspection appeared to show some yellowing within the catheter line. Radiation detection with a survey instrument was not able to provide localization of any areas of potential clumping due to being indistinguishable from elevated background. The delivery device/kit was returned to the vendor for

analysis. Their results indicate residual microspheres throughout, as well as high back pressure and low flow rate. This was likely due to use of a catheter with smaller inner diameter than indicated in the package insert.

In the original written report (dated 26 October), we indicated that this was the suspected cause. If you will recall from that report, as well as your discussion with the AU on 10/19, the physician intended to use a larger catheter, but the radiological technologists were unable to locate one.

In addition to the requested items, our office has pursued several avenues for increasing compliance with personnel dosimetry wear. These are as follows:

5) Update to ALARA Program: Unreturned and unused badges are now examined with the same scrutiny as those exceeding our established ALARA limits. This had been occurring on a haphazard basis since Spring of 2019, as indicated in the attached meeting minutes for the Machine-Produced Radiation Safety Committee (MPRSC, which governs machine-produced radiation, only). A later email from October 2019 shows an update on this initiative to reduce unused/unreturned dosimeters. Unfortunately, this program lost momentum during Covid because of staffing, delivery, and availability issues. This is now being pursued in full force to both machine-produced radiation users and radioactive material users under the purview of our Radionuclide Radiation Safety Committee (RRSC). In addition, readings of "M" ("Minimal", < 1 mrem) or "SL" ("Select Level", < 10 mrem) are being investigated for select subgroups, including Interventional Radiology and Nuclear Medicine/PET personnel.

6) The Permit Holder for TheraSphere use and AU, Director of Interventional Oncology, Chief of Vascular and Interventional Radiology, has worked with our office to develop an annual compliance acknowledgment for all physicians administering TheraSpheres. A copy of this acknowledgement is appended; please note emphasis on RSO authority and dosimetry wear indicated in items 7 and 8 of this acknowledgement.

7) I was able to speak directly to the IU Health Radiology Leadership Council Meeting on December 3rd. This meeting consists of division chiefs and leaders from all areas of radiology (e.g. interventional, nuclear, breast, etc). This talk emphasized the importance of dosimetry wear, including a "how-to" overview and several other points. Slides from this talk are appended.

As always, please do not hesitate to contact me if you require further information. I hope this will provide enough information for you to complete your inspection.

Sincerely,

T. Michael Martin

Digitally signed by T. Michael Martin
Date: 2021.02.12 14:29:42 -05'00'

T. Michael Martin, PhD, DABHP
IUPUI/IUMC Director of Health Physics & Radiation Safety Officer
(317) 274-0331
mimart@iu.edu / tmartin24@iuhealth.org

Personnel Dosimetry Estimate for Y-90 AUs

Personnel dosimetry was reviewed for all current TheraSphere Y-90 AUs from 2014-2019 (2014 is the earliest available data with number of Y-90 procedures per physician). Of the physicians reviewed, two were missing dosimetry data (unreturned/unused badges, or M/SL readings); IR Physician 1 (henceforth "IR1") (2012-present), and IR Physician 2 ("IR2") (2016-present). Dose estimates were conducted for both physicians. In addition, dosimetry data for IR1at IU Health Ball Memorial Hospital were collected for 2018-2020. This data indicated that dosimetry was generally not utilized by IR1 at this location, either.

Case load and dose estimates for fluoroscopy use were not available. Annual doses were plotted for all Y-90 AUs as a function of annual number of Y-90 cases to see if there was a correlation (Fig. 1). There is little to no correlation with DDR, LDE, or SDE; however, there is good correlation with Extremity dose. The downward slope in the trendlines for DDE and SDE may indicate that the more experienced users who do more Y-90s may also practice better fluoroscopy dose reduction techniques.

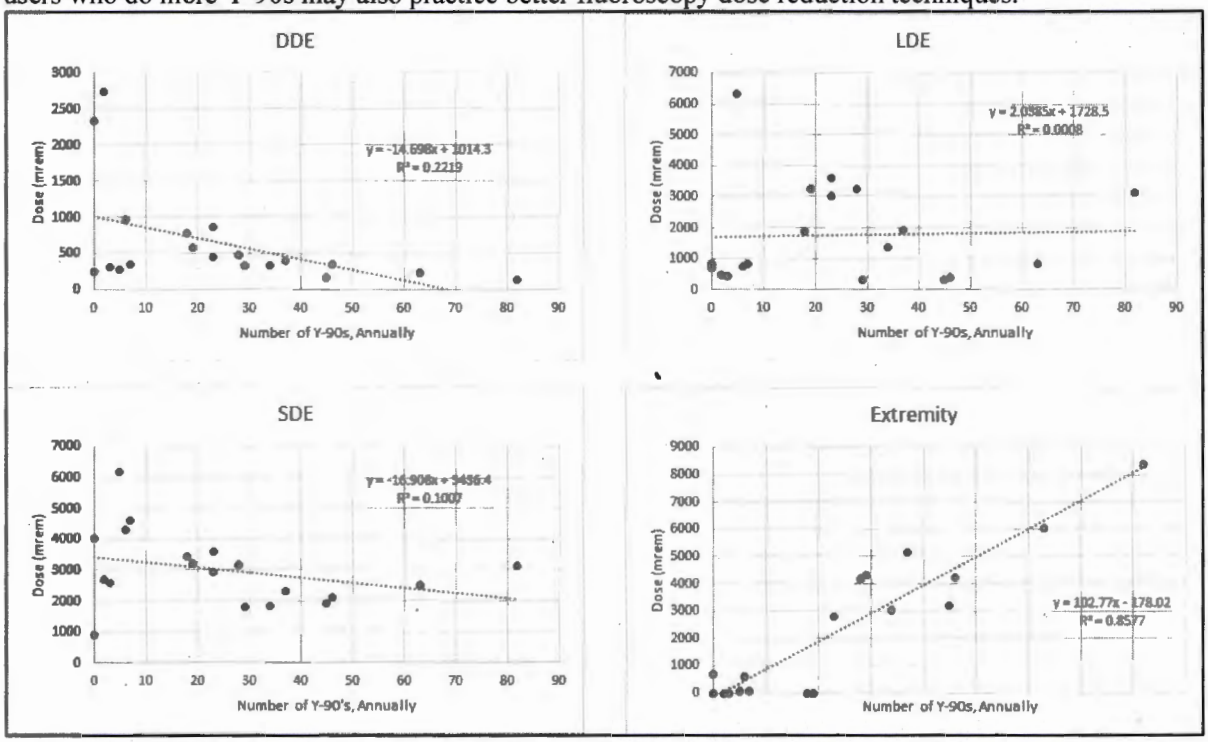


Figure 1. Reported doses plotted as a function of number of Y-90 administrations performed per year.

In an attempt to separate doses from fluoroscopy and Y-90 for DDE, LDE, and SDE, a basic estimate of dose received due to Y-90 was performed. Assuming an average activity of 50 mCi, a transit time during administration (i.e. time outside of shielding) of 1 minute, and a beta dose rate in air of 31.65 mrad/hr/mCi at 1 m (http://radprocalculator.com/Beta.aspx, Birky et al. 1998), the average physician dose at 1 m was estimated at ~ 30 mrem per administration. However, applying this correction and removing outliers did not significantly increase any correlation in doses (see Fig. 2).

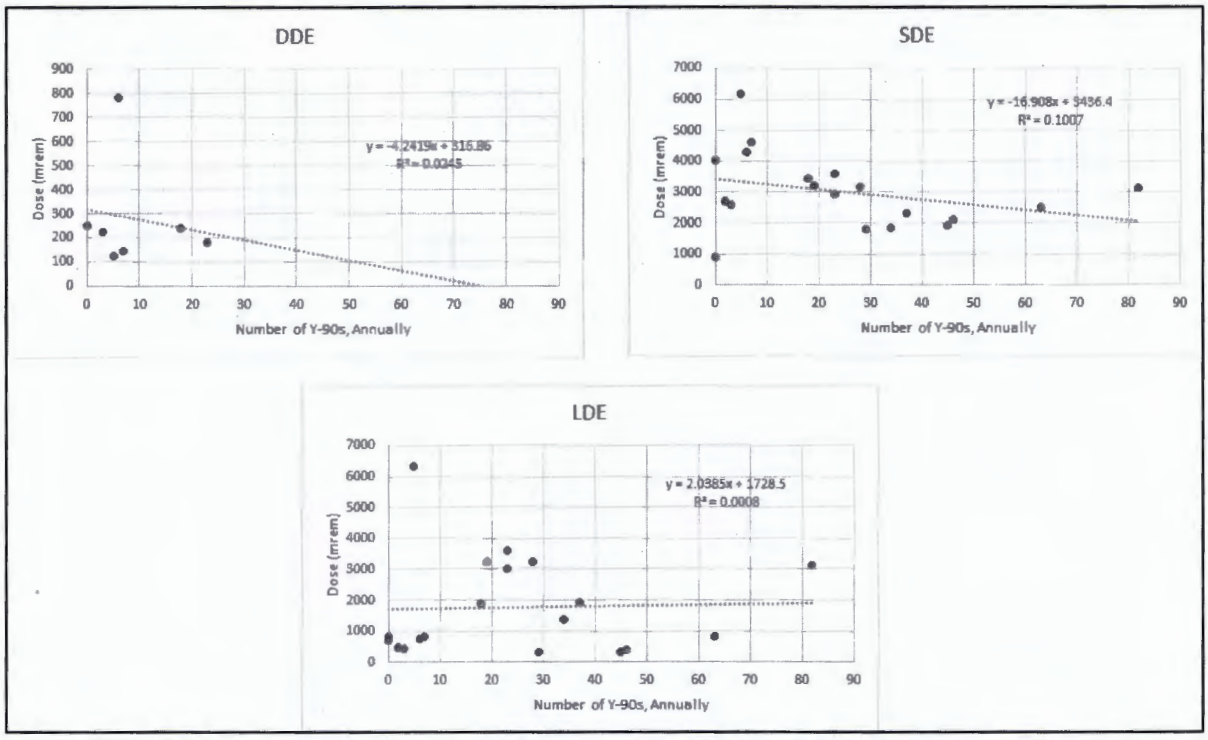


Figure 2. Annual doses with Y-90 correction applied; no increase in correlation was noted.

In order to estimate worst case doses (DDE, SDE, LDE) for IR1, annual maximums were noted for the entire cohort, and increased by 25% to ensure conservatism. These values were then scaled by the annual number of Y-90 cases. Average values derived from the entire cohort (0, SL, M doses were neglected in calculating the average), and added to these values to account for fluoroscopy dose. Extremity dose was estimated using the least squares fit provided in Fig. 1. Data was unavailable for 2012 and 2013, so the maximum from following years was used as an estimate. Data for 2020 may be incomplete, as the number of cases may change slightly. These estimates are provided in Table 1.

Table 1. Estimated annual doses for IR Physician 1.

Year	# of Y-90s	DDE (mrem)	LDE (mrem)	SDE (mrem)	Extremity (mrem)
2012*	?	4076	9693	10741	2186
2013*	?	4076	9693	10741	2186
2014	8	1842	4532	5704	644
2015	19	3480	8316	9398	1775
2016	23	4076	9693	10741	2186
2017	20	3629	8660	9733	1877
2018	10	2140	5220	6376	850
2019	15	2884	6940	8055	1364
2020	14	2736	6596	7719	1261

* Data was unavailable, so subsequent maximum was used

A similar methodology was applied to estimate doses for the missing portions of IR2's dose history. These are provided in Table 2. Values in red text indicate that they were present on reported dosimetry, and are not estimates. IR2 was authorized in 2016, so prior years are not reported. Data for 2020 may be incorrect, as cases are ongoing, and recent dosimetry results have not been returned from the vendor.

Table 2. Estimated annual doses for IR Physician 2. Values in red are measured data, and are not estimates.

Year	# of Y-90s	DDE (mrem)	LDE (mrem)	SDE (mrem)	Extremity (mrem)
2016	4	1140	3155	4361	233
2017	28	4076	11413	12419	400
2018	27	3953	11069	12084	2597
2019	18	779	1901	3449	1672
2020	19	581	3264	3209	1775

Indiana University Health

Origination:	*1/31/2007*
Effective:	*8/29/2019*
Last Approved:	*8/29/2019*
Last Revised:	*8/29/2019*
Next Review:	*8/28/2022*
Owner:	*Rochelle Curtin: Coord-Qual Reporting & Anlytcs*
Area:	*Radiology*
Tags:	*Education Level 1*
Applicability:	*Indiana University Health AHC*

Radiation Safety: Personnel Monitoring

I. PURPOSE

To ensure the proper assignment and use of dosimetry badges for personnel monitoring

II. SCOPE

This policy applies to all personnel assigned radiation monitor badges by the IUPUI/IUMC Radiation Safety Office.

III. EXCEPTIONS

None

IV. DEFINITIONS

None

V. POLICY STATEMENTS

This policy is designed to provide the standards for the proper monitoring of team members who are occupationally exposed to radioactive materials and/or machine-produced radiation.

PERSONNEL MONITORING

Total Effective Dose Equivalent (Whole Body)	5,000 mrem (50 mSv)/year
Dose Equivalent to any individual organ or tissue (other than the lens of the eye)	50,000 mrem (500 mSv)/year
Eye (Lens) Dose Equivalent	15,000 mrem (150 mSv)/year
Shallow Dose Equivalent to skin or extremity	50,000 mrem (500 mSv)/year
Dose equivalent to Embryo/Fetus due to occupational exposure of a Declared Pregnant Woman	500 mrem (5 mSv)/gestation at a uniform monthly rate

- These limits are derived from Nuclear Regulatory Commission (NRC) regulations and will be used for all radiation exposures, regardless of the source.
- The assigned dose equivalents must be for the part of the body receiving the highest exposure or based upon an approved method to calculate effective dose equivalent.

- For purposes of external exposure, the whole body is defined as the trunk to include the head, trunk, arms above the elbow, and legs above the knee. The lens of the eye has its own limit as does the thyroid.
- The annual effective dose equivalent limits apply to the properly weighted sum of external and internal exposures.

VI. PROCEDURES

A. General Guidelines

1. All individuals who are occupationally exposed to radiation on a regular basis and who may receive greater than one-tenth of the annual permissible limit to the whole body (i.e. greater than 500 mrem (5 mSv)/yr) will be issued a whole body personnel monitoring device. To initiate personnel monitoring, a Radiation Safety Form A-5 must be completed and returned to the IUPUI/IUMC Radiation Safety Office.
2. Individuals handling radioactive materials and/or individuals whose hands are frequently in the primary x-ray beam likely resulting in extremity exposures that exceed one-tenth of the annual permissible limit (i.e. greater than 5000 mrem (50 mSv)/yr) will be issued one ring badge to be worn on the hand that is likely to receive the highest exposure, or one ring badge for each hand.
3. All individuals who are occupationally exposed to significant radiation levels on an occasional basis, such as nurses caring for radiopharmaceutical therapy or implant patients, will be issued a "temporary" personnel monitoring badge or will have an electronic dosimeter available for use when caring for such patients.
4. Other individuals exposed to radiation on an occasional basis, such as security personnel who deliver packages, secretarial personnel who work in the nuclear medicine or radiation therapy clinics but do not work with patients, and nurses who occasionally care for patients who have received diagnostic dosages, will not normally be issued personnel monitoring devices as these individuals are not likely to exceed one-tenth of the annual limit.
5. Monitoring of the embryo/fetus of a Declared Pregnant Woman will be per Radiology policy, "*Radiation Safety: Pregnancy Policy for Radiologic and Nuclear Medicine Technologists.*"

B. Methodology

1. Personnel monitoring will usually take the form of a single personnel monitoring badge to reflect whole body exposure. The badge should be worn on the outside of any personal protection (e.g. outside the Pb apron) at the collar level.
2. The frequency of exchange of personnel monitoring badges is driven by the expected radiation exposure received. All personnel monitoring badges will be exchanged on a monthly or quarterly frequency.
3. Dosimetry reports are available for monitored individuals for review through the IUPUI/IUMC Radiation Safety Office, or may be accessed online (See Appendix A for instructions).
4. The personnel monitoring badge is not to be worn when the individual receives diagnostic or therapeutic radiation exposure as a patient.
5. When not in use, the personnel monitoring badge should be stored in a consistent location away from sources of radiation, excessive heat and moisture. Personnel monitoring badges should not be taken home unless the staff member travels to different facilities.
6. Personnel monitoring badges are to be worn only by the person whose name appears on the badge. Visitor badges are available from the IUPUI/IUMC Radiation Safety Office upon request to monitor

visitors, new personnel, and individuals who have lost a previously issued personnel monitoring badge.

7. Individuals wearing personnel monitoring badges are to notify the IUPUI/IUMC Radiation Safety Office if the badge has been inadvertently exposed (badge left in radiology room) or damaged (washed or dried) so that a replacement badge may be provided.
8. ALARA levels are established by the IUPUI/IUMC Radiation Safety Office and Radiation Safety Committees as action levels below the regulatory limits where investigations may be performed to determine the source of the exposure and any actions that may be appropriate to reduce future exposure. If an ALARA report is received by an individual, they should complete the report form and return it to the Radiation Safety Office.
9. Personnel monitoring dosimetry reports are sent to each monitoring group where individuals in that group can review their exposure.

VII. CROSS REFERENCES

Radiation Safety: Pregnancy Policy for Radiologic and Nuclear Medicine Technologists

VIII. REFERENCES/CITATIONS

None

IX. FORMS/APPENDICES

None

X. APPROVAL BODY, IF APPLICABLE

Geographic Medical Chiefs, the Radiology QA Committee, the Machine-Produced Radiation Safety Committee (MPRSC), the Radiation Safety Office, and the Radionuclide Radiation Safety Committee (RRSC)

Attachments

No Attachments

Approval Signatures

Step Description	Approver	Date
Sign	Todd Stanley: VP-Clinical Operations	8/29/2019
Sign	Jason Parker: Non-IU Health Leader	8/29/2019
Vet	Judy Hamilton: Project Coordinator	8/29/2019
	Rochelle Curtin: Coordinator-Quality Data	8/9/2019

Applicability

IU Health AHC

SECTION E. MAXIMUM PERMISSIBLE RADIATION DOSE LIMITS FOR INDIVIDUALS

CONTENTS:

I. EXTERNAL/INTERNAL EXPOSURE LIMITS FOR OCCUPATIONALLY EXPOSED INDIVIDUALS

	Adult (≥18 yrs old)	Minor (< 18 yrs old)
Whole body/TEDE*	5,000 mrem/yr (50 mSv/yr)	500 mrem/yr (5 mSv/yr)
Lens of eye	15,000 mrem/yr (150 mSv/yr)	1,500 mrem/yr (15 mSv/yr)
Extremities	50,000 mrem/yr (500 mSv/yr)	5,000 mrem/yr (50 mSv/yr)
Skin	50,000 mrem/yr (500 mSv/yr)	5,000 mrem/yr (50 mSv/yr)
Organ	50,000 mrem/yr (500 mSv/yr)	5,000 mrem/yr (50 mSv/yr)

* Total effective dose equivalent

A. For the purpose of external exposure, whole body includes the head and trunk area (i.e., arms above the elbows, legs above the knee, and the gonads). Extremities include the hand, elbow, arm below the elbow, foot, knee, or leg below the knee

B. The whole body/TEDE limit requires that internal and external exposures be summed. External exposure is determined by the use of personnel monitoring. Internal exposure may be determined by calculation and/or by the performance of bioassays (see PERSONNEL MONITORING - Bioassays).

C. Compliance with NRC regulations for internal exposure is determined by comparing the amount of radioactivity in the body to the appropriate Annual Limit on Intake (ALI) in 10 CFR 20, Appendix B. The limits for individuals under 18 years of age are 10% of the adult limits.

II. LIMITS FOR THE EMBRYO/FETUS OF DECLARED PREGNANT WORKERS

A. A number of studies indicate that the risks associated with radiation exposure to the embryo/fetus are greater than those to adults (see **NRC Reg Guide 8.13** in Appendix A). Pregnant women who are occupationally exposed to radiation have the option to "declare" their pregnancy by completing a Radiation Safety Form A-7, *Notice of Pregnancy*.

B. In keeping with this information, the NRC has established a regulatory limit of 500 mrem to the embryo/fetus of a "declared pregnant woman" for the entire gestation period. In addition, this dose must be distributed evenly throughout the gestation period (i.e.,

approximately 50 mrem per month). If the pregnant employee does not declare pregnancy, the exposure limits for occupational radiation users apply.

C. When pregnancy is declared, the RSO will review any previous exposures the employee may have received as well as the potential for future exposures during the pregnancy. Based upon the review, the RSO will provide specific recommendations and/or implement any additional precautions deemed appropriate.

D. The employee should notify the Radiation Safety Office when the pregnancy ends. Furthermore, the employee may elect to rescind her declaration of pregnancy at any time. In either case, the 500 mrem limit will no longer apply.

III. THE ALARA PROGRAM

The RSO evaluates radiation exposures for adherence to the University's program for maintaining exposures **A**s **L**ow **A**s **R**easonably **A**chievable (ALARA). Any excessive exposures and/or deviations from the ALARA program are investigated by the RSO and reported to the RRSC. The investigation levels and the basic procedures for maintaining the ALARA program are as follows:

INTERNAL EXPOSURE

Level I	**Level II**
10% of the applicable Annual Limit on Intake (ALI)	30% of the applicable Annual Limit on Intake (ALI)

EXTERNAL DOSE EQUIVALENT LIMITS

	Level I	**Level II**
Whole body/TEDE	125 mrem/qtr (1.25 mSv/qtr)	375 mrem/qtr (3.75 mSv/qtr)
Lens of eye	375 mrem/qtr (3.75 mSv/qtr)	1,250 mrem/qtr (12.5 mSv/qtr)
Extremities	1,250 mrem/qtr (12.5 mSv/qtr)	3,750 mrem/qtr (37.5 mSv/qtr)
	3,750 mrem/qtr (37.5 mSv/qtr)*	7,500 mrem/qtr (75 mSv/qtr)*
Skin	1,250 mrem/qtr (12.5 mSv/qtr)	3,750 mrem/qtr (37.5 mSv/qtr)
Organ	1,250 mrem/qtr (12.5 mSv/qtr)	3,750 mrem/qtr (37.5 mSv/qtr)

*This is used for PET Staff only

A. Exposures < Level I - Except when deemed necessary, no further action will be taken in those cases where an individual's exposure is less than those listed under Level I.

B. Exposures > Level I but < Level II
   1. Each individual whose exposure equals or exceeds Level I is required to complete an *Investigation of Elevated Exposure* form. The RSO will then review this form and the individual's exposure history.

2. The RSO will report the results of this review at the first RRSC meeting following the quarter when the exposure was recorded. If the exposure does not equal or exceed Level II, no action related specifically to the exposure is required unless deemed appropriate by the RSO and/or RRSC.
3. The RRSC will, however, consider each exposure in comparison with those of others performing similar procedures as an indication of the ALARA program quality and will record the review in the RRSC minutes.

C. Exposures > Level II
   1. Each individual whose exposure equals or exceeds Level II will be asked to complete an *Investigation of Elevated Exposure* form. The RSO will then review this form and the individual's exposure history.
   2. The RSO will investigate in a timely manner the cause(s) of all personnel exposures equaling or exceeding Level II, and if warranted, take action.
   3. A report of the investigation, actions taken, if any, and a copy of the individual's exposure history will be presented to the RRSC at the first quarterly meeting following completion of the investigation.
   4. The details of the investigation will also be made available to NRC inspectors for review at the time of inspection.

D. Exposure exceeding NRC and/or state limits
   1. These individuals will be instructed to stop work immediately.
   2. The RSO will investigate these exposures and will notify the NRC and/or state as applicable.

E. Establishment of higher ALARA levels
   1. In cases where a worker's or a group of workers' exposures are expected to routinely exceed an ALARA Level, a new, higher level may be established if it is consistent with good ALARA practices for that individual or group.
   2. Justification for a new ALARA Level will be documented.
   3. The RRSC must review and approve all revisions of ALARA Levels.

SECTION F. PERSONNEL MONITORING

CONTENTS:

I. PROCEDURES FOR INITIATING PERSONNEL MONITORING

A. Generally, nuclear medicine personnel who handle millicurie quantities of radiopharmaceuticals are required to utilize personnel monitoring devices.

B. All individuals who meet the personnel monitoring requirements must complete a Radiation Safety Form A-5, *Request for Personnel Monitoring Service*. There may be a month delay between the time the Rad. Safety Form A-5 is received by the RSO and the actual receipt of the individual's badge. (Personnel monitoring devices are provided by the vendor with the individual's name printed directly on the badge.)

C. If it is necessary to initiate personnel monitoring immediately, a temporary badge may be obtained from the RSO and utilized until the permanent badge is received.

II. TYPES OF PERSONNEL MONITORING

A. Whole body badge: The whole body badge is used to determine an individual's whole body deep and skin dose equivalent.
   1. Body badges should be worn on the torso of the body, somewhere between the waist and the upper chest (e.g., on a belt loop or on a lab coat chest pocket).
   2. In situations where protective devices (e.g., Pb aprons) are utilized frequently, multiple body badges may be issued.

B. Ring badge: Individuals who are issued whole body badges and routinely handle radioactive material are also required to wear a ring badge.
   1. Ring badges are available in small, medium, or large to accommodate different finger sizes. Medium rings will be ordered unless another size is specifically requested.
   2. Ring badges should be worn on one of the fingers of the hand expected to receive the highest dose (i.e., may be non-dominant hand).
   3. For the most accurate measurement, the wide part of the ring, which contains the participant information and the actual monitoring device, should be positioned toward the palm side of the hand.

4. When using radioactive material, ring badges should be worn under protective gloves to prevent contamination.
5. In some cases, a ring will be issued for each hand.

C. Fetal badge: A fetal badge may be issued for individuals who declare their pregnancy. This badge would be worn on the torso under a lead apron (if one is utilized).

III. EXCHANGING PERSONNEL MONITORING DEVICES

A. The length of time that an individual personnel monitor is used and the frequency of exchanging personnel monitors are dependent upon a number of factors including potential for exposure, frequency of radionuclide use, past exposures for a given type of use, etc. The typical exchange frequency is monthly for most individuals involved in clinical nuclear medicine procedures.

B. Generally, one individual within a group or department is designated as a contact for that group of badge recipients. A few days prior to the exchange date (end wear-date), the contact person will receive the new badges (via campus mail) and distribute the badges to his/her group. When the new badge is received, the used badge should be returned to the contact person who will return it to the RSO.

C. It is very important to exchange badges promptly. Failure to return used badges delays the badge readout process and in some cases results in an erroneous readout of the badge. If an individual does not receive a new badge at the appropriate time, the current badge should be utilized and the contact person and/or the RSO notified.

IV. GENERAL PROCEDURES FOR THE CARE AND USE OF PERSONNEL MONITORING DEVICES

The following guidelines should be observed to achieve accurate data from radiation monitoring devices:

A. Badges should only be utilized by the individual whose name appears on the badge.

B. Badges should never be cut, torn, or opened. All badges should be returned to the RSO in the same condition they were received.

C. A whole body badge should be worn on the torso between the neck and waist.

D. When not in use, personnel monitoring devices should be stored well away from sources of radiation exposure.

E. All personnel monitoring devices are issued for estimation of occupational exposure received at this institution only. Badges should not be taken home or otherwise

removed from the University premises; however, it is important to notify the RSO if you are occupationally exposed to radiation at another place of employment.

F. The RSO should be contacted immediately if any of the following events occur:
   1. A badge is left near a radiation source,
   2. A badge is contaminated with radioactive material,
   3. A badge is exposed to excessive heat and/or humidity (e.g., placed in a washing machine or a dryer),
   4. The badge is damaged in some way, or
   5. The badge is lost.

G. Upon termination of employment, all badges and holders should be returned to the RSO. At that time, a Radiation Safety Form A-13, *Employee Status Change,* should be completed and submitted to the RSO. This form should also be completed if there is a change of name of the badge user.

V. EXPOSURE REPORTS AND HISTORIES

A. The vendor-provided dosimetry report is initially received and reviewed by the RSO.
   1. There is usually a two to four week delay between the collection and reporting of individual exposures due to processing and mailing; however, the vendor will immediately notify the RSO by telephone of any exposures above a predetermined value established by the RSO.
   2. Once dosimetry reports are received from the vendor, the RSO investigates exposures as stipulated in the University's ALARA program.
   3. A copy of the dosimetry report is then forwarded to the contact person for each individual to review. Another report is retained by the RSO.

B. Individuals who have been issued personnel monitoring devices at other institutions are asked to provide the names and the addresses (including zip codes) of those institutions on the back of the Rad. Safety Form A-5. If an individual knows his/her exposure received at these institutions, it should be provided to the RSO.

C. Radiation exposure records are available from the Radiation Safety Office.
   1. An individual may request a copy of his/her exposure history at any time.
   2. After leaving the University this may be accomplished by sending a *signed* written memorandum to the RSO providing his/her name, social security number, department he/she worked in, and the dates of employment.
   3. An NRC Form 4 and Form 5 will be prepared for individuals who are required to be monitored by the NRC.
   4. Each individual will receive a copy of NRC Form 4 annually for review.

5. NRC Form 5 provides a lifetime history of each individual's dose equivalent.

D. In some cases, individuals may be exposed to radiation at multiple facilities. Due to the fact that the annual dose equivalent limits apply to individuals rather than facilities, special procedures must be implemented to assure that individual occupational limits are not exceeded. Individuals who receive radiation exposures from multiple institutions should:
    1. Obtain separate personnel monitoring devices from other institutions, and
    2. Provide the dosimetry information from these other facilities to the RSO.
    3. Likewise, other facilities may also require the dosimetry information from the University be provided to them. Individuals working at multiple institutions should contact the RSO to establish specific procedures to exchange this information with other facilities.

V. BIOASSAYS

A. The necessity of bioassays is determined by the RSO and/or the RRSC based upon the chemical form, the amount of the radioactive material being used, the intended use and the applicable regulations.

B. Bioassays may also be required if uptake of radioactive material is suspected (e.g., personal contamination).

C. The following are two types of required bioassays:
    1. Thyroid Bioassays:
        a. All individuals must have a baseline bioassay conducted before their initial use of unsealed (liquid) radioiodine.
        b. Individuals preparing and/or administering a therapeutic dose of liquid ^{131}I in excess of 33 millicuries (1.22 GBq) must have a bioassay performed within one week following the preparation/administration.
        c. Individuals preparing and/or administering <33 mCis (<1.22 GBq) of liquid ^{131}I are required to have a thyroid bioassay at the middle and the end of the calendar month (e.g., by the 15th and the 30th of a given month) in which the preparation/administration occurred.
        d. Individuals administering ^{131}I in capsule form are required to have a thyroid bioassay if the post-administration survey shows any readings higher than background in the dosing area, or if the patient sneezed, coughed, or vomited following administration.
        e. Thyroid bioassays are performed within the respective nuclear medicine areas utilizing the thyroid uptake probe with the results forwarded to the RSO.
        f. The necessity and/or frequency of thyroid bioassays for other procedures will be at the discretion of the RSO.

2. Urine Bioassays: The RSO may require urine samples from individuals who have been involved in cases of personal contamination or working with large quantities of activity.

INDIANA UNIVERSITY

OFFICE OF THE VICE PRESIDENT FOR RESEARCH
Office of Research Compliance

NOTICE OF EXPEDITED APPROVAL - RENEWAL WITH AMENDMENT

DATE:	May 08, 2020
TO:	MATTHEW SHILLING JOHNSON, Principal Investigator RADIOLOGY & IMAGING SCIENCES Paul Haste RADIOLOGY & IMAGING SCIENCES Max Pyko RADIOLOGY & IMAGING SCIENCES
FROM:	Turik, Michael A Chair - IRB-04
RE:	Protocol #: 1011003734R010 Protocol Type: Humanitarian Use Device (HUD) Protocol Title: A Humanitarian Device Exemption Use Protocol of TheraSphere For Treatment of Unresectable Hepatocellular Carcinoma, Cholangiocarcinoma, and Metastatic Liver Disease Funding Source: N/A

The Indiana University Institutional Review Board (IRB) IRB 00000219 | IRB-04 recently reviewed and approved the above-reference protocol. Approval of this protocol is based on your agreement to abide by the policies and procedures of the Indiana University Human Research Protection Program (HRPP) and does not replace any other approvals that may be required. Relevant HRPP policies and procedures governing Human Subject Research can be found at: https://research.iu.edu/compliance/human-subjects/guidance/index.html.

Submission and Review Information:

Type of Submission:	Renewal with Amendment
Level of Review:	Expedited
Expedited Category(ies), if applicable:	Expedited approval of non-research HDE
Approval Date of Submission:	May 08, 2020
Expiration Date:	May 07, 2021
Authorized IRB Signature	Kanti Crain Kanti Crain

Regulatory Determinations:

Documents Approved with this Submission (for Amendments and Renewals, documents appearing in bold were either added or replaced with the submission):

Attachment Type - Document Version #
Other - Inc Exc checklist Other - BTG Customer Letter

Other - FDA Confirmation Other - Package Insert Other - therasphere package insert - recently revised 10/11/16 (1 of 2 attachments) Other - 2 of 3 therapshere revised package insert Other - 3 of 3 Protocol - PRO

NOTE: If you submitted and/or are required to provide subjects with an informed consent document, please ensure you are using the most recent version of the document to consent subjects.

The following key personnel are approved to participate in the above titled research activities:

Investigator Name	Role	Training
MATTHEW SHILLING JOHNSON	Principal Investigator	Yes
DAVID M AGARWAL	Key Personnel	Yes
SABAH D BUTTY	Key Personnel	Yes
THOMAS CASCIANI	Key Personnel	Yes
WINSTON BROOKS DAVIS	Key Personnel	Yes
MARK C GORRIE	Key Personnel	Yes
Paul Haste	Co-PI Student/Fellow/Resident	Yes
SCOTT ALLEN PERSOHN	Key Personnel	Yes
Max Pyko	Co-PI Student/Fellow/Resident	Yes

Organizations:

Organization
IU HEALTH ESKENAZI HEALTH CENTER Indiana University IU Health Methodist Hospital IU Health University Hospital

You should retain a copy of this letter and all associated approved study documents for your records. Please refer to the assigned study number and exact study title in future correspondence with our office. Additional information is available on our website at https://research.iu.edu/compliance/human-subjects/guidance/index.html.

If you have any questions or require further information, please contact the HSO via email at irb@iu.edu or via phone at (317)274-8289.

Martin, Michael

From: Sayegh, Renee <Renee.Sayegh@bsci.com>
Sent: Wednesday, December 9, 2020 3:58 PM
To: Martin, Michael; Erb, Bob; Eric Li
Cc: Brody Ring; Clem, Eric T (IU Health); Muldoon, Steve; Bonilla, Isidro
Subject: [External] RE: TheraSphere Reportable Event at IU Health (CMP-0595)

Hi Michael,

Thank you for your patience, we have completed the examination of the post-treatment materials from Indiana University Health Methodist Hospital from treatment date 13-Oct-2020.

The investigation included visual inspection, radiation measurement, digital microscopy and pressure/flow testing of the returned components. The combined investigation results aligned with the hospital's report that the patient did not receive the full dose during the treatment.

- Residual microspheres were found throughout the Administration Set outlet tubing and also at the microcatheter hub and within the initial length of the microcatheter up to the Tuohy Borst adaptor. Some residual microspheres were also confirmed present within the dose vial. These findings are indictive of a very low flow rate and/or high backpressure situation.
- The Administration Set appeared normal and was shown to function as expected; no defective component was identified through any of the testing.
- Pressure and flow testing revealed high backpressure associated with the microcatheter. With an applied pressure well above the upper working limit of the Administration Set, the associated flow rate through the microcatheter was 15cc/min which is below the recommended flow rate outlined in the TheraSphere package insert.
- The microcatheter used was a Progreat 2.0F with inner diameter of 0.019 inch. The minimum microcatheter internal diameter required for TheraSphere administrations is 0.020 inch.

Based on the investigation findings, the inner diameter of the microcatheter that was used for the patient treatment did not meet the package insert requirements. This is considered the most likely cause of the high backpressure that was experienced during the investigation. We understand that a high resistance to flow can reduce the flow rate during treatment. Under reduced flow rates, microspheres can settle within the delivery system components in alignment with what was observed during this investigation.

Thank you for you continued support. Please feel free to contact me if you have any additional questions or concerns.
Renee

Renee Sayegh
Technical Specialist (Contractor)
Boston Scientific
Cell: +1 613 415 5985 | **Fax:** +1 613 701 4086
renee.sayegh@btgplc.com
www.bostonscientific.com

On behalf of BTG International Canada Inc.
11 Hines Road, Suite 200
Ottawa, Ontario, Canada, K2K 2X1

MACHINE PRODUCED RADIATION SAFETY COMMITTEE (MPRSC) MEETING

9 April 2019

Attendance: Eric Swank, Michael Martin, Gordon Guo, Michael Schacht**, Francis Marshalleck**, Matt Hadden*, Jay Jones, Yun Liang, Phillip Wong, Todd Stanley**, Janice Walker**

Guests: Stephanie Jones, Debbie Phillips, John Bullock, Chris Harvey, Rachel Schmidt

Regrets: Jeff Breall, Ryan Rhome

*Alternate for Jeff Mason
**via phone

1. The meeting was called to order at 12:03 pm
2. The committee unanimously approved the minutes from the August 23, 2018 meeting that had been distributed in advance.
3. Committee representation update:
    a. Jay Jones to replace Karen Hutchins – Mr. Jones is a new medical physicist in radiation oncology that has been added to the committee to replace Karen Hutchins. Mr. Jones also has experience as a radiation safety officer.
4. Summary of studies reviewed and approved since last meeting.
   Based on the threshold for reviews delegated to the RSO, most studies submitted since August were approved by the RSO on behalf of the committee. The approvals by RSO and by the full MPRSC via committee action were reviewed by the committee.
5. ALARA program summary – The ALARA summary for quarters 3 and 4 were presented to the committee and reflected several notifications in gastroenterology. The RSO is following up with these individuals to see if it is improper badge wear or improper techniques at the root of these readings. The RSO is looking to move to a new single badge system rather than the dual badge Webster correction for certain projects. Departments that had a large number of unused badges last year have received communication about this non-compliance. Radiation Safety will be incorporating unused badges into the ALARA notification program.
6. Fluoroscopy notification summary – There were no reported sentinel events. There were 125 reports, mostly in cardiology, with an average dose of approximately 5 Gy. Only 8 patients had multiple reports, with the maximum near 13 Gy.

   Todd Stanley joined during the fluoroscopy notification summary.

7. Fluoroscopy credentialing and training update – The Joint Commission's fluoroscopy training requirements came out last year and went into effect in January. The new training has been rolled out and RSO is working on how to get this to all the physicians that need it.

   The committee reviewed the requirements and unanimously voted to require that individuals operating the equipment complete the training, but not to extend the requirements to referring physicians who do not perform procedures.

8. Badge issues – RSO has been sending reminders to those who need to wear dosimetry badges. If it appears that individuals are still not wearing badges then the communications are escalated within departments as it is critical for them to wear the badge to accurately calculate their exposure. Todd Stanley volunteered to assist within IU Health.

Meeting adjourned at 12:32 pm.

M Schacht

Approved
Mike Schact, MD
Chairman, MPRSC

Martin, Michael

From: Martin, Michael
Sent: Tuesday, October 20, 2020 9:10 AM
To: Martin, Michael
Subject: FW: Unused Badge Reduction Update

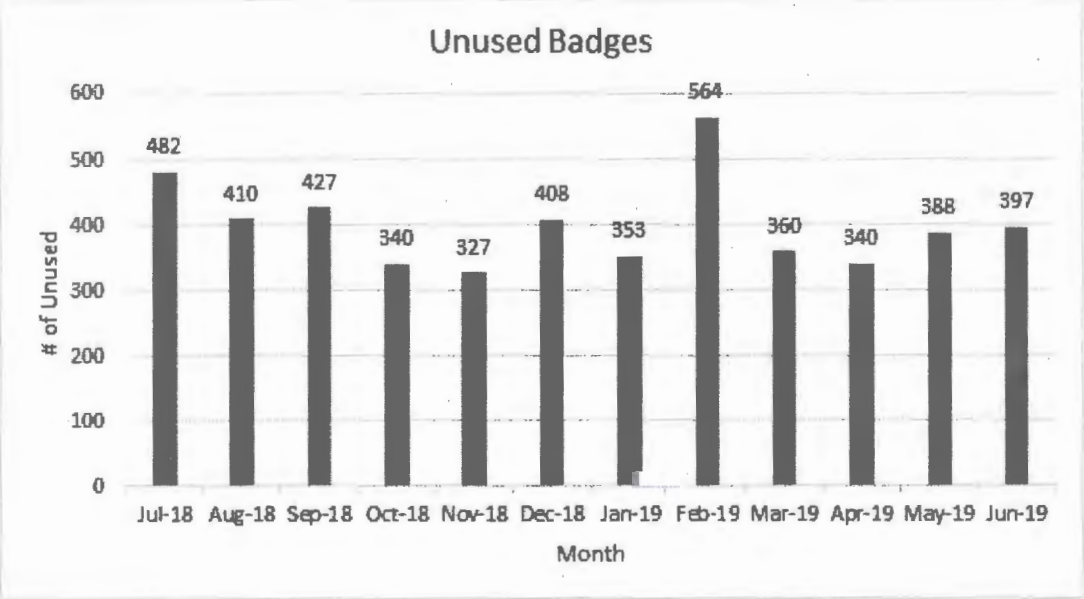
From: Bullock, John R <jorbull@iu.edu>
Sent: Tuesday, August 6, 2019 12:34 PM
To: Martin, Michael <mimart@iu.edu>; Harvey, Christopher Paul <charvey@iu.edu>; Kleyn, Tim David <tdkleyn@iu.edu>; Schmidt, Rachel J <rjschmi@iu.edu>; Chou, Emily <emchou@iu.edu>; Phillips, Deborah L <dphillip@iu.edu>
Subject: Unused Badge Reduction Update

Hey Friends,

June dose reports are in and we can see how things are working out.

It's difficult to notice with certainty if our attempts to increase badge wear (decrease UnUsed) are paying off. However, since we've started our initiative to change our radiation awareness culture we have not had a 400+ month. Five of the Eight previous months were 400+. That is one positive take away, I guess.

July badges consist of our last month of the EDE1 assessments and the last data set to really see an apples-to-apples comparison. We will see that report in about 4 weeks. FYI



Best regards,

John R. Bullock, MS, CNMT, NMTCB(CT)

Annual Statement of Compliance for IUH Users of TheraSphere

1) I am aware that in order to be allowed to use TheraSphere in IUH hospitals that I must comply with all of the requirements listed in this statement.
2) I understand that TheraSphere is approved through a Humanitarian Device Exemption (HDE) as a Humanitarian Use Device (HUD) and as such that its use is overseen by the IU Institutional Review Board (IRB), with training mandates and reporting requirements to the IRB.
3) I am aware that if I have any question regarding the TheraSphere HDE that I have been encouraged to contact Matt Johnson (matjohns@iu.edu) or Kim Collier (kimbcoll@iu.edu)
4) As the IRB mandates, I will remain compliant and up to date with required Collaborative Institutional Training Initiative (CITI) programs. I am aware that if I have questions regarding those requirements, I may contact Kim Collier or Jason Shine (jrshine@iupui.edu)
5) I understand that TheraSphere is merely one of many therapies employed in the treatment of patients with cancer, and that its optimal use requires understanding of other available therapies and that those therapies continue to evolve at a rapid pace. I understand that remote access to those conferences is readily available. As such, I will regularly attend one or more of the weekly IUH multidisciplinary cancer conferences, keep track of my attendance, and report it to Kim Collier annually.
6) I will comply with IRB reporting requirements, including annual reporting of number of cases and timely reporting of unanticipated adverse events (UAE), as outlined in appendix A. As such, I will provide those data to Kim Collier and Matt Johnson in a timely fashion in order for them to comply with reporting requirements as described in appendix A.
7) I understand that TheraSphere use is also overseen and managed by the Radiation Safety Office (RSO), that Michael Martin PhD (mimart@iu.edu) is the Director of Health Physics and Radiation Safety Officer, and that the RSO under Dr. Martin is responsible for all IU School of Medicine and IU Health (IUH) facilities, as well as for Eskenazi Hospital.
8) I am aware that IUH mandates the use of dosimetric badges for all interventional radiologists, that the RSO is able to calculate the dose a physician has received and compare to what is expected from the procedures he or she performs, and that my requirements as a physician who uses TheraSphere are as follows:
    a. I must wear my dosimetry badge during all TheraSphere planning and treatment procedures.
    b. I must return my dosimetry badge to the RSO at the end of each month.
    c. If my dosimetry badge is not returned at the end of a month or demonstrates that I have received an unexpectedly low amount of radiation, I will be deemed to be in noncompliance for that month.
    d. If I am found to be in noncompliance for 3 months during a one year period, I will receive a warning letter from the RSO. If I am found in noncompliance a second time, I will not be allowed to use TheraSphere or any other radioembolic for 3 months and I must take and pass a radiation safety review course prior to reinstitution of my privilege to do so. If I am found in noncompliance a third time, I will no longer be allowed to use TheraSphere or any other radioembolic in the hospitals overseen by the RSO.

Signed _____

Date. 12/1/2020

Personal Dosimetry Guidelines

Wearing Your Dosimetry is Required!

- State and Federal regulatory requirement (ISDH, NRC)
- IUH Policy (Radiation Safety: Personnel Monitoring)
- Accreditation requirement (TJC, ACR)

Consequences:

- Fines

  Feb 2019 - $14,500 fine to Providence Medical Center (AK)
  Aug 2020 - $7,500 fine to Avera McKennan (SD)
  Sep 2020 - $7,500 fine to St. Luke's Regional (ID)
  Oct 2020 - $7,500 fine to St. Joseph Regional (ID), $7,500 to Queen's Medical Center (HI)

- Increased scrutiny
- Onerous corrective actions

Personal Dosimetry Guidelines

Who needs a badge?

- Interventional, procedural with fluoro, CT-guided biopsy, NM

How to request a badge:

- Radiation Safety: radsafe@iupui.edu, 317-274-4797
- Online form**
- Badge contacts

Methodist	Marci McVeigh
University	Michelle Alting
Riley	Shelley Skinner
North	Jennifer Pavich
Saxony	Wes Schlegelmilch
Morgan	Cassi Henry
Tipton	Becky Ressler
Eskenazi	Lynn Wallace

West, Ball, Arnett, Frankfort, SCR – N/A

** https://research.iu.edu/doc/compliance/radiation-safety/a5-form-request-for-personnel-monitoring-service.pdf

Personal Dosimetry Guidelines

Where to store:

- Badge boards in most IR and general rad areas
- On lead is ok
- Keep with your ID, etc.

Multiple locations?

- Preferred: One badge per person, travels with you (like ID)
- Optional: Second set can be requested for other sites

How to wear?

- No lead – wear on torso
- Lead – wear at collar, outside of lead
- "Tab" on badges must be removed!