**Department of Veterans Affairs**

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In reply refer to: 583/001-AS

March 4, 2010

VA National Health Physics Program (115B)
Veterans Health Administration
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SUBJECT: **FOLLOW-UP INVESTIGATION- MEDICAL EVENT INVOLVING UNDERDOSING OF YTTRIUM-90 MICROSPHERES, VHA Permit No. 13-00694-03**

Please find attached the results of our Root Cause Analysis investigation of the December 30, 2009 medical event which occurred in the Interventional Radiology Suite at the Roudebush VA Medical Center, Indianapolis, IN. This report follows our original written report of January 11, 2010, and contains additional data and information on the circumstances and involved equipment. These investigations were carried out by our our staff in conjunction with technical representatives from Nordion®, the Therasphere® vendor. We have attached this original report as well.

It should be reiterated that the Therasphere® treatment was deemed clinically successful, and the patient involved was not harmed.

If you desire any further information regarding this matter, please contact our Radiation Safety Officer, Thomas A. Schumacher, MS, CHP, at telephone number (317) 988-2336, cell (317) 416-4307, or via e-mail at thomas.schumacher@va.gov.

Thomas Mattice
Medical Center Director

# Yttrium-90 Microsphere Medical Event

## Root-Cause Analysis and Follow-up Investigation of Delivery Apparatus

February 26, 2010

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Radiation Safety Officer
Roudebush VA Medical Center, Indianapolis, IN

## Background:

The Roudebush VA Medical Center holds VHA Permit No. 13-00694-03 for radioactive materials use under NRC Master Materials License 03-23853-01VA.

On 12/30/09, an infusion procedure using radioactive yttrium-90 (Y-90) labeled microspheres (Therasphere®) was performed at the Roudebush VA Medical Center in Indianapolis, IN. During several dozen previous such infusions, a target organ (liver) delivery percentage of no less than 90% was achieved, with most cases reaching 94%-99%. However, measurements of the residual tubing, vial, and other waste materials, made at the conclusion of this case, showed that only roughly three-quarters of the dose made it into the patient's liver, leaving approximately 25% of the material in the collected waste. Due to the extremely high radiation exposure rates just after the therapy, the waste materials were set aside for radioactive decay for 50 days, or approximately 18 Y-90 half-lives, until 2/19/10. Although the Y-90 at that point had decayed to $4 \times 10^{-6}$ of its original activity, the presence of the microspheres' residual radiocontaminants, principally $^{154}Eu$ ($t_{1/2}$ = 8.8 y) and $^{152}Eu$ ($t_{1/2}$ = 136 y), enabled the following localization of the residual activity in the apparatus. The goals of this investigation were

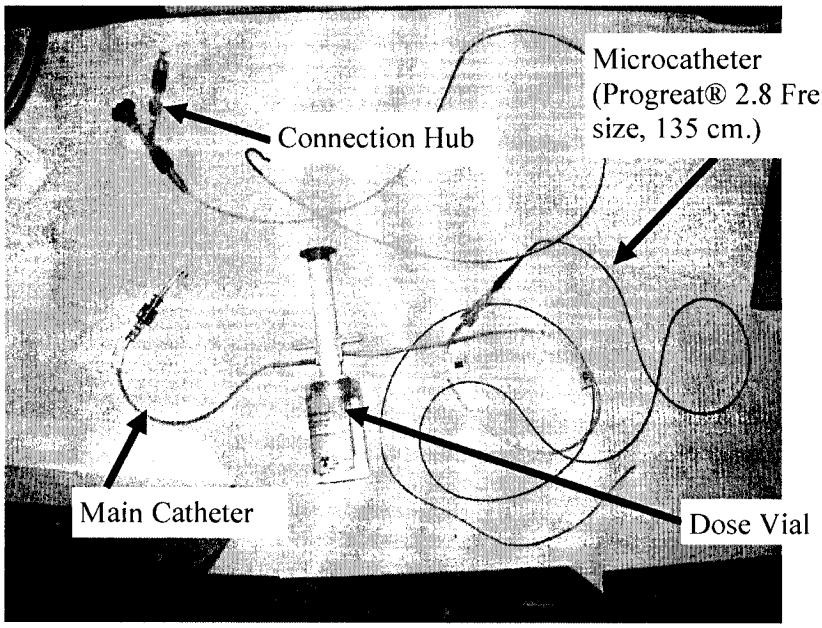


Fig. 1 Used Delivery Materials

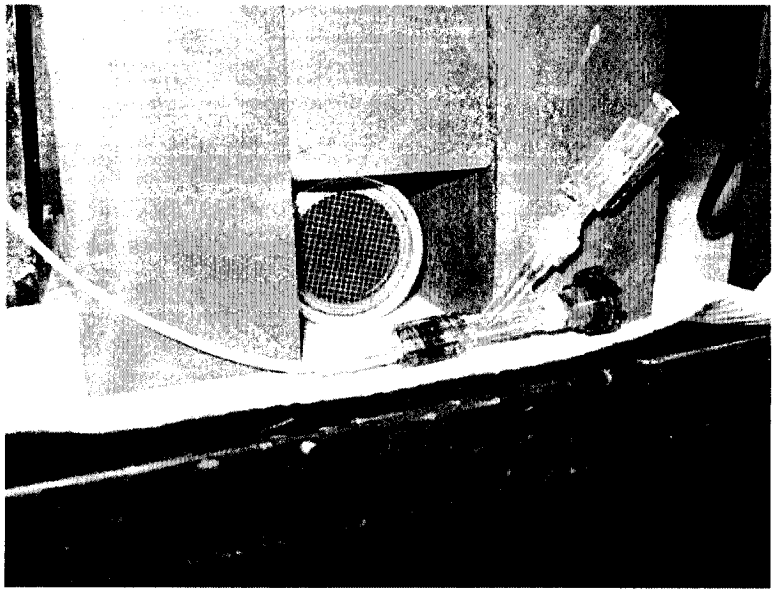

Fig. 2 Gross Survey

twofold: to discuss the incident with involved individuals, and to localize the residual microspheres among the waste materials. With information gleaned, a cause for the lower microsphere delivery might be inferred and shared with interested parties.

On 2/18/10, the following individuals met at the Roudebush VA Medical Center's Nuclear Medicine and Interventional Radiology areas, to discuss the incident:

1. Roudebush VAMC **Radiation Safety Officer Thomas Schumacher, MS, CHP**, who attended the infusion.
2. Roudebush VAMC **Chief Nuclear Medicine Technologist and Assistant Radiation Safety Officer Mary Ann Spilker, CNMT**, whose staff prepared and assayed the dose for proper activity level prior to delivery to Interventional Radiology for infusion;
3. **Nordion® clinical associate for Therasphere® operations Michael Pappas, BSRT, CNMT**
4. **VA Interventional Radiologist and Therasphere Authorized Therasphere® IR Physician Jeffrey Ramkaransingh, M.D.,** who performed the infusion.

Highlights of these discussions follow below. After the meetings with involved individuals, Messrs. Schumacher and Pappas set up the radiological investigation of the treatment's apparatus. Figure 1 shows the waste materials included the investigation.

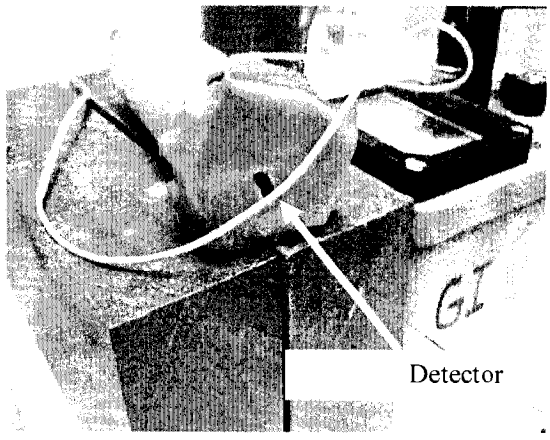


Fig. 3 Fine Survey of Catheter

## Measurement Setup:

A Ludlum Model 3 survey meter with detector model 44-7 (*s/n 71818, calibration date 5/4/09*) was arranged in two collimated configurations:

1. The first (fig 2) was used for a gross measurement of the apparatus. It consisted of

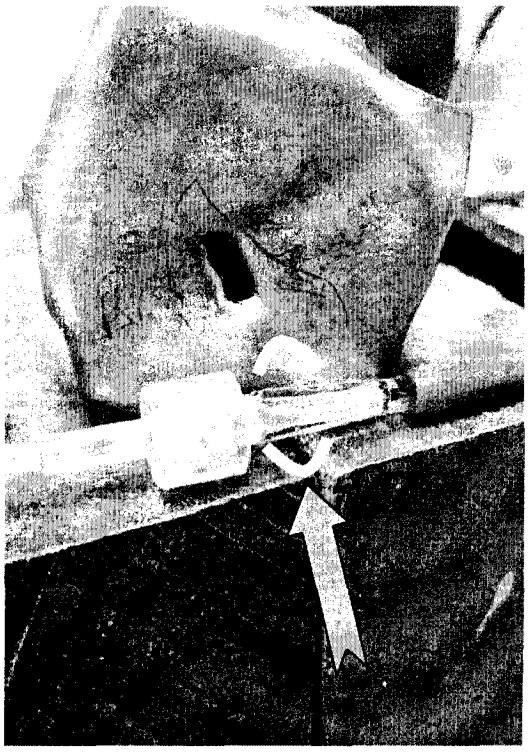

Fig. 4 Hot Area of Hub

a collimated trio of lead bricks with the detector face set back three centimeters from the material being surveyed.

2. The second configuration (fig. 3) was used for more precise localization of activity. It consisted of a small, rectangular detector slot approximately 2 mm wide by 5 mm height, cut out of a piece of 2 mm thick lead sheeting. Once the radioactivity's general location was found with the first method, it was investigated more closely with the second configuration. All materials that showed readings above natural background with the first step, were surveyed slowly along their entire length.

## Results:

The survey results are summarized in Table 1. A small amount of remaining radioactivity was observed in the source vial for the patient's dose, though no more than would be expected from previous experience. The large catheter measured at background, while the microcatheter uniformly read at 2-3 times background along its entire length. One area, the "hub" of the lexan® coupler (Fig. 4), contained significantly higher activity (*seven times background*). The hub includes a conical reduction of tubing diameter in the downstream direction. It was along this decreasing diameter that the residual activity was found.

| Location | Exposure Rate (mR/hr) |
|---|---|
| Background | 0.02 |
| Source Vial | 0.15 |
| Microcatheter | 0.05 |
| Large Catheter | 0.02 |
| **Catheter Coupling ("hub")** | **1.4** |

Table 1 Exposure Rates from Therasphere® Waste Materials

## Discussion:

The high concentration of microspheres in the roughly one-centimeter length of the connection hub is consistent with the initial report from Dr. Ramkaransingh, who stated that an unusually-high spike in exposure rate was seen during the second "push" of the saline solution/microsphere mixture through the delivery apparatus. Such a transiently high rate could be attributable to a higher concentration or aggregation of microspheres moving through the tubing, as opposed to a more uniformly-distributed suspension of spheres.

Some possible causes were proposed by Mr. Pappas. One involved the infusion of iodinated contrast media in the catheter. In order to confirm that the microspheres will

reach the desired area of the tumor, contrast is infused under fluoroscopy immediately before infusion of the radioactive microspheres. This contrast media has a higher viscosity than the saline solution/ microsphere suspension, so residual contrast may impede or trap any aggregations of microspheres along the same length of catheter. To avoid this possibility, he recommended that the catheter be flushed with plain saline solution to remove any such contrast remnants, before the microspheres are infused.

In March of 2009, a strikingly similar event occurred at the University of North Carolina Hospital in Chapel Hill. In that event, 26% of the Therasphere® dose appeared to remain in the source vial after repeated attempts to flush it into the patient's liver. Shortly thereafter, in April of 2009, a Therasphere® treatment at Indiana University medical Center resulted in approximately 28.6% of the material remaining in the delivery apparatus. At that time, it was thought that there was sticking of a significant portion of the spheres underneath the rubber septum ring of the inner dose vial. To prevent this, Nordion® recommended, and the NRC concurred in a licensee notice, that the vial be given additional agitation before being loaded in the delivery apparatus. In response to the NRC recommendation, the Roudebush VAMC instituted such a revision to the Therasphere® standard operating procedure, affixing an electric "Vortex Genie" shaker to the dose preparation cart, with instructions to perform the shaking as directed. Mr. Pappas observed this arrangement, and affirmed that it was advantageous. He added that a final, firm "tap" be additionally given to the dose vial just before delivery.

## Summary:

The location in the apparatus of the residual microspheres in the 12/30/09 case was determined; however, it is still undetermined *why* they were held up in this location. Subsequent patient administrations using the same techniques and routine, with the same catheters, connectors, etc., have been successful, with delivery rates of 92% and 99%. We will perform additional flushing of contrast media from the catheter prior to microsphere infusion, as recommended by the vendor. Our medical center personnel will continue to closely monitor future movement of microspheres through the source train by not only the mounted electronic dosimeters, but by real-time hand-held radiation surveys in the Interventional Radiology suite. ◆