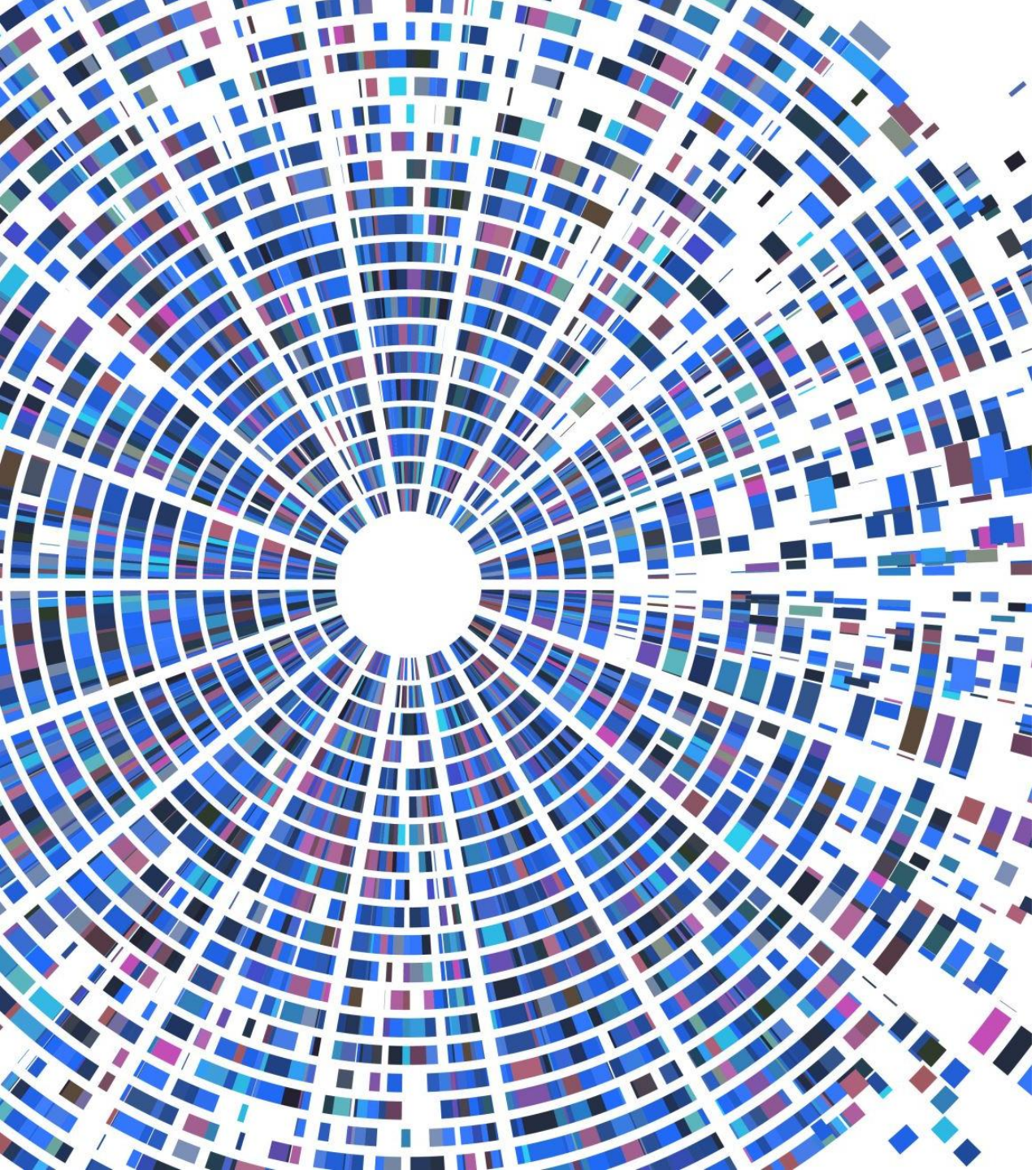


RADIOPHARMACEUTICAL THERAPY

RT4220 – Lecture #14

Kedree Proffitt

WSU

11/11/2025

LEARNING OBJECTIVES

- Review concepts of radiation protection and safety
- Discuss an overview of radiopharmaceutical procedures
- Explain the process of Lu-177 radiopharmaceutical procedures

REVIEW OF RAD PROTECTION AND SAFETY

So safe, so cool!

Types of Radiation Areas

- **Radiation Area:** an area, accessible to individuals, in which radiation levels could result in an individual receiving a dose equivalent in excess of 0.005 rem (0.05 mSv) in 1 hour at 30 centimeters from the radiation source or from any surface that the radiation penetrates.
- **High Radiation Area:** an area, accessible to individuals, in which radiation levels from radiation sources external to the body could result in an individual receiving a dose equivalent in excess of 0.1 rem (1 mSv) in 1 hour at 30 centimeters from the radiation source or 30 centimeters from any surface that the radiation penetrates.
- **Very High Radiation Area:** an area, accessible to individuals, in which radiation levels from radiation sources external to the body could result in an individual receiving an absorbed dose in excess of 500 rads (5 grays) in 1 hour at 1 meter from a radiation source or 1 meter from any surface that the radiation penetrates.

Dose Limits

Type	Annual Occupational Limit (Adults)	Annual Occupational Limit (Minors)	Embryo/ Fetus	Members of the Public
Total Effective Dose	5 rem (50 mSv)	0.5 rem (5 mSv)	0.5 rem (5 mSv)	0.1 rem (1 mSv); Per Year 0.002 rem (0.02 mSv); dose per hour in unrestricted areas 0.5 rem (5 mSv); Pear Year (visitors/ infrequent)
Individual Organ Excluding Lens	50 rem (500 mSv)	5 rem (50 mSv)		
Lens	15 rem (150 mSv)	1.5 rem (15 mSv)		
Skin	50 rem (500 mSv)	5 rem (50 mSv)		

Values from NCR 10 CFR 20.1201-1208.

Radiation Exposure Risk Estimates

Group	Risk Factor	NCRP Report 91	ICRP Publication 60	NCRP Report 116
Workers	Fatal cancer	1.25% per Sv	4% per Sv	4% per Sv
Workers	Non-fatal cancer	-	0.8% per Sv	0.8% per Sv
Workers	Severe genetic effects	0.4% per Sv	0.8% per Sv	0.8% per Sv
Members of the Public	Fatal cancer	-	5% per Sv	5% per Sv
Members of the Public	Non-fatal cancer	-	1% per Sv	1% per Sv
Members of the Public	Severe genetic effects	-	1.3% per Sv	1.3% per Sv
Embryo/Fetus	-	20% per Sv	-	~10% per Sv

Showing 1 to 7 of 7 entries

Radiation Worker Exposure Limits

	NCRP Report 91	ICRP Publication 60	NCRP Report 116
Based on Stochastic Effects	50 mSv annual effective dose limit 10 mSv × age (y) cumulative effective dose limit for workplace	50 mSv annual effective dose limit 100 mSv in 5 year cumulative effective dose limit	50 mSv annual effective dose limit 10 mSv × age (y) cumulative effective dose limit for workplace
Based on Deterministic Effects	150 mSv annual dose equivalent limit to lens 500 mSv annual dose equivalent limit to all other organs (e.g. red bone marrow, breast, lung, gonads, skin, extremities)	150 mSv equivalent dose limit to lens 500 mSv annual equivalent dose limit to skin, hands, and feet	150 mSv annual equivalent dose limit to lens 500 mSv annual equivalent dose limit to skin, hands, and feet
Annual Limits of Intake (ALI)	[50 mSv]/[HE (50) Bq-1]	[20 mSv]/[HE (50) Bq-1]	--
Annual Reference Levels of Intake	--	--	[20 mSv]/[HE (50) Bq-1]

Showing 1 to 4 of 4 entries

Public Exposure Limits

	NCRP Report 91	ICRP Publication 60	NCRP Report 116
Based on Stochastic Effects	1 mSv annual for continuous exposure 5 mSv annual for infrequent exposure	1 mSv annual A higher value may be acceptable if average annual over 5 years is less than 1 mSv	1 mSv annual for continuous exposure 5 mSv annual for infrequent exposure
Based on Deterministic Effects	50 mSv annual limit to lens, skin, and extremities	15 mSv annual limit to lens 50 mSv annual limit to skin, hands, and feet	50 mSv annual limit to lens, skin, and extremities
Embryo/fetus	5 mSv annual limit 0.5 mSv per month once pregnancy is known	2 mSv limit to woman's abdomen once pregnancy is declared Limit intake of radionuclides to 1/20 of ALI	0.5 mSv limit per month once pregnancy is known
Negligible Individual Dose (NID)	0.01 mSv annual per source or practice	--	0.01 mSv annual per source or practice

Showing 1 to 4 of 4 entries

Unit (Symbol)	Definition	Units
Exposure (X) $X = \frac{dQ}{dm}$	Amount of ionization per mass of air due to X-rays and gamma rays.	Roentgen (R) $1R = 2.58 \times 10^{-4} \frac{C}{kg}$
Absorbed Dose (D) $D = \frac{\text{Energy Deposited}}{\text{Mass}}$	Amount of energy imparted by radiation per unit mass.	SI: Gray (Gy) $1Gy = 1\frac{J}{kg}$ Traditional: rad 1 rad = 0.01Gy
Kerma (K) $K = \frac{dE_{tr}}{dm} = \psi(\frac{\mu_{tr}}{\rho})$	**K**inetic **E**nergy **R**eleased per unit **MA**ss Kinetic energy transferred by uncharged particles to charged particles per unit mass.	SI: Gray (Gy) $1Gy = 1\frac{J}{kg}$ Traditional: rad 1 rad = 0.01Gy
Equivalent Dose (H_T) $H_T = w_R D$	A measure of absorbed dose weighted for the biological effectiveness of the types(s) of radiation (relative to the low LET photons and electrons) to produce stochastic health effects in humans.	SI: Sievert (Sv) $1Sv = 1\frac{J}{kg}$ Traditional: rem 1 rem = 0.01Sv
Dose Equivalent (H) $H = QD$	A measure of absorbed dose weighted for the biological effectiveness of the types of radiation (relative to low LET photons and electrons) to produce stochastic health effects in humans.	Sievert (Sv) $1Sv = 1\frac{J}{kg}$ Traditional: rem 1 rem = 0.01Sv
Effective Dose (E) $E = \sum(W_T H_T)$	A measure of equivalent dose, weighted for the biological sensitivity of the exposed tissues and organs (relative to whole body exposure) to stochastic health effects in humans.	Sievert (Sv) $1Sv = 1\frac{J}{kg}$ Traditional: rem 1 rem = 0.01Sv
Effective Dose Equivalent (HE) $H_E = \sum(W_T H)$	A measure of equivalent dose, weighted for the biological sensitivity of the exposed tissues and organs (relative to whole body exposure) to stochastic health effects in humans.	Sievert (Sv) $1Sv = 1\frac{J}{kg}$ Traditional: rem 1 rem = 0.01Sv

C/kg is SI

Equivalent Dose (H)

Equivalent dose represents the stochastic health effects of low levels of ionizing radiation to the human body.

$$H_T = \sum_R (W_R \times D_{T,R})$$

Radiation Weighting Factors

Radiation Type	W_R
X-rays, gamma rays, electrons and muons	1
Neutrons	• <10keV: 5 • 10-100keV: 10 • 100keV - 2MeV: 20 • 2MeV-20MeV: 10 • >20Mev: 5
Protons > 2MeV	2
Alpha particles, fission fragments and non-relativistic heavy nuclei	20

Source: ICRP 60

Key Point: Although neutrons are indirectly ionizing, they have a high radiation weighting factor. This is because they transfer their energy to protons which have a high LET due to their charge and large mass.

Effective Dose (E)

Effective dose uses tissue weighting factors to compare the risk of stochastic effects from a specific distribution of doses to organs with the risk of stochastic effects of a uniform whole body dose. This is achieved by multiplying *equivalent dose* (H_T) to a tissue with a *tissue weighting factor* (w_T) and summing for all tissues.

$$E = \sum_T (w_T \times H_T)$$

Because the *tissue weighting factors* (w_T) were developed based on stochastic risks for a generic population of diversified age and gender, values of *effective dose* represent stochastic risk to a generic population rather than to any individual. Further, because these values are somewhat subjective, *tissue weighting factors* vary between the reports of different agencies.

Tissue Weighting Factors (W_T)

Organ	**W_T**
Gonads	0.20
Red bone marrow Colon Lung Stomach	0.12
Bladder Breast Liver Esophagus Thyroid	0.05
Skin Bone surface	0.1
Remainder	0.05
Total	**1.0**

Data from Table 1.1 of NCRP 116

1.1 Release of Patients Based on the Administered Activity

One means that licensees may use to comply with the dose limit in 10 CFR 35.75(a) is to release patients from licensee control if the dosage administered is not greater than the activity in Column 1 of Table 1. The total effective dose equivalent is approximately equal to external dose because the portion of the internal dose that contributes to the total external dose exposure is small or negligible (see Appendix B, Section B-3). The activities in Table 1 are based on a total effective dose equivalent of 5 mSv (0.5 rem) to an individual using the following conservative assumptions:

Average annual dose for an American is quoted to be about 6.4 mSv (3.2 mSv natural, 3.2 mSv man-made)

ALARA

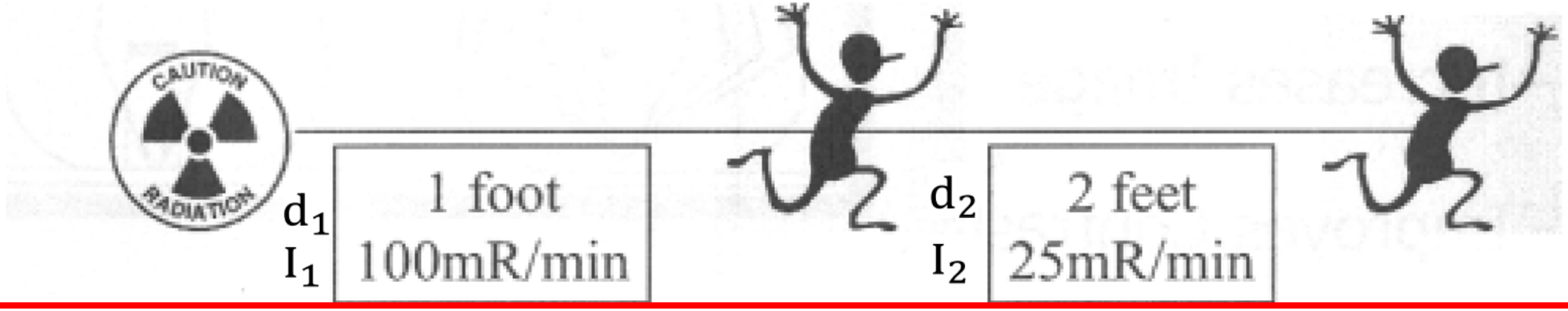
- AS LOW AS REASONABLY ACHEIVABLE

Use Factor (U)

Definition: Use factor is the fraction of the workload at which the treatment beam is directed at a given primary barrier.

- Lead aprons are near useless for HIGH ENERGY GAMMA EMISSIONS.
- GM survey meters are great for finding tiny, somewhat low activity things!

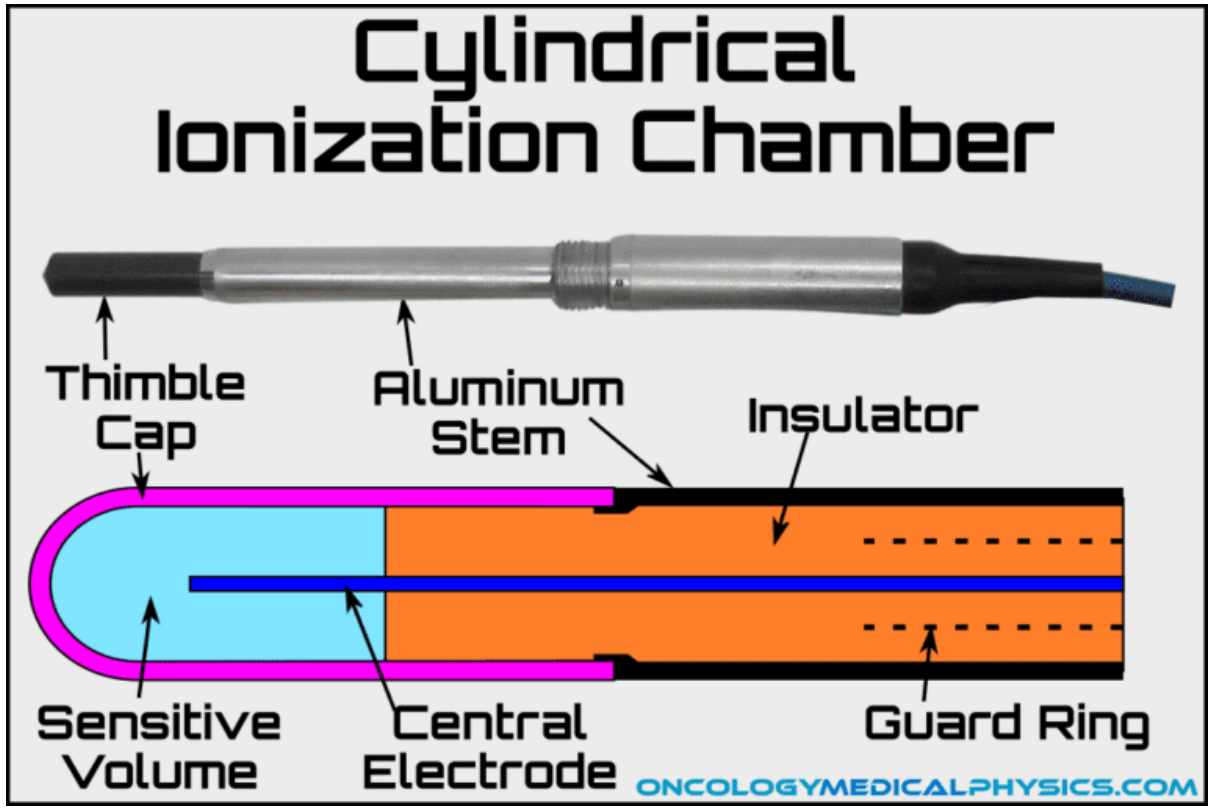
The Inverse Square Law: $\frac{I_1}{I_2} = \frac{(d_2)^2}{(d_1)^2}$

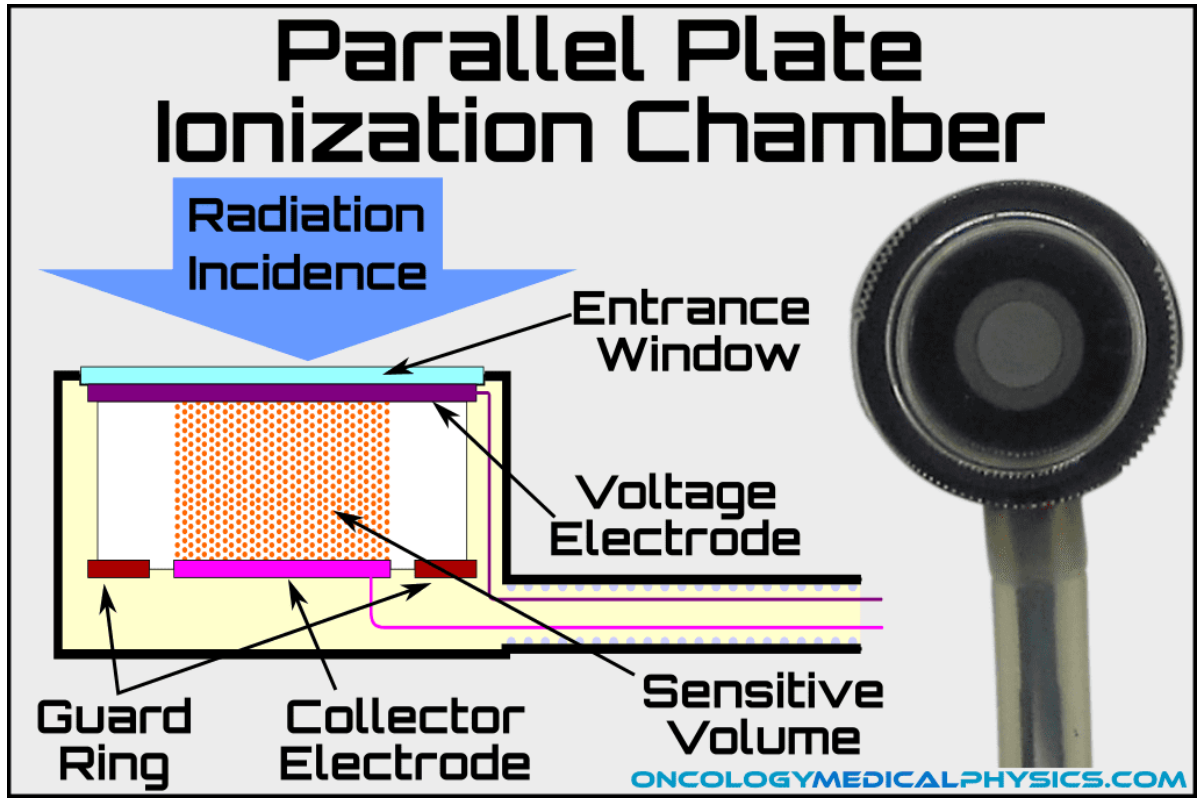


Exposure Rates are Example only - running from Radiation not a good idea.

POP QUIZ TIME

Please identify each correctly ☹


Cylindrical
Ionization Chamber
Thimble
Cap
Aluminum
Stem
Insulator
Sensitive
Volume
Central
Electrode
Guard Ring
ONCOLOGYMEDICALPHYSICS.COM


Parallel Plate
Ionization Chamber
Radiation
Incidence
Entrance
Window
Voltage
Electrode
Guard
Ring
Collector
Electrode
Sensitive
Volume
ONCOLOGYMEDICALPHYSICS.COM

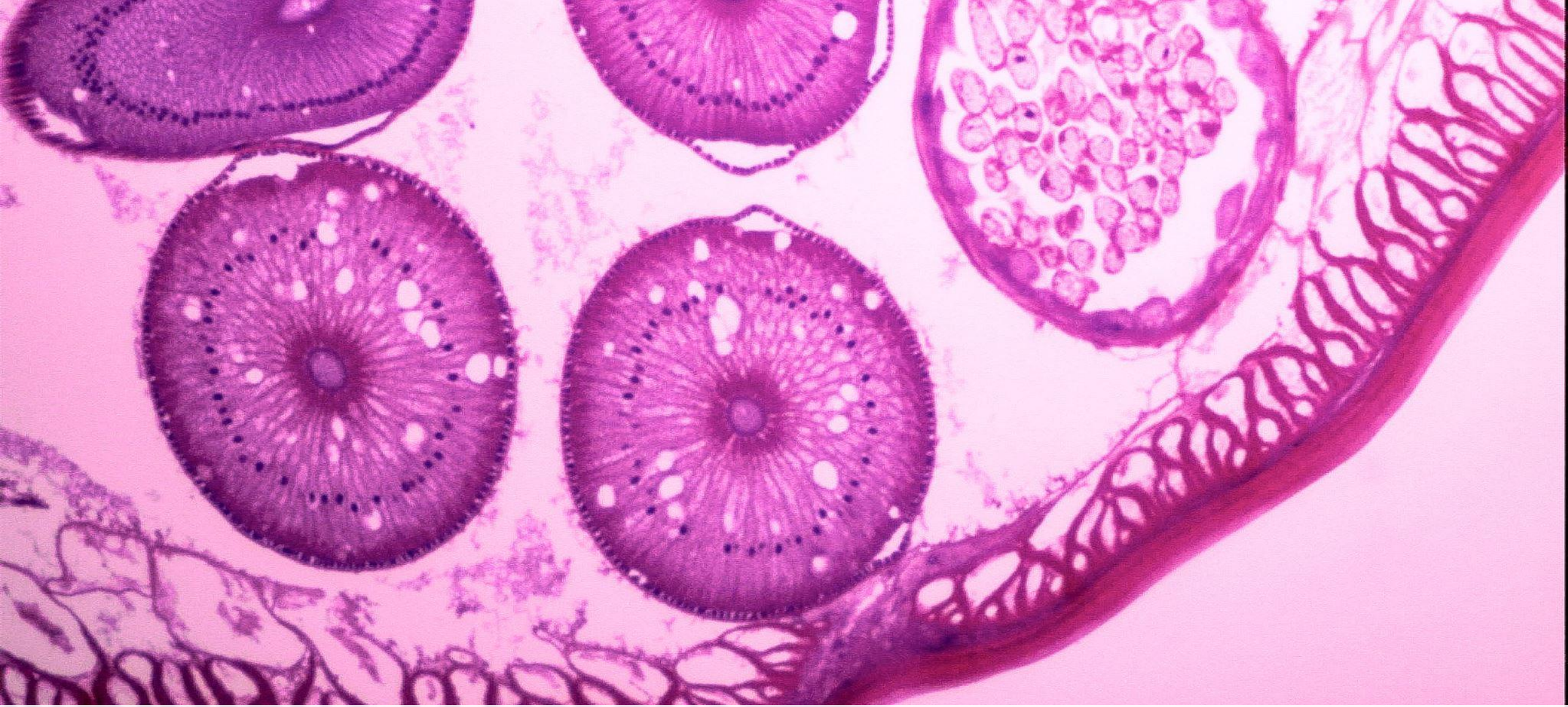
Pancake Probe Geiger Counter

Radiation: X-ray, Gamma, Beta, Alpha
Operating Voltage: 900V
Accuracy: +/-20%

ONCOLOGYMEDICALPHYSICS.COM

CAPINTEC, INC.
CRC-55t. 3.08
F18
Ga67
In111
Tc99m
I123
I131
Xe133
Tl201
Dose Decay
Sep 23 2013 14:48
5.80 uCi
Tc99m
Technetium 6.01 hr
Cal #: 080
Ch: 1, R
Print
Setup
CRC-55tR

Standard Probe Geiger Counter



AN OVERVIEW OF RADIOPHARMACEUTICAL PROCEDURES

Bird's Eye View,

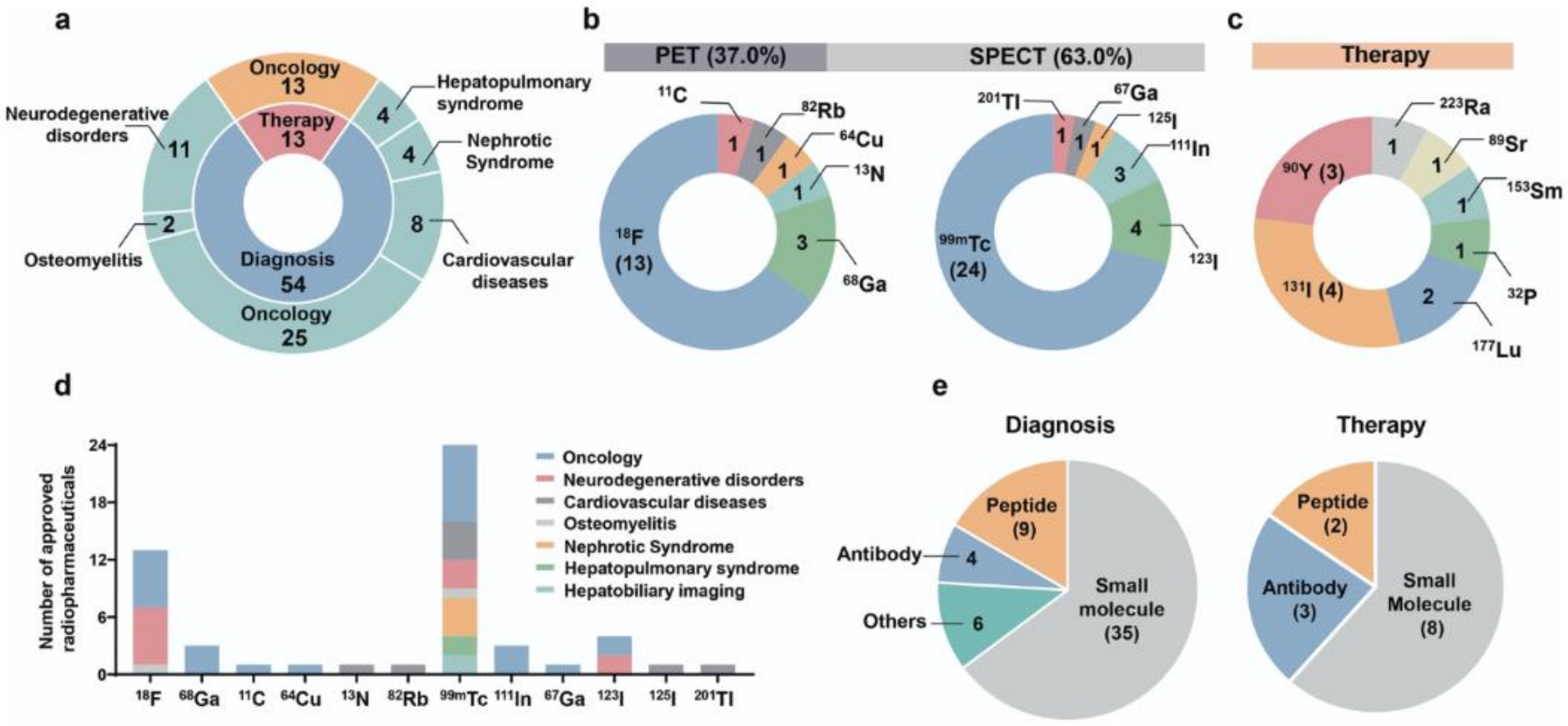
As The Crow Flys

Signal Transduction and Targeted Therapy www.nature.com/sigtrans

REVIEW ARTICLE OPEN

Radiopharmaceuticals and their applications in medicine

Siqi Zhang[1], Xingkai Wang[1], Xin Gao[1], Xueyao Chen[1], Linger Li[1], Guoqing Li[1], Can Liu[1], Yuan Miao[1], Rui Wang[1,2]✉ and Kuan Hu[1]✉



Radiotheranostics

"Theranostics" is a term derived from the combination of "therapeutics" and "diagnostics." Because the diagnostic molecule helps refine the treatment plan for each patient, such as selecting appropriate treatment options and adjusting dosages, theranostics can contribute to the development of personalized medicine.[45,46] Between 2016 and 2018, the FDA successively approved [^{68}Ga]Ga-DOTA-TATE and [^{177}Lu]Lu-DOTA-TATE for the diagnosis and treatment of well-differentiated neuroendocrine tumours (NETs).[47] In 2022, [^{177}Lu]Lu-PSMA-617 was approved for the treatment of metastatic castration-resistant prostate cancer (mCRPC) patients,[32] increasing the popularity of the theranostic approach in the field of nuclear medicine and indicating promising directions for its future development.

Table 3. Radiopharmaceutical therapy agents approved wordwide

	Radionuclides	Type	Agent	Targets	Indication
4 Bones	Radium-223	α	[^{223}Ra]$RaCl_2$	As a calcium mimic accumulating in bone[554]	Prostate cancer bone metastases
	Phosphorus-32	β	[^{32}P]Sodium orthophosphate	Major bone deposition[69]	Palliation of bone pain due to metastases
	Strontium-89	β	[^{89}Sr]$SrCl_2$	As a calcium mimic accumulating in bone[69,70]	Prostate cancer bone metastases
	Samarium-153	β	[^{153}Sm]Lexidronam	As a calcium mimic accumulating in bone[71]	Relieving pain associated with bone metastasis
2 Prostate	Lutetium-177	β	[^{177}Lu]Lu-PSMA-617	PSMA	mCRPC
			[^{177}Lu]Lu-DOTA-TATE	SSTR	NETs
3 Liver	Yttrium-90	β	[^{90}Y]Resin microspheres	Selective internal radiation therapy	Hepatocellular carcinoma
			[^{90}Y]Glass microspheres	Selective internal radiation therapy	Hepatocellular carcinoma
			[^{90}Y]Y-DTPA-ibritumomab tiuxetan	CD20	Non-Hodgkin's follicular lymphoma
4 Thyroid	Iodine-131	β	[^{131}I]MIBG	Norepinephrine tansporter[73]	NETs
			[^{131}I]Sodium iodinate	Sodium Iodide Symporter[555]	Hyperthyroidism and thyroid carcinoma
			[^{131}I]Metuximab	CD147[556]	Hepatocellular carcinoma
			[^{131}I]Tositumomab	CD20	Non-Hodgkin's follicular lymphoma

TEACHING YOU WHAT I KNOW

- I've only ever seen Lu-177 (prostate) and Ra-223 (bone) here at Karmanos
  - Pluvicto
  - Lutathera
  - Xofigo
- I watched a student lecture on Y-90 microspheres (Andrew Lucas!)

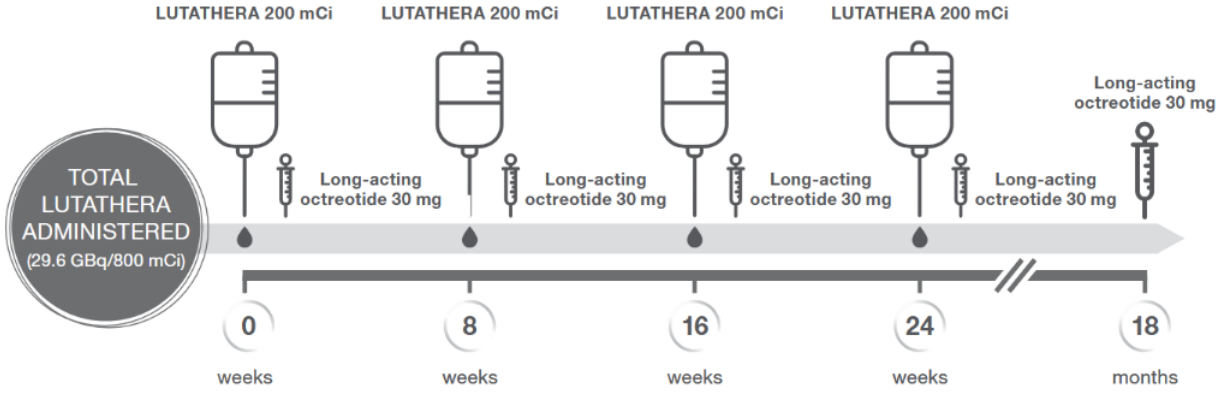
LUTATHERA

(Lu-DOTA-TATE)

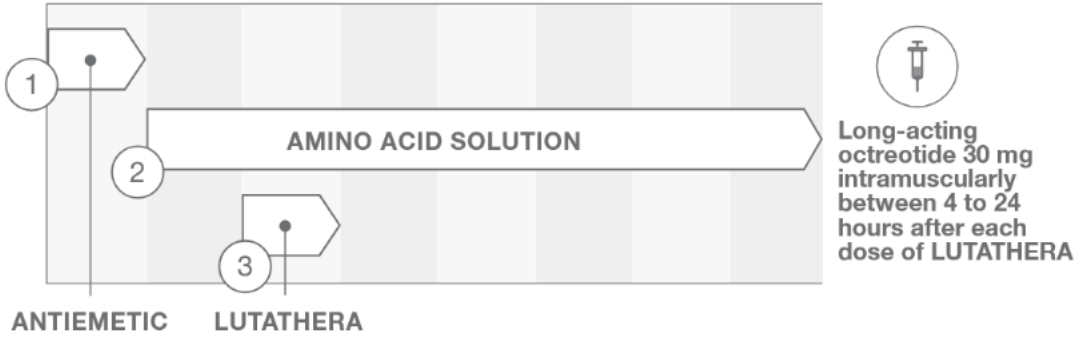
Injection of LUTATHERA containing 370 MBq/mL (10 mCi/mL) of lutetium Lu 177 dotatate is supplied in a colorless, Type I, glass, 30-mL, single-dose vial containing 7.4 GBq (200 mCi) ± 10% of lutetium Lu 177 dotatate at the time of injection. The solution volume in the vial ranges between 20.5 mL to 25 mL to provide a total of 7.4 GBq (200 mCi) of radioactivity.[1]

Treatment Regimen for LUTATHERA

Administer premedications and concomitant medications as recommended in the full Prescribing Information.[1]
Monitor patients with laboratory testing as needed.[1]

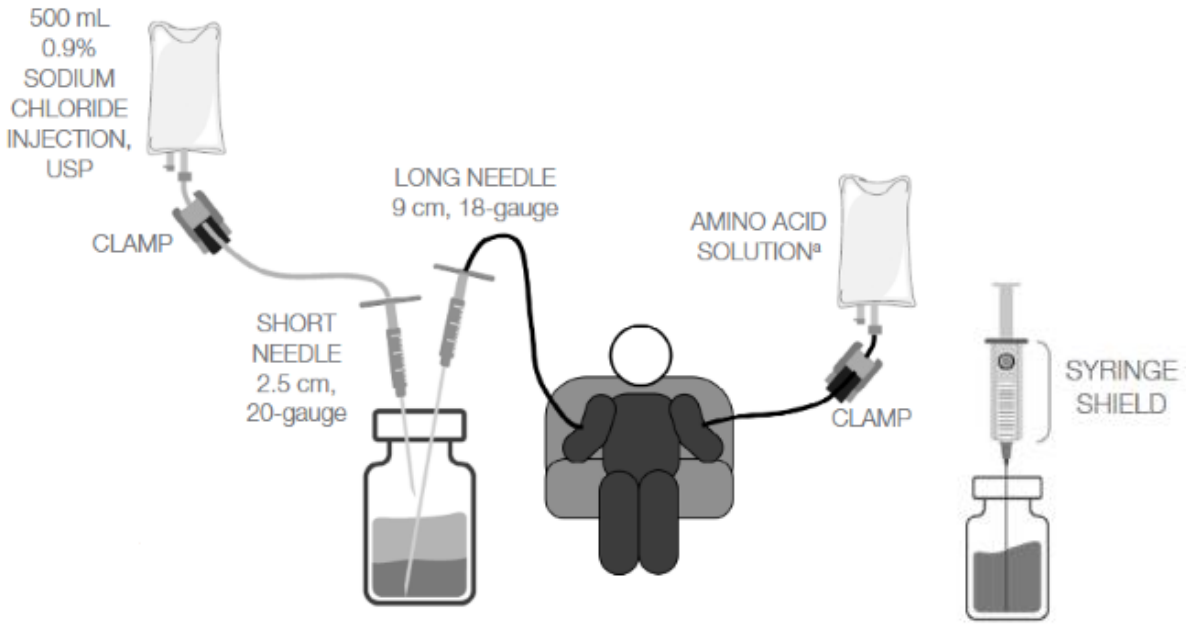


Example Timeline[1]

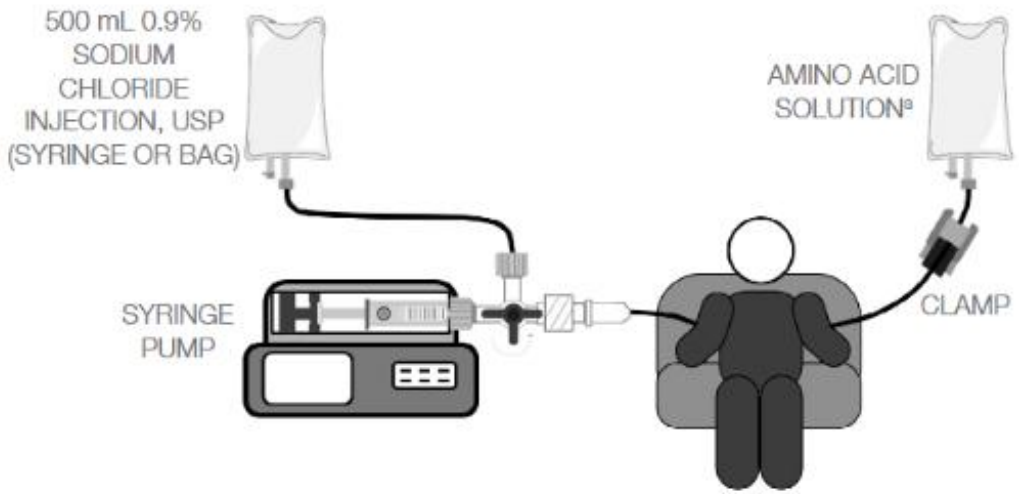


LUTATHERA METHODS

ADMINISTRATION SETUP OF GRAVITY METHOD



ADMINISTRATION SETUP OF SYRINGE PUMP METHOD



Physical Data	
Gamma constant	0.028 mrem/h per mCi at 1.0 meter (7.636E-6 mSv/h per MBq at 1.0 meter)[7]
Half-life (T½)	Physical T½: 6.647 d[1] Biological T½[a]: GI: ~1 d; lungs: ~30 d; incorporated fraction (<10%): ~4 y[7] Effective T½: GI: ~0.9 d; lungs: ~6 d; incorporated fraction (<10%): ~6.7 d[7]
Specific activity	1.1E5 Ci/g [4.1E15 Bq/g] maximum[7]

[a]Interpolation from intake retention factors at ~1% remaining, from NUREG/CR-4884 Interpretation of Bioassay Measurements (US Nuclear Regulatory Commission, 1987), p. B-295.

Recommended Shielding[7]		
Photons		
Lead	Half-value layer	0.6 mm (0.02 in)
	Tenth-value layer	2.1 mm (0.08 in)
Betas[a]		
Specific activity	Half-value layer	0.135 cm
The accessible dose rate should be background but must be <2 mR/h		

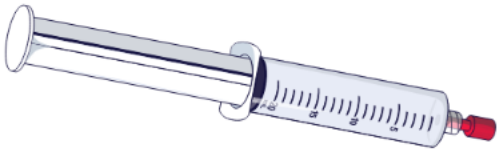
Example of patient bathroom preparation

PLUVICTO

(Lu-PSMA-617)

Not actual size.

Single-dose vial[1]



Not actual size.

Pre-filled syringe[1,2]

TREATMENT ROOM AND BATHROOM PREPARATION[9,*]

- A **treatment room** with a dedicated bathroom in proximity is helpful to have for the day. Consider using caution with patients who have urinary incontinence. For patients with urinary incontinence, be sure to follow guidelines from your institution. Vomit, urine, and feces should be disposed of according to regulations as possible radioactive waste
- Prepare **bathroom** to minimize potential radioactive contamination from bodily fluids in accordance with institutional guidelines

*Based on institutional practices or guidelines.

Timline:
THERE IS NONE! HAH
1 min push at Karmanos, no other medications

SYRINGE METHOD[1,*]

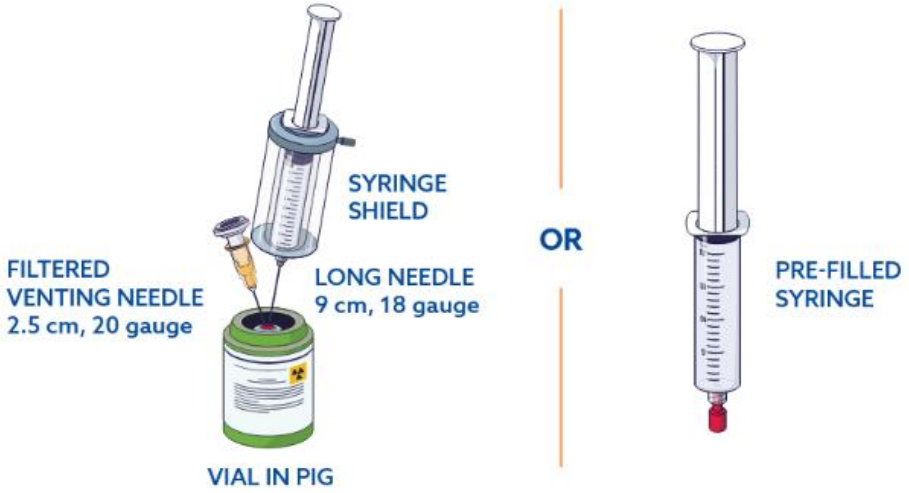
SETUP

WHEN USING A PRE-FILLED SYRINGE, BEGIN AT STEP 2.

STEP 1:

Withdraw desired radioactivity dose from PLUVICTO vial using a syringe fitted with a syringe shield and disposable sterile needle.

Other methods of intravenous administration may be chosen per institutional practice.



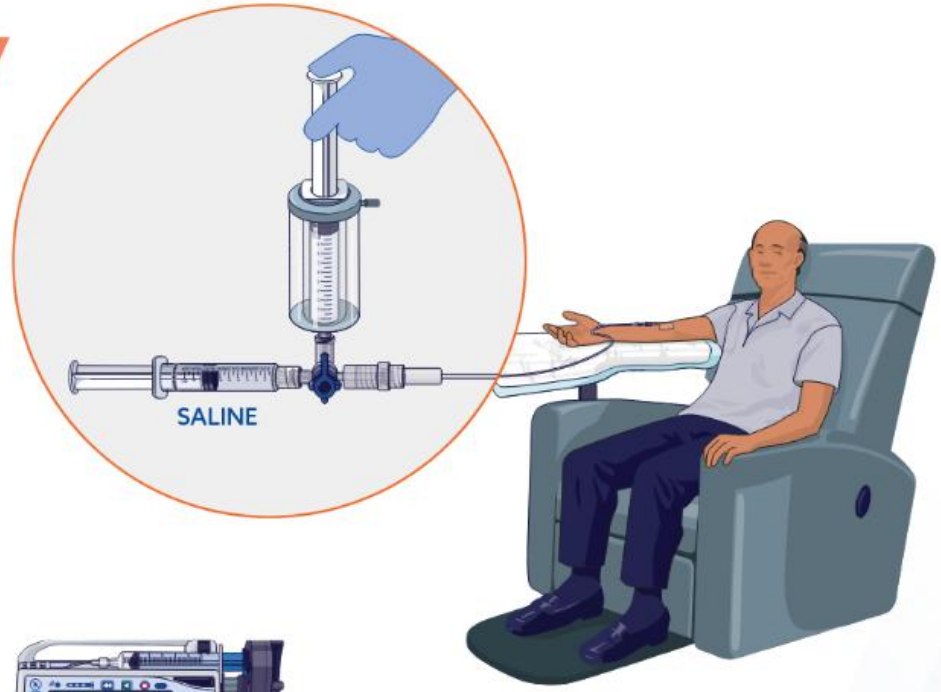
ADMINISTRATION

STEP 2:

Using the syringe, administer PLUVICTO by **slow intravenous push** within approximately 1 to 10 minutes (with a syringe pump or manually).

STEP 3:

Flush port with ≥10 mL of 0.9% sterile sodium chloride solution.



SYRINGE PUMP

*The illustration above shows the syringe method without a syringe pump. The syringe method may also be used with a syringe pump.

Images are for illustrative purposes only. Illustrations may show different positioning and/or scale of equipment than actual clinical setup for administration.

GRAVITY METHOD[1,*]

When using the gravity method for a reduced dose, adjust the PLUVICTO dose before the administration to avoid the delivery of an incorrect volume of PLUVICTO.

PLUVICTO is administered slowly via intravenous route, preceded and followed by a saline flush. PLUVICTO may be administered by 3 methods: As an injection using a disposable syringe fitted with a syringe shield (with or without a syringe pump), as an infusion using the gravity method (with or without an infusion pump), or as an infusion using the vial (with a peristaltic infusion pump).[1]

A reduced dose of PLUVICTO should be administered using the syringe method (with or without a syringe pump) or the vial method (with a peristaltic infusion pump).[1]

SETUP

STEP 1:

Connect the short needle via a catheter to 500 mL of 0.9% sterile sodium chloride solution (used to transport PLUVICTO during infusion).

Insert the short needle into the PLUVICTO vial.

The short needle **must not** touch the solution of PLUVICTO in the vial.

Do not connect the short needle directly to the patient.

Do not allow the 0.9% sterile sodium chloride solution to flow into the PLUVICTO vial prior to initiation of infusion.

Do not inject PLUVICTO solution directly into the 0.9% sterile sodium chloride solution.

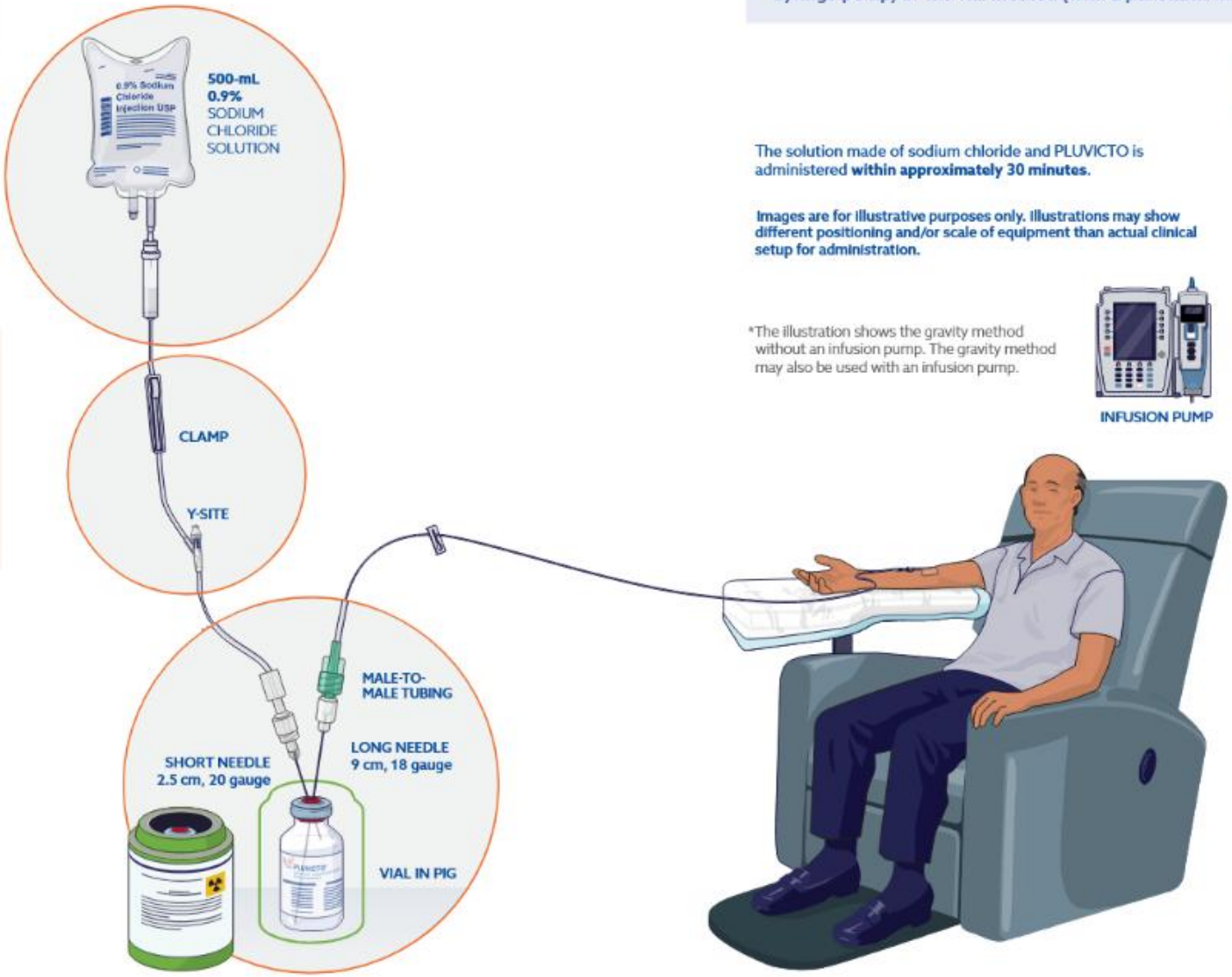
STEP 2:

Insert the long needle into the PLUVICTO vial.

The long needle **must touch** and be secured to the bottom of the PLUVICTO vial during the entire infusion.

STEP 3:

Connect the long needle to the intravenous catheter or access via a catheter that is pre-filled with 0.9% sterile sodium chloride solution (used only for PLUVICTO infusion into the patient's arm).



The solution made of sodium chloride and PLUVICTO is administered **within approximately 30 minutes.**

Images are for illustrative purposes only. Illustrations may show different positioning and/or scale of equipment than actual clinical setup for administration.

*The illustration shows the gravity method without an infusion pump. The gravity method may also be used with an infusion pump.

INFUSION PUMP

ADMINISTRATION

STEP 4:

Use a clamp or an infusion* pump to regulate the flow and ensure that the level of the solution in the PLUVICTO vial remains constant.†

The 0.9% sterile sodium chloride solution entering the vial through the short needle will carry PLUVICTO from the vial to the patient.

†Monitor variations in the level and take appropriate action per your institutional practices or guidelines.

STEP 5:

Once the level of radioactivity is stable for at least 5 minutes, clamp or stop the infusion pump to stop the flow of 0.9% sterile sodium chloride solution into the vial, and disconnect the vial from the long needle line.

STEP 6:

Flush the patient's intravenous catheter with ≥10 mL of 0.9% sterile sodium chloride solution.

XOFIGO

($Ra\text{-}Cl_2$)

given at 4-week intervals for 6 injections

Volume to be administered (mL) =

$$\frac{\text{Body weight (kg)} \times (55\ \text{kBq})/\text{kg body weight}}{\text{Decay factor} \times 1{,}100\ \text{kBq/mL}}$$

or:

$$\frac{\text{Body weight (kg)} \times (1.49\ \mu\text{Ci})/\text{kg body weight}}{\text{Decay factor} \times 30\ \mu\text{Ci/mL}}$$

STEPS FOR ADMINISTRATION:

Step 1:
Assay the dose immediately before and after administration (see dose calibration procedure flashcard for further instructions on how to determine a dial setting for Ra 223).

Step 2:
Prepare the infusion environment by placing absorbent materials in the immediate area where the injection will take place.

Step 3:
Insert the intravenous cannula or instrument as required per your institution for injection. Connect a 2- or 3-way stopcock to the IV device.

Step 4:
Open the stopcock to allow for flushing of the infusion set-up prior to injection of Xofigo, in order to minimize the risk of extravasal administration. Flush the infusion set to confirm IV patency.

Step 5:
If IV patency is confirmed, remove the red cap from the syringe containing Xofigo and attach to the open port of the stopcock. Turn the stopcock so that it is closed to the saline syringe and open from the Xofigo syringe to the patient.

Step 6:
Administer Xofigo by slow intravenous injection over 1 minute. When the infusion is complete, turn the stopcock to shut off the Xofigo syringe and open the saline syringe. Flush the infusion system thoroughly with isotonic saline per institutional procedure.

Step 7:
Remove the syringes and injection set-up. Assay for residual activity and dispose of according to institutional policies (please see the Storage and Handling Guide for additional information).

OPTIONAL:

A syringe shield may be utilized according to institutional policy.

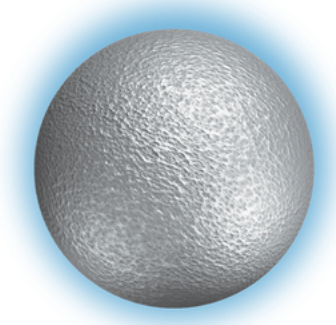
Y-90 MICROSPHERES

Mechanism of action = radiation

TheraSphere is uniquely engineered to have unmatched radiation per microsphere (RPM), maximizing lethal hits to tumor DNA and driving tumor cell death.

TheraSphere Y-90 Glass Microsphere

Radiation is embedded within the glass matrix, providing greater RPM

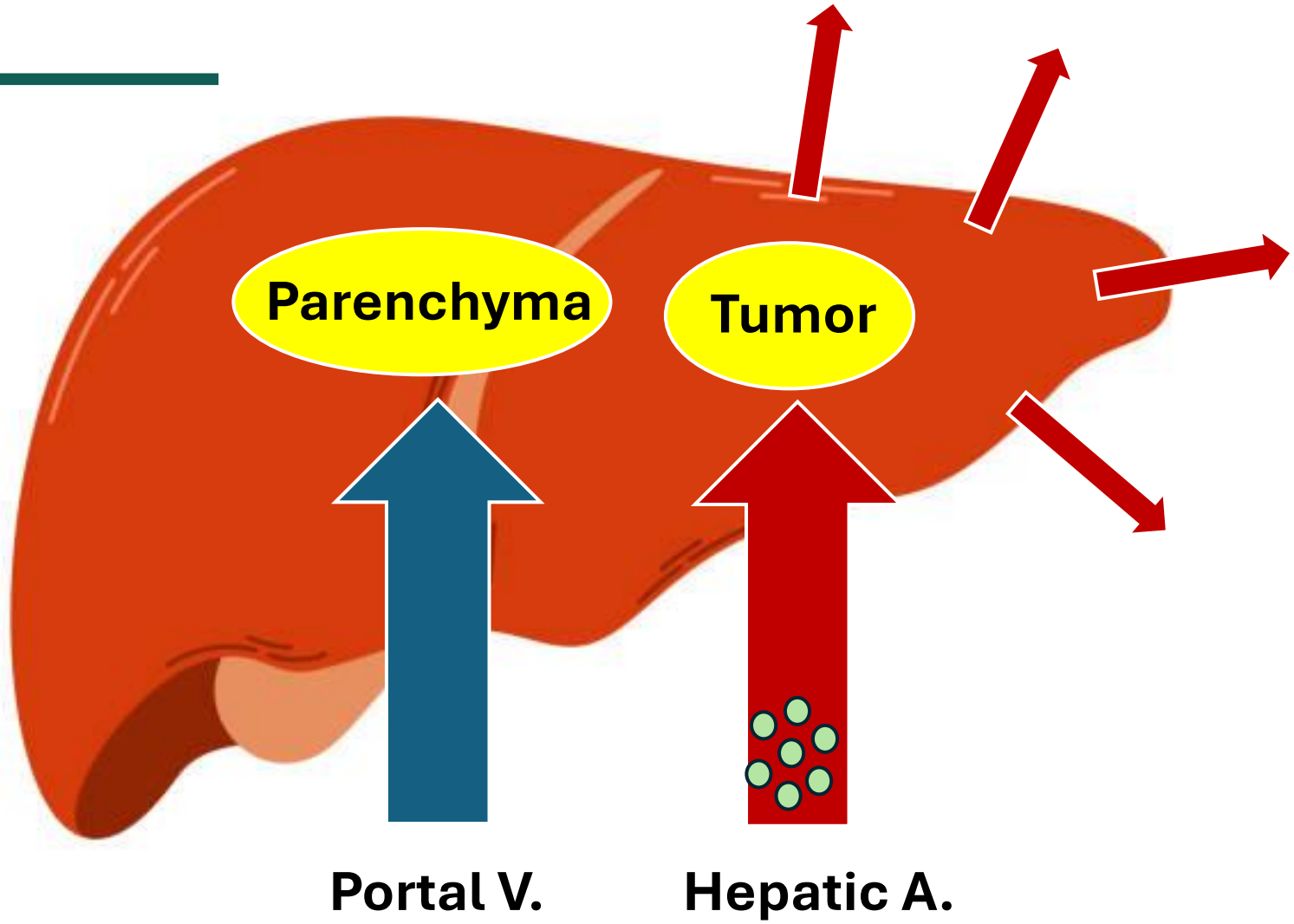


Y-90 Resin Microsphere

Radiation is only coated onto the surface area of the resin sphere,[1] limiting RPM

What is it?

- Tumors / mets are initially supplied by the portal v.
- Their size compresses the veins, destroying them
- Angiogenic factors signaled in hepatic artery
- New, leaky hepatic vessels sprout around tumors



Dose Regimens

- Single, permanent implant (LDR)
  - Dose rates ~ 200 Gy / 64 hrs = 3 Gy/hr
  - 40-80 million spheres, 300 Bq / sphere

- SIRT may induce cold spots that SBRT can help:
  - May be delivered in 1, 3, or 5 fractions (8-16 Gy/fx)
  - Given either daily or every other day

- "Fractionation":
  - Treat one lobe, let it recover (4-6 weeks), then treat the other
  - Treat one segment, let it recover (8-12 weeks), then treat it again

What to expect

After reviewing all treatment options with you, your cancer care team may recommend Y-90 treatment. The first step is to examine your liver's blood supply. A series of CT or MRI scans help map out the liver's blood vessels. These images also determine the size and location of your liver tumors.

Next, the team determines a treatment plan and identifies which vessels will be injected with Y-90. They also will recommend the number of treatments.

An interventional radiologist inserts a small tube, called a catheter, into an artery in the groin or wrist and threads it to the identified vessels that supply blood to your tumors. The radioactive beads are injected through the catheter into the blood vessels. The beads emit radiation into the tumor's blood supply for a short period.

Y-90 treatments are completed in a hospital procedure room, and you can go home the same day as the treatment. Side effects are usually limited but may include fatigue or mild abdominal pain. Multiple treatments may be necessary depending on the stage and location of your liver cancer.