Establishing a Dosimetry Planning Program for Theranostic Radiopharmaceutical Therapy in a Large Community Hospital

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feel whole.

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Disclosures

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Objectives

01

PROGRAM SETUP

The attendee will learn the basics of setting up a radiopharmaceutical program in a community hospital setting.

02

DOSIMETRY BASICS

They will learn the basics of dosimetry planning for radiopharmaceuticals.

03

COMMUNITY RPT

They will learn the nuances of establishing the RPT dosimetry process in the non-academic setting.

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Brief Introduction

- Central Florida since 1994
- TRP License #16 (Therapy)
- Been doing RPTs for all of that time
- Dosimetry Program for RPT (Theranostics)
- Faculty, John Patrick University, Medical Dosimetry/Physics program- Brachytherapy
- Served with AAPM:
  - RPT Science Subcommittee
  - WG for Medical Errors in Brachytherapy
  - FLAAPM-State Chapter President - 2024-2026

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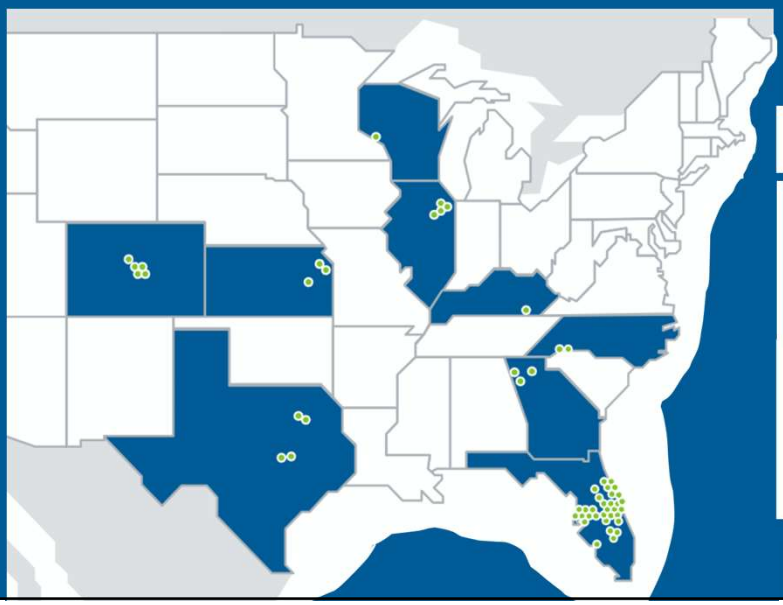

55 Hospital campuses in NINE states

27 Offsite EDS

17 Home health and hospice agencies

58 Urgent care facilities

100,000+ Team Members

9 MILLION + Patients served annually

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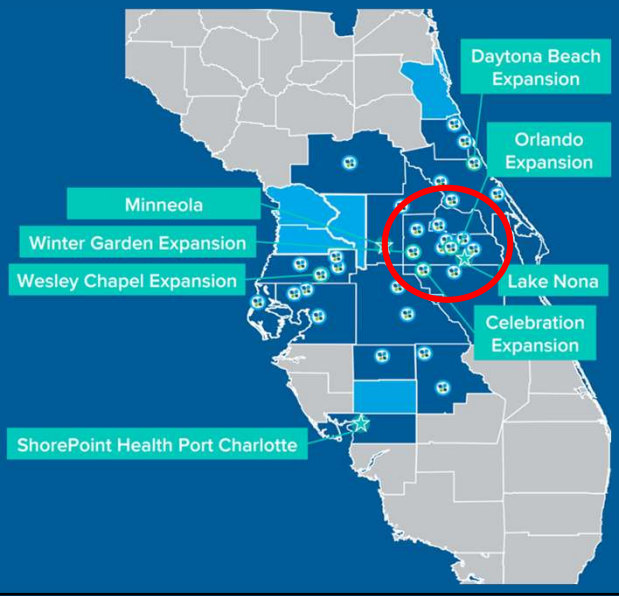
Adventhealth | Regional Footprint



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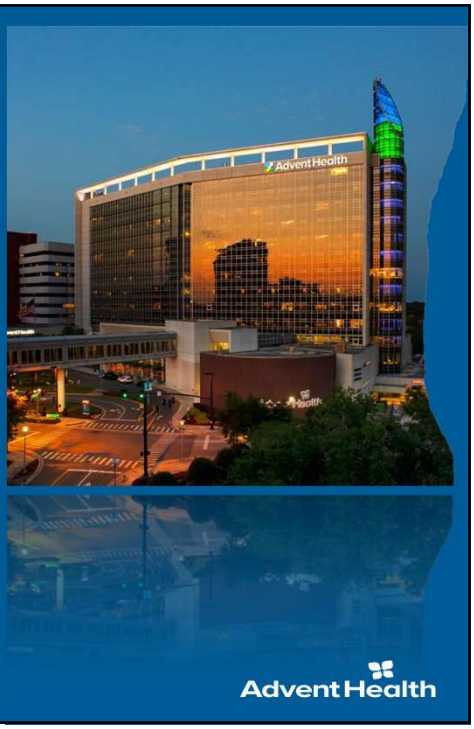
HISTORY OF RPT at AdventHealth

- Radioactive I-131- Suppression /Ablation/ In-patient / Liquid application / Special renal precautions I131 and dialysis
- Metastron (Sr-89) for bone mets *(past)*
- Quadramet (Sm-153 for bone mets) *(past)*
- Xofigo Ra-223
- Liquid I-125 GliaSite brain treatments *(past)*
- Busy Y90 radioembolization program

Started dosimetry program more recently and are starting several clinical trials, including a couple with alpha emitters



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Push for Radiopharmaceuticals

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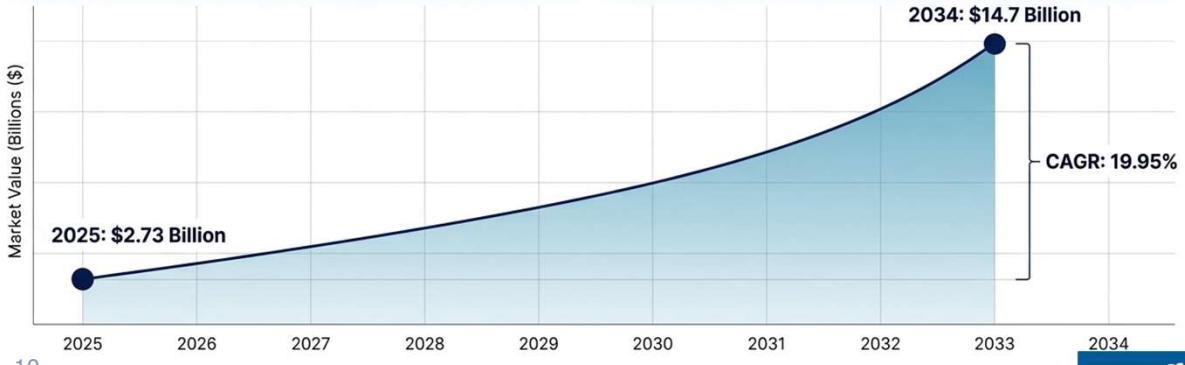
Macro Trajectory: A $14.7B Market by 2034

Geographic Dominance

North America is driving 80.95% of current global market share, supported by robust reimbursement and domestic production capabilities.

Widening Indications

Expanding beyond prostate (PLUVICTO) and neuroendocrine (LUTATHERA) tumors into glioblastoma, medulloblastoma, and pediatric applications.



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The Big Pharma Stampede Validates the Science

2021
- **Bristol Myers Squibb** — $3.1B acquisition of RayzeBio (Dec 2023)

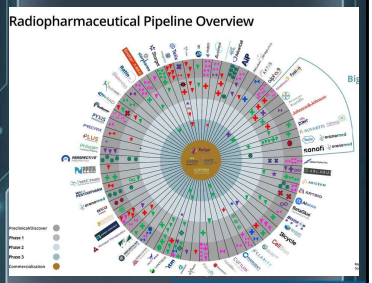
2022
- **Eli Lilly** — $1.4B acquisition of Point Biopharma (Dec 2023) & $1.0B acquisition of Radionetics Oncology (Jul 2024)

2023
- **Novartis** — $1.75B acquisition of Mariana Oncology (May 2024)
- **Novartis**

2024
- **AstraZeneca** — $2.5B acquisition of Fusion Pharmaceuticals (Mar 2024)
- **AstraZeneca**

>90 Deals
Executed in just 3 years

>$400M
In recent IPO financing



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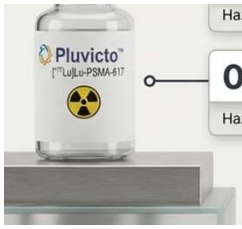
Radiopharmaceutical Therapy is a New Pillar of Cancer Care

Recent phase 3 trials (VISION, NETTER-1) have solidified RPT's role, achieving clinically relevant hazard ratios (OS HR of 0.62, PFS HR of 0.18).

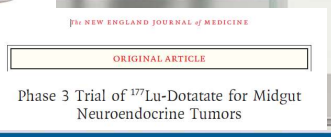
Overall Survival (OS):	15.3 months vs. 11.3 months
OS Hazard Ratio:	0.62 (38% risk reduction)
rPFS Hazard Ratio:	0.40 (60% risk reduction)

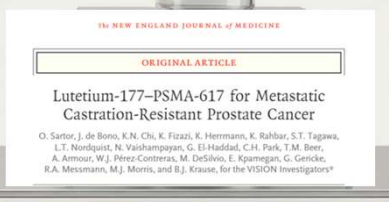
Median OS:	48.0 months vs. 36.3 months (+11.7 mo)
PFS Hazard Ratio:	0.18 (82% risk reduction)
Safety Profile:	Low long-term severe nephrotoxicity (5%)



0.40 PFS
Hazard Ratio (VISION)

0.18 PFS
Hazard Ratio (NETTER-1)





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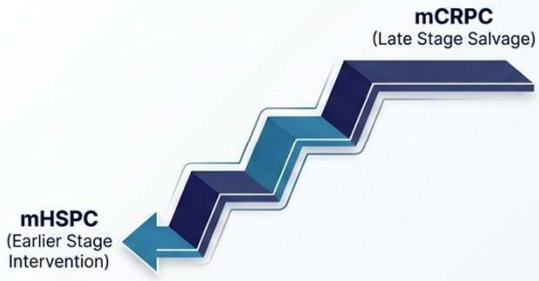
Expanding the Horizon: Earlier Intervention

The Clinical Shift



Quality of Life

The PSMAddition Trial

Moving Pluvicto into metastatic hormone-sensitive prostate cancer.

Efficacy: 28% reduction in the risk of progression or death (HR 0.72).

Longitudinal Patient-Reported Outcomes (PROs)

A modest, transient decline in functional well-being occurs during active therapy, but scores reliably return to standard-therapy baselines. No sustained deterioration is observed.

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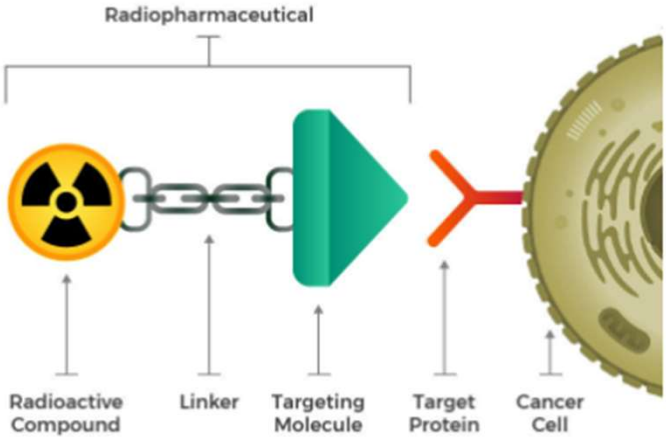
What is a r

Drug with radiation (cl
radiation)

Targeting molecule – l
radioactive compound

Therapy versus diagnc
what's the difference ?
a good/bad imaging a
good/bad therapeutic



Radiopharmaceuticals consist of a radioactive molecule, a targeting molecule, and a linker that joins the two.

Credit: National Cancer Institute

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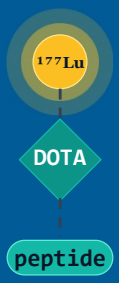
MECHANISM OF ACTION

How Radiopharmaceuticals Work

A targeting molecule delivers a radioactive payload directly to diseased cells — sparing healthy tissue.

01 · ANATOMY
Three-part molecule

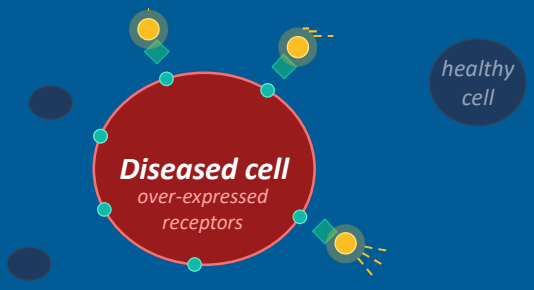


Radionuclide
Unstable isotope that emits the radiation — β^- or α for therapy, γ or β^+ for imaging.

Chelator
Cage-like molecule (e.g., DOTA) that locks the radionuclide to the targeting vector.

Targeting vector
Peptide or antibody that recognizes a receptor over-expressed on diseased cells (e.g., PSMA, SSTR).

02 · IN THE BODY
Targeted binding & local emission



The vector locks onto its receptor; the radionuclide then deposits its dose over a short range — a few cell-diameters for β^- (^{177}Lu), micrometers for α (^{225}Ac).

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FDA-Approved Radiopharmaceuticals for Therapy

Includes withdrawn and limited-use agents · As of 2025

Brand Name / Agent	Radionuclide	Emission	Indication	Approval Year	Status	Mechanism of Targeting
Sodium Iodide ^{131}I (various brands)	Iodine-131	β^-, γ	Thyroid cancer; hyperthyroidism	1951	Active	NIS-mediated iodine uptake in thyroid tissue
Sodium Phosphate ^{32}P (generic)	Phosphorus-32	β^-	Polycythemia vera; bone mets	~1952	Limited / Rare	Phosphate metabolism → bone/marrow incorporation
Metastron® (Strontium-89 chloride)	Strontium-89	β^-	Bone pain palliation (osteoblastic mets)	1993	Limited / Rare	Calcium mimetic → hydroxyapatite in bone mets
Quadramet® (Samarium-153 lexidronam)	Samarium-153	β^-, γ	Bone pain palliation (osteoblastic mets)	1997	Limited / Rare	EDTMP chelate → hydroxyapatite in bone mets
Zevalin® (^{90}Y ibritumomab tiuxetan)	Yttrium-90	β^-	Relapsed/refractory follicular NHL	2002	Limited / Rare	Anti-CD20 monoclonal antibody (ibritumomab)
Bexxar® (^{131}I tositumomab)	Iodine-131	β^-, γ	Relapsed/refractory follicular NHL	2003	Withdrawn	Anti-CD20 monoclonal antibody (tositumomab)
Xofigo® (Radium-223 dichloride)	Radium-223	α, γ	mCRPC with symptomatic bone mets, no visceral mets	2013	Active	Calcium mimetic → osteoblastic bone mets (alpha emitter)
Azedra® (^{131}I iobenguane / MIBG)	Iodine-131	β^-, γ	Iobenguane-avid pheochromocytoma/paraganglioma	2018	Active	Norepinephrine transporter (NET) uptake in chromaffin tumors
Lutathera® (^{177}Lu DOTATATE)	Lutetium-177	β^-, γ	Somatostatin receptor+ GEP-NETs (SSTR2)	2018	Active	Somatostatin analogue (DOTATATE) → SSTR2 overexpression
Pluvicto® (^{177}Lu vipivotide tetraxetan	Lutetium-177	β^-, γ	PSMA-positive mCRPC (post-AR	2022	Active	Small molecule PSMA ligand → PSMA

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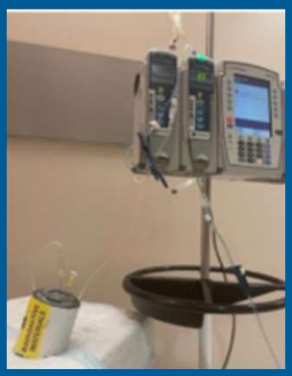
How do we "do" radiopharmaceuticals?

U.S.NRC
United States Nuclear Regulatory Commission
Protecting People and the Environment



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The First ^{131}I Administration for Graves' Disease: Theronostics' Birthplace

- Saul Hertz, M.D. (April 20, 1905 – July 28, 1950) laid the foundation of iodine physiology that made radioactive iodine therapy possible
- Dr. Hertz (at age 35) performed the first ^{131}I treatment, administering 2.1 mCi to a patient with Grave's disease on March 31st, 1941

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DEFINITION AND ROUTES OF ADMINISTRATION

Radiopharmaceutical Therapy = Unsealed source therapy (NRC 10 CFR 35.300)

Route of Administration: (various methods)

1. *Ingestion (oral)*
2. *Infusion into the circulatory system (IV)*
3. *Injection into a body cavity (Instillation)*

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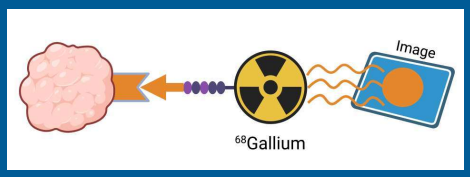
The theranostics paradigm

Theranostics is a precision medicine approach that combines the diagnosis and treatment of disease using radioactive agents that selectively target cancer cells

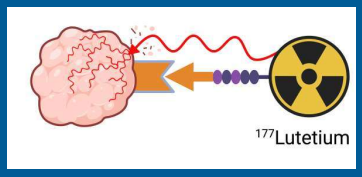
Common examples:
- **Lu-177 DOTATATE**
- **Lu-177 PSMA**
- **I-131**
- **Y-90 microspheres**

Combination of diagnostic and therapeutic modalities targeting the **same biological target**

DIAGNOSTICS



THERAPEUTICS



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Why Theranostics Matters

- Precision treatment using targeted radiopharmaceuticals
- Imaging and therapy linked by the same molecular target
- Shift from administered activity to absorbed dose
- Personalized treatment planning in nuclear medicine

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IODINE-131 SODIUM IODIDE

- Treatment of hyperthyroidism
  - Imaging and Diagnosis
  - Rx: 4-30 mCi
  - Route of Administration: Oral (capsule or liquid)
- Treatment of thyroid carcinoma
  - Imaging and Diagnosis
  - Rx: 50-200+ mCi
  - Route of Administration: Oral (capsule or liquid)

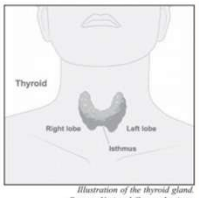
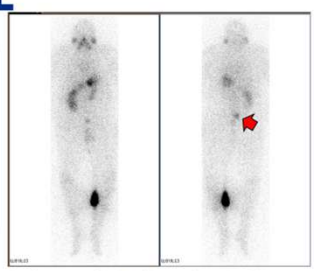
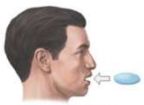
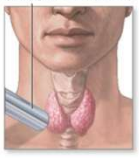


Illustration of the thyroid gland. Source: National Cancer Institute.



https://www.snmmi.org/AboutSNMMI/Content.aspx?ItemNumber=1785

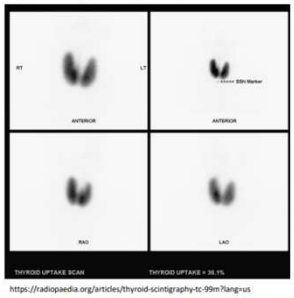




ADAM.

Radioactive iodine uptake test is a type of nuclear test performed to evaluate thyroid function. The patient ingests radioactive iodine (I-123 or I-131) capsules or liquid. After a time (usually 6 and 24-hours later), a gamma probe is placed over the thyroid gland to measure the amount of radioiodine uptake in the thyroid gland. The values are then compared.

https://www.mountsinai.org/health-library/tests/radioactive-iodine-uptake



https://radiopaedia.org/articles/thyroid-scintigraphy-tc-99m?lang=us

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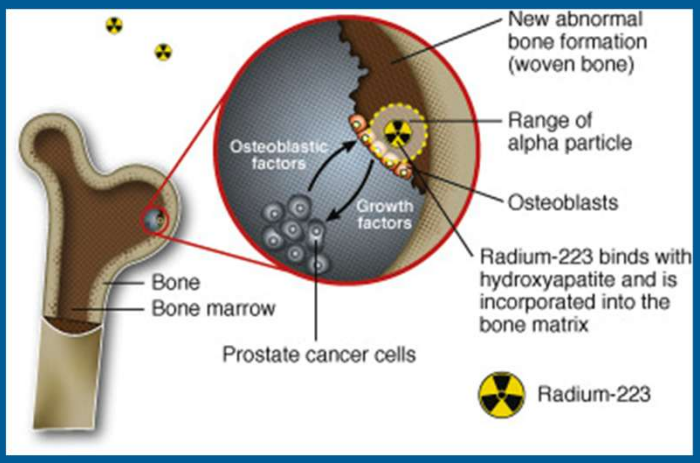
Alpha-Emitter $^{223}RaCl_2$ (XOFIGO) Mimics Calcium to Treat mCRPC Bone Metastases



Isotope = ligand!

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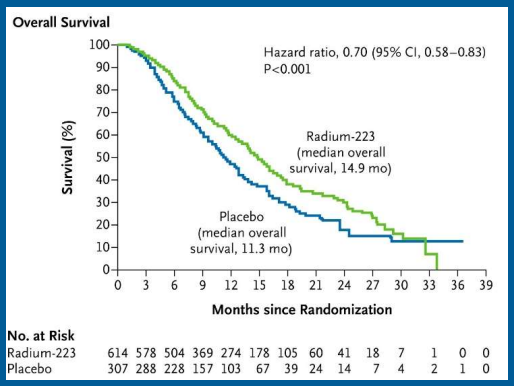

Radium-223 (XOFIGO)

$^{223}RaCl_2$
50 kBq/kg q4wk x 6

2013 FDA approval of $^{223}RaCl_2$ for men with castrate resistant metastatic prostate cancer with symptomatic bone metastases

Concern for hematotixicity

OS benefit in phase III ALSYMPCA trial, as well as time to skeletal event

Parker et al, NEJM 2013

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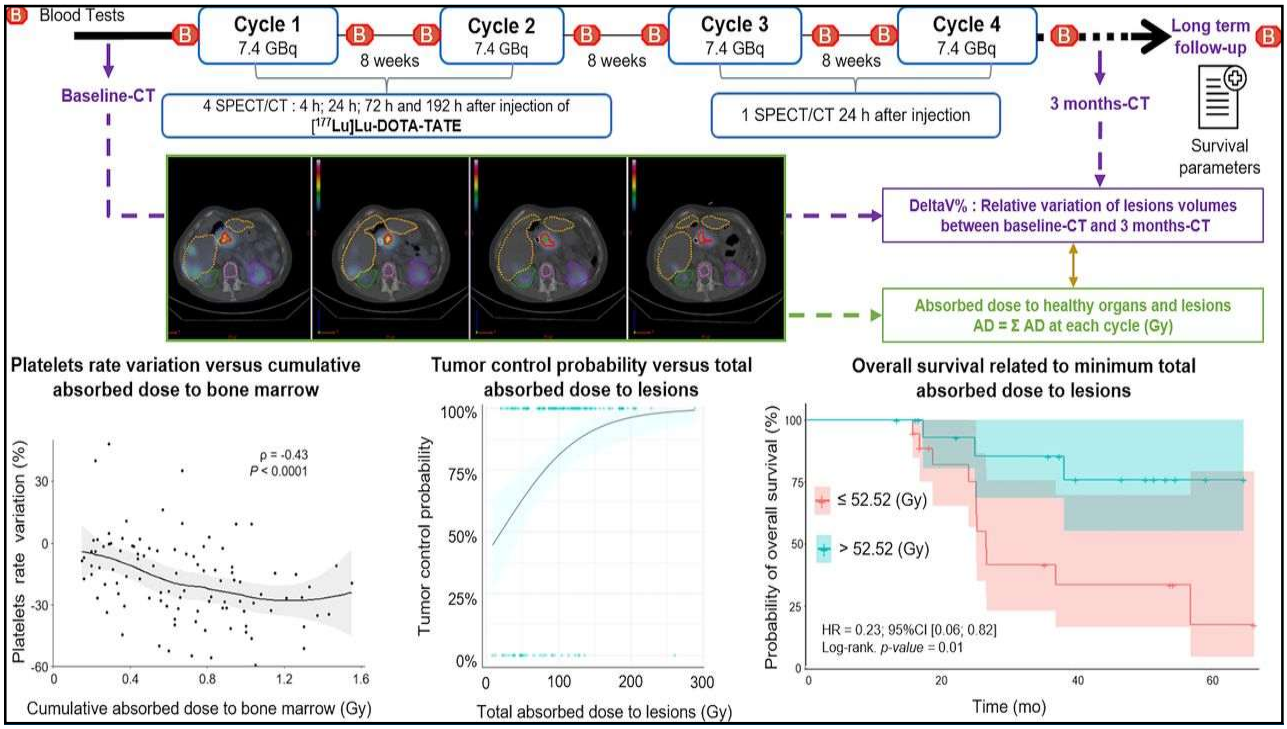
Blood Tests
Cycle 1
7.4 GBq
8 weeks
Cycle 2
7.4 GBq
8 weeks
Cycle 3
7.4 GBq
8 weeks
Cycle 4
7.4 GBq
Long term follow-up
Baseline-CT
4 SPECT/CT : 4 h; 24 h; 72 h and 192 h after injection of [177Lu]Lu-DOTA-TATE
1 SPECT/CT 24 h after injection
3 months-CT
Survival parameters
DeltaV% : Relative variation of lesions volumes between baseline-CT and 3 months-CT
Absorbed dose to healthy organs and lesions
AD = Σ AD at each cycle (Gy)
Platelets rate variation versus cumulative absorbed dose to bone marrow
ρ = -0.43
P < 0.0001
Platelets rate variation (%)
Cumulative absorbed dose to bone marrow (Gy)
Tumor control probability versus total absorbed dose to lesions
Tumor control probability
Total absorbed dose to lesions (Gy)
Overall survival related to minimum total absorbed dose to lesions
≤ 52.52 (Gy)
> 52.52 (Gy)
HR = 0.23; 95%CI [0.06; 0.82]
Log-rank. p-value = 0.01
Probability of overall survival (%)
Time (mo)

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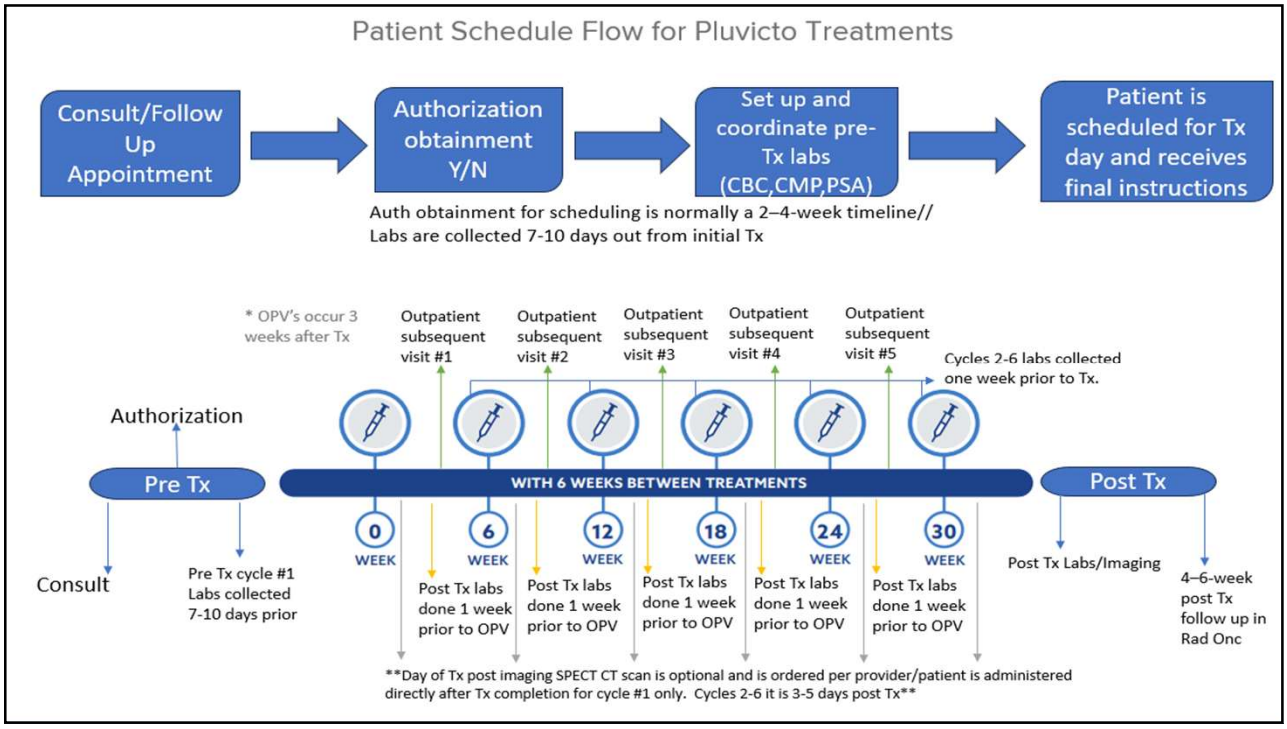
Patient Schedule Flow for Pluvicto Treatments
Consult/Follow Up Appointment
Authorization obtainment Y/N
Set up and coordinate pre-Tx labs (CBC,CMP,PSA)
Patient is scheduled for Tx day and receives final instructions
Auth obtainment for scheduling is normally a 2–4-week timeline//
Labs are collected 7-10 days out from initial Tx
* OPV's occur 3 weeks after Tx
Outpatient subsequent visit #1
Outpatient subsequent visit #2
Outpatient subsequent visit #3
Outpatient subsequent visit #4
Outpatient subsequent visit #5
Cycles 2-6 labs collected one week prior to Tx.
Authorization
Pre Tx
WITH 6 WEEKS BETWEEN TREATMENTS
Post Tx
0 WEEK
6 WEEK
12 WEEK
18 WEEK
24 WEEK
30 WEEK
Consult
Pre Tx cycle #1 Labs collected 7-10 days prior
Post Tx labs done 1 week prior to OPV
Post Tx Labs/Imaging
4–6-week post Tx follow up in Rad Onc
Day of Tx post imaging SPECT CT scan is optional and is ordered per provider/patient is administered directly after Tx completion for cycle #1 only. Cycles 2-6 it is 3-5 days post Tx

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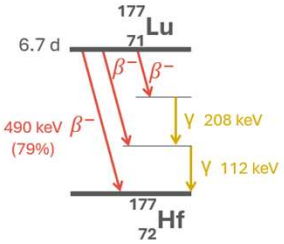
Beta Emitter ^{177}Lu-DOTATATE (LUTATHERA) Targets Somatostatin Receptor in Neuroendocrine Tumors

Lu-DOTATATE

- **Radiopharmaceutical**: ^{177}Lu-DOTATATE
  - Also referred to as "peptide receptor radionuclide therapy"
  - Commercial name: **Lutathera**
- **Indication**: somatostatin receptor–positive gastroenteropancreatic neuroendocrine tumors
- **Mechanism**:
  - Administration: intravenous
  - Administered over 4 injections of a maximum 200 mCi each; 8+ weeks apart
  - DOTATATE is a **peptide analog of somatostatin**; which then **binds to somatostatin receptors** on the surface of neuroendocrine tumors



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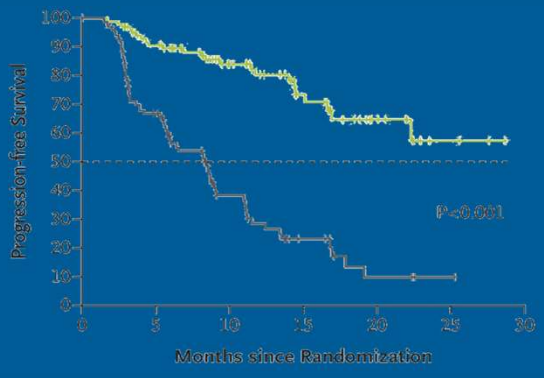

^{177}Lu-DOTATATE (LUTATHERA)

Median Progression-Free Survival:
--- ^{177}Lu-DOTATATE 40 mo
--- Control 8.4 mo
P<0.001

2018 FDA approval of ^{177}Lu-DOTATATE for pts with advanced neuroendocrine gut cancer
PFS benefit in phase III NETTER-1 trial
Concern for renal toxicity and hematotoxicity
Low imaging photon energy (~200 keV) with low branching ratio (10-20 %)

7.4 GBq q8wk x 4
Pre-administration of peptides

Strosberg et al, NEJM 2017

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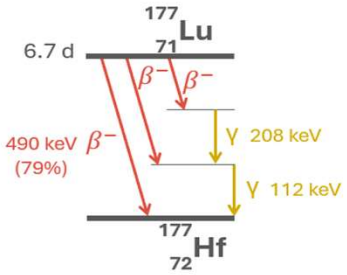
Prostate Specific Membrane Antigen

Lu-PSMA

- **Radiopharmaceutical**: ^{177}Lu-PSMA-617
  - Commercial name: **Pluvicto**
- **Indication**: metastatic castration-resistant prostate cancer (already treated with hormone therapy and chemotherapy)
- **Mechanism**:
  - Administration: intravenous
  - Administered over 6 injections of a maximum 200 mCi each; 6 weeks apart
  - **PSMA-617 is a small molecule inhibitor of PSMA**, a protein that is highly expressed on the surface of prostate cancer cells



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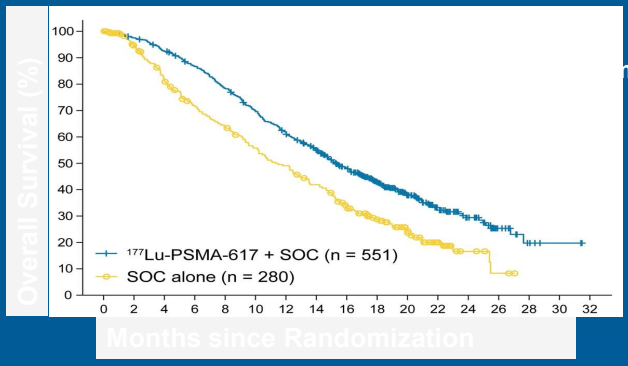
^{177}Lu-PSMA-617

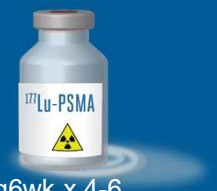


2022 FDA approval of ^{177}Lu-PSMA-617 in mCRPC with prior taxane, ARPI

OS benefit in phase III VISION trial

New FDA-production site in USA in 2023

Concern for renal toxicity and salivary gland toxicity



7.4 GBq q6wk x 4-6

Sartor et al, NEJM 2021

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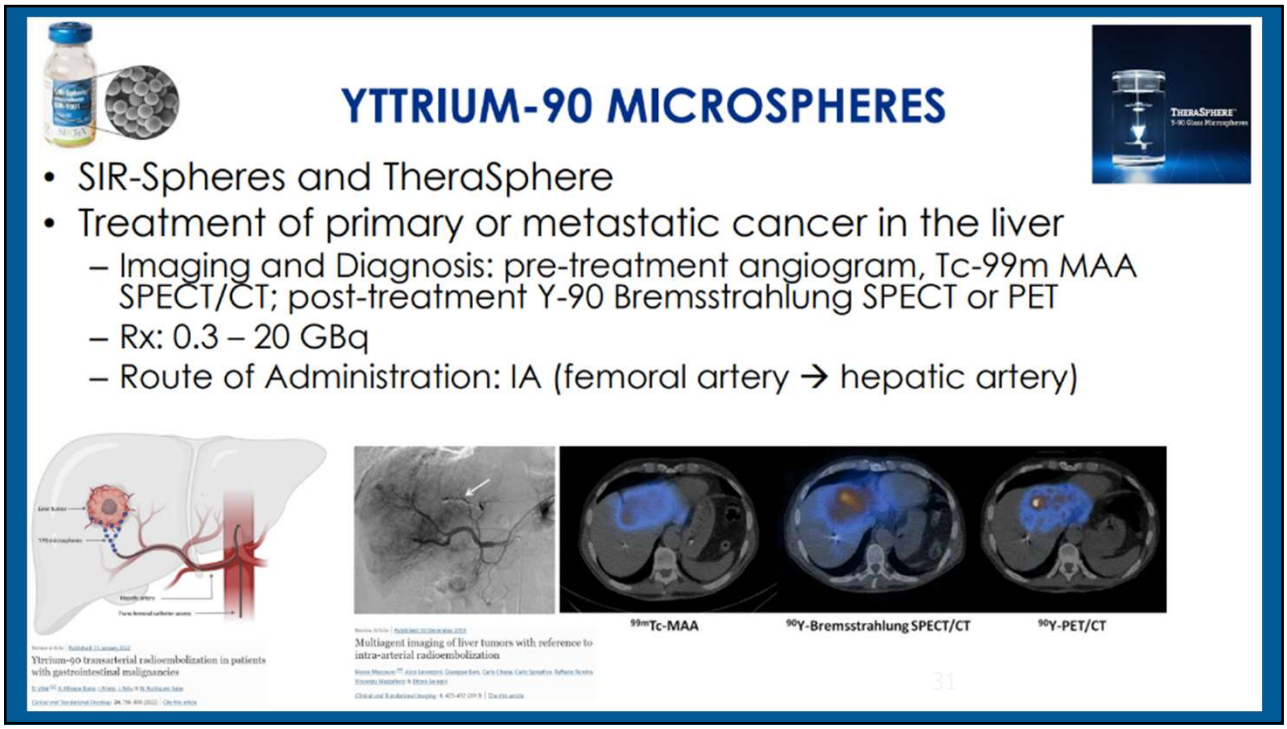

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Y-90 Microspheres

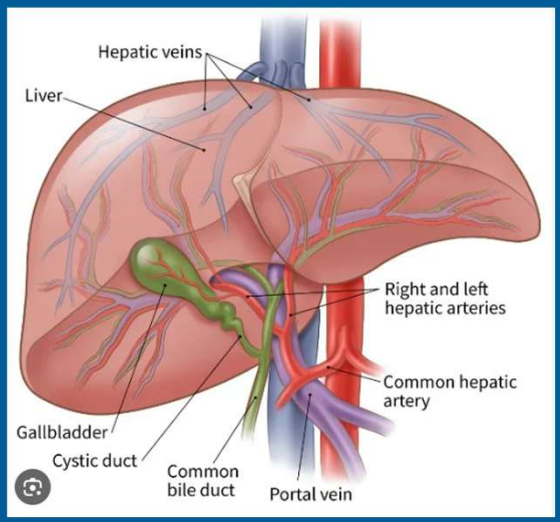
Nano-particles, not molecules: ~10 million beads of resin or glass (~20-50 μm)

Targeting is not bio-chemical, but physiological or bio-mechanical. Dual blood supply to the liver. **Normal tissue received most of its blood from the portal vein, tumor receives most of the blood supply from the hepatic artery**

Interventional Radiology places a catheter and delivers activity to (usually) right or left hepatic artery

The particles embolize, that is, they stick and do not re-localize as with RPT. It is not a systemic therapy.

Activity is calculated based on an average absorbed dose to the treated (liver volume) using simple numberic activity to absorbed dose conversion (typical prescribed dose is 120 Gy)



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RPT Dosimetry

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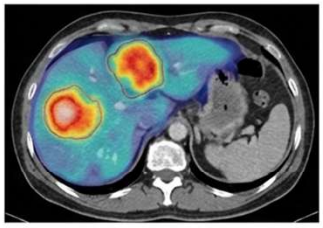
We Measure What We Inject, Not What the Tumor Absorbs

Administered Activity (Bq)	Absorbed Dose (Gy)
	
Definition: The total amount of radioactivity given to the patient (e.g., fixed 7.4 GBq).	**Definition:** The cumulative radiation energy absorbed by a specific tissue.
Location: Measured in the vial.	**Location:** Measured in the patient's cells over time.
Limitation: Ignores patient-specific pharmacokinetics.	**Advantage:** Drives the actual biological response and clinical outcomes.

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Why Dosimetry?

- Same administered activity can produce very different absorbed doses
- Patient variability affects pharmacokinetics
- Organ-at-risk protection is critical
- Potential for adaptive therapy

- Precision oncology using targeted radiopharmaceuticals
- Imaging and therapy linked by the same molecular target
- Shift from administered activity to absorbed dose
- Personalized treatment planning in nuclear medicine

- "dosimetry is not performed because dose–response data are lacking, and dose–response data are lacking because dosimetry is not performed." (Stabin, Letter to Editor, JNM, 2022)

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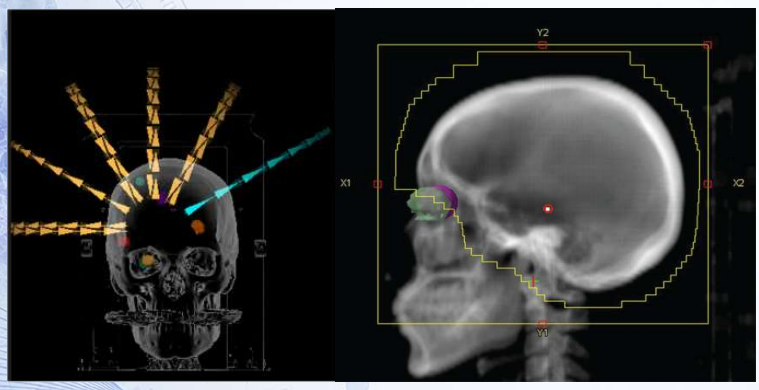
Giving the same activity for RPT...

Give every patient 500 MU, should be close....



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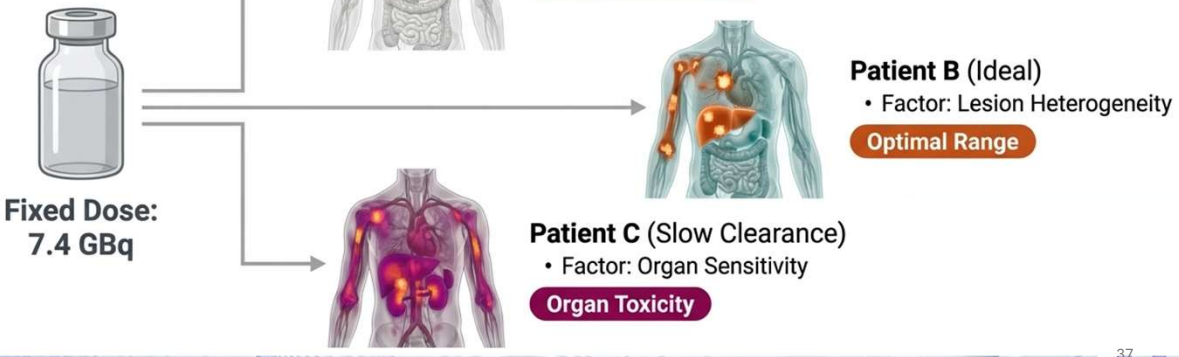
The Fallacy of the 7.4 GBq Standard Cycle

Fixed activity protocols cannot account for profound inter-patient variability, leading to reduced therapeutic index, incomplete tumor response, or severe toxicity.



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Clinical Dosimetry Reveals a Vast and Unpredictable Range of Tumor Absorbed Doses

Unlike in EBRT where doses are prescribed, RPT results in a wide spectrum of delivered doses to lesions, with no clear, simple correlation to outcome.

[177Lu]Lu-DOTA-TATE{NETs)	[177Lu]Lu-PSMA-617{mCRPC)	[223Ra]Ra-Cl2 {mCRPC)
2 to 77 Gy per cycle	**3.4 to 73.9 Gy/GBq** in bone lesions	**0.6 to 44.1Gy**

Mean absorbed dose alone is insufficient to predict treatment response or toxicity.

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Role of dosimetry in personalized medicine
Clinical Impact

Enhances **precision medicine** by tailoring therapy to tumor biology and patient-specific kinetics.

Improves **safety** by verifying organ dose thresholds.

Supports **resource-limited settings** through simplified protocols and scalable software solutions.

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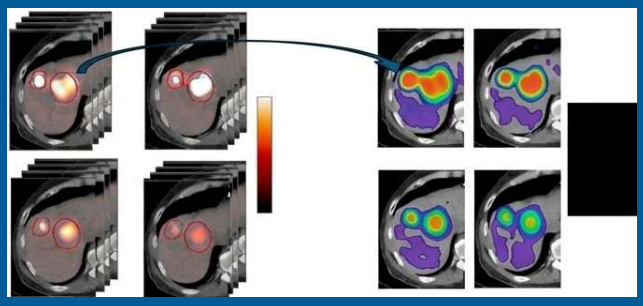
We Measure What We Inject, Not What the Tumor Absorbs

Administered Activity (Bq)	Radiation Absorbed Dose (Gy)
The total amount of radioactivity given to the patient (e.g., 7.4 GBq).	The cumulative radiation energy absorbed by a specific tissue, which varies dramatically between tumors and organs in the same patient.
A fixed amount of a drug in a vial. Ignores patient-specific pharmacokinetics.	The actual drug concentration achieved within the tumor over time.



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It is the radiation absorbed dose, specific to each patient, that mediates the tumour-killing effect, and is therefore responsible for tumour response.

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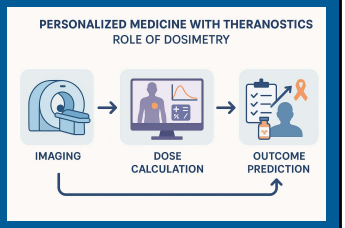
Role of dosimetry in personalized medicine

Dosimetry calculates **absorbed radiation doses** in tumors and normal organs during radiopharmaceutical therapy. Its main contributions:

Personalized Treatment Planning
Instead of fixed dosing, dosimetry enables patient-specific activity selection to:
- Maximize tumor control.
- Minimize toxicity to critical organs (kidneys, bone marrow). [jnm.snmjournals.org]

Predictive and Prognostic Value
Studies show strong correlations between absorbed dose and:
- Tumor response (e.g., ≥135 Gy linked to 90% partial response in prostate cancer).
- Survival outcomes and toxicity profiles (hematologic changes linked to spleen/bone marrow dose). [go.mimsoftware.com]

Adaptive Therapy
Early-cycle dosimetry can predict outcomes and guide adjustments in subsequent cycles (e.g., PRRT for GEP-NETs).



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Role of the Medical Dosimetrist

Image segmentation
Define organs and tumor volumes

Workflow coordination
Sequence imaging, dose, sign-off

Dose reporting
Calculate and document organ doses

Data management
Curate imaging and dose records

Quality assurance
Verify accuracy and consistency

Clinical communication
Brief physicians, techs, RSO

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PARADIGM FOR PATIENT-SPECIFIC DOSIMETRY

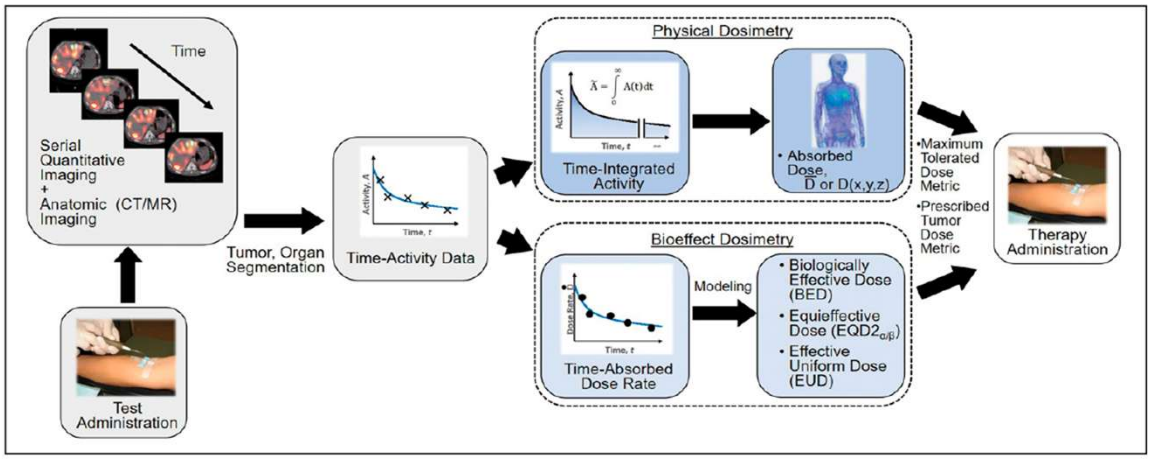

FIGURE 2. General workflow for RPT dosimetry. Process begins with test administration (may be either pretherapy administration or first cycle of multi-dose therapy regimen). Serial quantitation measurements can then support calculation of absorbed doses, either in terms of tumor and organ mean doses (D) or dose distributions (D[*x,y,z*]). Dose estimation per unit of administered activity can then be used to tailor treatment. The term *dose metric* may refer to absorbed dose (for physical dosimetry) or biologically effective dose (BED), equieffective dose (EQD2$_{\alpha/\beta}$), or effective uniform dose (EUD) (for bioeffect dosimetry).

Dosimetry

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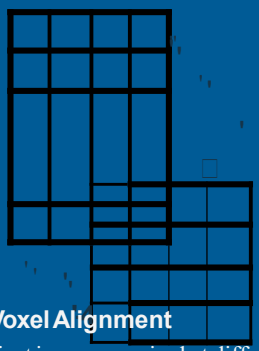
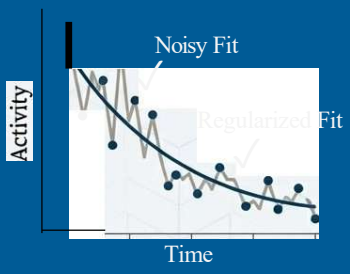
Addressing the Practical Challenges of Integration



1. Voxel Alignment

Patient images acquired at different time points must be spatially registered to ensure that each voxel corresponds to the same anatomical location across the entire image series.



2. Curve Fitting and Regularization

Mathematical techniques are required to fit a curve to the time-activity data points, with regularization methods often employed to manage image noise and ensure a biologically plausible fit.

$$\int A(t)\,dt \qquad \int \dot{D}(t)\,dt$$

Time-Activity | Time-Dose-Rate

3. Time-Activity vs. Time-Dose-Rate Integration

Atechnical distinction exists between integrating activity over time (the standard approach) and integrating the dose-rate over time. The choice can impact the final dose calculation, particularly for complex decay schemes.

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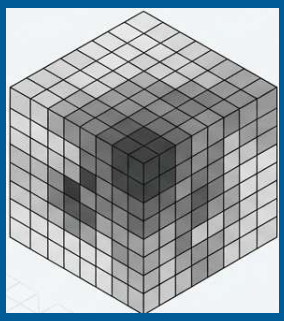
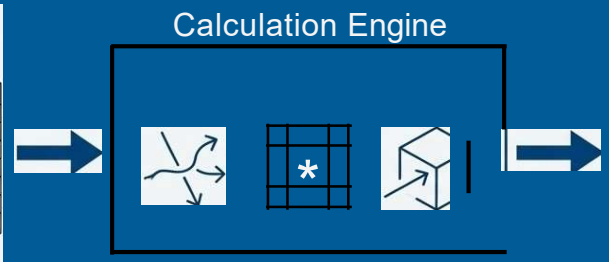
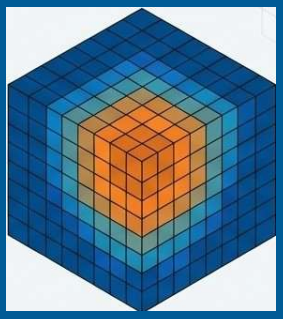
Dose Calculation Converts Activity to Absorbed Dose



Activity Map (A)



- Monte Carlo Simulation
- Dose Kernel Convolution
- Local Energy Deposition



Dose Map (D)

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Dose Map Interpretation for Clinical Evaluation

The Final Product: The result is a patient-specific 3D dose map, which can be visualized as a colorwash overlay on the patient's own CT or MRI scans.

Clinical Utility: This allows clinicians to:

- Visually inspect the dose distribution in relation to target volumes and organs at risk.
- Quantify dose metrics for specific anatomical structures.
- Evaluate the dose-response relationship for both tumors and normal tissues.

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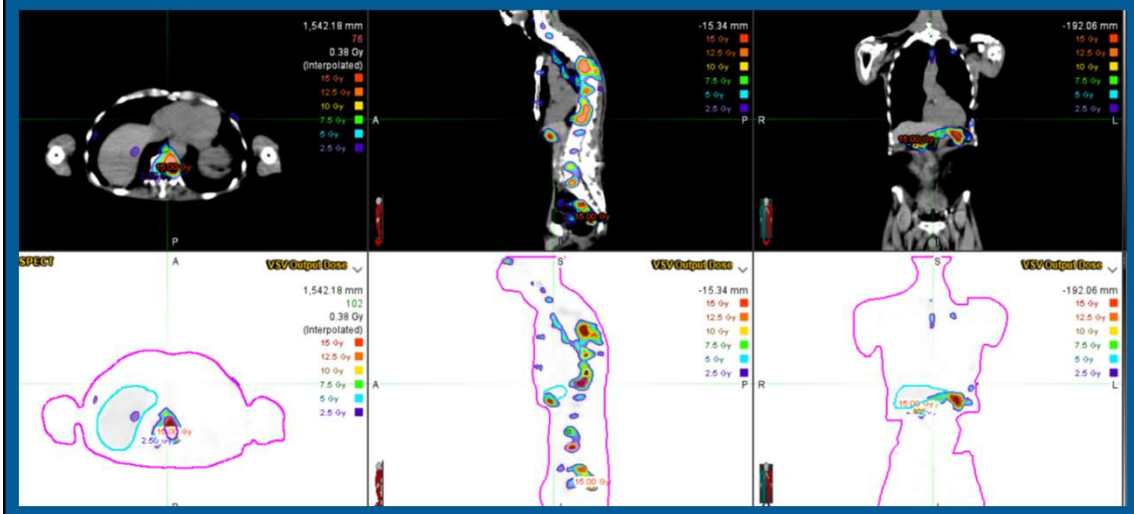
Dosimetry Examples

Pluvicto



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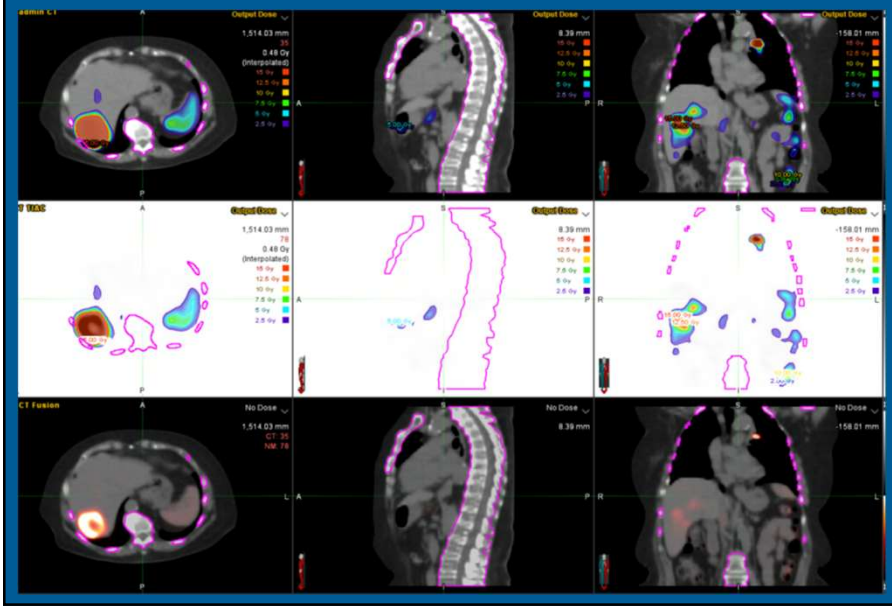
MIM Dosimetry Examples

Lutathera



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Setting Up a Dosimetry Program

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Before you start…

- **Premise:** A community hospital can launch a safe, credible theranostics program — without being an academic center on day one.
- **Team:** AU/NM physician, medical physicist, therapy-capable techs, radiation safety, pharmacy, nursing, oncology.
- **Start narrow:** One platform first — ^{177}Lu-DOTATATE or ^{177}Lu-PSMA-617 — with standardized post-therapy imaging.
- **Phase dosimetry:** Protocolized WB/SPECT-CT first; expand to patient-specific once throughput is stable.
- **Real risks aren't technical:** referral leakage, scheduling, physicist time, safety consistency, reimbursement.

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Why now: the community hospital opportunity

Approved theranostic pathways have moved RPT from niche practice toward mainstream oncology, especially in neuroendocrine tumors and metastatic castration-resistant prostate cancer.

Patients often prefer treatment close to home. Community programs can reduce travel burden, improve retention within the health system, and strengthen oncology service lines.

Theranostics also creates a referral flywheel: diagnostic PET → multidisciplinary review → therapy → post-therapy imaging → follow-up imaging and supportive care.

Hospitals do not need to offer every radionuclide or every dosimetry model at launch. They need a reproducible first indication, dependable logistics, and a defensible quality framework.

Strategic benefits

- Keeps oncology patients in-network
- Differentiates regional cancer care
- Builds PET / NM / oncology integration
- Creates platform for future agents

What community sites do well

- Operational discipline
- Standardized care pathways
- Close links with local oncologists
- Pragmatic phased growth

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Why dosimetry matters

Dosimetry estimates absorbed dose to organs and, when feasible, tumors. It supports treatment optimization, documentation of practice quality, and learning over time.

Even when label-driven fixed activity is used, dosimetry can identify outliers, explain toxicity, support retreatment discussions, and prepare the program for future personalized protocols.

For a new community program, dosimetry is less about theoretical perfection and more about disciplined measurement: calibrated imaging, consistent timing, defensible assumptions, and physicist

Safety

- Kidney, marrow, salivary, or other organ monitoring
- Explains dose-limiting toxicity

Quality

- Checks imaging consistency
- Builds local outcome database

Growth

- Prepares for trials and future adaptive therapy

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Pick the first service line intentionally

Common first-platform options	Selection criteria	Recommendation
177Lu-DOTATATE for somatostatin receptor-positive NETs	Referral base and oncology champions	Start with one indication
177Lu-PSMA-617 for eligible prostate cancer	Drug access and payer pathway	Run 3–6 months with a standard protocol
I-131 programs may offer a stepping stone if site already has capability	SPECT/CT availability	Expand only after stable scheduling, imaging, and documentation
	Physicist availability for dosimetry	
	Radiation safety burden	
	Nursing/supportive care readiness	

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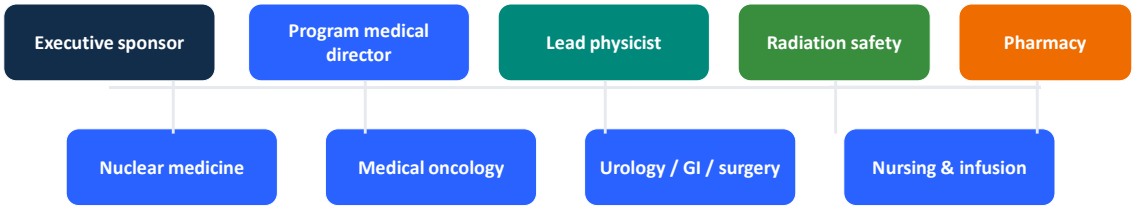
Multidisciplinary program structure



Governance cadence

Weekly operational huddle during launch; monthly quality review; quarterly strategic review with leadership.

Formal treatment selection board is strongly recommended, especially for borderline eligibility, retreatment, or unexpected toxicity.

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Equipment, software, and space

Must-have	Strongly preferred	Can be outsourced initially
SPECT/CT with quantitative capability or reproducible calibration workflow	Dedicated dosimetry software or validated in-house workflow	Advanced dosimetry analysis
Dose calibrator and QC program	Phantom-based calibration support	Some physicist tasks
Hot lab / radiopharmacy process	Body contouring and VOI tools	Some radiopharmacy support
Therapy administration room with contamination controls	Electronic templates for therapy, safety, and dosimetry reporting	Selected protocol design / peer review
Access to post-therapy imaging time slots		

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Practical dosimetry workflow for launch

Level 1: minimum viable	Level 2: selective	Level 3: mature program
Standard post-therapy imaging time points	Additional time points for complex cases	Routine longitudinal dose tracking
Whole-body + one quantitative SPECT/CT region when appropriate	Tumor dosimetry for selected patients	Adaptive treatment decisions
Protocolized organ measurements	Retreatment or toxicity-focused analysis	Research registry / trials readiness
Document assumptions and calibration method	Peer review by physicist	Automated analytics dashboards

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Radiation safety and contamination control

Therapy workflows need patient-specific release instructions, handling precautions, spill response, waste segregation, and contamination monitoring.

Roles must be explicit: who verifies activity, who handles residual assay, who clears the room, who documents surveys, and who gives discharge instructions.

Community programs succeed when radiation safety is integrated from the start rather than consulted after the drug is ordered.

Treatment-day checklist

- Room prep
- PPE
- Absorbent covering
- Survey meter ready
- Waste path defined
- Post-visit room release

Patient instructions

Hydration, toilet hygiene, contact restrictions if required, caregiver guidance, emergency contact

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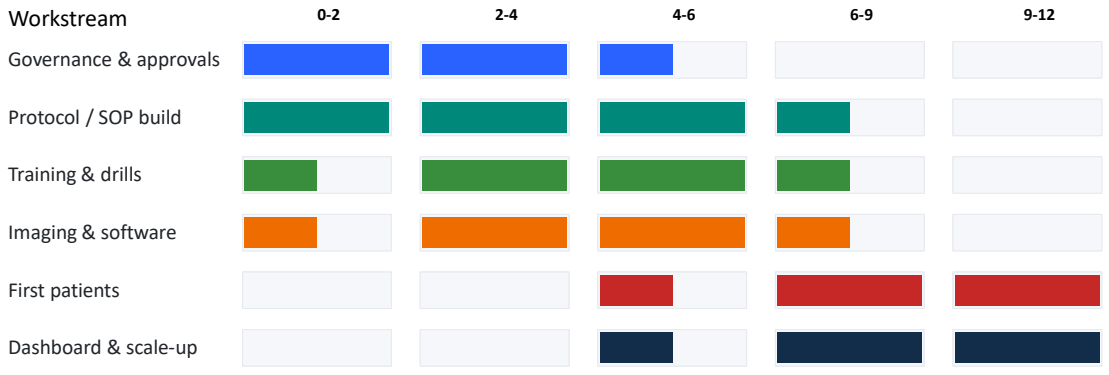
12-month implementation roadmap



Launch gate

Proceed to first patient only after a documented dry run, validated imaging chain, written safety procedures, and named owners for every handoff.

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Common questions from community sites

Do we need full patient-specific dosimetry for every patient on day one?

Can we outsource physics and still run a credible program?

How much scanner time should we reserve after therapy?

Should we begin with DOTATATE or PSMA if we can only choose one?

What volume threshold warrants more in-house investment?

Practical answer pattern

Begin with the simplest workflow that is safe, reproducible, and teachable. Outsource what you must, but keep local ownership of patient selection, treatment-day safety, imaging quality, and follow-up.

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Reimbursement / Billing

CPT Code	Description	APC HOPPS	APC ASC	2025 Rate	2026 Rate
77295	3-dimensional radiotherapy plan, including dose-volume histograms	5613	5613	$1,368.26	$1,430.97
77300	Basic radiation dosimetry calculation, central axis depth dose calculation, TDF, NSD, gap calculation, off axis factor, tissue inhomogeneity factors, calculation of non-ionizing radiation surface and depth dose, as required during course of treatment, only when prescribed by the treating physician	5611	5611	$132.77	$138.85
77370	Special medical radiation physics consultation	5611	5611	$132.77	$138.85

Source: SNMMI Reimbursement Hospital Educational Material — Revision Date: July 17, 2025. CPT codes © AMA.

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Dosimetry Challenges

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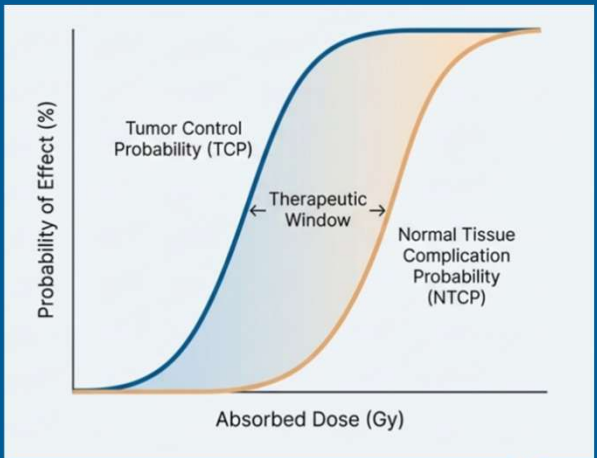
RPT is Radiotherapy, But We Haven't Been Treating It That Way

In External Beam Radiotherapy (EBRT), efficacy (Tumor Control Probability - TCP) and toxicity (Normal Tissue Complication Probability - NTCP) follow a sigmoid curve based on Absorbed Dose.

The goal is to operate within the therapeutic window: maximizing TCP while keeping NTCP acceptable.

A fundamental disconnect: In EBRT, we plan to a prescribed Absorbed Dose (Gy). In RPT, we have historically used a fixed Administered Activity (Bq).



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Applying EBRT Principles to RPT Is Not Straightforward

The irradiation pattern in RPT is fundamentally different from EBRT, which profoundly impacts the biological response.

Feature	External Beam Radiotherapy (EBRT)	Targeted Radionuclide Therapy (RPT)
Dose Rate	**High** (Acute, >2 Gy/min)	**Low** (Continuous, <1 Gy/h)
Dose Distribution	**Pre-defined,** relatively uniform	**Heterogeneous,** patient-specific
Duration	Spans a defined treatment period	Continuous for hours to days per cycle
Fractionation	Standard practice to protect normal tissue	Repeated cycles are **not** true fractionation

Low dose rates in RPT may allow for more tissue repair, meaning higher total absorbed doses are required to achieve the same biological effect.

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FOR EXAMPLE: Kidney Tolerance in RPT

- **Historical (EBRT):** 23 Gy limit
- **Current RPT thresholds:** 27–40 Gy range
- **Conservative:** 28 Gy for patients with risk factors

Why higher in RPT? Low dose-rate effects allow better renal repair compared to external beam

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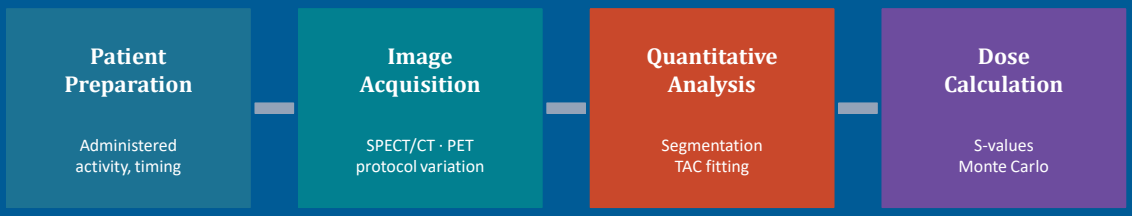
The Dosimetry Uncertainty Chain



Uncertainties Accumulate at Each Stage → Final dose estimate: typically ±20–30% (1σ)

Physical

Attenuation · scatter · PVE
Collimator response · noise

Biological

Uptake variability · clearance
Organ motion · inter-patient

Computational

Segmentation · TAC fitting
Kernel vs. Monte Carlo

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Dosimetry Calculation Uncertainties

Time-Activity Curve Fitting

- Sparse time-point sampling (2–3 scans): under-determined exponential fits
- Choice of integration method (trapezoidal vs. mono/bi-exponential)
- Pre-peak activity assumption if no early time-point acquired
- Reported TIAC uncertainty: 10–25% depending on sampling schedule

Absorbed Dose Computation

- MIRD S-value (stylised phantoms): ±30–50% in heterogeneous patient anatomy
- Voxel S-value kernels: tissue homogeneity assumed, fail near boundaries
- Monte Carlo (MC): gold standard but propagates all upstream uncertainties
- Organ mass/volume: CT-derived delineation errors directly scale dose

Biological & RBE Factors

- Radiobiological effectiveness (RBE) of Auger/α emitters: poorly constrained
- BED extrapolation: α/β ratios for tumour vs. normal tissue vary widely
- Tumour heterogeneity: sub-volume dosimetry vs. mean absorbed dose
- Dose-rate effects: repair kinetics uncertain for protracted ^{177}Lu exposures

TIAC = Time-Integrated Activity Coefficient · BED = Biologically Effective Dose · RBE = Relative Biological Effectiveness

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Quantifying & Propagating Uncertainties

Reported Uncertainty Magnitudes (1σ)

Source	Typical Range
Activity measurement (dose calibrator)	1–3%
SPECT/CT organ quantification	5–15%
TAC integration (sparse sampling)	10–25%
Organ volume segmentation	5–15%
S-value (stylised vs. patient-specific)	15–50%
Combined (quadrature)	~20–35%

GUM = Guide to the Expression of Uncertainty in Measurement (JCGM 100:2008)

Approaches to Uncertainty Quantification

GUM / Error Propagation
Analytical uncertainty propagation through dosimetry chain; assumes independent Gaussian errors

Monte Carlo Sampling
Repeated simulation drawing from input distributions; captures non-linear interactions and correlated errors

Bootstrap Resampling
Resamples image noise and time-point data; accounts for fitting model uncertainty in TACs

Sensitivity Analysis
Identifies dominant uncertainty sources; guides where effort reduces total uncertainty most

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Clinical Impact & Mitigation Strategies

Why Uncertainties Matter Clinically

- Activity prescription: ±30% dose uncertainty prevents tight therapeutic windows
- Organ-at-risk thresholds: kidney absorbed dose limits (23–28 Gy) are sensitive
- Comparative trials: dose-response data unreliable without uncertainty reporting
- Adaptive dosimetry: mid-therapy replanning requires tight confidence intervals
- Regulatory/reimbursement: EANM/SNMMI dosimetry reports require uncertainty bounds

Strategies to Reduce Uncertainty

Harmonised protocols
EANM dosimetry committee guidelines, phantom cross-calibration, multi-centre QA

Patient-specific MC
GATE/FLUKA-based absorbed dose engines integrated with clinical workstation (EQS, Hermes, MIM)

AI-assisted segmentation
Deep learning auto-contouring reduces inter-observer variability in organ & tumour delineation

Optimised time-point sampling
Optimal design theory to maximise TAC information from minimum scans (2–3 time-points)

Uncertainty reporting
Dosimetry reports should include point estimate + 1σ uncertainty for each organ

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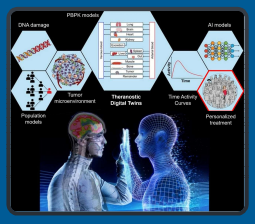
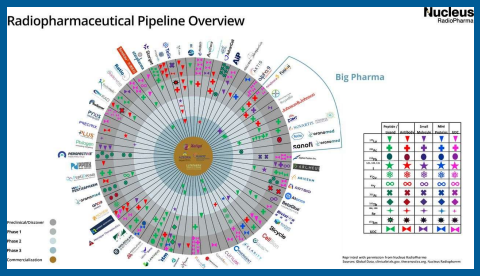
Future of RPT Dosimetry

- AI-driven auto-dosimetry pipelines / Theranostic digital twins with patient-specific organ phantoms
- Advanced isotopes: Alpha particles / Auger electrons
- Prospective dose-response studies with harmonised uncertainty metrics, use diagnostic imaging → predict therapy doses
- Move beyond prostate and NETs
- Radiobiologic refinement: Patient-specific BED calculations





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Rationale for Combination: Why EBRT + RPT?

Complementary Spatial Coverage

EBRT delivers precise high-dose volumes to macroscopic disease; RPT reaches distant micrometastases and ligand-expressing cells beyond the EBRT field — together providing whole-body + focal control

DNA Damage Synergy

EBRT-induced DNA double-strand breaks sensitise cells to the subsequent low-dose-rate irradiation of $^{177}Lu/^{225}Ac$. Impaired repair pathways amplify RPT lethality in the pre-irradiated volume

Receptor Upregulation

Sub-lethal EBRT can upregulate PSMA, SSTR2, and other target receptors, increasing RPT uptake in the treated field — a radiobiological priming effect confirmed in preclinical models

Tumour Microenvironment

EBRT normalises tumour vasculature and reduces hypoxia, improving RPT agent delivery. Combined EBRT + RPT can overcome the hypoxia-driven resistance that limits each modality alone

PSMA = Prostate-Specific Membrane Antigen · SSTR2 = Somatostatin Receptor 2 · RPT = Radiopharmaceutical Therapy · DSB = Double-Strand Break

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Conclusions

1 Exponential Growth

The future of theranostics and dosimetry is poised for rapid expansion across the field.

2 Team Collaboration

Physicists can't deliver this alone — will need more help and might rollover to dosimetrists

3 EBRT + RPT

EBRT combined with RPT unlocks transformative clinical potential for patients.

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