Supplemental Appendix:

Imaging Protocols for Dosimetry

The following equipment are needed to collect the data necessary for a dosimetry evaluation: gamma-camera with low and medium energy collimator (if a SPECT/CT is not available, a separate CT can be used for attenuation correction); gamma-counter with multichannel analyzer to determine ^{177}Lu activity in blood and urine samples if desired; and a dose calibrator to measure radioactivity in reference sources and the injected radioactivity. Typically, quantitative SPECT/CT with attenuation and scatter correction (typically using the triple energy window technique, with (e.g.) a 15% photopeak window at 208 keV and 4% windows at 189 and 229 keV) are used to obtain absolute activity quantification in all regions of interest (ROIs), correlated with the SPECT volumes of interest (VOIs). The OLINDA/EXM software is often used for multi-organ dose calculations (*1*).

There are two ways one can perform dosimetry. First, would be to acquire multiple time points to perform an accurate quantification. Clearance of ^{177}Lu-DOTATATE is biphasic, and multi-time-point whole body imaging at 1, 3-4, 16-24, 40-48, and 64-80 hours post injection can be used to characterize whole body and organ biokinetics and thus dosimetry (*2*). This may present challenges in patient management, in requiring a series of images over 3 days, but Bodei et al noted an approximate range of kidney doses from 8-37 Gy and marrow doses from 0.5-1.3 Gy in only 12 patients (*3*), thus patient-individualized dosimetry may be considered during the first treatment cycle, if possible. Second, would be to extrapolate data from a single time point imaging study post-treatment. For ^{90}Y-DOTATOC, the use of a well-chosen single time point for imaging can provide reasonable (±10%) estimates of areas under time-activity

curves for single exponential clearance case (*4*). A similar successful single time-point approach for estimating renal dose from ^{177}Lu-DOTATATE has also been reported recently (*5*). For kidney dosimetry, it is important to adjust for individual patient renal mass for accurate dose determination using patient specific kidney mass estimates (*6*). Additionally, separate assignment of activity to the kidney cortex and medulla, can be used with a multiregion kidney model to improve renal dosimetry (*7*).

Although assessment of marrow dose to individual patients is challenging, there are two methods for estimating marrow dose of radiopeptides – the blood-based approach, and the image-based approach (*8*). When using the blood based approach, blood activity is considered equivalent to marrow activity, and so marrow/blood concentration ratio of close to 1.0 is appropriate. Blood time-activity curves can be used to directly estimate marrow time-activity curves and thus marrow self-dose. In the image-based approach, activity clearly delineated marrow regions (e.g. sacrum, lumbar vertebrae) may be derived from and total marrow time-activity curves may be estimated by applying some standard fraction of total bone marrow assumed to be in the imaged region.

Supplemental Table 1: Description of administration methods

Method 1: Gravity method administration
• Insert a 2.5 cm, 20 gauge needle (short needle) into the radiopeptide vial and connect via a catheter to 250mL 0.9% sterile sodium chloride solution (used to transport radiopeptide during infusion) • Ensure short needle does not touch the radiopeptide solution in the vial and do not connect this short needle directly to the patient • Do not allow the sodium chloride solution to flow into the radiopeptide vial prior to the initiation of the radiopeptide infusion and do not inject radiopeptide directly into the sodium chloride solution • Insert second needle that is 9 cm, 18 gauge (long needle) into the radiopeptide vial ensuring that the long needle touches and is secured to the bottom of the radiopeptide vial during the entire infusion • Connect the long needle to the patient by an intravenous catheter that is prefilled with 0.9% sterile sodium solution and that is used exclusively for the radiopeptide infusion into the patient • Use a clamp or pump to regulate the flow of the sodium chloride solution via the short needle into the radiopeptide vial at a rate of 50ml/hr to 100ml/hr for 5 to 10 minutes and 200ml/hr to 300ml/hr for an additional 25 to 30 minutes (the sodium chloride solution entering the vial through the short needle will carry the

radiopeptide from the vial to the patient via the catheter connected to the long needle over a total of 30 to 40 minutes)

- During the infusion ensure the fluid level of the radiopeptide remains constant
- Disconnect the vial from the long needle line and clamp the saline line once the level of radioactivity is stable for at least five minutes
- Follow the infusion with and intravenous flush of 2 mls of 0.9% sterile sodium solution

Method 2: Pump method with the vial

- Position tubing into pump and prime the needle and tubing with saline, then attach tubing to IV using double male adapter.
- Insert a 3.5 inch 20-gauge spinal needle into a 10 mLs vial of sterile saline, and attach to tubing set from pump manufacturer. An example infusion pump would be the Curlin/Moog 6000 CMS ambulatory pump.
- Remove the 3.5-inch needle from the saline vial and pierce the therapy vial, and ensure that the tip of the needle touches the bottom of the vial.
- Place 0.25 inch 25-gauge vent needle in therapy vial with tip above level of solution level. Place three-way stopcock and then activated charcoal 0.22-micron filter on the end of the vent needle.
- Set pump to administer the volume of the ^{177}Lu-DOTATATE over 25-30 minutes. ^{177}Lu-DOTATATE is distributed in 20-25 mLs of volume, so an administration rate of 0.8-0.9 mL/minute will result in an infusion between 25 and 30 minutes.

- At the end of the infusion, flush the therapy vial with 10 mLs of sterile saline from a syringe using the three-way stopcock. Saline flushes can be administered at 2.5 mL/minute.

Method 3: Pump method with a syringe

- Prepare the shielded infusion pump: Hang a 250 ml saline bag and prime tubing with saline, prime the patient dose microbore tubing and the 3-way stopcock with saline and connect both sets of tubing into the 3-way stopcock. Set the infusion rate at 50 ml/hr.
- Stand the vial on a plastic wedge covered with chux to tilt the vial
- Insert a vent needle at an angle just until it punctures through the vial septum (one option is to attach a 20 g needle to a tuberculin syringe without the plunger).
- With a 30 ml syringe in a syringe shield, change the regular needle and attach a 3.5" spinal needle to the syringe. Insert this needle into the vial until it touches the bottom of the vial.
- Slowly withdraw all liquid from the vial.
- Using tongs, carefully raise the vial to ensure all liquid has been withdrawn.
- Slowly pull up the syringe to remove it from the vial
- Slightly pull back the plunger on the syringe to remove any liquid from the needle hub.
- Using gauze, carefully twist off the spinal needle, discard it in the designated ^{177}Lu sharps container, and attach a regular needle onto the syringe

- Pull out the vent syringe and discard in the designated ^{177}Lu sharps container
- Measure the vial residual and syringe in the dose calibrator using the appropriate ^{177}Lu setting
- Technologist loads the syringe into the shielded infusion pump

Supplemental Table 2: Radiation Dose Estimates for the Reference Adult for ^{177}Lu-DOTATATE

	Estimated Dose	
Target Organ	mSv/MBq	rem/mCi
Adrenals	6.87E-02	2.54E-01
Brain	5.04E-02	1.86E-01
Esophagus	5.42E-02	2.01E-01
Eyes	5.04E-02	1.86E-01
Gallbladder Wall	6.30E-02	2.33E-01
Left colon	5.51E-02	2.04E-01
Small Intestine	5.47E-02	2.02E-01
Stomach Wall	5.55E-02	2.05E-01
Right colon	5.56E-02	2.06E-01
Rectum	5.47E-02	2.02E-01
Heart Wall	5.48E-02	2.03E-01
Kidneys	5.95E-01	2.20E+00
Liver	3.63E-01	1.34E+00
Lungs	5.36E-02	1.98E-01
Pancreas	5.68E-02	2.10E-01
Prostate	5.54E-02	2.05E-01
Salivary Glands	5.14E-02	1.90E-01
Red Marrow	4.10E-02	1.52E-01

Osteogenic Cells	5.97E-02	2.21E-01
Spleen	9.10E-01	3.37E+00
Testes	5.13E-02	1.90E-01
Thymus	5.24E-02	1.94E-01
Thyroid	5.18E-02	1.92E-01
Urinary Bladder Wall	4.98E-01	1.84E+00
Total Body	6.72E-02	2.49E-01
Effective dose*	8.43E-02	3.12E-01

* Note that 'Effective dose' is not a relevant quantity when therapy levels of dose are involved.

Supplemental Table 3: Photon and Beta (β-) emissions from ^{177}Lutetium (*9*).

Photon Emission	Mean Energy (MeV)	Frequency
γ	0.208	0.110
γ	0.113	0.064
γ	0.321	0.002
γ	0.250	0.002
γ	0.072	0.002
γ	0.137	0.001
Beta (β-) Emission	Mean Energy (MeV)	Frequency
β-	0. 497	0.786
β-	0.176	0.122
β-	0.384	0.091

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