Retention of Lu-177 Peptide in Dose Vial and Administration Tubing

Nic J. Mastascusa, Pharm.D, BCNP, James A. Ponto, MS, BCNP

University of Iowa, Iowa City, IA

INTRODUCTION

Following the success of Lutetium-177 dotatate, other clinical trials to treat receptor-expressing tumors have been initiated.[1-4] Previous investigations have used the flebo infusion method[5] (Figure 1) or the Rotterdam method[6] (Figure 2) for administration of the radiopharmaceutical. Our objective was to empirically demonstrate that our modified Rotterdam administration method[7] delivered a reproducible and accurate dose of an investigational Lu-177 radiolabeled peptide to the patient.

Figure 1. Schematic drawings of the flebo method[5]. Saline solution from an inverted vial (*4*) flows by gravity into the shielded radiopharmaceutical vial (*1*) via a short needle (*52*); the increased pressure within the radiopharmaceutical vial causes aspiration of radiopharmaceutical solution through a long needle (*60*) and is infused into the patient (*62*).

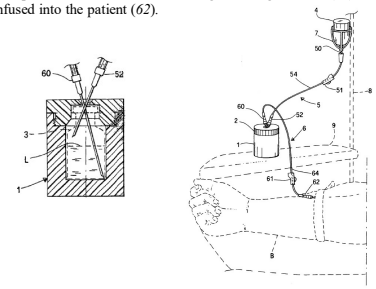
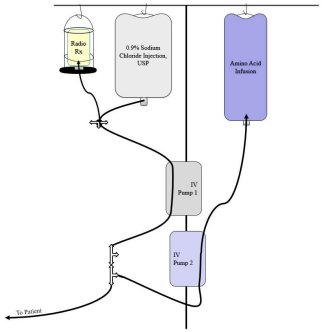


Figure 2. Schematic drawing of the original Rotterdam method. An IV pump is used to infuse the radiopharmaceutical solution into the patient from an inverted vial suspended in a wire frame. Normal saline is used keep line patency and to flush the administration line. A second pump is used to continuously infuse the amino acid solution

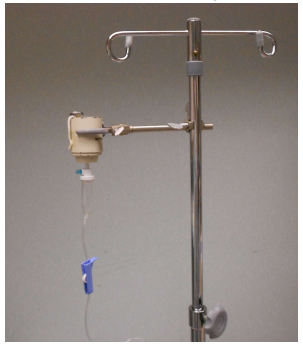


METHODS

Under the IND protocol, the Lu-177 radiolabeled peptide was supplied in a volume of approximately 10-14 mL in a 20 mL vial. Prior to administration, the volume of the vial was adjusted down to the correct activity of the prescribed dose. For administration, the vial diaphragm was punctured with an IV spike infusion set (Figure 3) and upon completion of the infusion, the IV line was flushed with normal saline. The residual activity in the administration vial and tubing was measured separately in a dose calibrator shortly after the completion of administration. Due to the short interval to residual measurement (generally within an hour) and the long half life of Lu-177 (6.6 days) values were not corrected for decay. To prevent contamination of the dose calibrator, the tubing set was bunched up, secured with a rubber band and placed inside of an extra large examination glove before it was placed in the dipper and measured on the appropriate setting. Mean and standard deviation for retention in dose vials and in administration tubing for all administrations to date (n=17) were calculated as percentages of the initial activity in the dose vial.

Figure 3. Components of administration set-up. Left to right: vented IV spike infusion set (SmartSite® Infusion Set, CareFusion, San Diego, CA), radiopharmaceutical vial, screw-top lead vial shield with lead cover for access opening, and flask clamp.

Figure 4. Shielded vial spiked and hung for infusion. Infusion pump (not pictured) Alaris®, CareFusion, San Diego, CA



RESULTS AND DISCUSSION

Retention in the dose vial averaged 0.24% ± 0.07% with a range of 0.10-0.40%. Retention in the administration tubing averaged 1.62% ± 0.31% with a range of 1.27-2.60%. As a result, in all cases ≥ 97.1% of the radiopharmaceutical dose was administered. In all administrations, 98.07% to 104.24% with an average of 100.19% of the ordered dose was administered to the patient (Table 1 and Figure 5).

In contrast to the flebo method, our modified administration method allowed for short (average 14.4 min), efficient and reproducible (Figure 6) infusion of the radiopharmaceutical without being further diluted with normal saline. In contrast to the original Rotterdam method, we used a lead vial shield to provide radiation protection.

Table 1. Residual vial and tubing contents using our modified method for our first 17 administrations of Lu-177 peptide.

	vial residual					tubing retention		total not infused		Amt infused	% vs. Rx
Dose #	orig mCi	orig vol	mCi resid	mL resid	%	mCi	%	mCi	%	mCi	%
1	210	9.8	0.40	0.02	0.19%	2.9	1.38%	3.30	1.57%	206.7	103.4%
2	212	8.4	0.44	0.02	0.21%	3.08	1.45%	3.52	1.66%	208.5	104.2%
3	205	9.7	0.38	0.02	0.19%	2.67	1.30%	3.05	1.49%	202.0	101.0%
4	202	9.0	0.32	0.01	0.16%	3.28	1.62%	5.60	2.77%	196.4	98.2%
5	209	7.9	0.46	0.02	0.22%	3.69	1.77%	4.15	1.99%	204.9	102.4%
6	200	9.0	0.41	0.02	0.21%	3.29	1.65%	3.70	1.85%	196.3	98.2%
7	203	9.9	0.58	0.03	0.29%	3.12	1.54%	3.70	1.82%	199.3	99.7%
8	205	8.4	0.48	0.02	0.23%	3.42	1.67%	3.90	1.90%	201.1	100.6%
9	204	9.3	0.81	0.04	0.40%	3.37	1.65%	4.18	2.05%	199.8	99.9%
10	203	9.7	0.20	0.01	0.10%	2.65	1.31%	2.85	1.40%	200.2	100.1%
11	201	9.0	0.36	0.02	0.18%	2.78	1.38%	3.14	1.56%	197.9	98.9%
12	202	8.0	0.62	0.02	0.31%	5.25	2.60%	5.87	2.91%	196.1	98.1%
13	205	7.9	0.52	0.02	0.25%	3.43	1.67%	3.95	1.93%	201.1	100.5%
14	203	8.1	0.44	0.02	0.22%	3.69	1.82%	4.13	2.03%	198.9	99.4%
15	203	9.5	0.65	0.03	0.32%	3.34	1.65%	3.99	1.97%	199.0	99.5%
16	203	8.3	0.46	0.02	0.23%	2.57	1.27%	3.03	1.49%	200.0	100.0%
17	203	8.1	0.69	0.03	0.34%	3.77	1.86%	4.46	2.20%	198.5	99.3%
		Ave	0.48	0.02	0.24%	3.31	1.62%	3.91	1.92%	200.38	100.19%
		St.Dev	0.15	0.01	0.07%	0.62	0.31%	0.83	0.42%	3.49	1.75%
		MAX	0.81	0.04	0.40%	5.25	2.60%	5.87	2.91%	208.48	104.24%
		MIN	0.20	0.01	0.10%	2.57	1.27%	2.85	1.40%	196.13	98.07%

Figure 5. Graphical representation of the data in Table 1

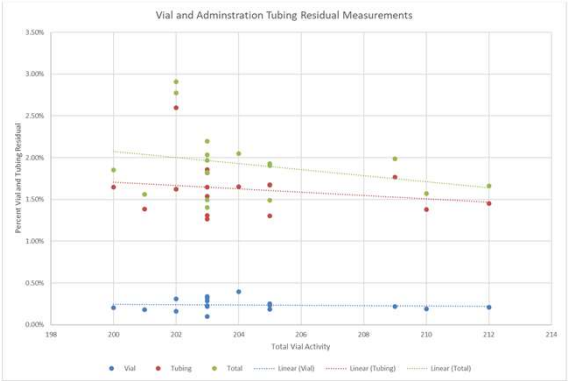
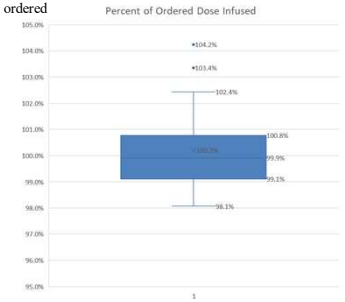


Figure 6. Percent of dose infused for the first 17 doses ordered



CONCLUSION

Our modified method for administration of Lu-177 peptide allows simple and efficient infusion of the radiopharmaceutical. Measurement of the residual radiopharmaceutical in the dose vial and administration tubing following infusion of the Lu-177 radiolabeled peptide confirmed ≥97% of the initial radiopharmaceutical therapy dose was consistently administered to the patient. More recent data of an additional 13 patients result in continued consistency of dose delivery with vial retention 0.27% ±0.11% (range 0.10-0.63%), tubing retention of 1.62% ±0.26% (range 1.27-2.60%). All doses were still within 98.07% to 104.24% of the ordered dose with an average of 99.94% of the ordered dose delivered to the patient.

REFERENCES

1. Baum RP, Kulkarni, HR, Schuchardt C, et. al. ^{177}Lu-Labeled Prostate-Specific Membrane Antigen Radioligand Therapy of Metastatic Castration-Resistant Prostate Cancer: Safety and Efficacy. J Nucl Med. 2016; 57:1006-1013
2. Nicolas GP, Mansi R, McDougall L, et. al. Biodistribution, Pharmacokinetics, and Dosimetry of ^{177}Lu-, ^{90}Y-, and ^{111}In-Labeled Somatostatin Receptor Antagonist OPS201 in Comparison to the Agonist ^{177}Lu-DOTATATE: The Mass Effect. J Nucl Med 2017 Sep;58(9):1435-1441
3. Reynolds TS, Bandari RP, Jiang Z, Smith CJ, Lutetium-177 Labeled Bombesin Peptides for Radionuclide Therapy. Curr Radiopharm. 2016;9(1):33-43.
4. Schottelius M, Osl T, Poschenrieder A, et. al. [^{177}Lu]pentixather: Comprehensive Preclinical Characterization of a First CXCR4-directed Endoradiotherapeutic Agent. Theranostics. 2017 Jun 11;7(9):2350-2362
5. Chinol M, Paganelli G. Container for vial of radiopharmaceutical and set for its infusion in a patient or for its transfer elsewhere. U.S. Patent 7,842,023 B2. November 30, 2010.
6. Kwekkeboom DJ, Bakker WH, Kooij PPM, et al. [^{177}Lu-DOTA^{0}, Tyr^{3}] octreotate: comparison with ^{111}In-DOTA^{0}] octreotide in patients. Eur J Nucl Med. 2001; 28:1319-1325.
7. Ponto J, Smith, J, Bricker J, Modified Method for Administration of Lu-177 Peptide [abstract]. J Am Pharm Assoc. 2014;54(2):148.