Washington University in St. Louis

Environmental Health & Safety | Radiation Safety Office

February 14, 2017

U.S. Nuclear Regulatory Commission
Region III
Nuclear Materials Licensing Section
2443 Warrensville Road, Suite 210
Lisle, Illinois 60532-4352

Attn: Regional Administrator

RE: License No. 24-00167-11
Docket No. 030-02271

Subject: Report of §35.3045 event in accordance with "Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance" (February 12, 2016, Revision 9)
Event Report No. 52520

In accordance with §35.3047(d), this written report is being submitted following our January 31, 2017 telephone notification to the NRC Operations Center of a medical event that occurred on April 8, 2016.

Licensee's name: Washington University in St. Louis

Name of prescribing physician: Perry W. Grigsby, M.D.

Brief description of the event:

The patient was being treated for liver cancer. The patient was administered a first dose of Y-90 TheraSpheres on March 3, 2016. The authorized user (AU) for this written directive prescribed 5.22 GBq Y-90 TheraSpheres to deliver a 118 Gy dose to the right liver lobe, and 5.14 GBq was the delivered activity. The first administration of Y-90 TheraSpheres was done in accordance with the manufacturer's procedures without incident. The patient was administered a second dose of Y-90 TheraSpheres on April 8, 2016. The prescribing physician was the AU for the second written directive. He prescribed 4.15 GBq Y-90 TheraSpheres to deliver a 117 Gy dose to

Washington University in St. Louis, Campus Box 8053, 660 S. Euclid Avenue, St. Louis, MO 63110-1093
(314) 362-3476, *Fax:* (314) 362-4776, radsafety@wustl.edu, https://radsafety.wustl.edu

the left liver lobe, and 4.07 GBq was the delivered activity. The second administration of Y-90 TheraSpheres was done in accordance with the manufacturer's procedures without incident.

On April 8, 2016, the patient was imaged using a PET/MRI scanner to obtain PET images (via detection of pair production/annihilation radiation from Y-90 beta particles) for post-treatment dosimetry evaluations. The patient's PET/MRI images were evaluated for post-treatment dose by the Radiation Oncology GI service chief on April 16, 2016. This physician noted that the Y-90 TheraSpheres appeared to have been primarily deposited in the right liver lobe (approximately 95%) rather than the left liver lobe (approximately 5%). The physician alerted the chief medical physicist who then alerted the radiation safety officer (RSO). The RSO and chief medical physicist discussed the possible cause of the deposition of microspheres in the right lobe and the event reporting criteria in NRC's "Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance" (February 12, 2016, Revision 9). They considered the cause of the incident to be patient intervention and decided to meet on the next Monday to review the angiogram and discuss other possible causes to determine if the incident constituted a medical event.

On April 18, 2016, the RSO and chief medical physicist reviewed the procedure information and images, which showed that the interventional radiologist who administered the Y-90 TheraSpheres on April 8, 2016 had angiographically confirmed and documented placement of the catheter tip to deliver the microspheres to the left lobe of the liver with contrast agent administration. It was noted that the catheter tip was placed 0.5-1 cm beyond the left hepatic artery origin to ensure microspheres delivery to the middle hepatic artery as well as the left hepatic artery. The RSO and chief medical physicist decided that following proper completion of the manufacturer's written procedure to provide high confidence that the administration was in accordance with the written directive, the cause of the deposition of the TheraSpheres in the right liver lobe rather than in the left liver lobe, was movement of the catheter tip due to patient intervention as defined in 10 CFR 35.2:

> "*Patient intervention* means actions by the patient or human research subject, whether intentional or unintentional, such as dislodging or removing treatment devices or prematurely terminating the administration."

The RSO discussed the determination of patient intervention with the Radiation Safety Committee chairman and the Washington University management representative and they agreed with this conclusion.

Despite the University's determination that the Y-90 TheraSpheres incident was not a medical event, the RSO, the prescribing physician, the interventional radiologist and others who make up the microspheres authorization team participated in the hospital's patient safety review of the incident to evaluate all aspects of the patient therapy for additional process improvement opportunities.

The RSO first discussed the Y-90 TheraSpheres incident with a NRC Region III inspector on January 11, 2017, and discussed the circumstances of the incident, and the University's determination of patient intervention, and the conclusion that the incident was not a medical event. On January 30, 2017, the Inspector let the RSO know that NRC Headquarters and Region III had determined that the incident was a medical event, and requested that the RSO report the medical event to the NRC Operations Center.

Why the event occurred

The review team concluded the April 8, 2016 Y-90 TheraSpheres administration had been done in accordance with the manufacturer's procedures and the incident occurred due to unintentional action by the patient shifting the catheter tip due to breathing, coughing, or other movement. The incident would most likely not have been identified if the post-administration PET/MRI imaging had not been done.

Effect, if any, on the patient

No overt clinical effect was observed. On a subsequent imaging examination months later, it was apparent that the right hepatic lobe had atrophied and this was accompanied by appropriate and expected compensatory hypertrophy of the left lobe. In becoming larger as a response to the right lobe atrophy, the left lobe can and did compensate for any loss of hepatic function from the right. It is impossible to know for sure how much, if any, additional atrophy occurred to the right lobe after the second (unintended) infusion of Y-90 because we do not typically image the patient until three months after treatment. Further, we typically see atrophy of a lobe after just one treatment, so it is hard to know how much additional loss of size and function occurred.

The patient remains under the care of the University. The patient was last seen in Radiation Oncology on January 23, 2017. The patient had no significant changes to liver function that were inconsistent with his liver cancer; and had no pain in the abdomen.

What actions, if any, have been taken or are planned to prevent recurrence

As similar incidents are identified by employing improved post-administration imaging techniques, we believe these incidents should be considered a known risk of the procedure. This is a similar situation as GI irradiation from Y-90 microsphere brachytherapy noted in the NRC Advisory Committee on the Medical Uses of Isotopes (ACMUI) "Final Report on Yttrium-90 (Y-90) Microsphere Brachytherapy Medical Event Criteria" (September 29, 2014). The ACMUI recognized that such a known risk of the procedure "is in large part dependent on the practice of

medicine, recognizing that:

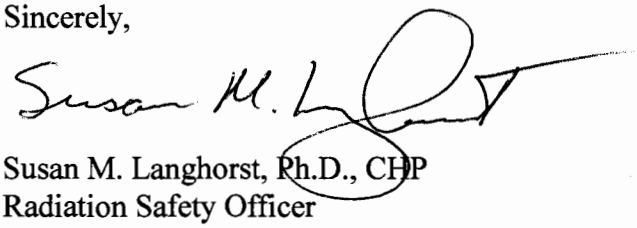
- the placement of the infusion catheter tip at the time of Y-90 microsphere infusion is in alignment with the prior preparation;
- once injected into the vascular pathway to the treatment target at the catheter tip, flow of the microsphere brachytherapy sources and their sites of final implantation are entirely dependent on the patient's unique vascular anatomy and blood flow dynamics."

Certification that referring physician and patient were notified

The interventional radiologist who administered the Y-90 TheraSpheres was the patient's referring physician and was notified of the incident by email on April 16, 2016. The referring physician spoke with the patient about the incident on April 20, 2016. The interventional radiologist was notified the same day (January 30, 2017) that the RSO was informed the NRC had determined that the incident was a medical event. The NRC Inspector informed us during his reactive inspection that the patient would not need to be re-notified of the medical event.

Please let me know if you need further information or have additional questions concerning this report. My e-mail address is slanghorst@wustl.edu and my phone number is (314) 362-2988.

Sincerely,



Susan M. Langhorst, Ph.D., CHP
Radiation Safety Officer

cc: Referring Physician
P.W. Grigsby, M.D.
J.M. Michalski, M.D.
D.E. Hallahan, M.D.
B.A. Siegel, M.D.
B.D. Backus
C.W. Goddard