UNITED STATES
NUCLEAR REGULATORY COMMISSION
OFFICE OF NUCLEAR REACTOR REGULATION
OFFICE OF NUCLEAR MATERIAL SAFETY AND SAFEGUARDS
WASHINGTON, DC 20555-0001

September 17, 2025

NRC INFORMATION NOTICE 2025-05: RECENT REPORTED MEDICAL EVENTS INVOLVING GASTROINTESTINAL DEPOSITION OF YTTRIUM-90 MICROSPHERES

ADDRESSEES

All U.S. Nuclear Regulatory Commission (NRC) medical-use licensees and NRC master materials licensees that are authorized for the use of yttrium-90 (Y-90) microspheres in accordance with Title 10 of the *Code of Federal Regulations* (10 CFR) 35.1000, "Other Medical Uses of Byproduct Material or Radiation from Byproduct Material." All Agreement State Radiation Control Program Directors and State Liaison Officers.

PURPOSE

The NRC is issuing this information notice (IN) to inform licensees of recent reported medical events that involved gastrointestinal (GI) deposition of Y-90 microspheres. The NRC expects that recipients will review the information for applicability to their facilities and consider actions, as appropriate, to minimize the potential for similar medical events.

INs may not impose new requirements, and nothing in this IN should be interpreted to require specific action. The NRC is providing this IN to the Agreement States for their information and for distribution to their medical licensees, as appropriate.

DESCRIPTION OF CIRCUMSTANCES

The NRC requires reporting of events involving Y-90 microspheres that meet medical events criteria in 10 CFR 35.3045 and licensee's approved conditions per 10 CFR 35.1000(b). The purpose of reporting medical events is to identify their causes in order to correct them, prevent their recurrence, and allow the NRC to notify other licensees so they can avoid similar incidents. Both the NRC staff and the Advisory Committee on the Medical Uses of Isotopes (ACMUI) regularly review medical event reports to identify generic issues or concerns and to identify any inadequacies or the unreliability of specific equipment or procedures. The recent Y-90 medical events were discussed during the April 7, 2025, ACMUI meeting and are included in the meeting slides (ML25162A113). Past presentations are posted in the Medical Events section of the NRC Medical Uses Licensee Toolkit public webpage at https://www.nrc.gov/materials/miau/med-use-toolkit.html#events.

Medical events involving Y-90 microsphere brachytherapy constitute the majority of medical events reported to the NRC each year. Most of these events are due to underdoses and/or administrative errors, as described previously in NRC Information Notice (IN) 2019-12, "Recent Reported Medical Events Involving the Administration of Y-90 Microspheres for Therapeutic Medical Procedures," dated December 31, 2019 (ML19262G231). More recently, however,

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between May and September 2024, four medical events were reported that indicated significant deposition of Y-90 microspheres to the GI system. All four events were included in NUREG-0090, Volume 47, Report to Congress on Abnormal Occurrences Fiscal Year 2024 (ML25150A343). These four medical events were deemed to be significant to safety as each resulted in a dose that exceeded the intended dose to an organ or tissue by 10 grays (Gy) (1,000 rad).

The GI deposition is a known complication of microsphere brachytherapy which could lead to significant health effects to the patient including GI ulceration and death. Historically, the NRC has received very few reported medical events involving GI deposition and the recent Y-90 events were identified as an uptick. The staff noted that all four reported events involved Therasphere® Y-90 microspheres; however, medical events involving GI deposition associated with the use of other types of microspheres have also been reported in the past.

Manufacturer instructions for Y-90 microsphere products list noticeable blood flow from the point of infusion toward the GI system to be a contraindication for treatment. However, the decision of an authorized user (AU) to treat a patient based on their individual circumstances is outside the regulatory authority of the NRC. As such, the NRC is providing recent examples of Y-90 GI deposition for awareness. The purpose of this IN is to inform licensees and their AUs of operational experience related to medical events involving GI deposition for their consideration in their medical decision-making process.

In one event, macroaggregated albumin (MAA) mapping was unable to adequately predict blood flow to the GI system. Initial MAA mapping indicated flow to the GI system. A second MAA mapping procedure was performed the morning of the treatment, which did not indicate any potential deposition to the GI system. Because the second mapping procedure did not show any contraindications to treatment, the treatment proceeded. Upon post-treatment imaging the licensee found that only 86% of the prescribed dose was received by the target site and discovered uptake of microspheres to the stomach wall, resulting in a stomach dose between 1,400 and 2,000 centigray (cGy) (rad). Because this dose met the criteria listed in the additional reporting criteria required for Y-90 microsphere use, the licensee reported the event as a medical event.

In a second event, misinterpretations of the patient's anatomy led to GI deposition. The MAA mapping procedure revealed no flow to the GI system. On the day of treatment, the microcatheter placement was confirmed using digital subtraction angiography images. Post-treatment imaging revealed no microsphere deposition in the patient's liver but major deposition in the patient's stomach. The patient's stomach received 100% of the activity delivered, resulting in a dose of 19,880 cGy (rad) while the patient's liver received no dose. Upon discovery of this unintended dose, the licensee reported the incident as a medical event. The licensee determined that the root cause of the event was misinterpretation of the blood supply to the liver[1]. The patient was subsequently treated for adverse effects to the GI system, including GI-related pain, loss of appetite, vomiting, gastritis, and ulcers. As a corrective action, the licensee added cone beam computed tomography (CBCT) to their internal Y-90 microsphere mapping procedure.

[1] Using a two-dimensional image, the physician believed the catheter to be in the target vessel to deliver microspheres to the liver. However, the catheter had actually been positioned inside the gastric artery. The licensee determined that the physician would have been able to identify the error had three-dimensional imaging been used.

In a third event, the patient was scheduled to receive treatment in two steps: one dose for each lobe of the liver, delivered in separate treatment procedures. Two months prior to the event, a pre-treatment Tc-99m MAA mapping procedure was conducted for the right lobe of the liver. The first treatment to the right lobe was performed without issue. No additional MAA mapping procedure was performed for the left lobe of the liver. Post treatment imaging revealed the majority of the microspheres were delivered to the patient's GI system instead of the liver during treatment of the left lobe. The licensee reported that a majority of the dose was received by the patient's stomach, resulting in severe health consequences for the patient. The licensee's corrective actions included implementation of new procedures that emphasize Tc-99m MAA mapping and angiography techniques, including CBCT, prior to every administration.

In a fourth event, a licensee reported equipment failure leading to GI deposition. Upon post-treatment imaging, the licensee discovered extrahepatic deposition. The licensee determined that only an estimated 42% of the prescribed activity of Y-90 microspheres was delivered to the liver and that the remainder of the microspheres were deposited in the patient's duodenum, resulting in an organ dose of 9,900 cGy (rad). Upon discovering the deposition in the duodenum, the licensee reported a medical event. The licensee believed that the cause of the event was an occlusion of microspheres within the distal portion of the microcatheter. The physician noted resistance during administration of the microspheres. The licensee believed the microcatheter ruptured when the physician attempted to clear the resistance by flushing the microcatheter, which changed the point of delivery and altered flow dynamics, allowing microspheres to travel to the GI system.

DISCUSSION

This IN is intended to provide licensees with awareness of recent medical events involving GI deposition of Y-90 microspheres. Deposition of Y-90 microspheres in the GI system has been associated with major health complications and poor patient outcomes. Evidence of potential GI deposition during pre-treatment imaging is listed as a contraindication for Y-90 microsphere brachytherapy by manufacturers. While the decision to treat and manage possible adverse effects is at the discretion of the AU, it is assumed that there will be a minimal expected dose to the GI system for most Y-90 microsphere administrations due to this contraindication.

The Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-Spheres® Licensing Guidance (ML21089A364) and the Yttrium-90 Microsphere Brachytherapy Sources and Devices Eye90® Microspheres Licensing Guidance (ML24247A254) provides medical event reporting criteria for Y-90 microsphere medical events. The criteria include reporting of a dose to the skin or an organ or tissue other than the treatment site that exceeds by 0.5 Sv (50 rem) to an organ or tissue and 50 percent or more of the dose expected from the administration defined in the written directive, excluding shunting, as defined in the licensing guidance, when shunting was evaluated prior to the treatment in accordance with the manufacturer's procedures. Shunting, as defined by the licensing guidance, is blood flow through pathway or bypass due to patient vasculature causing the Y-90 microspheres to flow to an unwanted location. Unexpected dose or activity to an organ or tissue other than the treatment site that is caused by catheter placement during delivery of the Y-90 microspheres is not considered shunting if the licensee commits to the licensing guidance.

GI deposition is most likely to be detected through either post-treatment imaging or follow-up after a patient experiences negative side effects. While post-treatment imaging is not required

by the NRC, it is often performed for purposes of treatment verification or for clinical trials. In the four events described above, post-treatment imaging detected the GI deposition of Y-90 microspheres. Once post treatment imaging discovered the GI deposition, the licensees were required to report the dose to an unintended organ as a medical event as required by 10 CFR 35.3045, “Report and notification of a medical event.”

The events discussed in this IN highlight that GI deposition events are occurring during Y-90 microsphere procedures and licensees should consider methods to minimize the potential of future events. These events highlight the importance of careful pre-treatment evaluation of patient vascular anatomy. For corrective actions, several licensees emphasized the use of CBCT for vascular imaging and detecting blood flow to extrahepatic tissue, whether performed during pre-treatment mapping procedures or on the day of the procedure. Licensees also draw attention to the limitations of MAA as an analog for microspheres due to differences in size and flow dynamics. It is considered a best practice for licensees to stay abreast of current manufacturer, professional society, and industry recommendations to limit the likelihood of future GI deposition events.

CONTACTS

This information notice requires no specific action or written response. Please direct any questions about this matter to the technical contact listed below or to the appropriate regional office.

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Note: NRC generic communications may be found on the NRC public website, http://www.nrc.gov, under NRC Library/Document Collections.

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ADAMS Accession No.: ML25178A313

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