# Technical Aspects and Administration Methods of $^{177}$Lu-DOTATATE for Nuclear Medicine Technologists

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At Banner M.D. Anderson Cancer Center in Arizona, we have gained valuable knowledge of the different infusion methods for $^{177}$Lu-DOTATATE peptide receptor radionuclide therapy. **Methods:** Our nuclear medicine department has used 2 different methods of administration: the gravity infusion method and the infusion pump protocol. **Results:** Our experience with the gravity infusion method allowed us to identify problematic aspects and led us to search for and implement the infusion pump protocol. **Conclusion:** The pump protocol ensures that the infusion of $^{177}$Lu-DOTATATE is safe and delivers a consistent dose to every patient.

**Key Words:** Lutathera; neuroendocrine cancer; PRRT; pump protocol; gastroenteropancreatic neuroendocrine tumor

**J Nucl Med Technol 2019; 47:288–291**
DOI: 10.2967/jnmt.118.221846

The NETTER-1 clinical trial, an expanded-access protocol for therapeutic use of the somatostatin analog $^{177}$Lu-DOTATATE, was established in Arizona in 2017 (*3*). Our center was the first in Arizona to administer this therapy to patients with inoperable, somatostatin receptor–positive, gastroenteropancreatic–neuroendocrine tumors of the foregut, midgut, and hindgut (*2*).

In October 2017, the first Arizona patient was treated with peptide receptor radionuclide therapy, and to date, we have treated 12 patients. On January 26, 2018, the Food and Drug Administration approved $^{177}$Lu-DOTATATE (Lutathera; Advanced Accelerator Applications USA, Inc.) (*1*). Patients with gastroenteropancreatic–neuroendocrine tumors are traveling great distances to receive this now commercially available drug. The aim of this article is to describe our facility's experience with the standard operating procedure–recommended gravity infusion method and with the infusion pump protocol.

## MATERIALS AND METHODS

Twelve expanded-access-protocol patients were treated with $^{177}$Lu-DOTATATE (7.4 GBq [200 mCi] ± 20%). The treatment was discontinued in 3 of these 12 because of toxicity (*3*). The remaining 9 patients received a total of 4 $^{177}$Lu-DOTATATE infusions. There was an interval of 8 wk between each administration, with a 1-wk extension for those experiencing toxicity that resolved (*3*). Two methods of administration were used between 2017 and 2018 for delivery of $^{177}$Lu-DOTATATE into patients enrolled in the expanded-access-protocol clinical trial at our facility: the gravity infusion method and the infusion pump protocol. In this paper, we discuss the methods used, the difficulties faced, and the current protocol created with the collaboration of fellow technologists at other facilities.

## RESULTS

### Recommended Gravity Infusion Method

The first method of administration, derived from the NETTER-1 clinical study investigator brochure, is the gravity infusion method (*3*). The expanded-access protocol for therapeutic use of $^{177}$Lu-DOTATATE uses the gravity infusion method as the standard operating procedure to administer the liquid therapy agent. The premise of this method suggests that the flow of saline into the $^{177}$Lu-DOTATATE vial induces pressure, which, in turn, pushes the radiopharmaceutical out of the vial and into the intravenous catheter of the patient. The gravity infusion method calls for an infusion pole, a 250-mL bag containing a 9 mg/mL solution of saline, a long-needle (90–100 mm) gravity intravenous infusion set, a short-needle (3 cm, 18 gauge) gravity intravenous infusion set, and a pair of forceps (*3*). The $^{177}$Lu-DOTATATE vial is encased in a lead pig. A 250-mL bag of saline is hung, and the tubing is connected to the short needle (*3*). The short needle is used to puncture the $^{177}$Lu-DOTATATE vial at an angle, with the needle tip sitting in the air pocket at the top of the $^{177}$Lu-DOTATATE vial (*3*). The short needle is used for the saline drip into the vial (*3*). Next, the long needle is attached to the intravenous catheter tubing and used to puncture the $^{177}$Lu-DOTATATE vial at an angle, with the needle tip sitting at the bottom of the vial and inside the radiopharmaceutical liquid (*3*). The long needle is used to transfer the $^{177}$Lu dose into the patient (*3*). Once the flow of saline begins, the radiopharmaceutical is pushed into the intravenous catheter of the patient (*3*). The flow of saline is controlled by a pump at a rate of 50–100 mL/h for 10 min and then is increased to 200–300 mL/h for an additional 30 min (*3*).

### Challenges of the Gravity Infusion Method

There were several challenges with the gravity infusion method. First, it was difficult to assess how much of the

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Published online Apr. 24, 2019.




JNMT-221846 ■ 11/25/19

radiopharmaceutical was administered over time. The amount of dose infused over time was important at our facility as there were occasions on which our radiologist chose to infuse only a portion of the 7.4-GBq (200-mCi) dose because of abnormal bloodwork results or toxicity. In theory, the amount of saline administered should directly relate to the amount of radiopharmaceutical administered. However, in our experience, this was not the case. The time it took to administer each dose varied significantly despite use of the same rate and volume of saline flow for every infusion. The second difficulty of the gravity infusion method was loss of air pressure in the vial, which occurred during 4 of the 37 drug administrations. We found that loss of air pressure could be avoided by stabilizing the needles and puncturing the vial at the outer, thicker, portion of the septum. This technique ensures that the puncture holes of the vial do not become enlarged during infusion, which can cause loss of air pressure. Loss of air pressure, in turn, can result in loss of the air pocket, which can cause the radiopharmaceutical to bubble out of the top of the vial and slow or stop the infusion. To remedy the loss of air pressure, we needed to infuse 5 mL of air into the saline line to recreate an air pocket in the vial. The need to constantly monitor the vial for loss of the air pocket was also exposing the technologist to additional radiation. During 1 infusion, the loss of air pressure prevented us from infusing the dose. In this instance, the only alternative was to draw up and hand-inject the remaining dose. The hand injection rescue method subjected the physician and the surrounding personnel to additional exposure even when shielded.

### Possible Solutions to the Challenges

We corrected the issues of the gravity infusion method by placing the $^{177}$Lu-DOTATATE vial (with lead pig) into an acrylic box to prevent exposure from contamination in case the radiopharmaceutical bubbled outside the top of the vial. We also placed a digital pocket dosimeter on top of the acrylic box to measure mR/h and found that the reading was directly related to the dose administered (as the peptide receptor radionuclide therapy decreased in the vial, the mR/h reading decreased). Once these issues were resolved, we found that this method was feasible but still increased the exposure of the technologist, who had to closely monitor the vial throughout the infusion. The gravity infusion method was also difficult to reproduce successfully when attempted by all technologists.

The many challenges of the gravity infusion method and the high radiation exposure of the physician needing to hand-inject the dose after a failed infusion led us to search for a more reliable method. Knowing that $^{177}$Lu-DOTATATE would soon be approved by the Food and Drug Administration and that the demand would increase, we decided to search for a more reliable method of infusion. We developed the infusion pump protocol and successfully implemented it at our facility. This protocol has proven to be reliable and efficient, reducing the exposure of all involved. It is a consistent method of liquid dose infusion with a low possibility for contamination or error.

### Alternate Method of Administration, the Infusion Pump Protocol

The infusion pump protocol uses any commercially available infusion pump, a male-to-male adaptor, a 3-way stopcock, infusion pump tubing, an 18-gauge (3.5-in) spinal needle, a micron filter, an 18-gauge (1.5-in vent needle), forceps, and a 10-mL saline vial (Fig. 1). The logic behind the infusion pump protocol is simple. The infusion pump pulls the liquid therapy out of the vial via an 18-gauge spinal needle and infuses it into the patient. First, the $^{177}$Lu-DOTATATE vial is ventilated with a micron filter (Fig. 2). Then, the infusion pump tubing is primed and inserted into the pump. The liquid therapy is infused at a rate of 0.8 mL/min for 30 min. At the end of infusion, 10 mL of saline are injected into the $^{177}$Lu-DOTATATE vial through the micron filter and the pump is set to an infusion rate of 2 mL/min for 5 min (Figs. 3 and 4). The 5-min saline infusion is used to rinse the vial of any residual dose. [**Fig. 1**] [**Fig. 2**] [**Fig. 3**] [**Fig. 4**]


**FIGURE 1.** Materials for pump protocol. Moog pump is shown on left and injection supplies on right.

### Challenges to the Infusion Pump Protocol

The recommended standard operating procedure for $^{177}$Lu-DOTATATE administration requires the dose to be diluted with 250 mL of saline solution

**FIGURE 2.** Vent needle set-up.

throughout a 30-min infusion. This was the first major challenge of the infusion pump protocol. The recommended saline dilution was not possible with the infusion pump protocol we developed. For this reason, we needed approval from our radiologist and physicians to alter the standard operating procedure and remove the need for saline dilution during infusion of the liquid therapy. Another minor hurdle of this method was the need to allot extra time for set-up of the equipment before administration. Equipment set-up typically takes an additional 10 min. The final challenge of this method was the extra cost of an infusion pump. However, the need for a more efficient, reliable, and predictable method of administering $^{177}$Lu-DOTATATE justified the cost of the equipment. The decreased chance of contamination and radiation exposure of the staff alone made the purchase worthwhile.

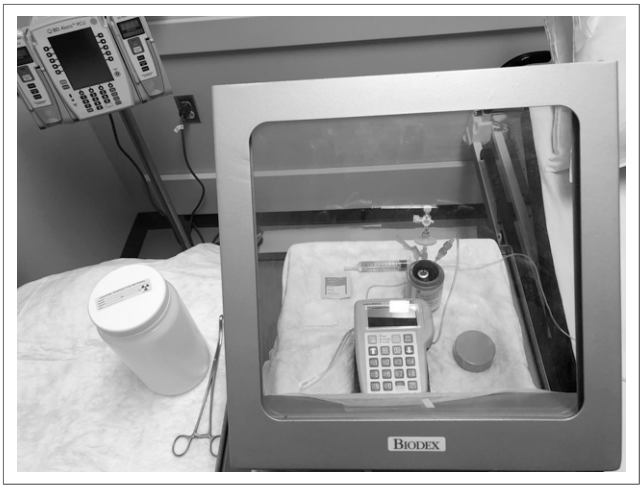


**FIGURE 3.** $^{177}$Lu-DOTATATE patient set-up using pump protocol.

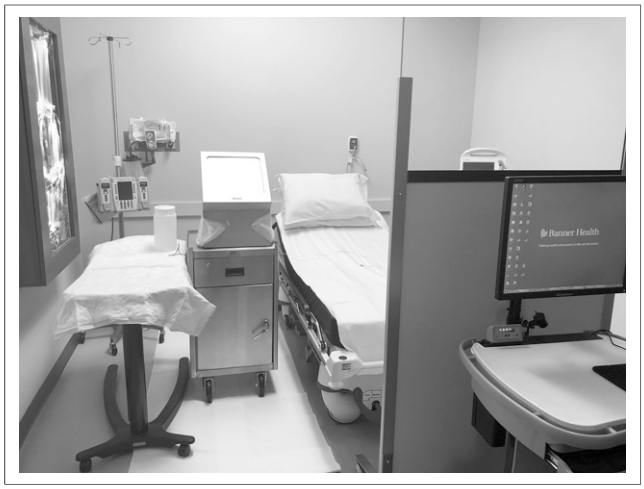


**FIGURE 4.** Room set-up for pump protocol.

## DISCUSSION

We have experienced great success with the infusion pump protocol but believe that it needs further rigorous testing. Because of the rise in demand for liquid nuclear therapies, there is a worldwide requirement for proven standardized methods of administration.

## CONCLUSION

Although the gravity infusion method is cost-effective, we identified some challenges that increased the possibility of error, contamination, and excessive radiation exposure. Consequently, we developed the infusion pump protocol. Our facility currently uses the Curlin pump manufactured by Moog Inc.; however, the method can be done with any commercially available infusion pump. This new method also reduces error, the possibility of contamination, and, most importantly, radiation exposure. Our facility has used this method for 6 mo, and we have not experienced any of the contamination or leakage issues that we encountered with the gravity infusion method. The new method has proven to be beneficial to our patients and department staff and provides safe and consistent dose delivery. The benefits of this method far outweigh the additional expense of purchasing an infusion pump.

## DISCLOSURE

This article discusses different methods of $^{177}$Lu-DOTATATE infusion. Nuclear medicine professionals should choose the



JNMT-221846 ■ 11/25/19

method that suits their department's needs in accordance with their respective institution's regulations and radiation safety standards. The protocol and drug referred to in this article have not been tested by Moog Inc., and Moog Inc. did not contribute financially to the development of the new protocol. No other potential conflict of interest relevant to this article was reported.


## ACKNOWLEDGMENTS

We thank Dr. Boris Naraev, a gastrointestinal medical oncologist from Banner M.D. Anderson Cancer Center in Arizona, for believing in compassionate, personalized cancer care that focuses on a patient's quality of life. The drive that Dr. Naraev has for his patients and his energy for pursuing the latest and greatest in cancer care allowed us to participate in the expanded-access-protocol clinical trial for $^{177}$Lu-DOTATATE. We thank Scott Graham, CNMT, from the University of California, San Francisco, for sharing his liquid-therapy pump infusion method with our facility. Our director of radiology, Tonya Brownell, and nuclear medicine supervisor, David Branch, were excellent facilitators during this entire experience. We are especially grateful for our radiology nurses, Silvy Vallapan and Cynthia Devera, for their excellence in patient care.


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