

Chapter 9

Advanced techniques and research in nuclear medicine

Dr. Sc. Siria Medici

with material from Dr. Sc. Silvano Gnesin

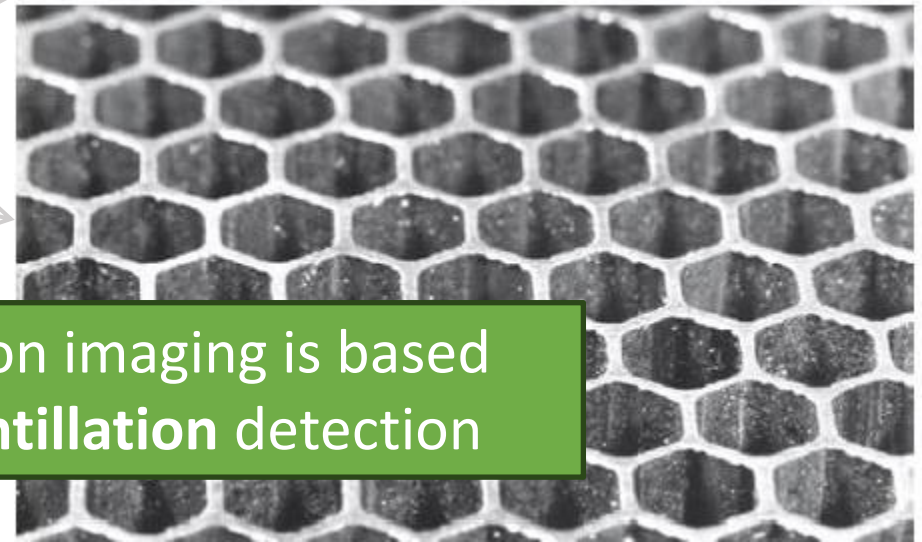
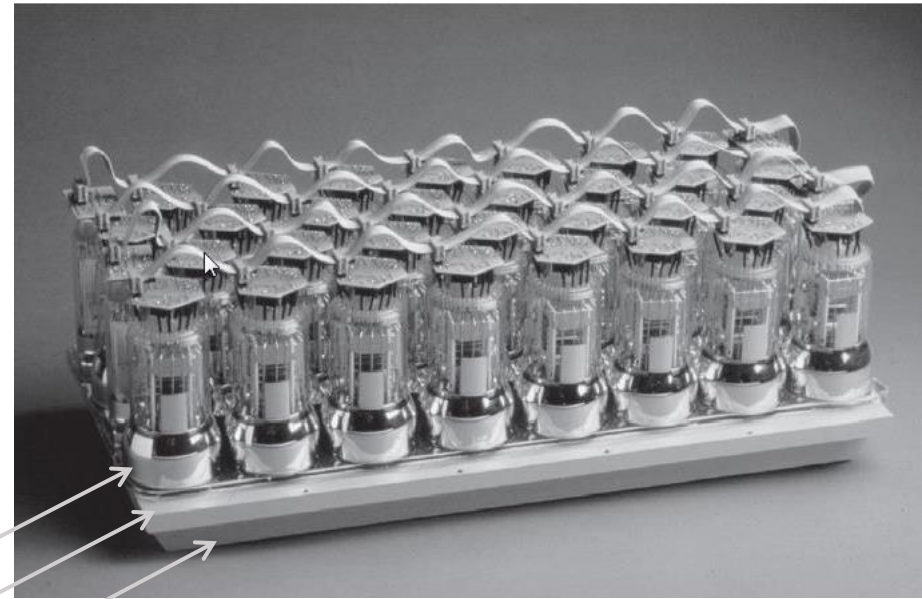
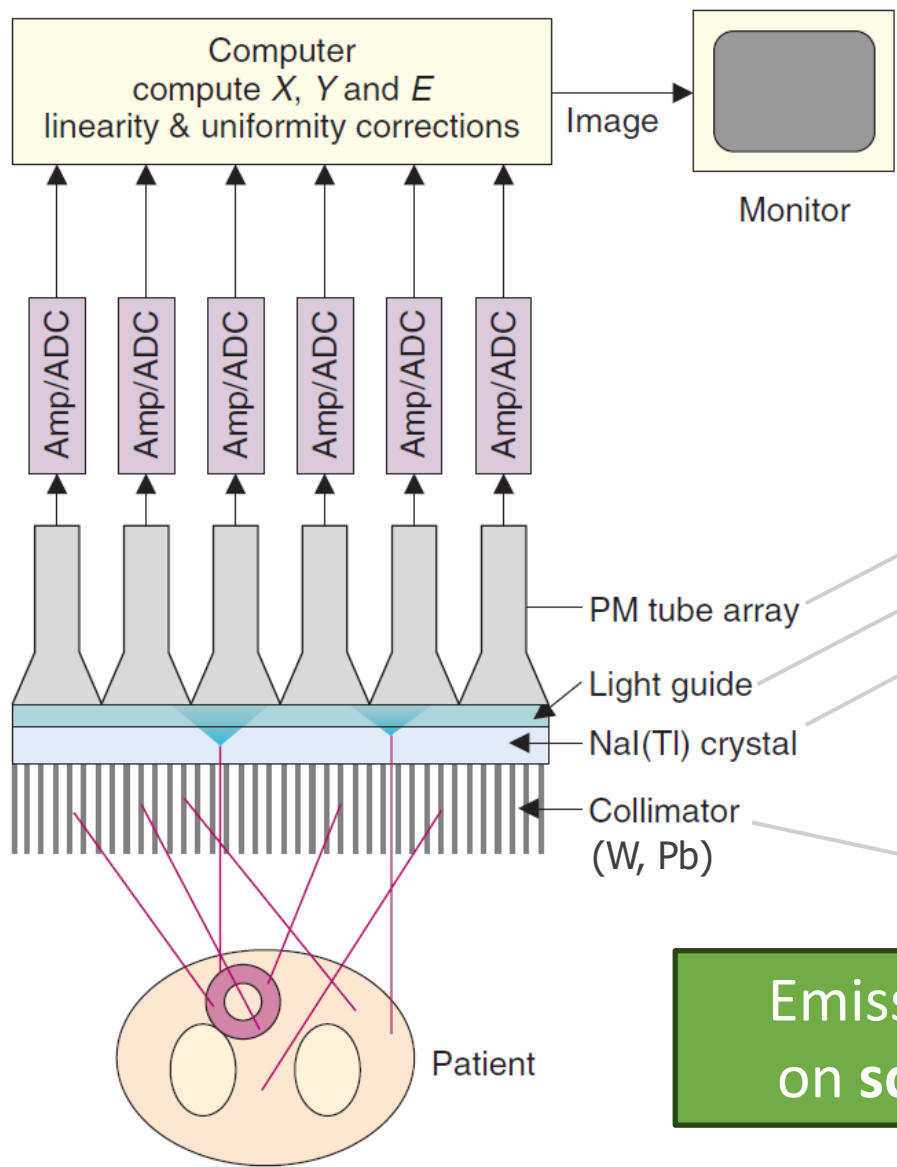
EPFL - PHYS 455

Introduction to Medical Physics

Learning objectives

- Briefly describe the **most promising advanced techniques** in nuclear medicine
- Describe the different **therapeutic applications** of nuclear medicine and **theranostics**
- Explain the **workflow** required to perform **dosimetry** in nuclear medicine

New trends in SPECT



Emission imaging is based on scintillation detection

Parallel hole collimator

New trends in SPECT

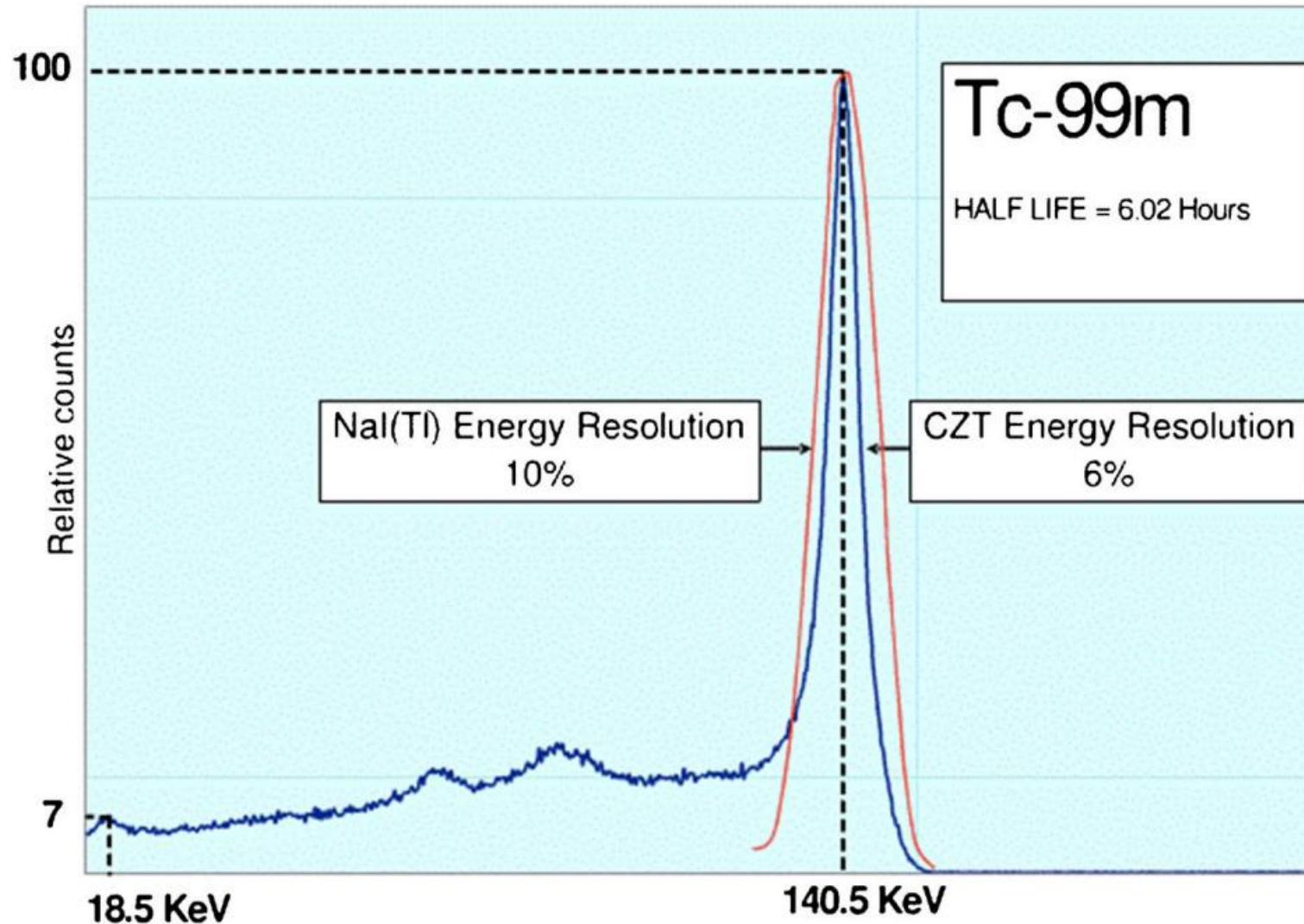
1. Detectors - from scintillators to solid-state detectors:

- Cadmium-zinc-telluride (CZT):
 - More expensive than NaI(Tl)
 - Improved energy response (improved scatter reduction)
 - Improved spatial resolution:
 - Direct conversion (CZT) vs. indirect conversion (NaI)
 - Reduced signal spread
 - Pixelated array → more precise signal localisation
 - No need of PMT → more compact design
 - Efficiency?
 - CZT is denser than NaI (higher stopping power), but has limited manufacturing thickness
→ in clinical practice the difference is less pronounced



Energy resolution comparison

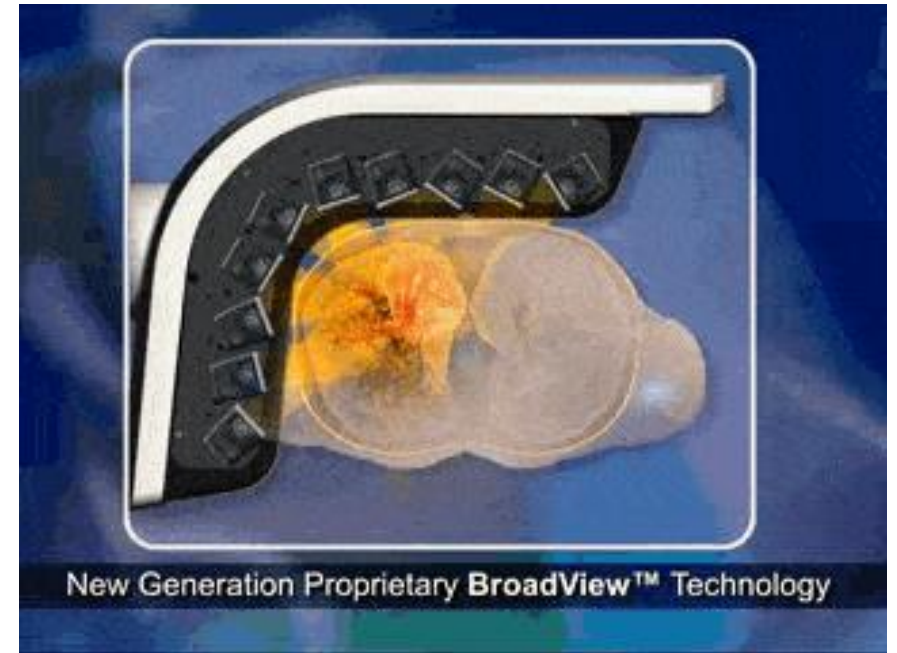
Eur J Nucl Med Mol Imaging (2016) 43:2423–2432



New trends in SPECT

2. Collimators and design:

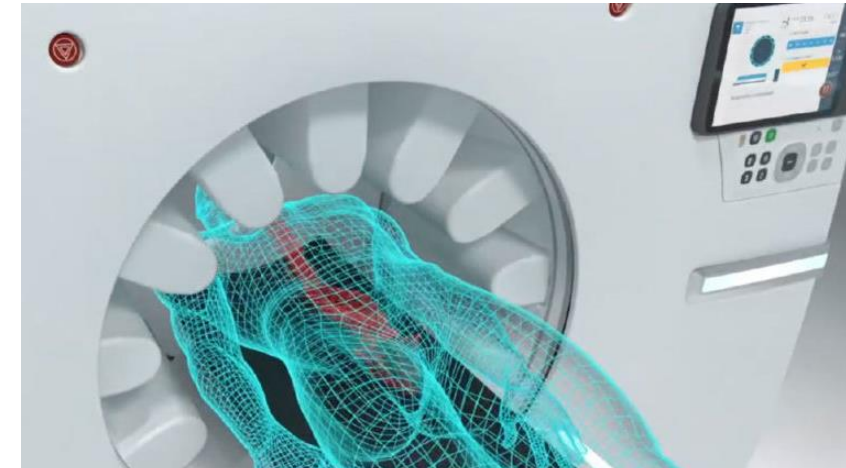
- Solid-state systems use specific design to maximise sensitivity:
- Special designs for **cardiac** imaging
 - Static or dynamic collimation
 - Multiple projections still allow for tomographic image reconstruction
 - Close to the organ of interest
 - Improved resolution
 - Improved sensitivity



New trends in SPECT

2. Collimators and design:

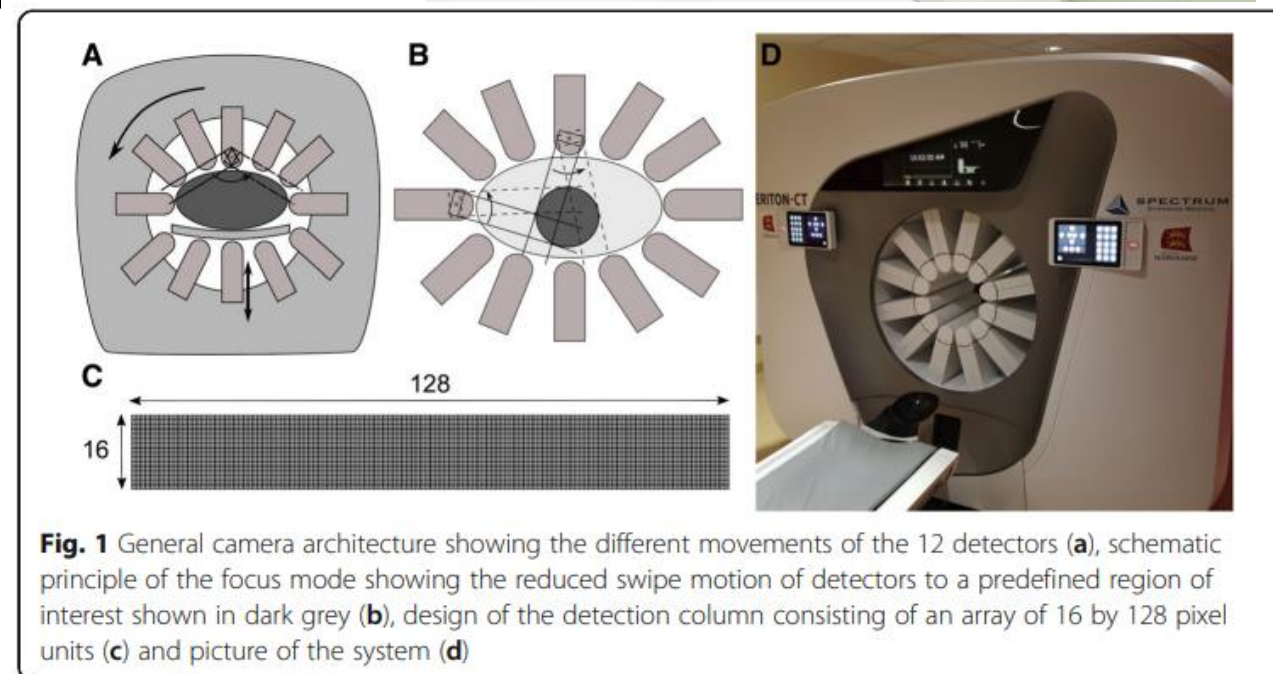
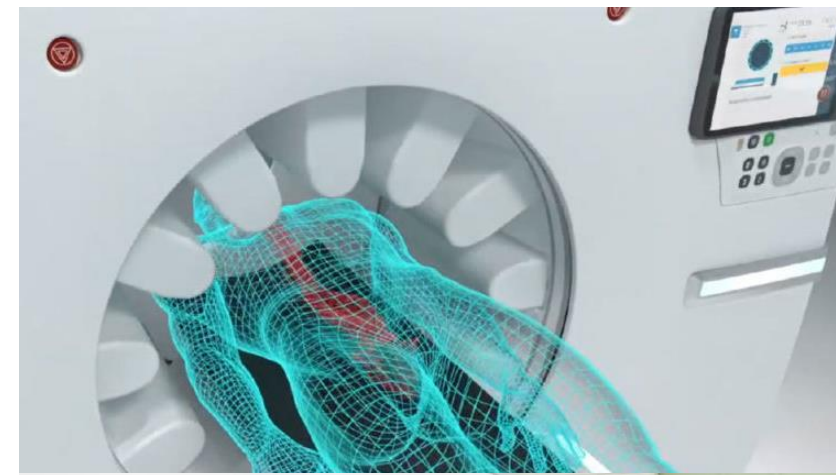
- Special designs for **whole-body** imaging
 - multiple CZT detectors (e.g. 12)
 - Ring configuration around the patient
 - Approach/retract to follow body contour
 - Sweeping motion of the detectors
 - Multiple projections still allow for tomographic image reconstruction
 - Only a predefined collimator (independently on the energy)
 - Close to the organ of interest
 - Improved resolution
 - Improved sensitivity



New trends in SPECT

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New trends in SPECT

3. Quantitative SPECT:

- Historically, SPECT has been qualitative : yes / no uptake, often for relative metrics (lesion uptake vs background region).
- Improved corrections in SPECT (iterative methods, correction of partial volume effects, scatter and attenuation correction) allow to perform absolute quantification (cps / mL \rightarrow Bq/mL).
- This allows to the use of standardized uptake value (SUV) metrics, as already the case for PET.
- Possible use in the clinics for monitoring of response, objective and multicentric comparison (i.e. independent on the centre acquisition/reconstruction algorithms).
- Need to define standardisation procedures!

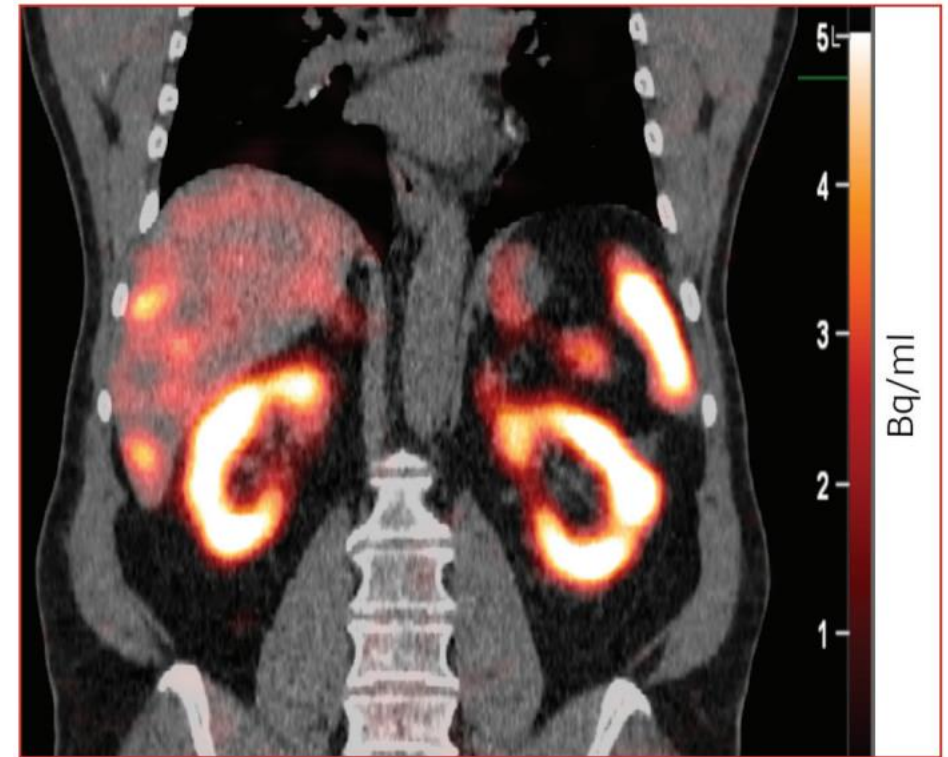


Figure 1: Quantitative fused (i.e., SPECT + CT) image with colorbar showing units of Bq/ml.

European Journal of Nuclear Medicine and Molecular Imaging (2023) 50:980–995
<https://doi.org/10.1007/s00259-022-06028-9>

GUIDELINES

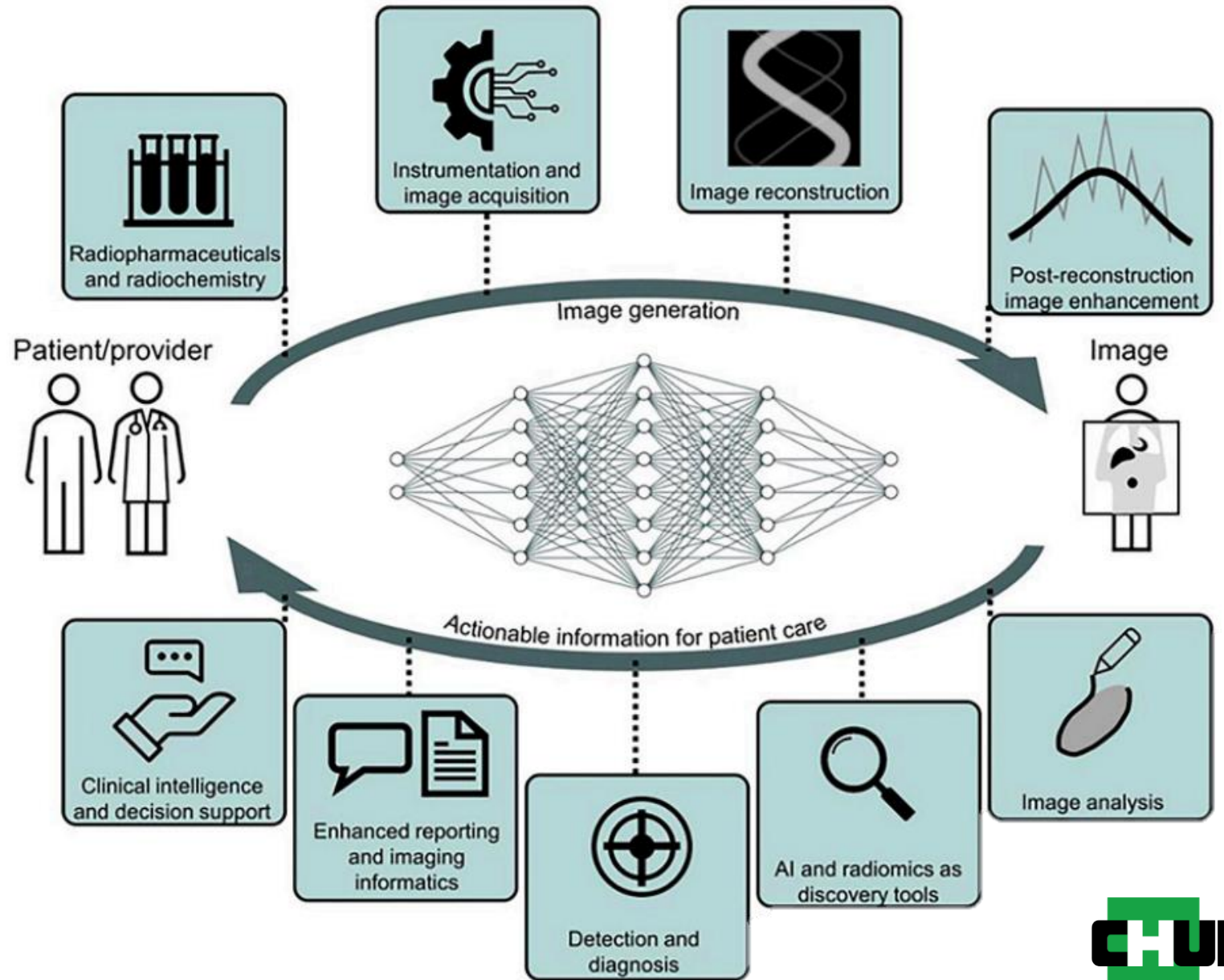
EANM practice guideline for quantitative SPECT-CT

John C. Dickson¹ · Ian S. Armstrong² · Pablo Minguez Gabiña^{3,4} · Ana M. Denis-Bacelar⁵ · Aron K. Krizsan⁶ · Jonathan M. Gear⁷ · Tim Van den Wyngaert^{8,9} · Lioe-Fee de Geus-Oei^{10,11} · Ken Herrmann¹²

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New trends in SPECT

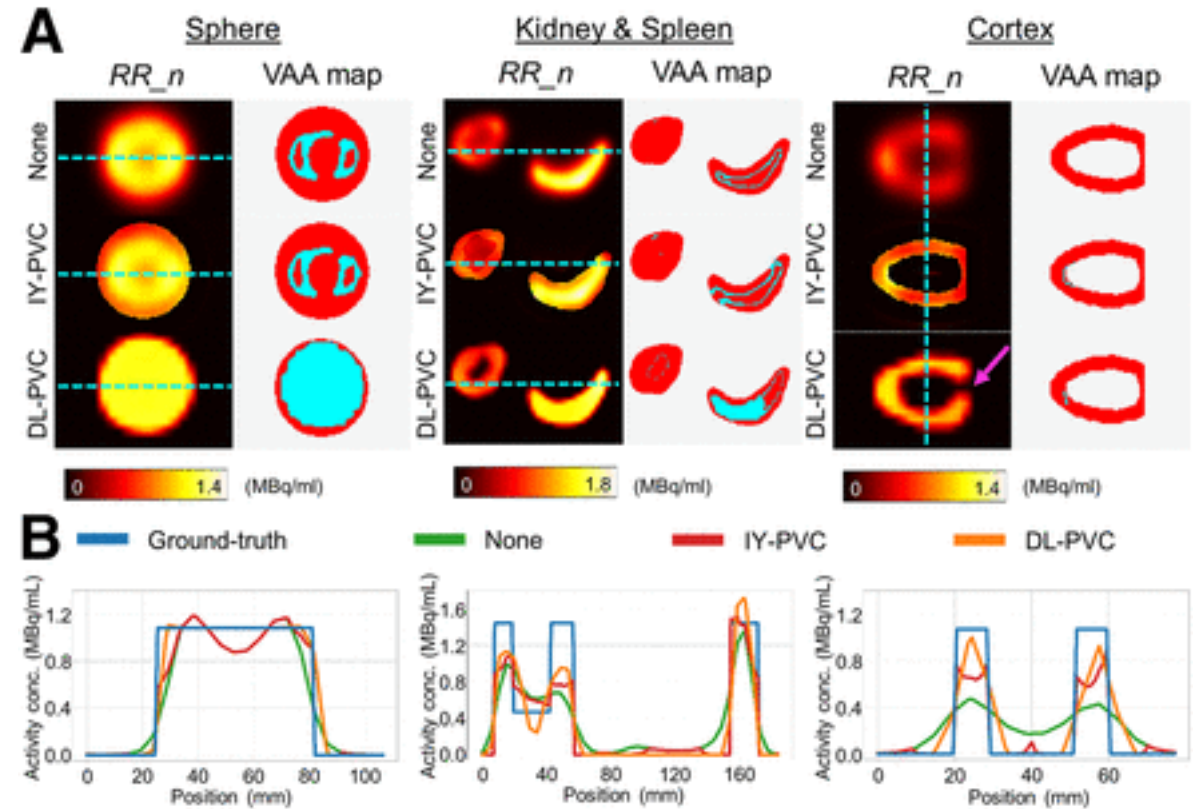
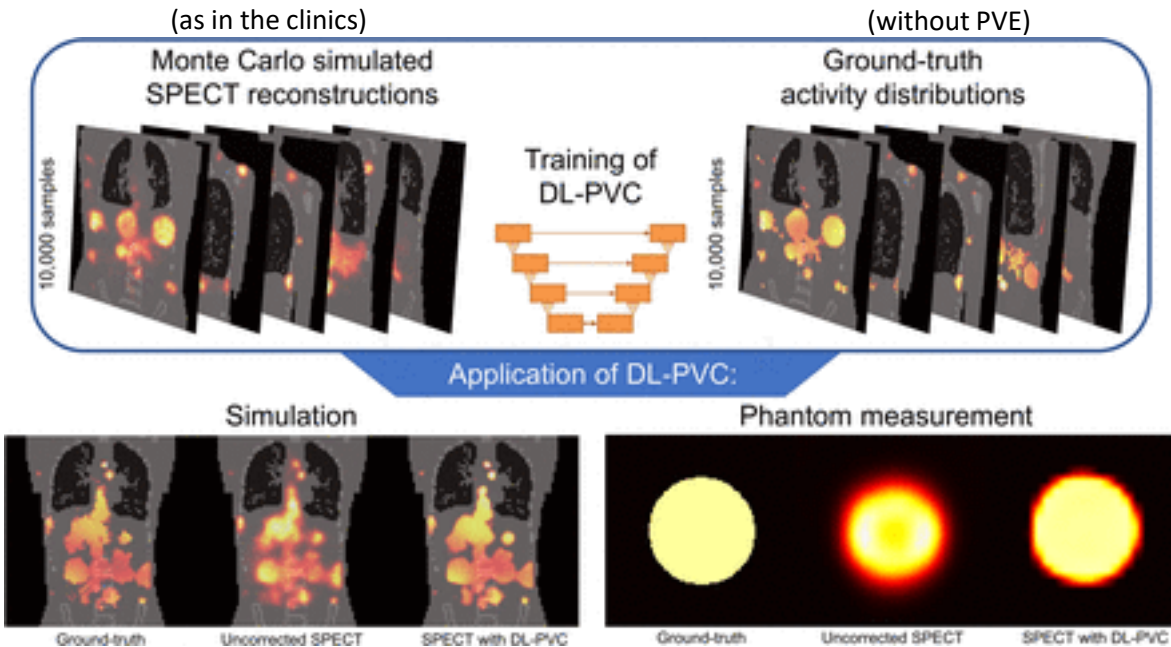
4. Artificial intelligence:



New trends in SPECT (AI examples)

deep learning assisted partial volume effect (PVE) correction

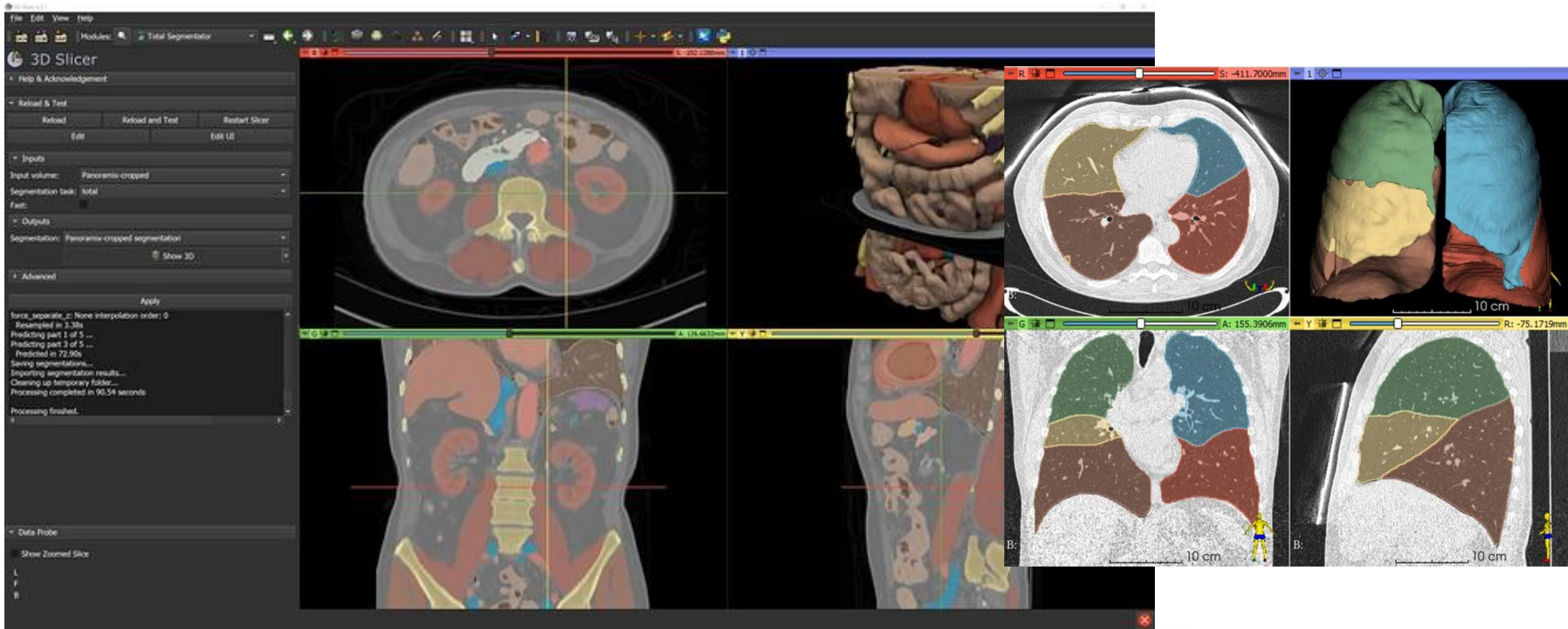
For small objects, PVE limits the accuracy of activity quantification.



Future deployment on clinical image data.

New trends in SPECT (AI examples)

automatic organ segmentation



Fully automated AI-based organ segmentation

New trends in PET

1. Increase axial field of view:
 - Better patient coverage
 - Higher sensitivity
 - Lower dose / shorter time
2. From analog (PMT) to digital detectors (SIPMs)
 - Improved sensitivity
 - Better spatial localisation
 - Better timing resolution (improved TOF)
3. Artificial intelligence

New trends in PET

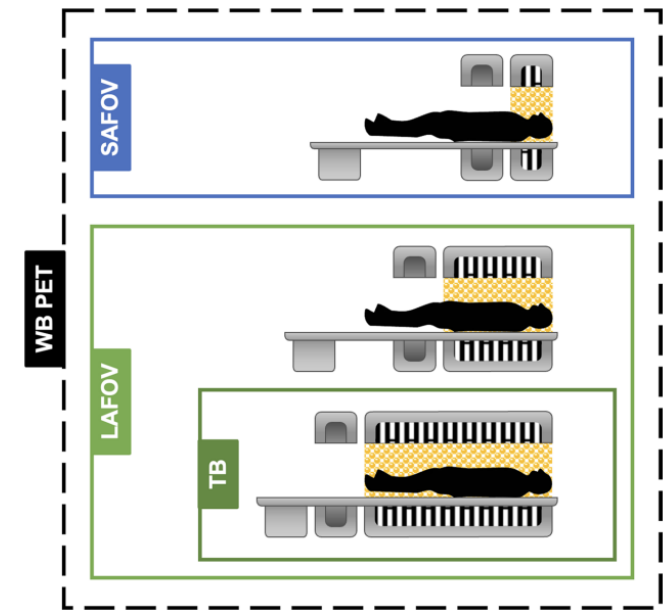
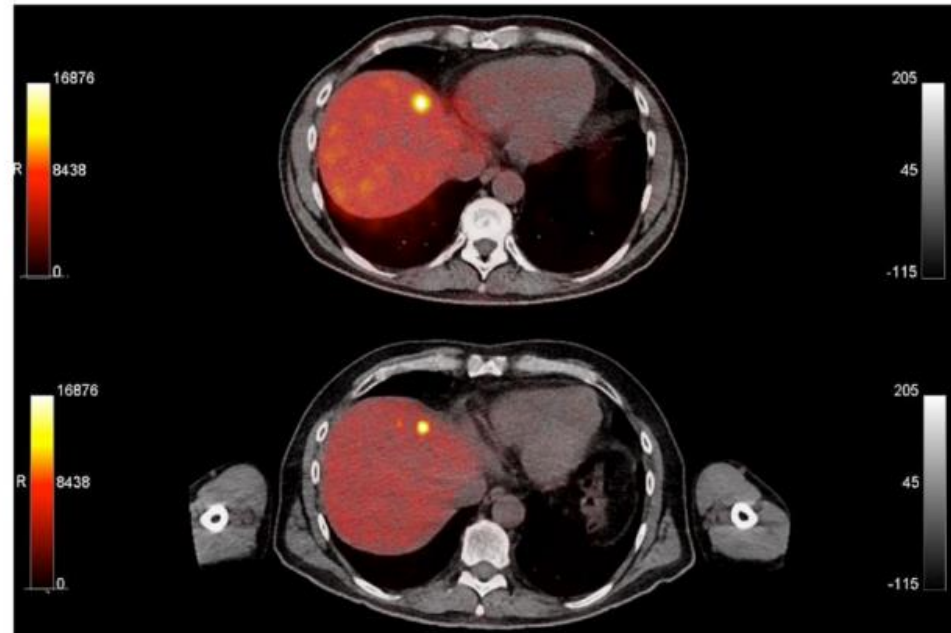


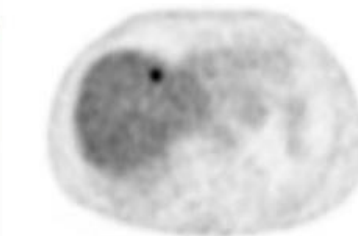
Fig. 1 Graphical representation of different PET/CT scanners based on axial field-of-view clinical classification. WB, whole-body imaging; SAFOV, short-axial field-of-view; LAFOV, long-axial field-of-view; TB, total-body

Fig. 1 a Comparison of a [^{68}Ga]-DOTATOC study in a patient with liver metastases of a neuroendocrine carcinoma with a conventional PET-CT scanner 1 h p.i. (Biograph mCT, upper row) and a LAFOV PET-CT system 2 h p.i. (Biograph Vision Quadra, lower row). Apart from the larger metastatic lesion in the cranial part of the organ, a second smaller liver metastasis is delineated with the LAFOV scanner in the transversal slices despite the delayed scanning due to the higher sensitivity of the new system.

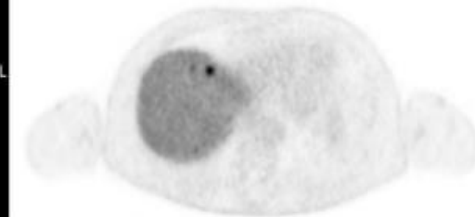
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Conventional PET/CT



LAFOV PET/CT



New trends in PET

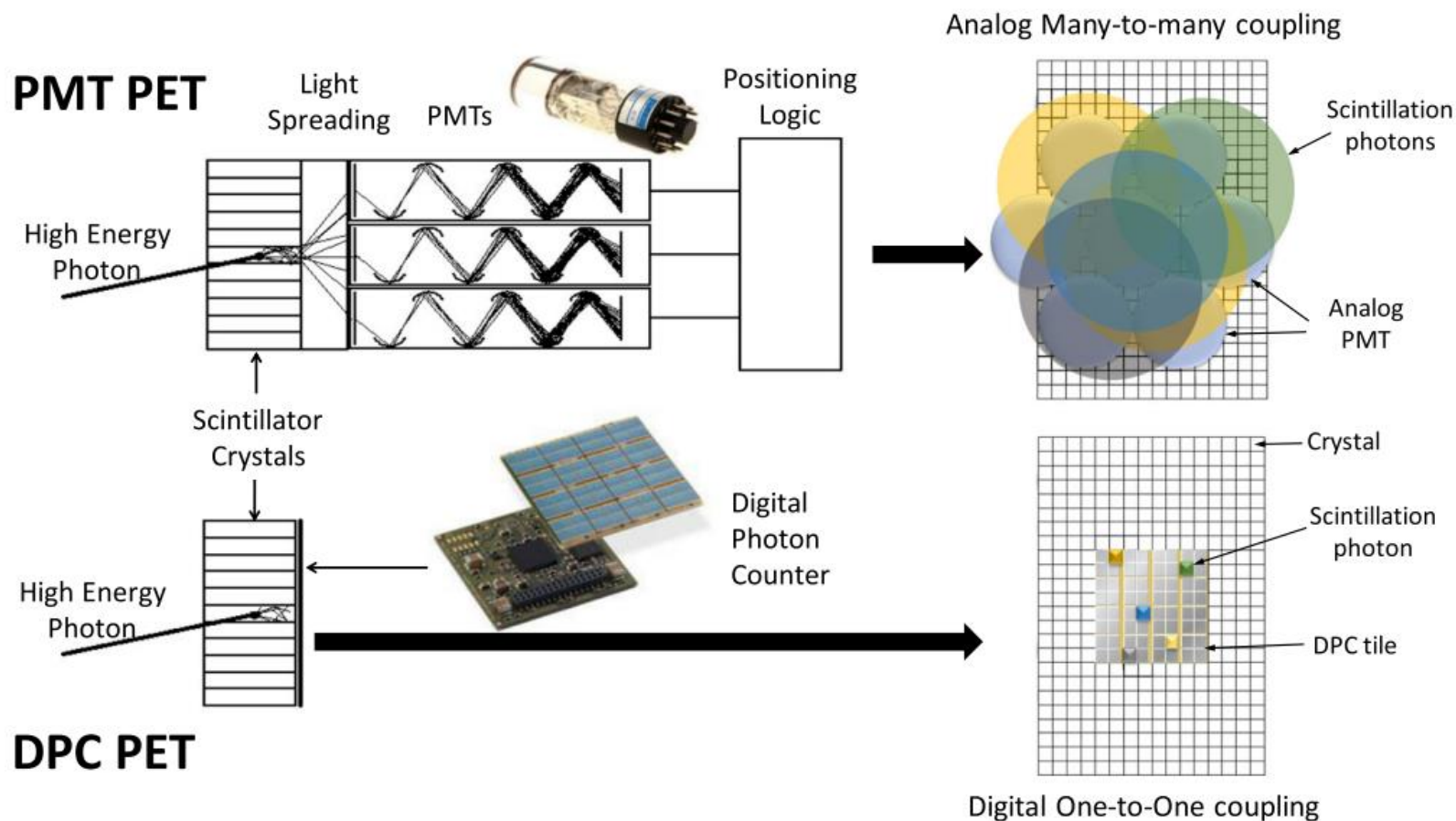
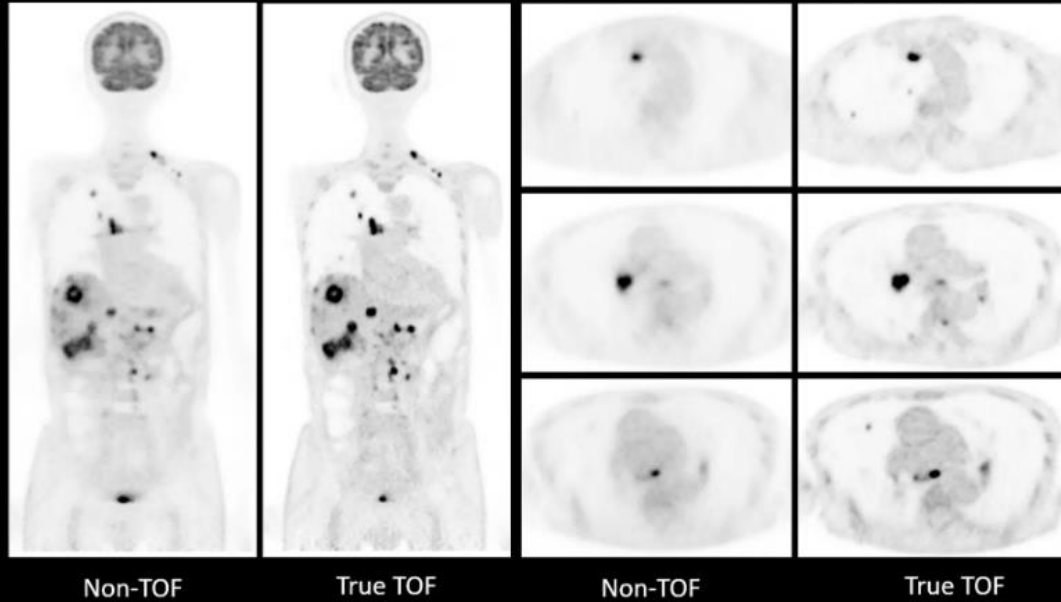


Fig. 3 Comparison of PMT PET detector and DPC PET detector approach. For PMT PET, incident photons are converted to visible light via interaction with scintillators coupled with multiple PMTs to generate and multiply electronic signals for further Anger-logic positioning decoding which exhibits significant dead time. For DPC PET, 1:1 coupling of scintillator and digital detector directly channels lights from a crystal to its 'own' detector with a digital signal output that is virtually dead time free

New trends in PET



Data courtesy of Research Institute for Brain and Blood Vessels-Akita, Akita, Japan.

True time of flight (TOF) performance improves definition and contrast

- High contrast and sharp definition of supraclavicular lung mediastinal and liver metastases with TOF, reflect potential for improved small lesion detectability

Biograph Vision PET/CT

PET

Scan acquisition: 13.48 minutes

Image reconstruction: 440 x 440 matrix, OSEM+PSF 3i5s

440 x 440 matrix, PSF+TOF 3i5s

All-pass filter

Injected dose: Fludeoxyglucose F 18 (^{18}F FDG) Injection^[a]

5.5 mCi (204 MBq)



New trends in PET (AI examples)

Attenuation correction without need to perform a CT

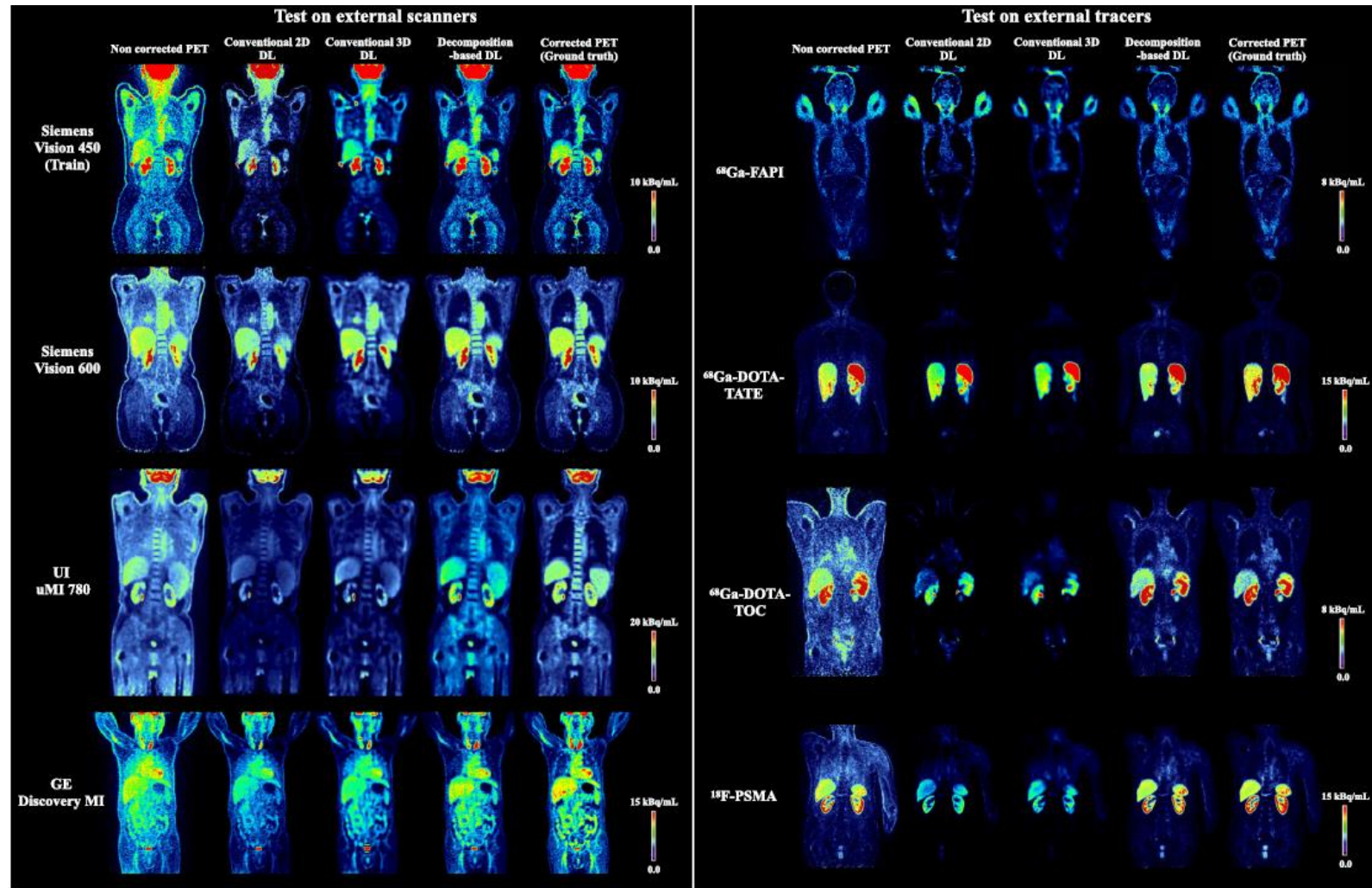


Fig. 3 | Exemplary test results of external scanners and external tracers.
Exemplary test results of ^{18}F -FDG imaging from Siemens Vision 450, Siemens Vision 600, UI uMI 780, and GE Discovery MI and imaging from ^{68}Ga -FAPI (Vision 450-SH),

^{68}Ga -DOTA-TATE (Vision 450-SH), ^{68}Ga -DOTA-TOC (Vision 600-Bern) and ^{18}F -PSMA (Vision 600-Bern). Note that the color bars used for non-corrected PET are in the range of 15% of the presented color bars.

New trends in PET (AI examples)

Attenuation correction without need to perform a CT

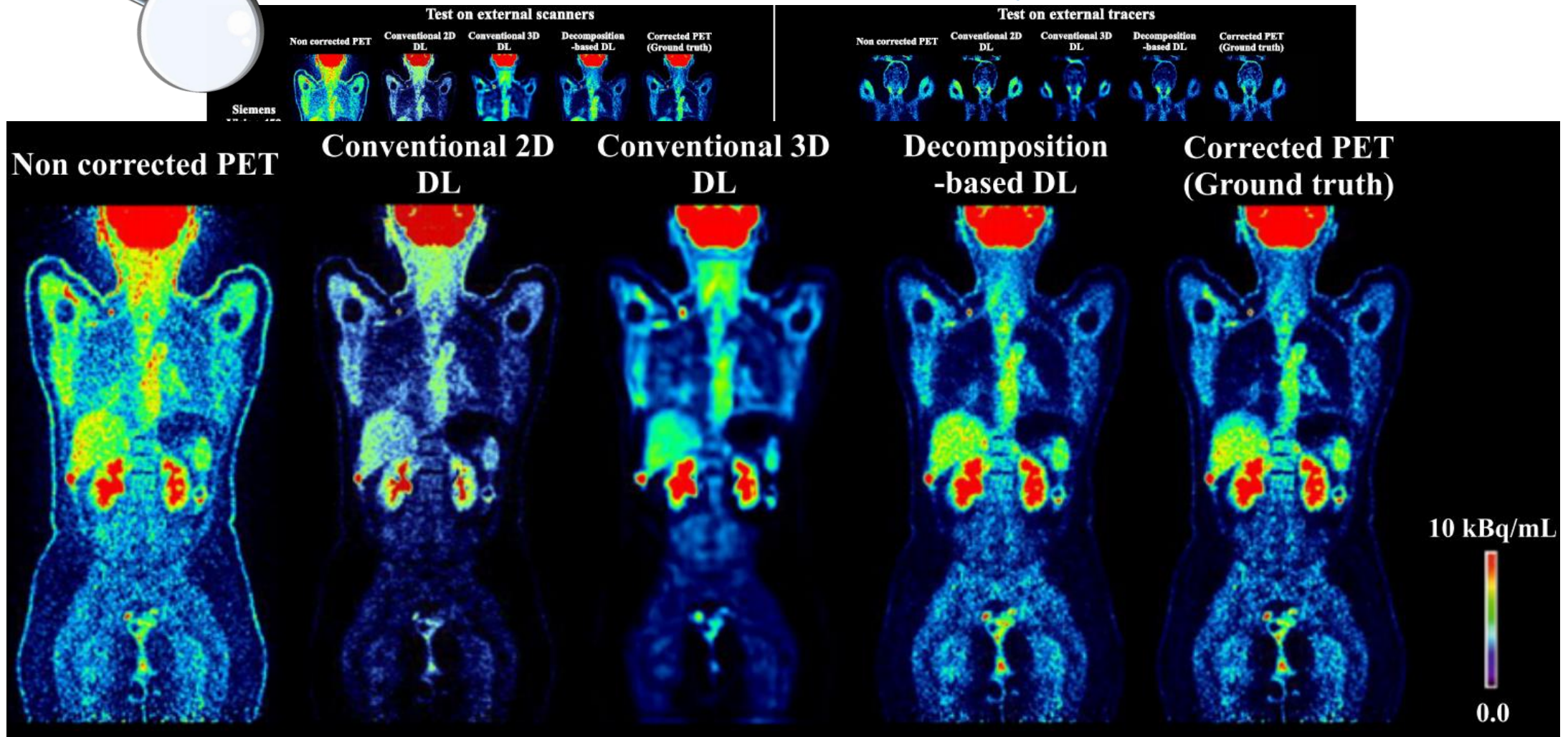


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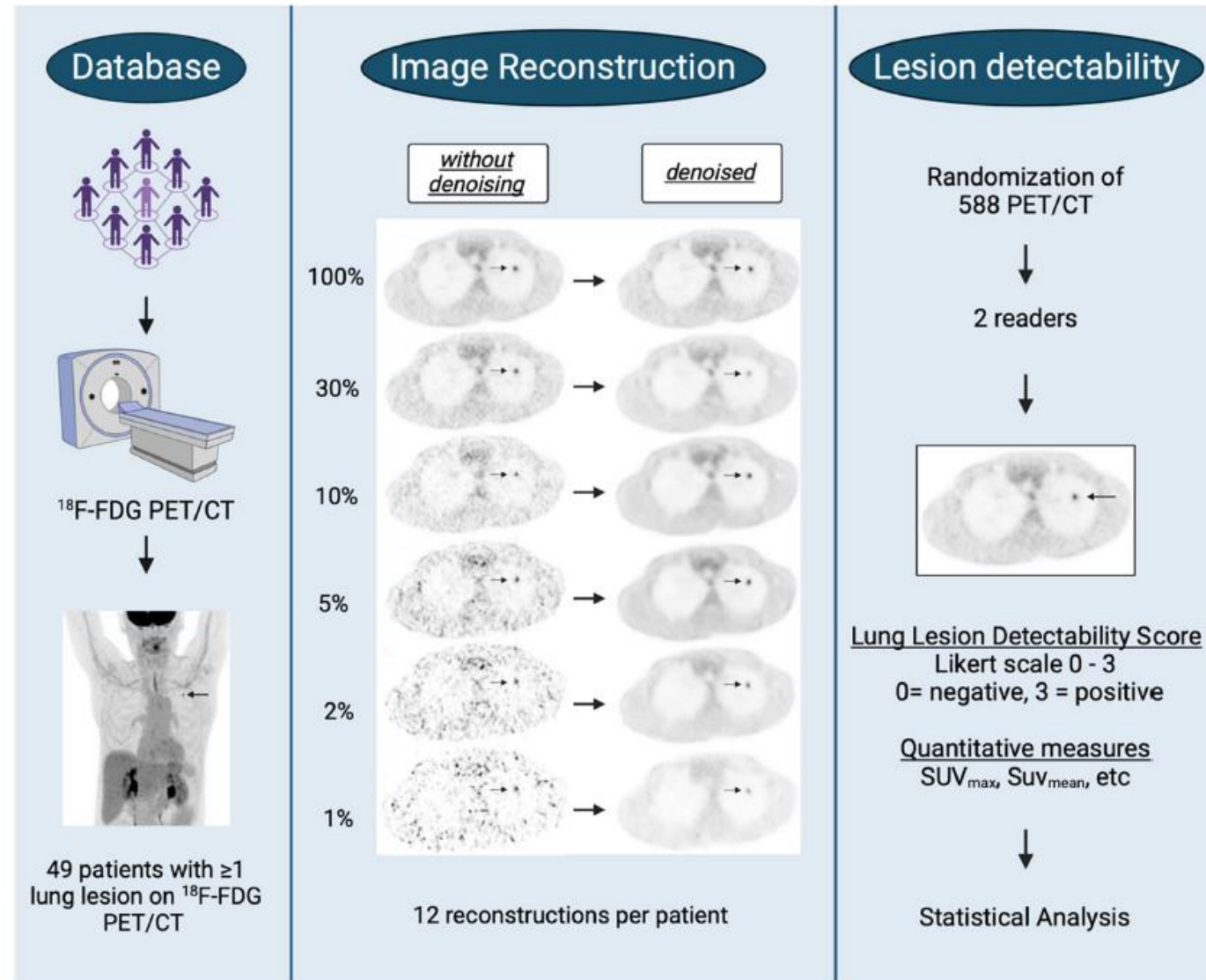
^{68}Ga -DOTA-TATE (Vision 450-SH), ^{68}Ga -DOTA-TOC (Vision 600-Bern) and ^{18}F -PSMA (Vision 600-Bern). Note that the color bars used for non-corrected PET are in the range of 15% of the presented color bars.

New trends in PET (AI examples)

convolutional neural network denoising for low PET statistics

4458

European Journal of Nuclear Medicine and Molecular Imaging (2025) 52:4456–4466



New trends in PET (AI examples)

convolutional neural network (CNN) denoising for low PET statistics

- Inject down to 1% of the initial activity and use CNN to try to restore the original signal.
- Possible application : very low-dose lung screening.

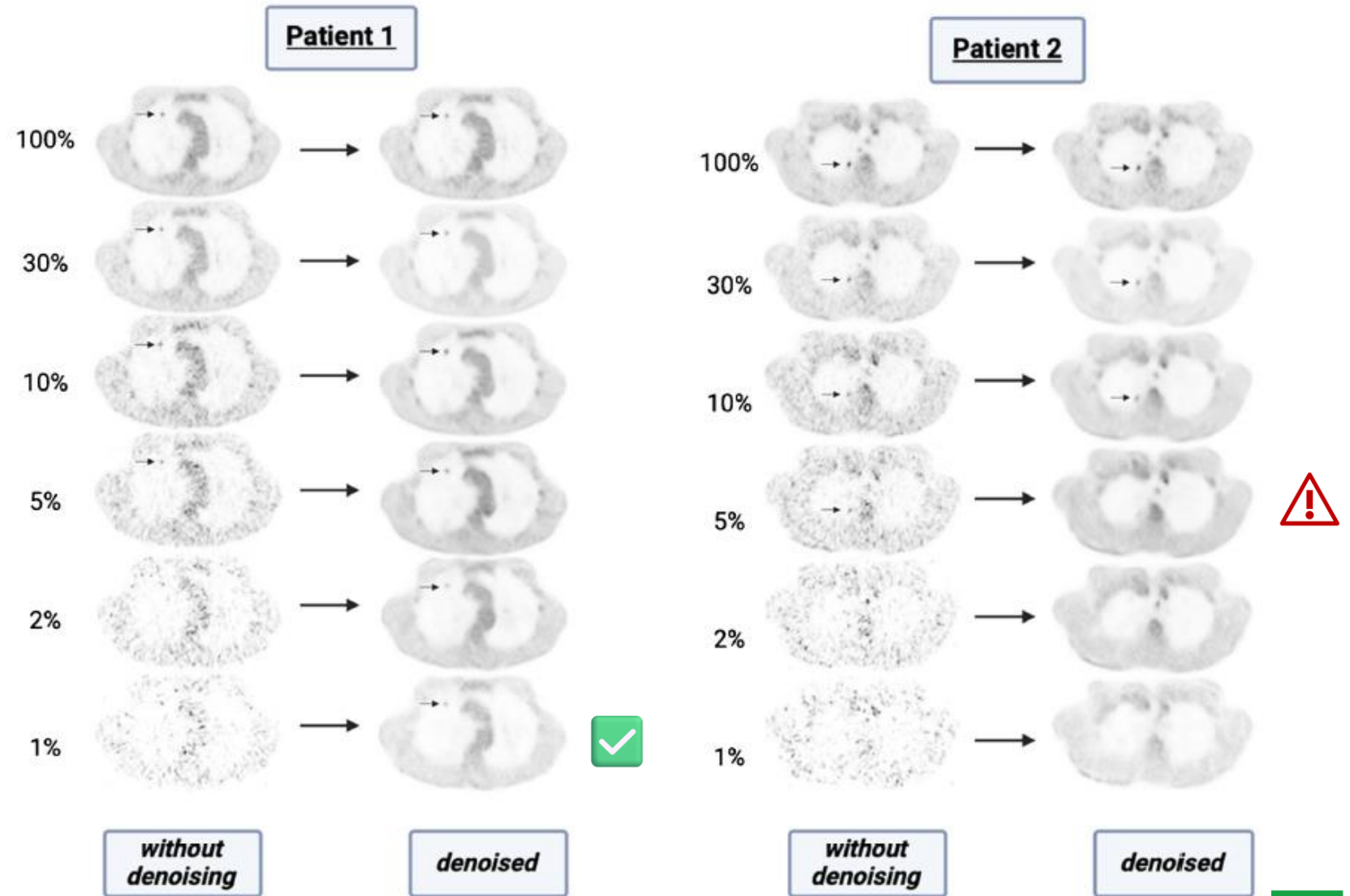


Fig. 3 Example of 5 decimation levels of $[^{18}\text{F}]$ -FDG PET with and without denoising in two patients. The lung lesion score stays positive for all reconstructions on patient 1. On patient 2 the lung lesion detectability score becomes negative in the 2% and 1% decimations

New trends in PET (AI examples)

deep learning-based time-of-flight (ToF) for non-ToF PET

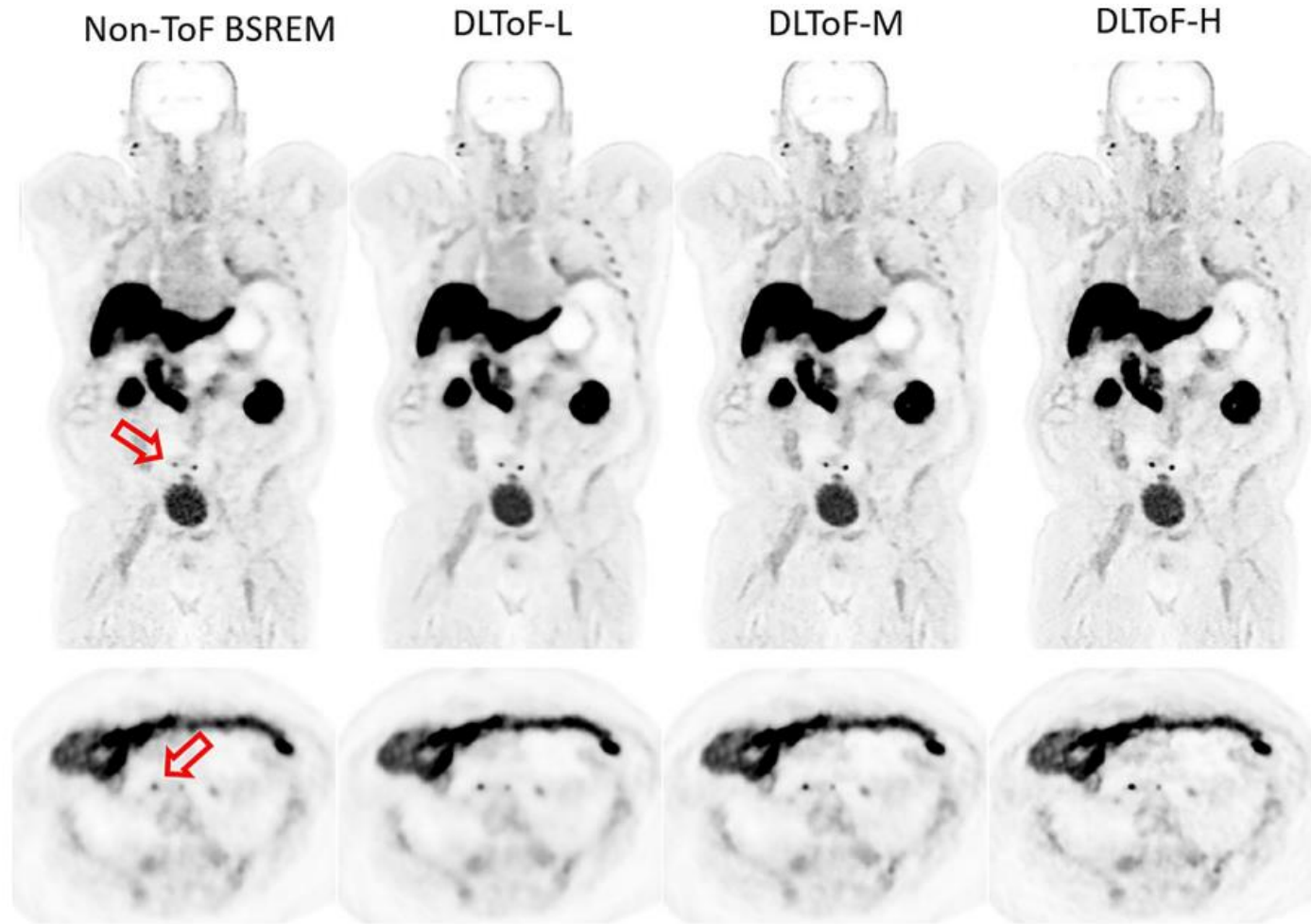
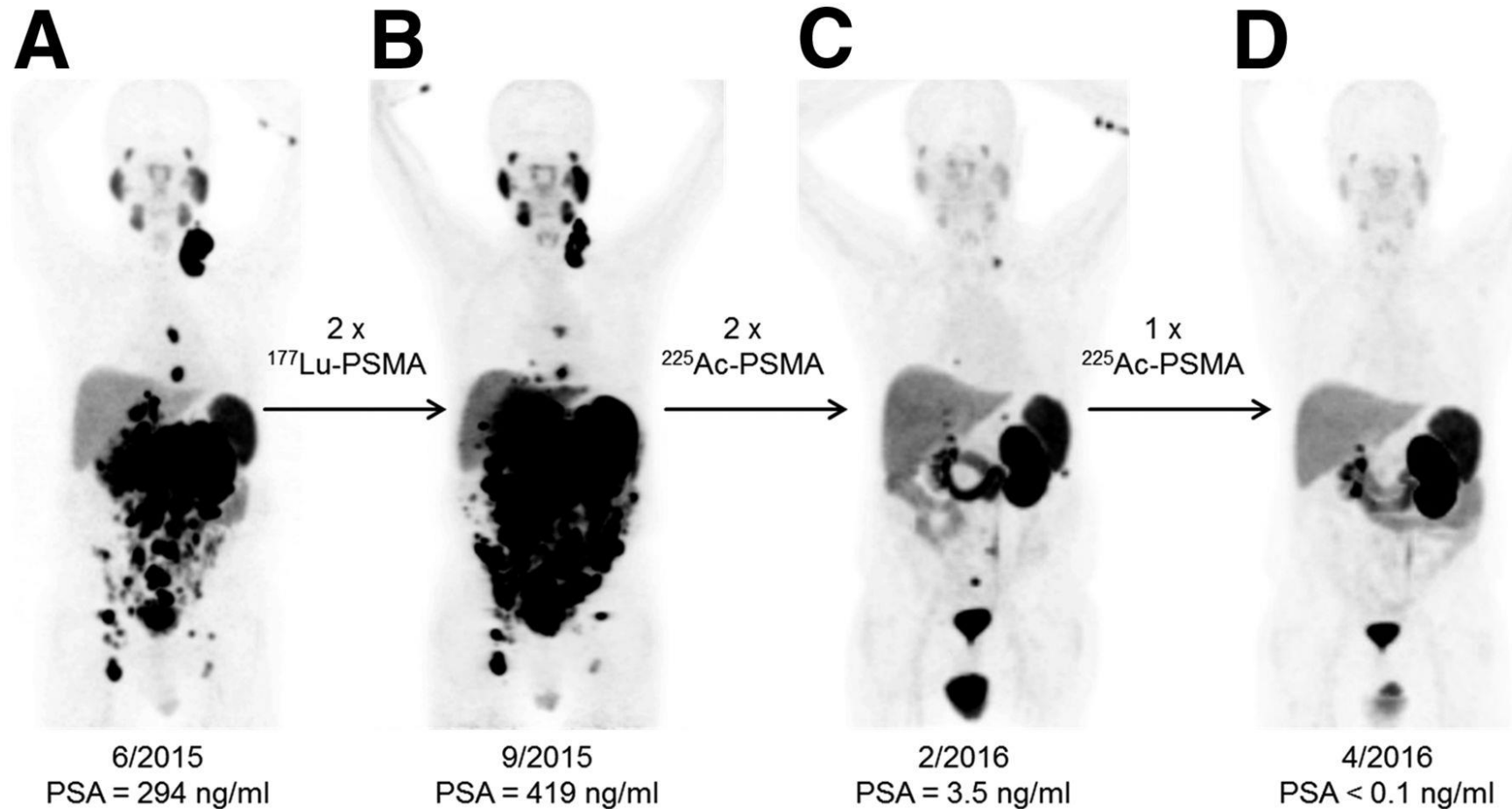


Fig. 7 DL-ToF enhancement of a representative ^{18}F -PSMA-1007 test subject with a BMI of 39.1 kg/m^2 with an injected activity of 249 MBq scanned on a GE Omni LegendTM PET/CT scanner. Demonstrating

two sub-5 mm PSMA avid retroperitoneal nodes at the L5 level. Display window: 0–6 SUV

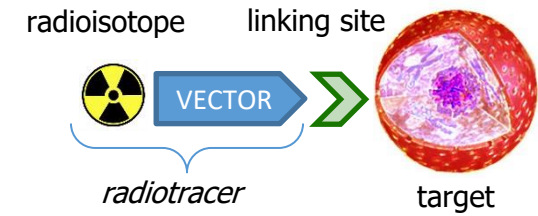
Therapeutic applications in NM

BONUS: radionuclide therapy, the future of NM?



68Ga-PSMA-11 PET/CT scans of patient B. In comparison to initial tumor spread (A), restaging after 2 cycles of β -emitting $^{177}\text{Lu-PSMA-617}$ presented progression (B). In contrast, restaging after second (C) and third (D) cycles of α -emitting $^{225}\text{Ac-PSMA-617}$ presented impressive response.

Recap : Nuclear Medicine applications



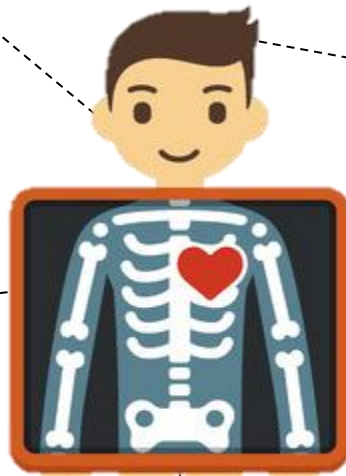
Diagnostics
Therapy

... and many more!

Oncology
F-18 FDG (PET)

Thyroid diseases
I-131 (T+SPECT)
I-124 (PET)
I-123 (SPECT)

Brain diseases
F-18 FET/FDG (PET)
I-123 DaTscan (SPECT)



Heart Disease
Rb-82 (PET)
Tl-201 (SPECT)
Tc-99m MIBI (SPECT)

Neuroendocrine tumors
Lu-177-peptide (T+SPECT)
Y-90-peptide
Ga-68/Sc-44-peptide (PET)
I-131-MIBG (T+SPECT)

Lymphoma (NHL)
Y-90-mAb (T + Scintigraphy)
In-111 (SPECT)/Zr-89 (PET)

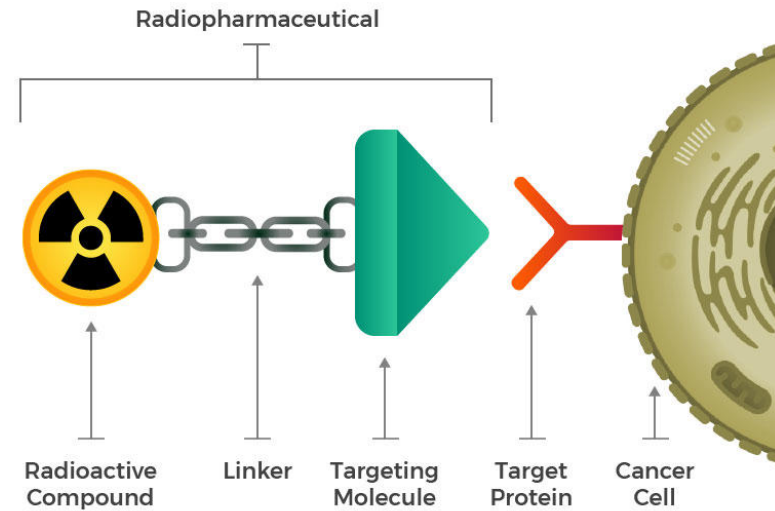
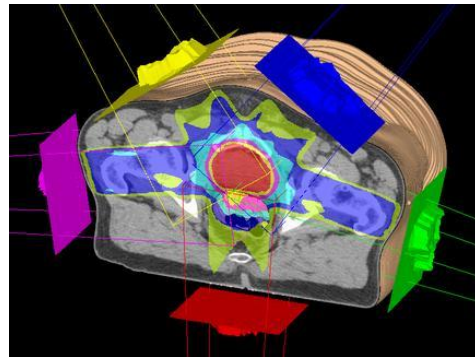
Bone & joint pain
Sr-89 (T + Scintigraphy)
P-32 (T + Scintigraphy)
Sm-153-EDTMP (T + Scintigraphy)
Re-188-HEDP (T + Scintigraphy)
Y-90-HEDP
Ra-223 (T + Scintigraphy)
Y-90, Re-186, Er-169
Tc-99m DTPA

Liver tumors
Selective Internal
Radiotherapy (SIRT)
Y-90 microspheres
(T+PET+SPECT)
Tc-99m-MAA (SPECT)

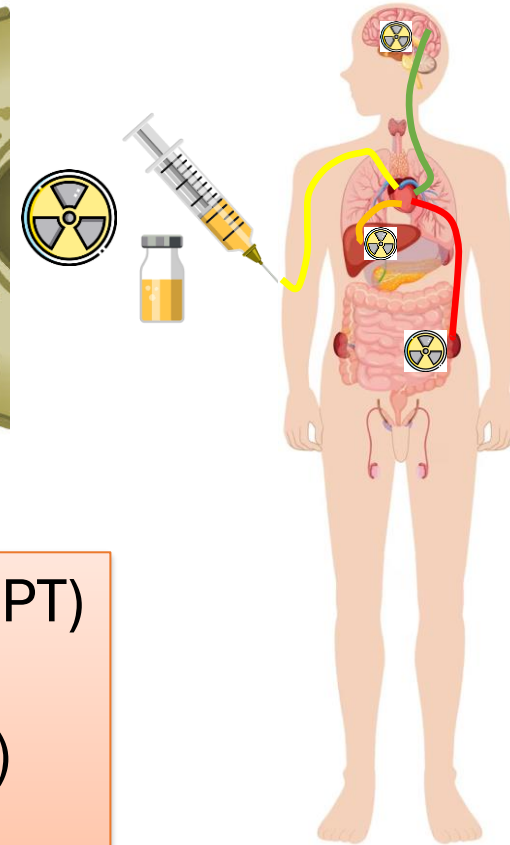
Prostate cancer
Lu-177-PSMA (T+SPECT)
Ga-68/Sc-44-PSMA (PET)

Bases of therapy and dosimetry in NM

External beam radiation therapy
(EBRT)



Systemic administration



Radiopharmaceutical therapy (RPT)
Targeted radiotherapy (TRT)
Molecular Radiotherapy (MRT)
Radioligand therapy (RLT)
Radioisotope therapy ...
Many names for similar principles!

Bases of therapy and dosimetry in NM

Systemic administration

External Beam

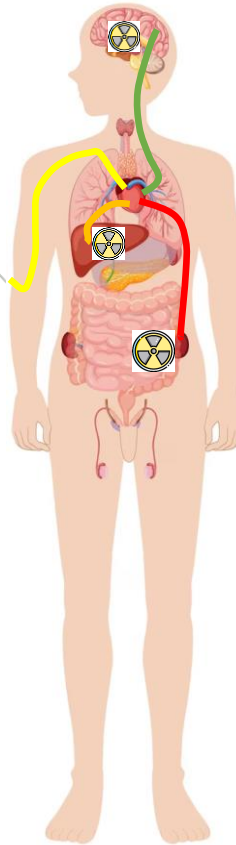
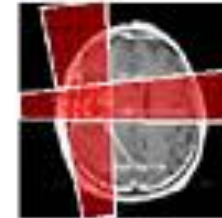
Targeted Radionuclide



Requires knowledge of tumor location



Requires knowledge of tumor biology



- **Brain Tumor Targeted Radiotherapy:**
 - Less toxic effects to normal brain
 - Can be designed for treating small deposits of tumor cells infiltrating normal brain

Dose calculation to a target r_T – MIRSD formalism

Absorbed dose in target region r_T [Gy]



r_T : thyroid

$$D(r_T) = \sum_{r_S} \tilde{A}(r_S) S(r_T \leftarrow r_S)$$

$$\tilde{A}(r_S) = \int_{t_0}^{\infty} A(r_S, t) dt$$

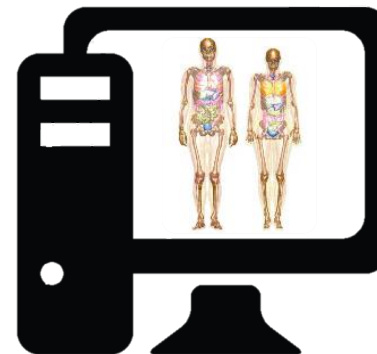
number of decays in r_S

$$S(r_T \leftarrow r_S) = \sum_i \frac{\Delta_i \phi(r_T \leftarrow r_S, i)}{M(r_T)}$$

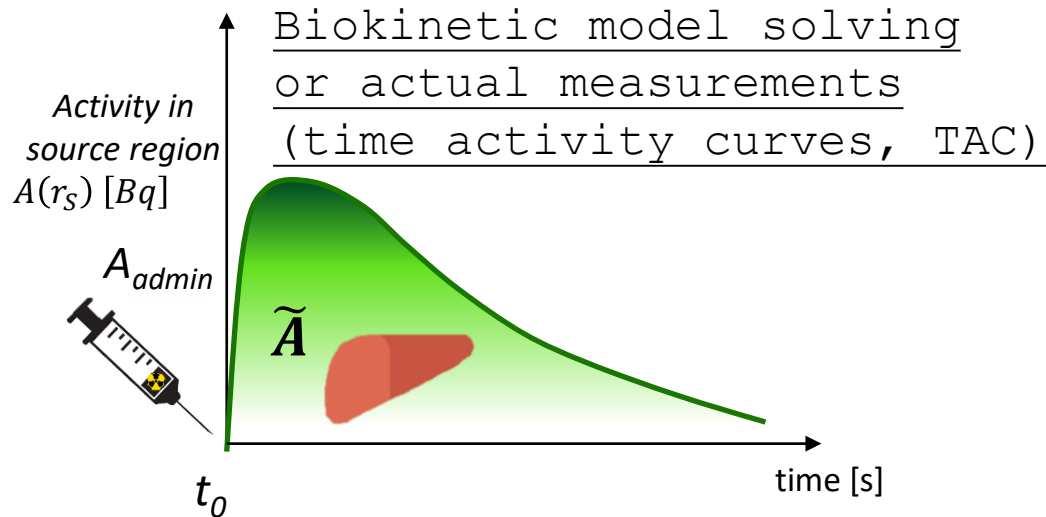
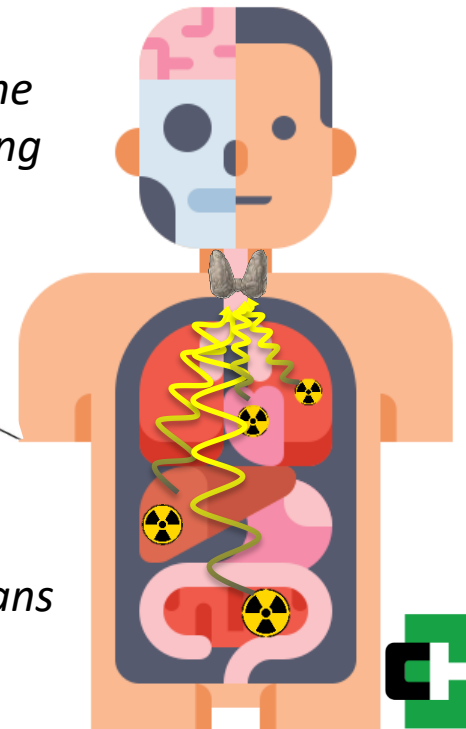
S-factor [Gy/(Bq.s)]:

Absorbed dose delivered to the target tissue r_T per decay taking place in the source tissue r_S

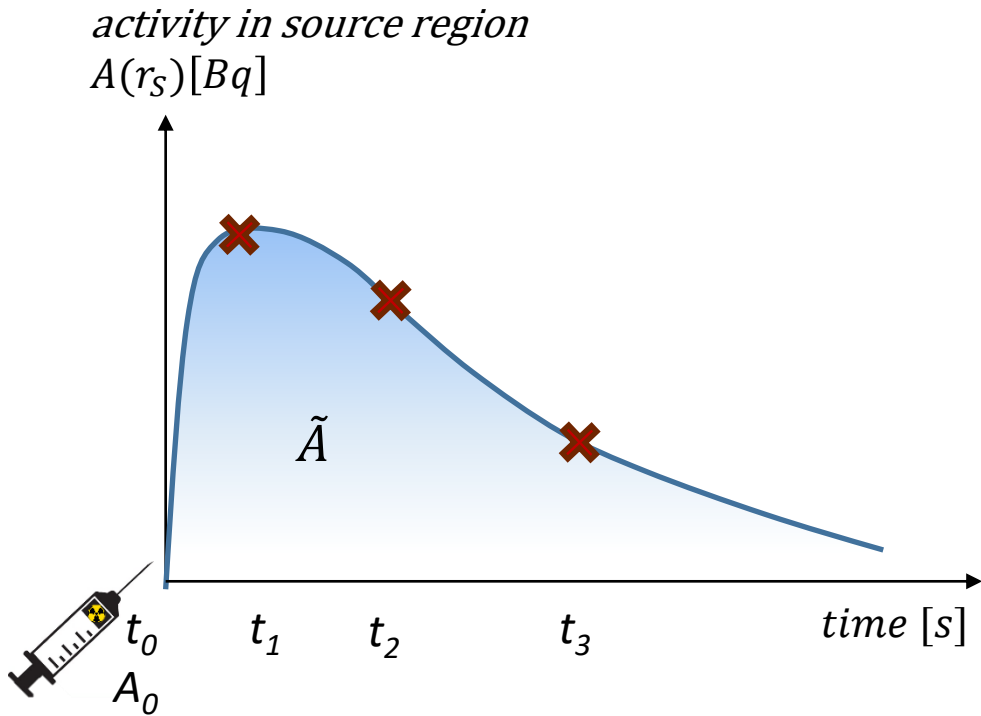
Dosimetric models



r_S : organs



Dose calculation to a target r_T – MIRD formalism



$$\tilde{A}(r_S) = \int_{t_0}^{\infty} A(r_S, t) dt$$

TAC = time activity curve
 (number of decays in r_S)

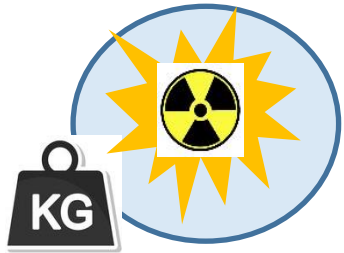
$$S(r_T \leftarrow r_S) = \sum_i \frac{\Delta_i \phi(r_T \leftarrow r_S, i)}{M(r_T)}$$

S-factor [Gy/(Bq.s)] :
 absorbed dose delivered
 to r_T per nuclear
 transformation in r_S
 (radiation weighted).

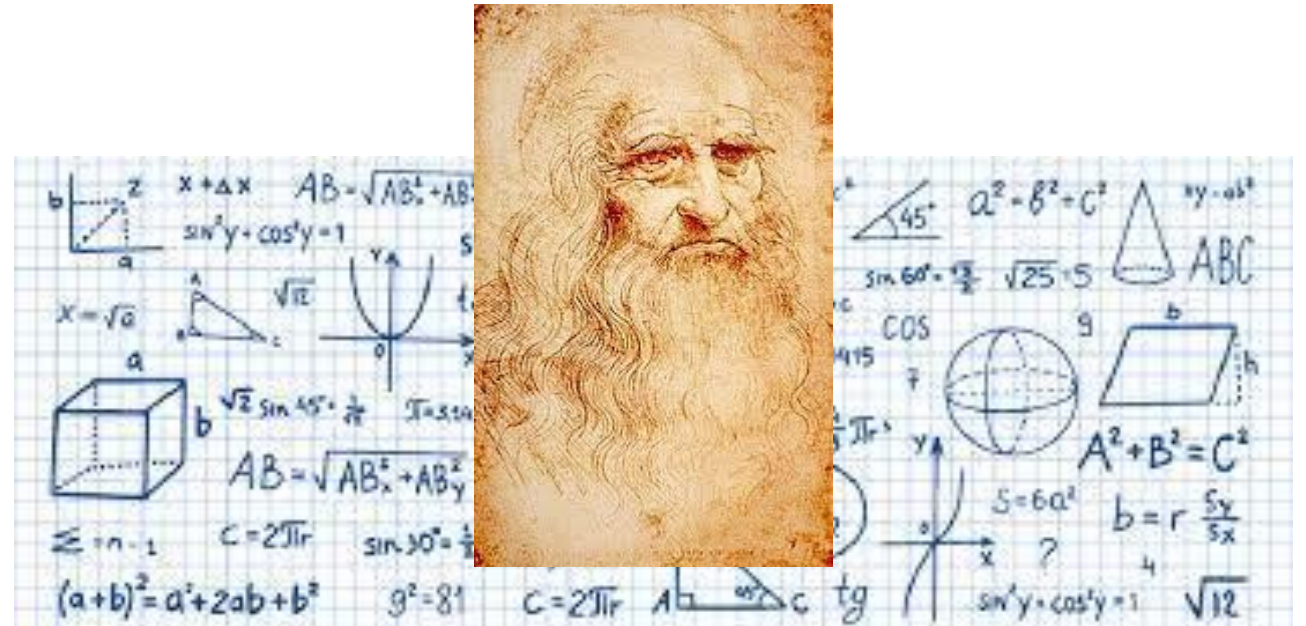
$$D(r_T) = \sum_{r_S} \tilde{A}(r_S) S(r_T \leftarrow r_S) \quad \text{absorbed dose in } r_T \text{ [Gy]}$$

*But WHY do we care about **dose**?*

Bases of therapy and dosimetry in NM

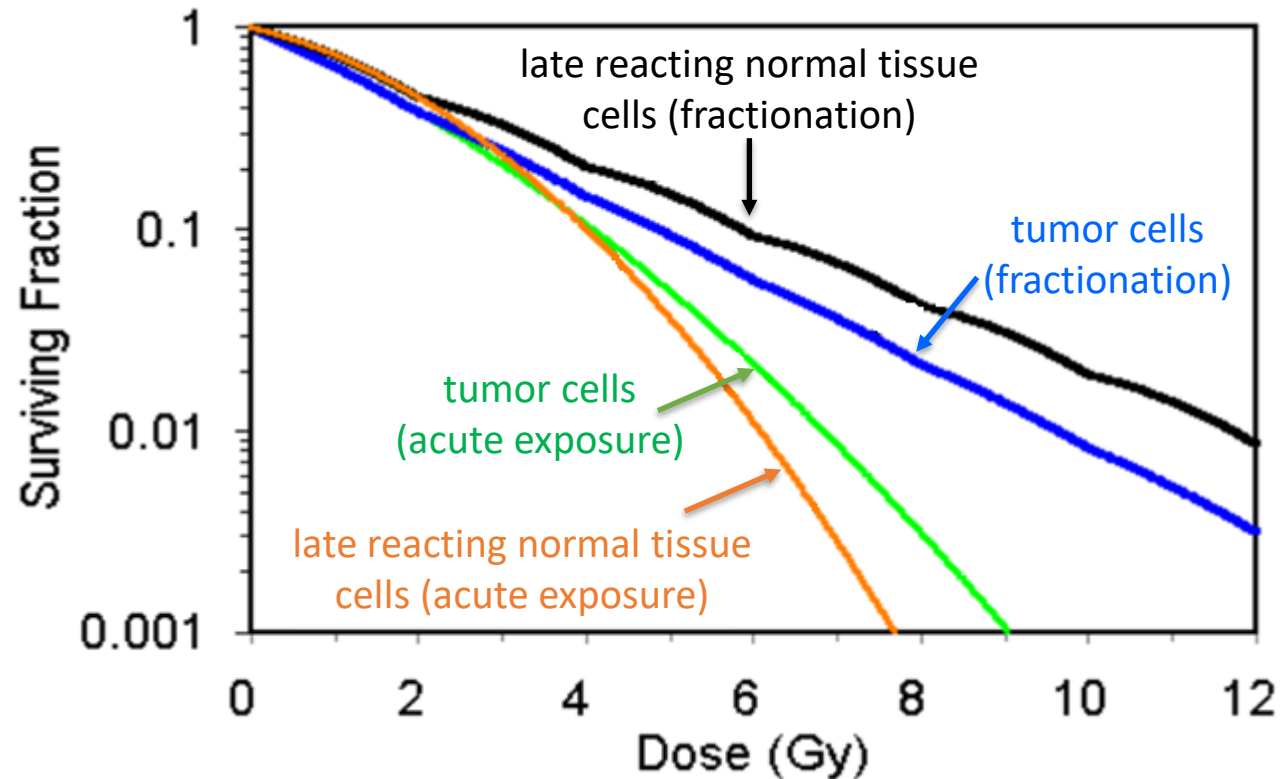


$$D(\text{Gy}) = \frac{\text{Energy (J)}}{\text{Mass (kg)}}$$



Bases of therapy and dosimetry in NM

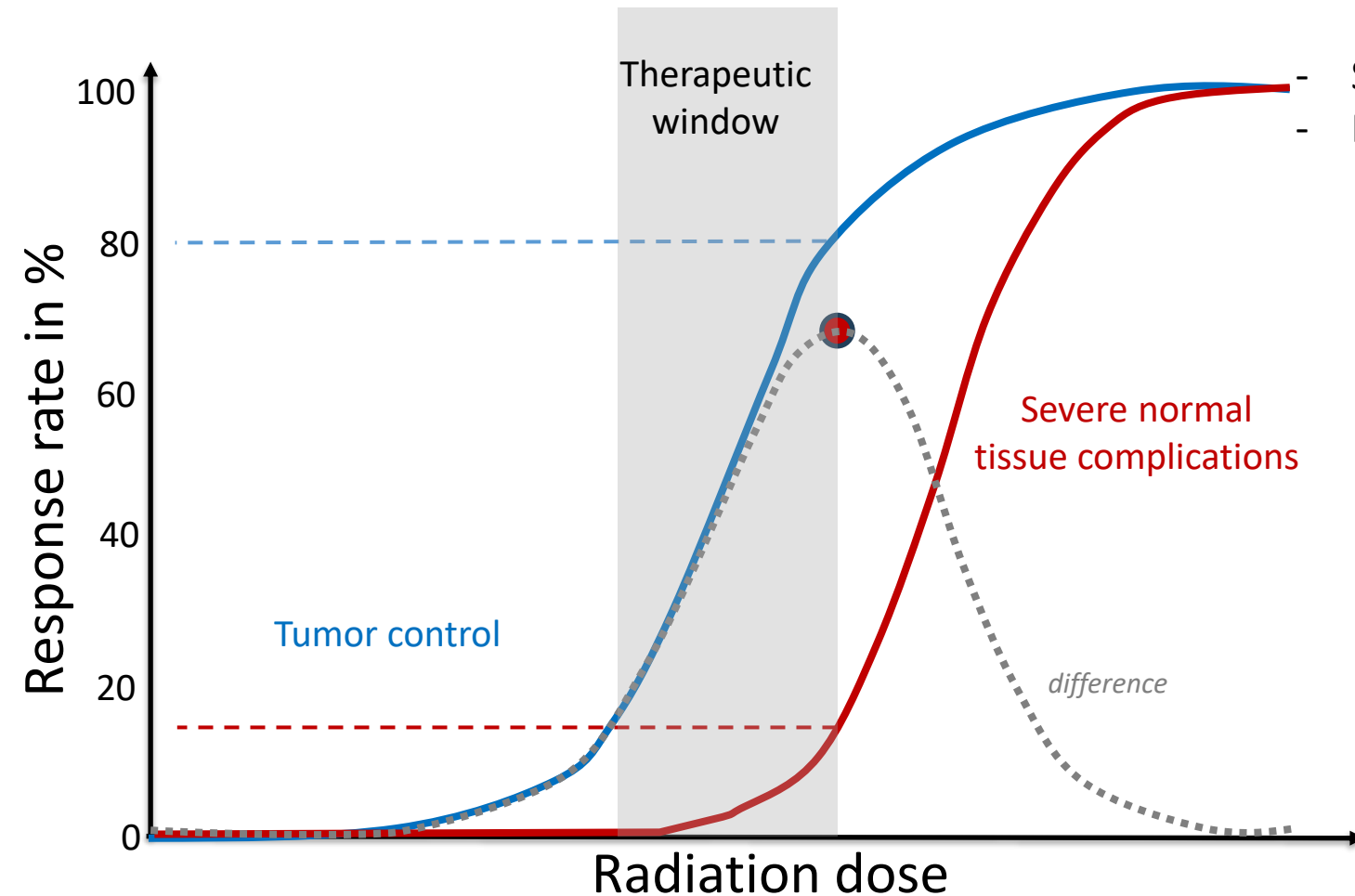
Model of cell survival under ionizing radiation (i.e. vs. radiation absorbed dose)



Under appropriate conditions the cell-killing probability is **higher in tumor** than in normal tissues

Bases of therapy and dosimetry in NM

Optimal treatment point: ●



- Sufficiently high tumor control probability (80%)
- Max. tolerable level of complication probability (15%)

The concept of **dose** is necessary to:

- determine whether the treatment will be effective in achieving the desired biological response.
- Predict possible toxicity to healthy tissue
- (ideally) individualize the treatment (by adjusting administered activity)
- comply with safety standards
- Dose – response relationship (?)

⚠ where do the data come from?

External beam
radiotherapy

Bases of therapy and dosimetry in NM

Dose–Response Relationships

E.M. Abbott et al. / Clinical Oncology 33 (2021) 735–743

737

- Dose-response for radionuclide therapy
- in particular toxicity - can have significant differences with respect to external beam radiotherapy (EBRT) (*cf. next lectures!*) :
 - Different spatial heterogeneity
 - Different dose/rates

Need for more investigation!

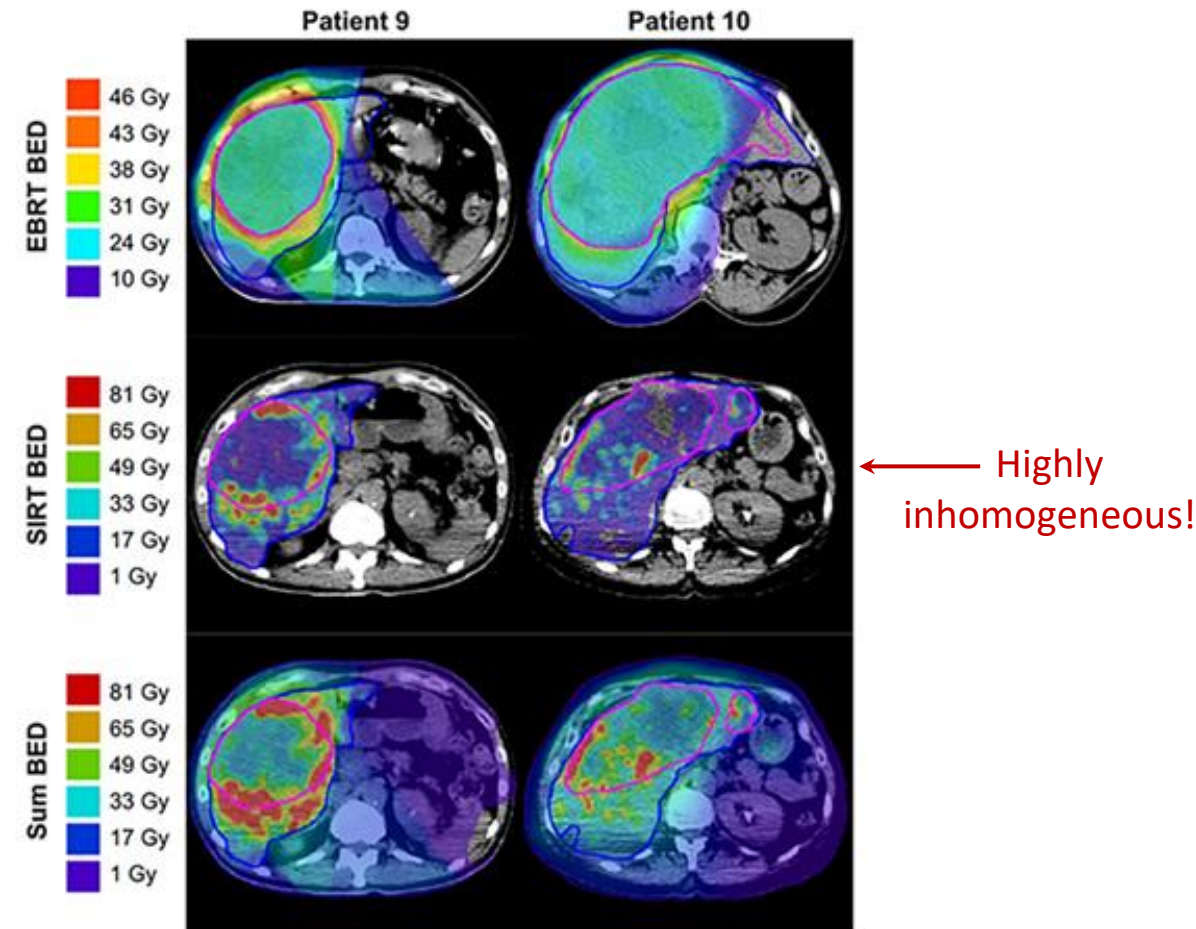
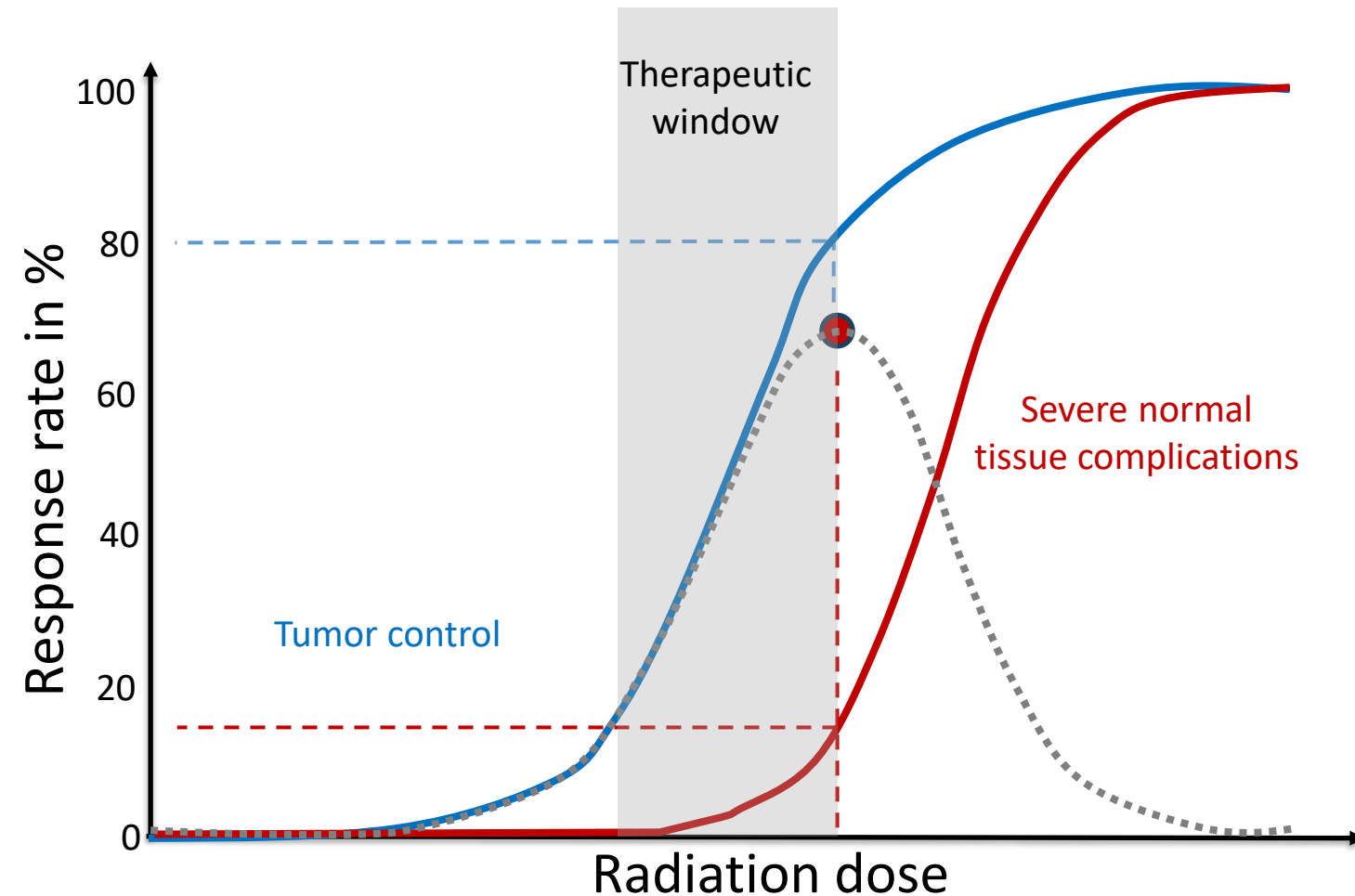


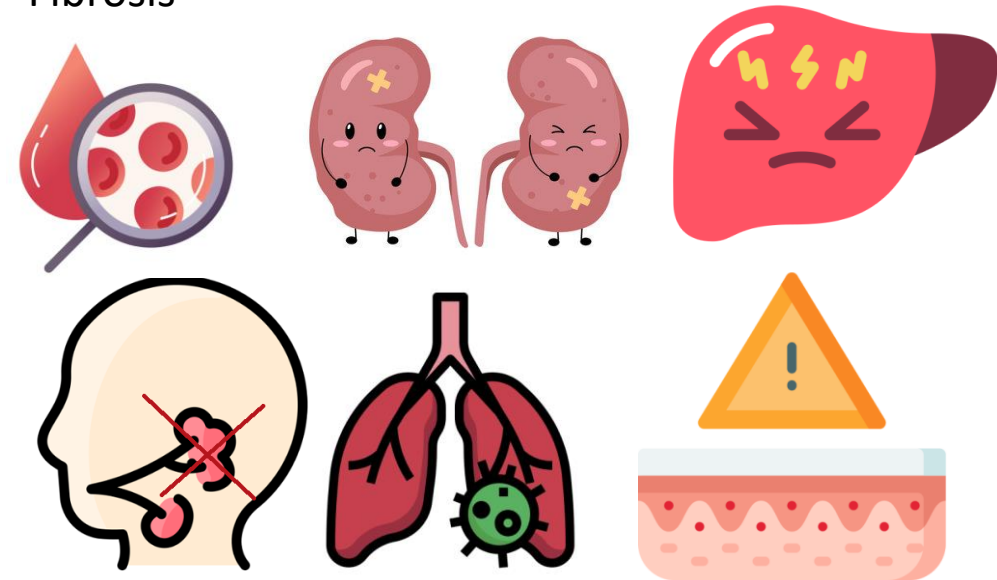
Fig 1. Biological effective dose (BED) maps for two representative patients who received external beam radiotherapy (EBRT) followed by yttrium-90 selective internal radiation therapy (^{90}Y -SIRT) for hepatocellular carcinoma.

Bases of therapy and dosimetry in NM



Toxicities in MRT (tissue):

- Hematotoxicity (red bone marrow)
- Renal toxicity
- Hepatotoxicity
- Xerostomia (salivary glands)
- Pneumonia (lungs)
- Fibrosis



Adapted from : https://doi.org/10.1007/978-3-031-08601-4_13

Pictures: https://www.freepik.com/icon/blood-cells_2096630; <https://stock.adobe.com/search?k=unhealthy+kidney>; https://www.freepik.com/icon/liver_3390186#fromView=search&page=3&position=63&uuid=432c01c3-39a3-4617-a16e-fb73304e6891; https://www.freepik.com/icon/pneumonia_5144364#fromView=search&page=1&position=33&uuid=8611fb2b-ba2b-4541-8768-ae62a875f936; https://www.freepik.com/icon/warning_11009128#fromView=search&page=2&position=32&uuid=1b3972ee-b122-467c-8506-bd36cde0da0a

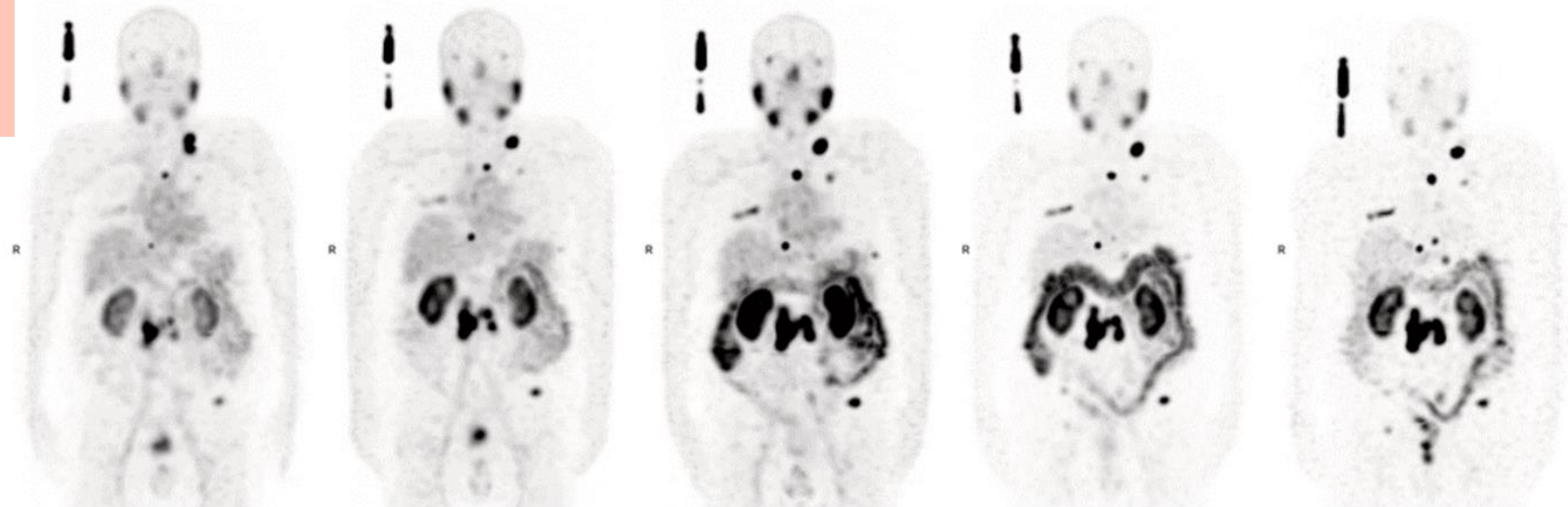
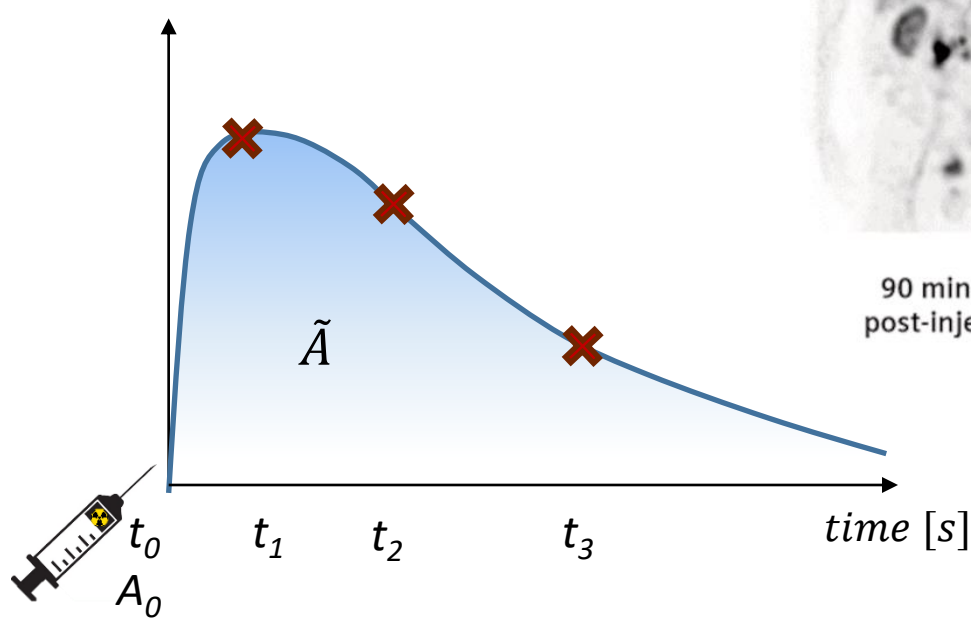
From «counts» to dose → activity quantification!

absorbed dose in r_T [Gy]

$$D(r_T) = \sum_{r_S} \tilde{A}(r_S) S(r_T \leftarrow r_S)$$

activity in source region

$A(r_S)$ [Bq]



90 minutes
post-injection

6 hours
post-injection

24 hours
post-injection

48 hours
post-injection

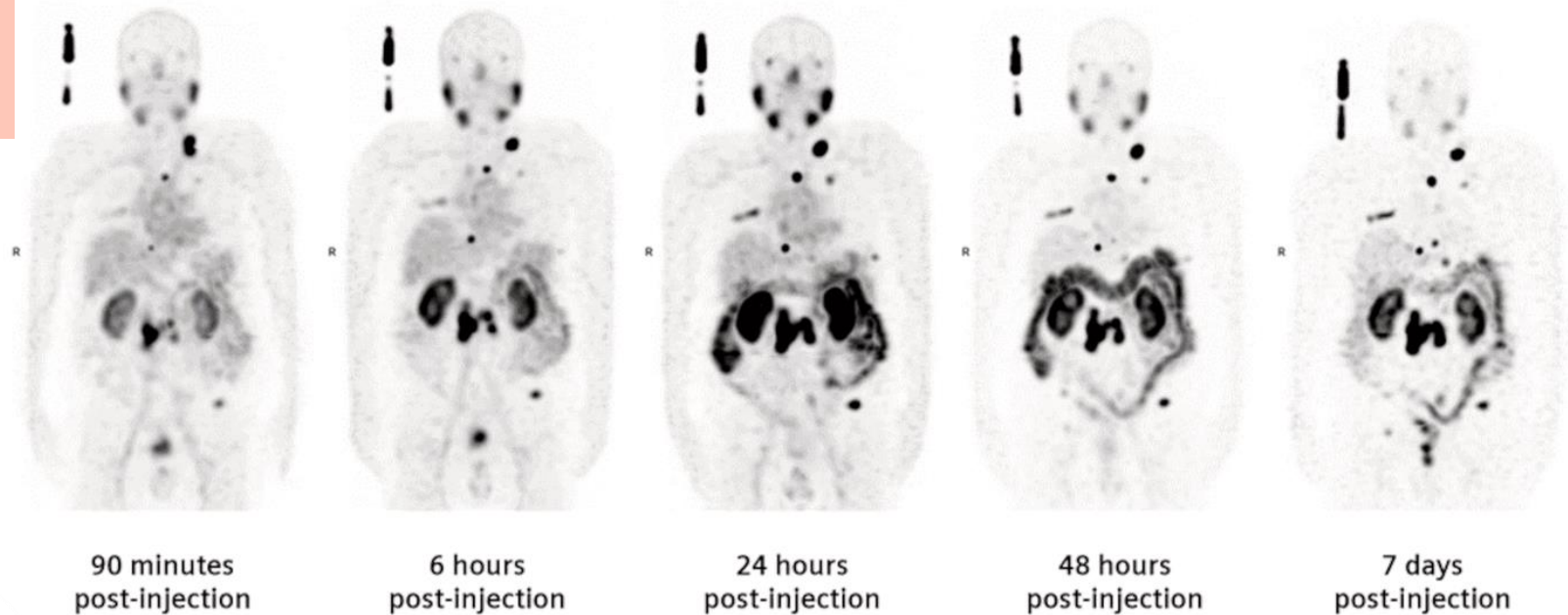
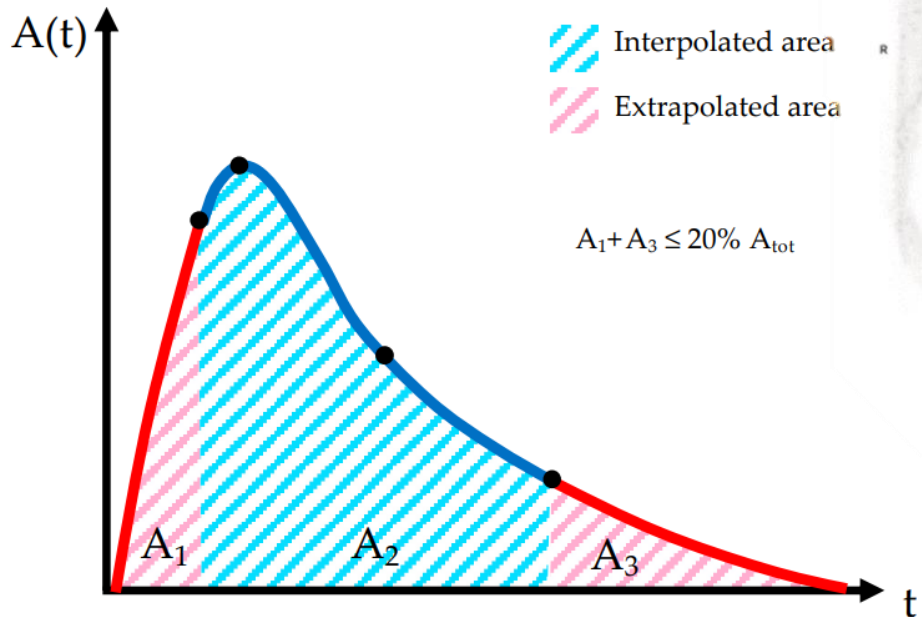
7 days
post-injection

*Choosing wisely the timing of imaging post-administration is fundamental to describe the time activity curve!
In this example : sequential imaging after Lu-177 PSMA injection.*

From «counts» to dose → activity quantification!

absorbed dose in r_T [Gy]

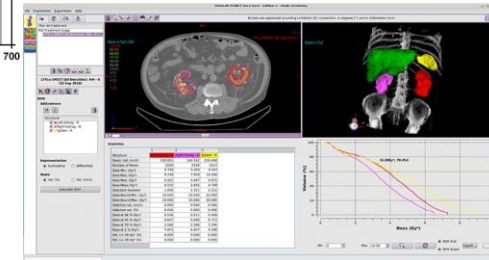
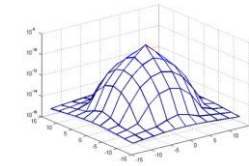
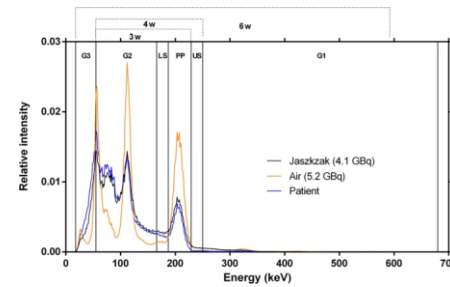
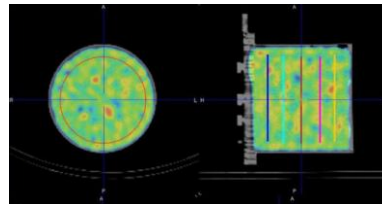
$$D(r_T) = \sum_{r_S} \tilde{A}(r_S) S(r_T \leftarrow r_S)$$



Choosing wisely the timing of imaging post-administration is fundamental to describe the time activity curve!
In this example : sequential imaging after Lu-177 PSMA injection.

Figure 2. Time-activity curve (TAC) with interpolation and extrapolation areas.

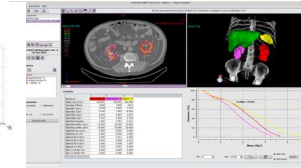
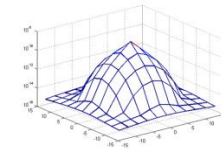
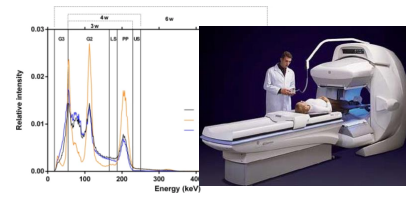
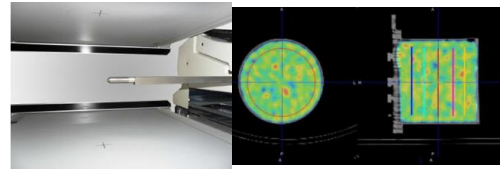
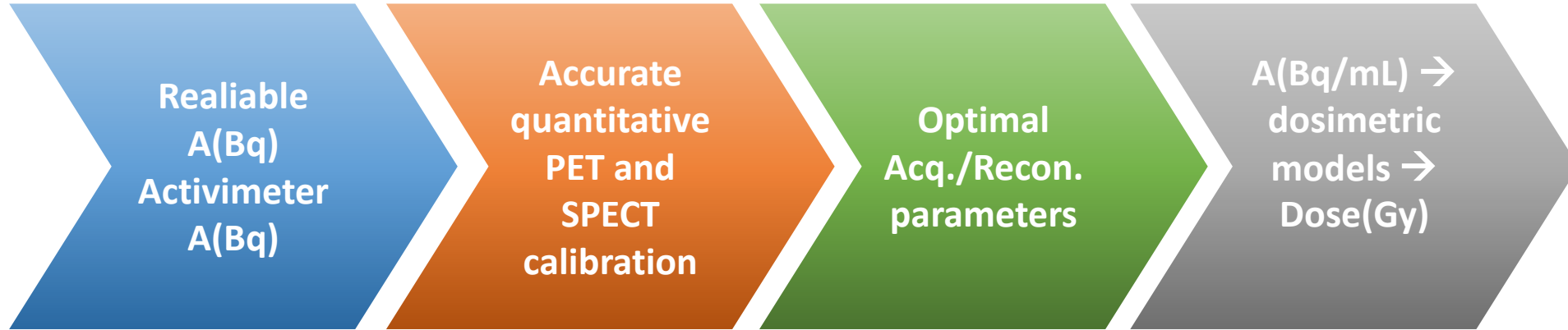
Quantitative PET and SPECT: how to...



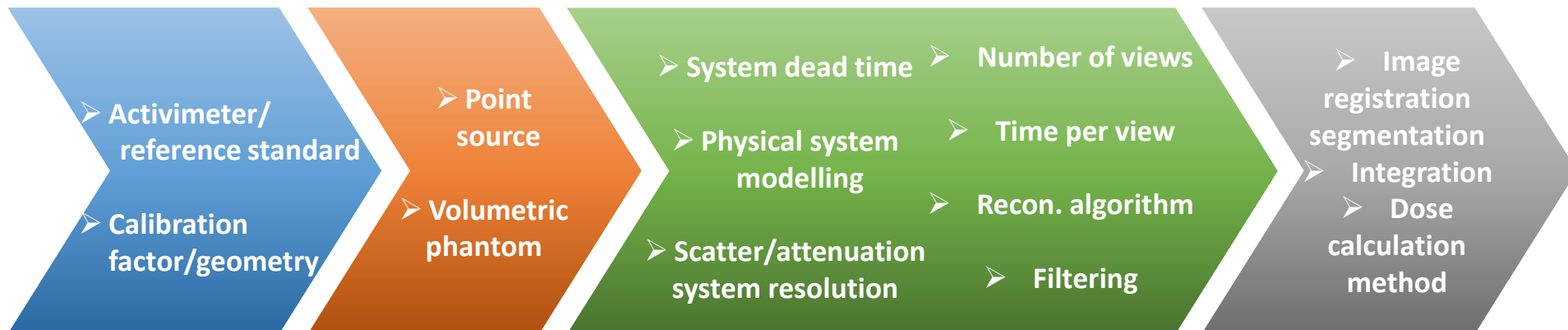
From Activity (Bq) in the syringe

→ Activity concentration (Bq/mL) in the PET or SPECT image

Quantitative PET and SPECT: how to...



Sources of quantitative bias and variability



From raw data to quantification (PET and SPECT)

Raw Sinogram Data

remove randoms (PET only)

normalize detector responses

correct for deadtime

correct for scatter

Sinogram
Ready for Reconstruction

correct for attenuation

System calibration

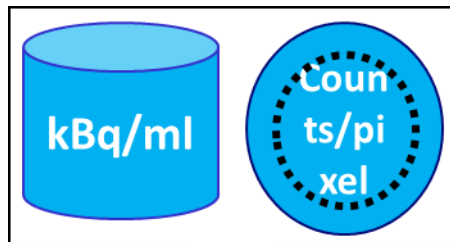
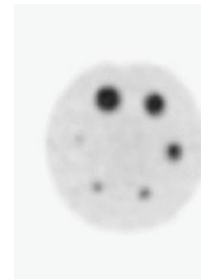
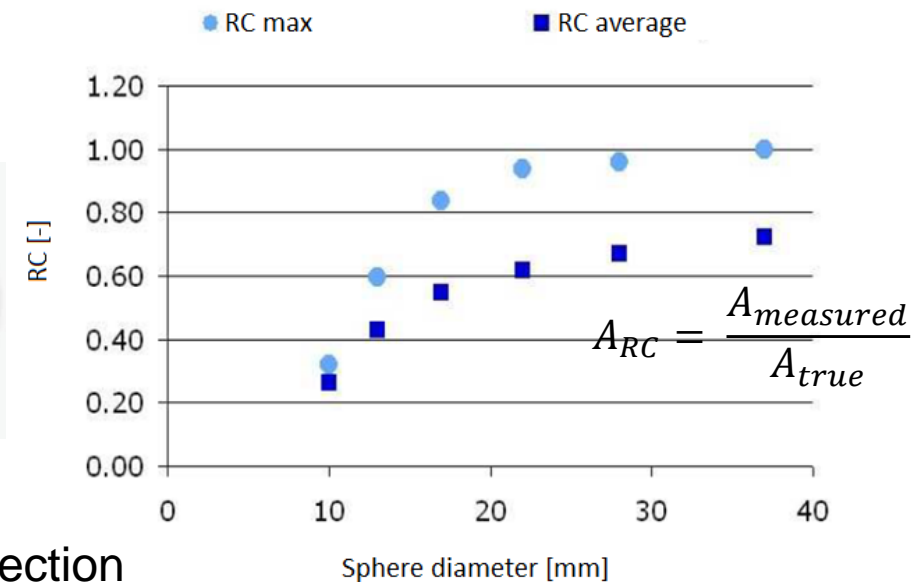


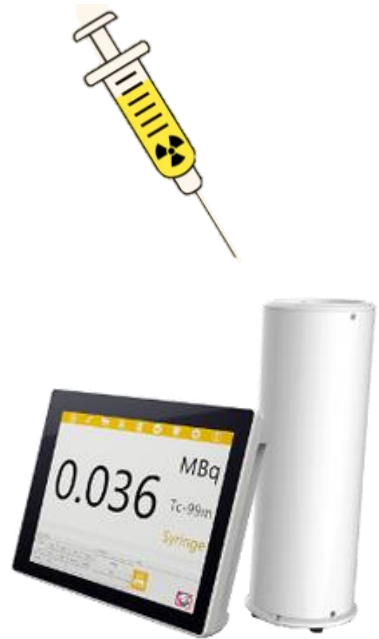
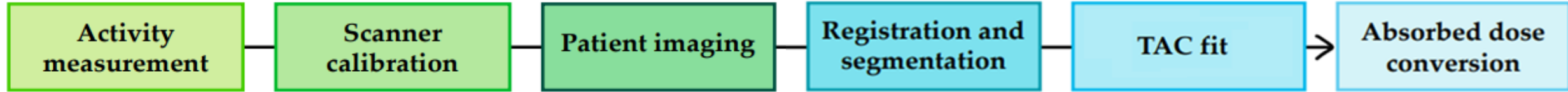
Image in kBq/ml



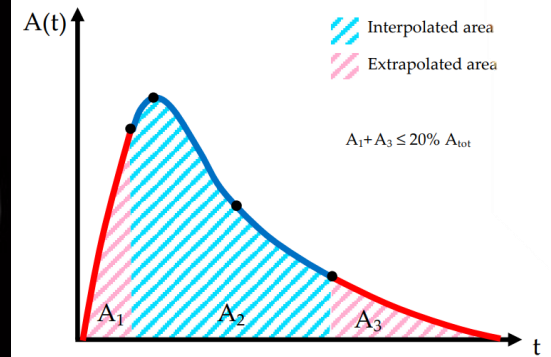
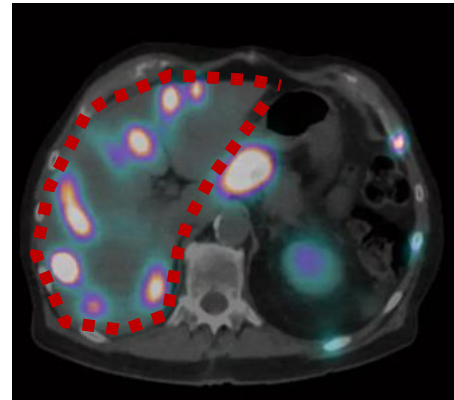
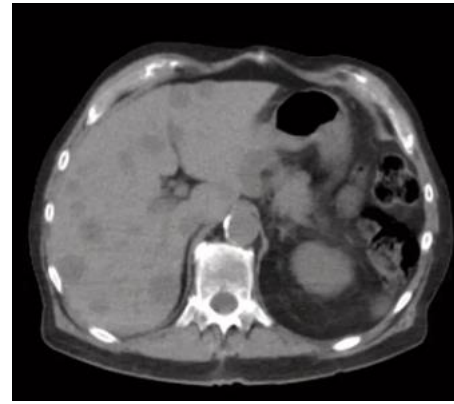
PVE correction



Simplified dosimetry workflow



48 hours post-injection



e.g. MIRD formalism:

$$D(r_T) = \sum_{r_S} \tilde{A}(r_S) S(r_T \leftarrow r_S)$$

Source : workflow adapted from DOI: 10.3390/jpm12020205

Images: <https://www.shutterstock.com/fr/image-vector/vector-radioactive-syringe-danger-death-dependence-666719677> ; https://cdn.shopify.com/s/files/1/1750/9895/t/2/assets/mega-menu-6592-comecer-vdc606icon-2028035036_320x.png?10165514685249898252 ; <https://www.dr-w-koch.de/index.php/Nuklearmedizin-und-Radiologie/Methoden-und-Strahlenexposition/die-gamma-kamera-spect-kamera.html> ; <https://www.siemens-healthineers.com/molecular-imaging/mi-clinical-corner/clinical-case-studies/tumor-organ-dosimetry-sequential-quantitative-spect-ct> ; <https://www.siemens-healthineers.com/en-us/molecular-imaging/mi-clinical-corner/clinical-case-studies/tumor-organ-dosimetry-sequential-quantitative-spect-ct>

What kind of therapies exist in nuclear medicine?

(non exhaustive list)

Radioactive iodine therapy (RAI)

- Thyroid cancer
- Hyperthyroidism (Graves' disease)

Targeted radionuclide therapy (TRT)

- Neuroendocrine (NET) tumors, meningiomas and neuroblastomas (vector : DOTA)
- Castration-resistant prostate cancer (vector: PSMA)
- Neuroendocrine (NET) tumors (vector: MIBG)
- Bone metastases (α)

Selective internal radiotherapy (SIRT)

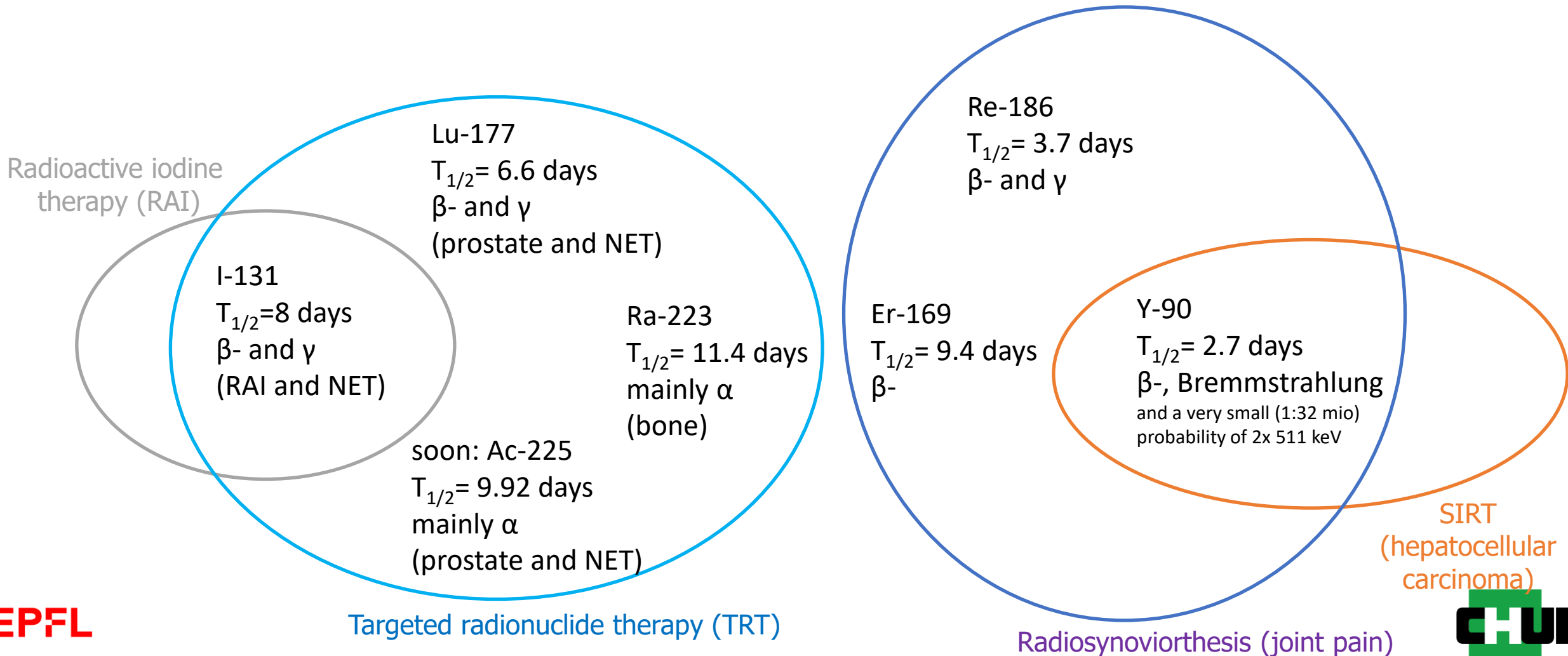
- Hepatocellular carcinoma (liver tumor)

Radiosynoviorthesis

- Joint pain

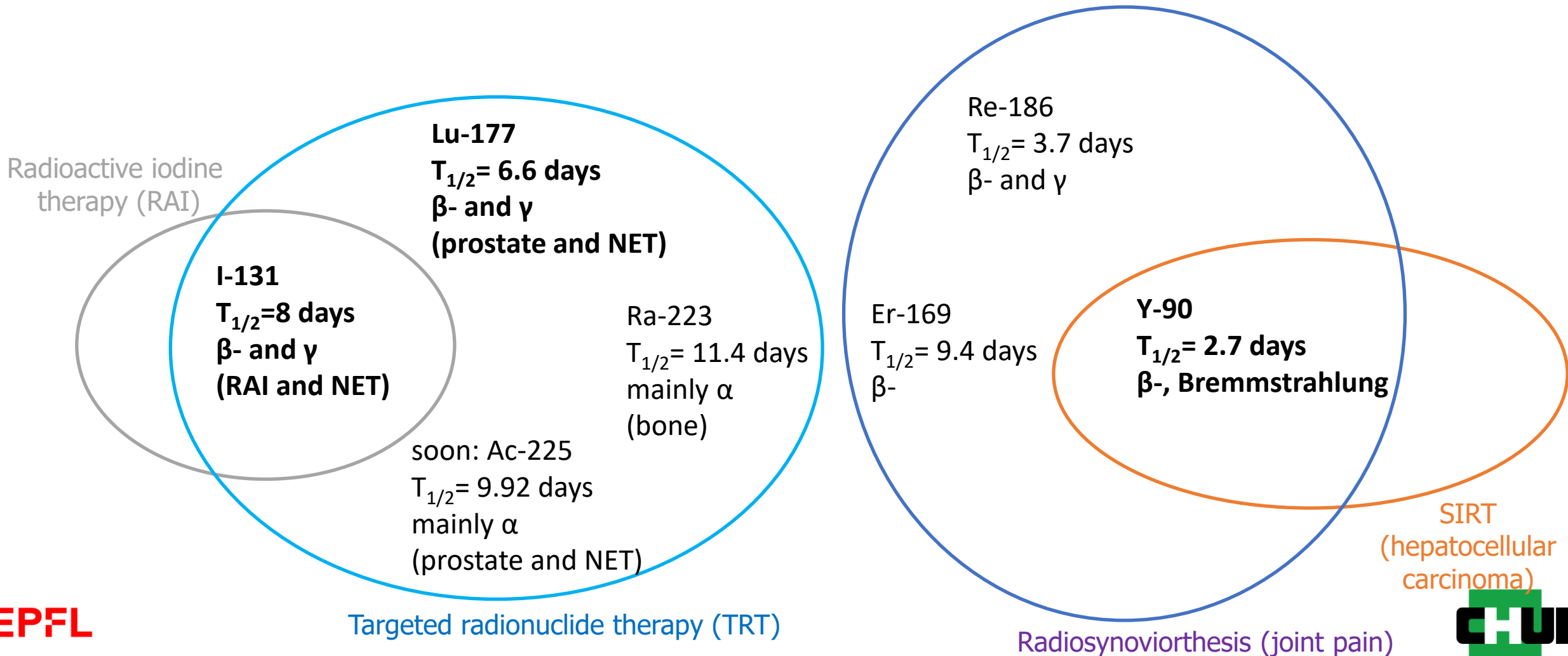
What radionuclides for therapies in nuclear medicine?

(non exhaustive list)



What radionuclides for therapies in nuclear medicine?

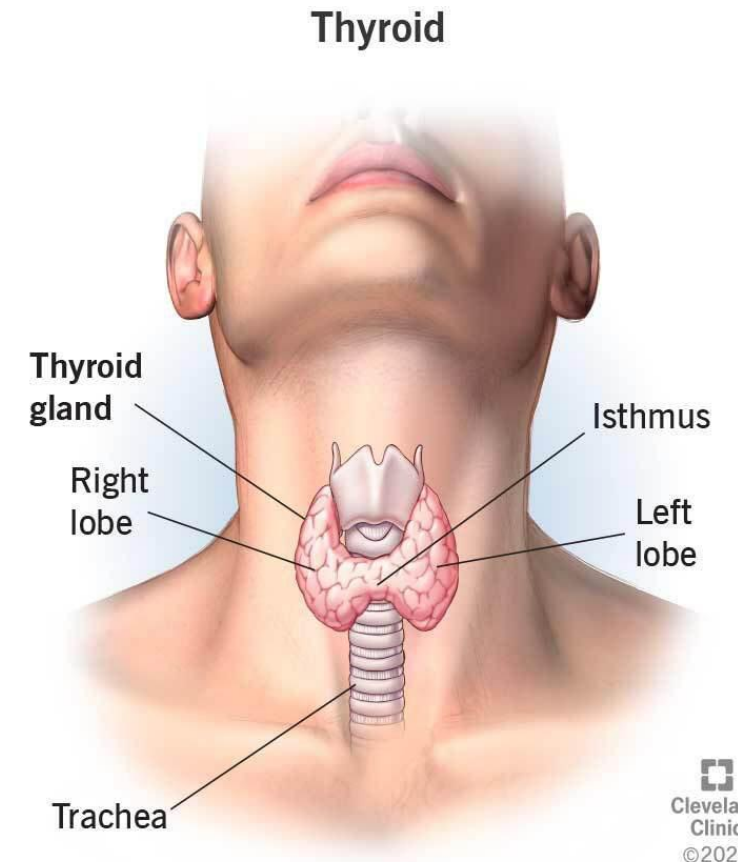
(non exhaustive list)



More detail about the therapies

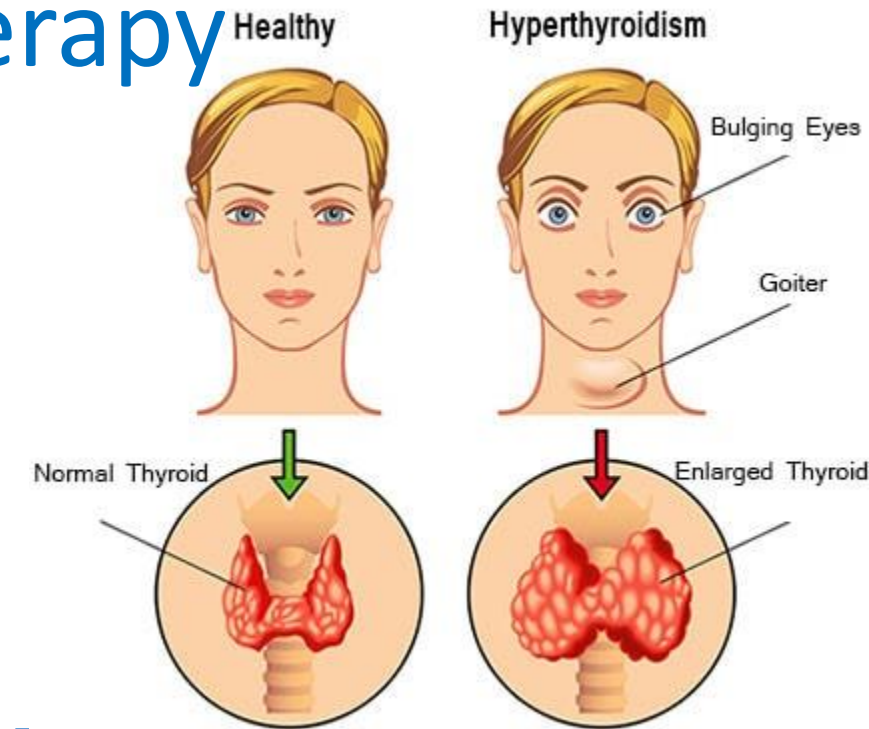
Radioactive iodine therapy

- The thyroid is a gland located at the front of the neck and it's part of the endocrine system, which produces hormones that regulate many body functions.
- It produces hormones that regulate metabolism, including heart rate, weight, body temperature and energy consumption.
- It has strong affinity for iodine (element).
- Some of the thyroid diseases include :
 - Hypothyroidism: underactive thyroid → fatigue, weight gain, cold intolerance.
 - Hyperthyroidism: overactive thyroid → weight loss, rapid heartbeat, anxiety, heat intolerance.
 - Goiter: Enlarged thyroid, neck swelling, difficulty in breathing/swallowing.
 - Thyroid nodules or cancer: benign or malignant growth.



Radioactive iodine therapy

- **Hyperthyroidism** and thyroid cancer can be treated with RAI.
- Hyperthyroidism : pre-therapy dosimetry is done either with
 - I-123 (diagnostic, costly, lower energy gammas)
 - small activities of I-131 (therapeutic, high energy gammas)
 - → both are imaged with SPECT
- The pre-therapy scan is used to evaluate thyroid function.
- The activity to be delivered to the patient is then individually determined based on the clinical purpose:
 - Functional dose concept → reverse hyperthyroidism, reach euthyroidism
 - 100-150 Gy
 - Ablative dose concept → achieve hypothyroidism as soon as possible
 - 200-300 Gy



European journal of nuclear medicine and molecular imaging (2023) 50:3324–3348
<https://doi.org/10.1007/s00259-023-06274-5>

GUIDELINES

The EANM guideline on radioiodine therapy of benign thyroid disease

Alfredo Campenni¹ · Anca M. Avram² · Frederik A. Verburg³ · Ioannis Iakovou^{4,5} · Heribert Hänscheid⁶ · Bart de Keizer⁷ · Petra Petranović Ovcariček^{8,9} · Luca Giovannella^{10,11}

Received: 22 March 2023 / Accepted: 18 May 2023 / Published online: 3 July 2023
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Typical activities : from 10-15 mCi up to 30-50 mCi of I-131

$$A_a [MBq] = \frac{1}{\bar{E}} \cdot \frac{M [g] \cdot D [Gy]}{\int_0^{\infty} RIU(t) dt [d]}$$

A_a : activity administered to the patient

M : thyroid mass

D : target dose

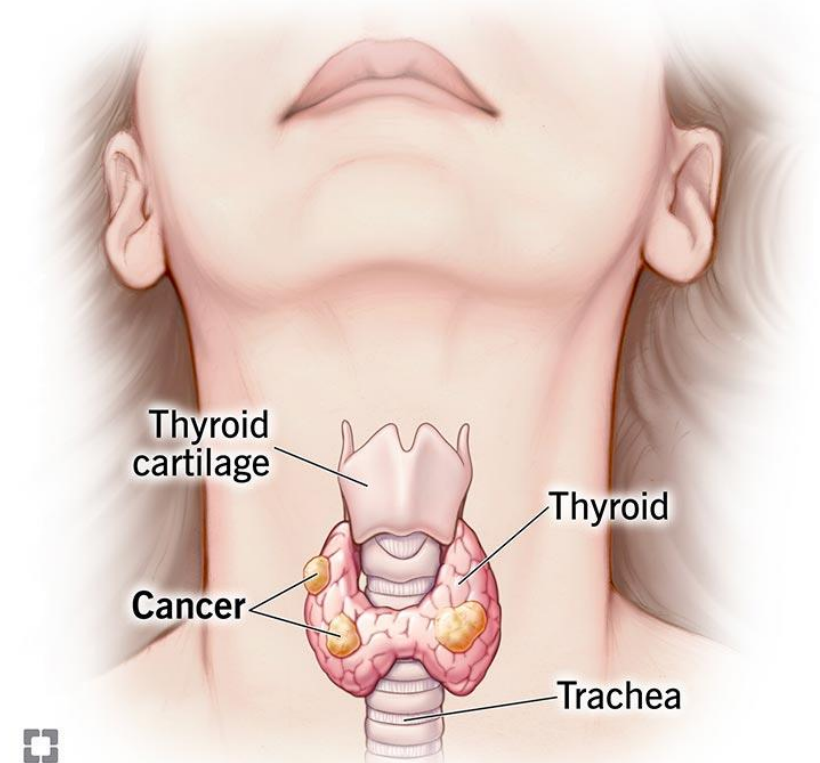
\bar{E} : mean energy deposited in the thyroid per I-131 decay (fixed)

RIU : radioiodine uptake =fraction (unitless) of the administered activity in M at a given time t after the administration

Radioactive iodine therapy

- Hyperthyroidism and **thyroid cancer** can be treated with RAI.
- The activity administered depends on the treatment type.
 - Remnant ablation : the thyroid has been removed, I-131 is given afterwards to kill any remnant thyroid cells in low-risk of recurrence patients → typical : 30-50 mCi
 - Adjuvant therapy the thyroid has been removed, I-131 is given afterwards to kill any remnant thyroid cells in high-risk of recurrence patients → typical 50-100 mCi.
 - Metastatic disease: → typical 100-150 mCi. Escalation possible up to 200 mCi if supported by personalized dosimetry.
- Target doses are typically in the order of 100-300 Gy to remnants and metastasis.
- Limiting organ (radiotoxicity) in RAI?
 - Bone marrow → hematotoxicity
 - Blood as surrogate : maximum dose = 2 Gy

Thyroid Cancer



SNMMI Procedure Standard/EANM Practice Guideline for Nuclear Medicine Evaluation and Therapy of Differentiated Thyroid Cancer: Abbreviated Version

Anca M. Avram (cochair)¹, Luca Giovannella (cochair)², Bennett Greenspan³, Susan A. Lawson⁴, Markus Luster⁵, Douglas Van Nostrand⁶, Justin G. Peacock⁷, Petra Petranović Ovcariček⁸, Edward Silberstein⁹, Mark Tulchinsky¹⁰, Enderik A. Vachuro¹¹, Alexia Vrachini¹²

Radioactive iodine therapy and radiation protection

- Special conditions on patient release apply to radionuclide therapy in NM.
- In Switzerland, ambulatory (in-hospital) treatment with I-131 can be performed up to 200 MBq.
- Beyond this activity, the patient needs to be hospitalized in special therapy rooms.
- Every object or waste (including biological waste, urine, feces, bed sheets,...) needs to be collected and checked.
- Release criteria?
 - At least 2 days of hospitalization **and**
 - Dose rate measured 1 meter away from the patient < 10 uSv/h

Tableau 1 Critères déterminant le choix d'une radiothérapie métabolique en résidentiel, durée minimale de l'hospitalisation, critères de sortie

Isotope / produit radiopharmaceutique	Résidentiel à partir de	Durée minimale d'hospitalisation après l'application*	Critère de sortie supplémentaire
I-131	200 MBq	48 h	DD < 10 µSv/h à 1 m **



Directive
Radiothérapie métabolique
V2 24.06.2025
www.bag.admin.ch/fr/radioprotection-directives

Contact
Tél : 058 058 462 96 14
Courriel : str@bag.admin.ch

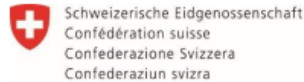
Radiothérapie métabolique



Exemple d'installation de contrôle des eaux usées. Photo: P. Koch

Radioactive iodine therapy and radiation protection

- Even after release, patients are provided with specific recommendations to follow to reduce public exposure.



Département fédéral de l'intérieur DFI
Office fédéral de la santé publique OFSP
Division radioprotection

Patient(e) traité(e) au I-131 Hyperthyroïdie ou goitre

Recommandations concernant les mesures de radioprotection
à la sortie de l'hôpital

A la maison et au travail

Dormir séparément

Durant **deux semaines**, **dormez seul/e**, de préférence dans une pièce séparée.

Il est recommandé de ne pas concevoir d'enfant dans les **six mois** suivant la thérapie.



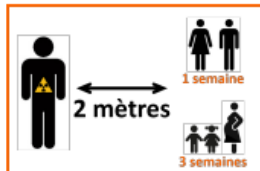
Garder ses distances

Gardez une distance d'au moins **deux mètres** avec les personnes de votre entourage durant :

Une semaine avec **vos proches et vos collègues de travail**.

Trois semaines avec **les enfants et les femmes enceintes**

Limitez les contacts prolongés (plus de quinze minutes par jour) à une distance inférieure. Le fœtus et les enfants sont plus sensibles aux radiations



Hygiène

Durant **trois semaines**, **tirez** la chasse d'eau à **deux reprises**, **nettoyez** les souillures **avec du papier toilette** et jetez-le **dans les toilettes**.

Lavez-vous soigneusement les mains.

Vos urines contiennent encore de la radioactivité.



Déchets

Pendant **trois semaines**, gardez les **sacs poubelles** contenant vos éventuelles couches ou protections urinaires dans des endroits peu fréquentés (p.ex. cave ou balcon) **jusqu'au dernier moment** avant la collecte des déchets ménagers afin d'éviter d'irradier des tiers.



Protéger les autres

Personnel soignant

Pendant **trois semaines**, si vous êtes admis à l'hôpital ou nécessitez des soins, **veuillez informer le personnel médical** de votre traitement en médecine nucléaire.

Information pour médecin / personnel soignant



Tous les autres

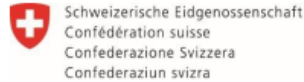
Pendant **une semaine**, limitez vos trajets en **transports publics** à des trajets d'un **maximum de quatre heures**.

Vous pouvez côtoyer vos **amis et collègues** et recevoir des personnes chez vous en limitant les durées et en maximisant la distance entre vous.



Radioactive iodine therapy and radiation protection

- Even after release, patients are provided with specific recommendations to follow to reduce public exposure.



Département fédéral de l'intérieur DFI
Office fédéral de la santé publique OFSP
Division radioprotection

Patient(e) traité(e) au I-131 Hyperthyroïdie ou goitre

Recommandations concernant les mesures de radioprotection
à la sortie de l'hôpital

A la maison et au travail

**Dormir
séparément**

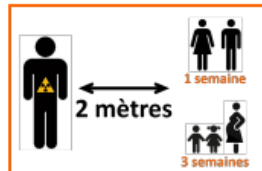
During 2 weeks, sleep alone.
Wait at least 6 months before
conceiving



**Garder ses
distances**

Gardez une distance d'au moins **deux mètres** avec les

Keep a distance of two meters
for 1 week with family and
colleagues and for 3 weeks with
pregnant women and children



Hygiène

For 3 weeks, flush the toilet
twice and clean any drops with
toilet paper.



Déchets

For 3 weeks, keep the waste bin
containing urinary pads in low frequented
areas (basement, balcony) until the next
waste collection day



Protéger les autres

**Personnel
soignant**

During 3 weeks, if you need to be
hospitalized, inform the healthcare
professionals of your iodine treatment



Tous les autres

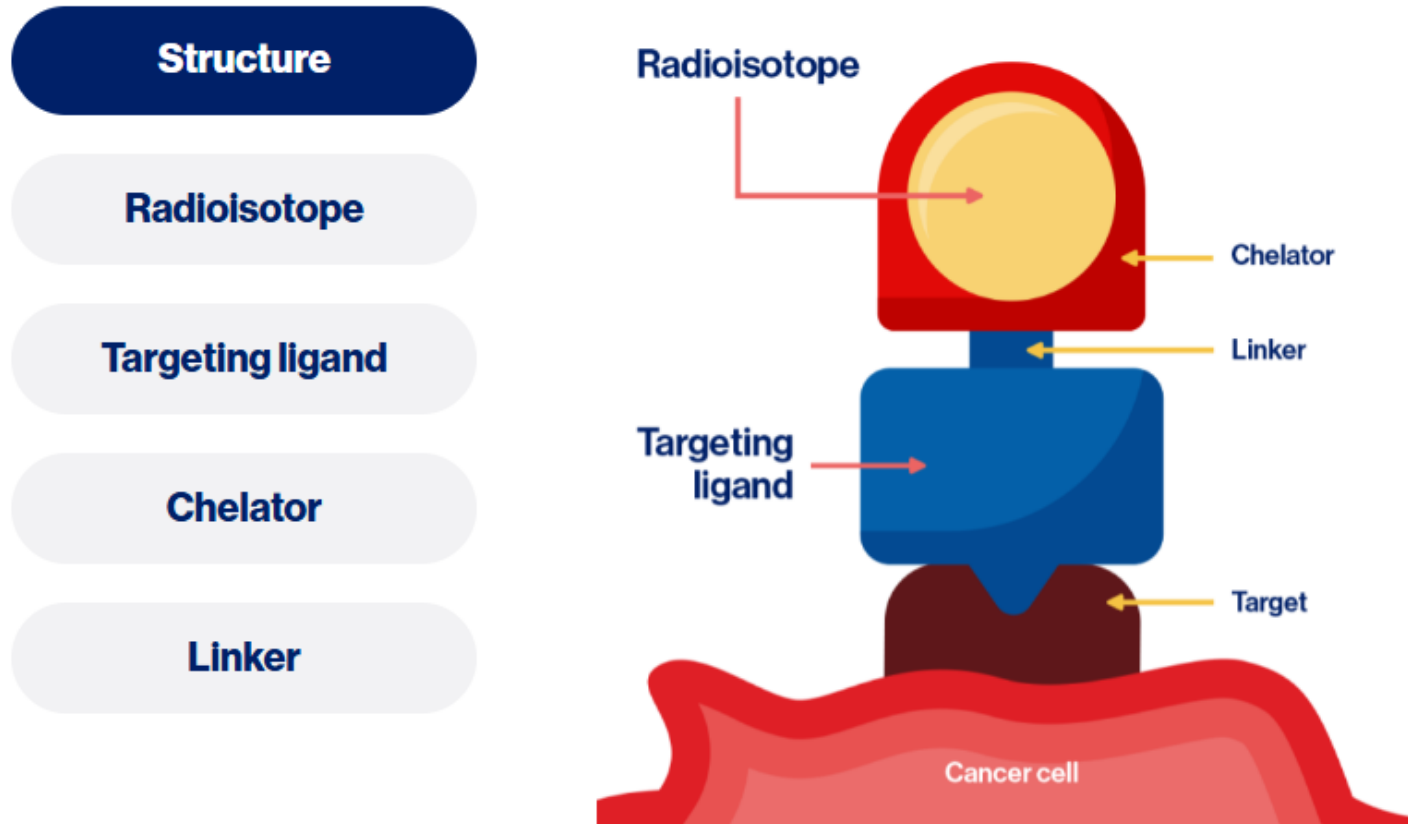
During 1 week, limit your commuting
using public transports to less than 4 h.
When you are at home or at work,
maximise distance with family and friends



Targeted radionuclide therapy

(the case of radioligand therapy)

Radioligand therapy is a particular case of targeted radionuclide therapy. It targets disease by using a combination of a ligand (targeting molecule) and a radioisotope.

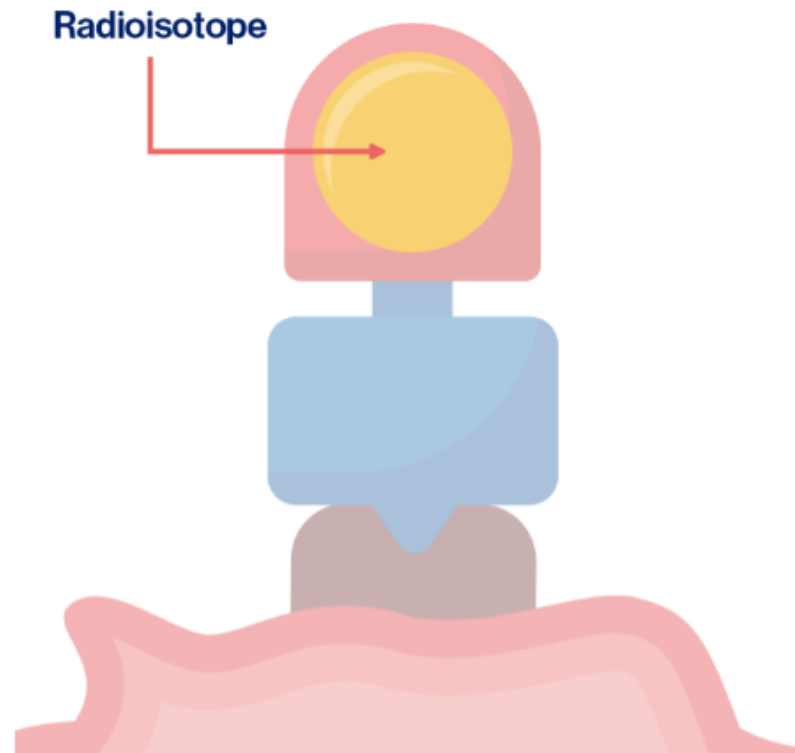


Radioligands are built with a well-defined structure composed of 4 key components.²

Targeted radionuclide therapy

(the case of radioligand therapy)

Radioligand therapy is a particular case of targeted radionuclide therapy. It targets disease by using a combination of a ligand (targeting molecule) and a radioisotope.

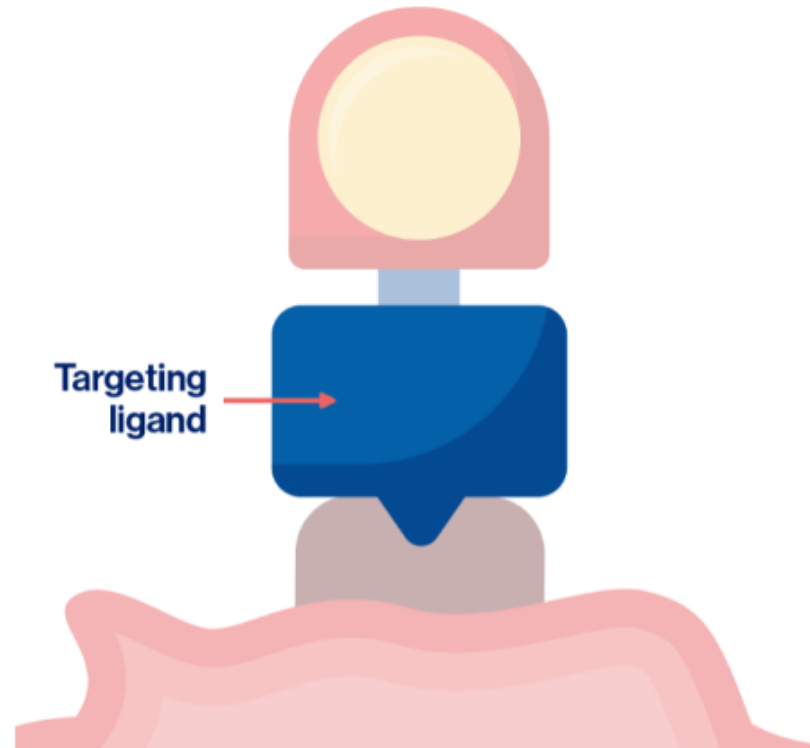


The radioisotope is the radioactive component used in RLI/RLT and can either emit γ radiation for imaging (diagnostic use) or deliver targeted β^- or α radiation (therapeutic use) to cancer cells.²

Targeted radionuclide therapy

(the case of radioligand therapy)

Radioligand therapy is a particular case of targeted radionuclide therapy. It targets disease by using a combination of a ligand (targeting molecule) and a radioisotope.

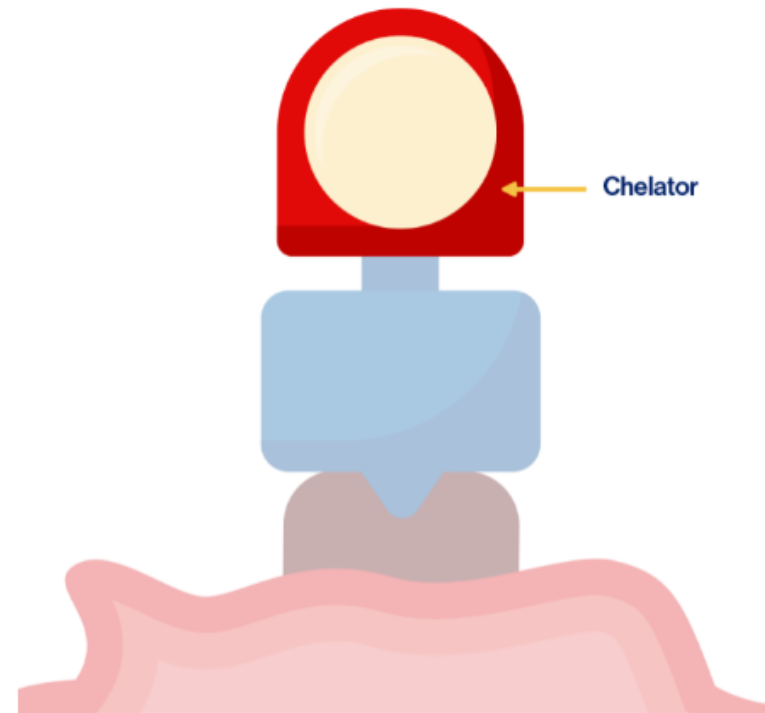


The targeting ligand is the molecule that identifies and binds to specific markers on cancer cells and is designed to selectively deliver therapeutic radiation to tumor cells or cells of the tumor microenvironment with potentially limited damage to healthy cells.^{2,4}

Targeted radionuclide therapy

(the case of radioligand therapy)

Radioligand therapy is a particular case of targeted radionuclide therapy. It targets disease by using a combination of a ligand (targeting molecule) and a radioisotope.

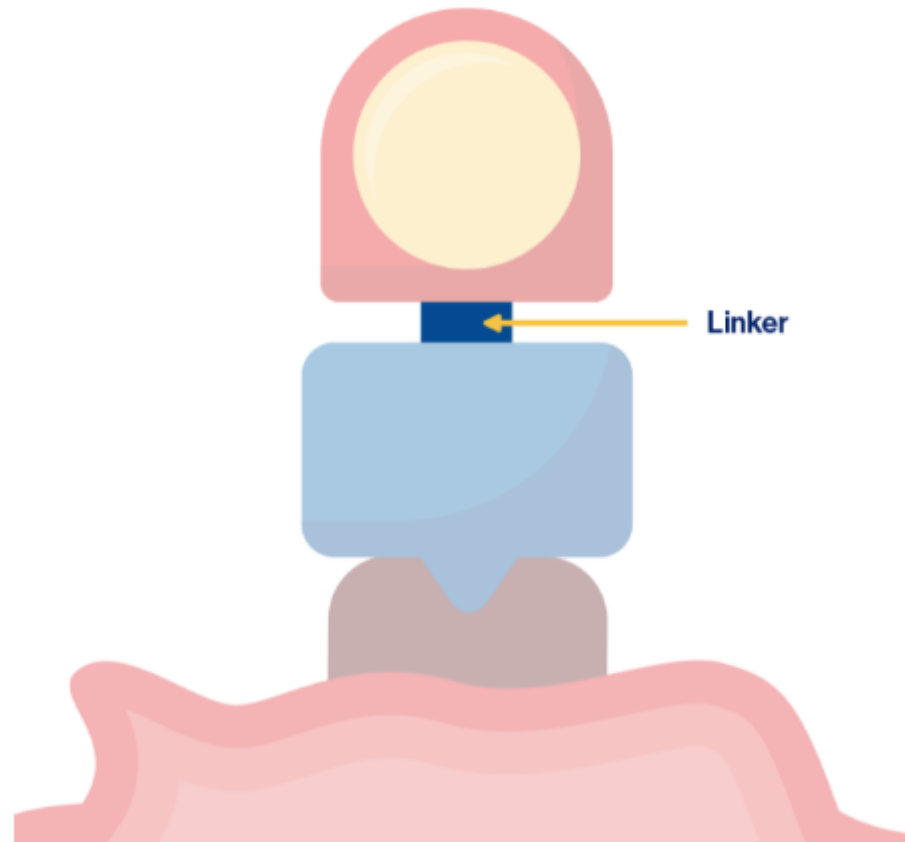


The chelator is a chemical agent that securely binds to the radioisotope, ensuring its stable attachment and proper delivery to the target cancer cells. The chelator plays an important role in preventing the radioisotope from dissociating, which could lead to unintended radiation exposure.²

Targeted radionuclide therapy

(the case of radioligand therapy)

Radioligand therapy is a particular case of targeted radionuclide therapy. It targets disease by using a combination of a ligand (targeting molecule) and a radioisotope.



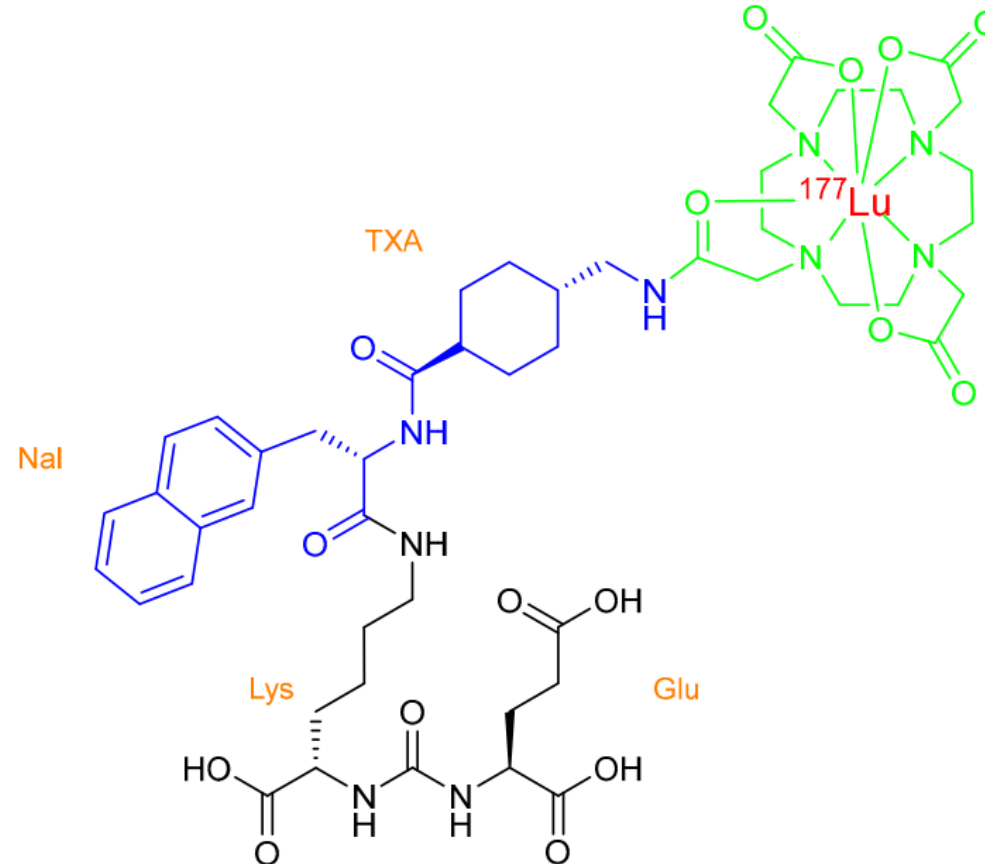
The linker is a molecular structural component that connects the targeting ligand to the chelator. The linker maintains the stability and integrity throughout the process, allowing it to bind effectively to cancer cells.²

Targeted radionuclide therapy

(the case of radioligand therapy)

Radioligand therapy is a particular case of radiopharmaceutical therapy (RPT). It targets disease by using a combination of a ligand (targeting molecule) and a radioisotope.

Lu-177 DOTA
(neuroendocrine tumors)



radionuclide (^{177}Lu) + chelator (DOTA) + linker + targeting motif (Glu-NH-CO-NH-Lys)

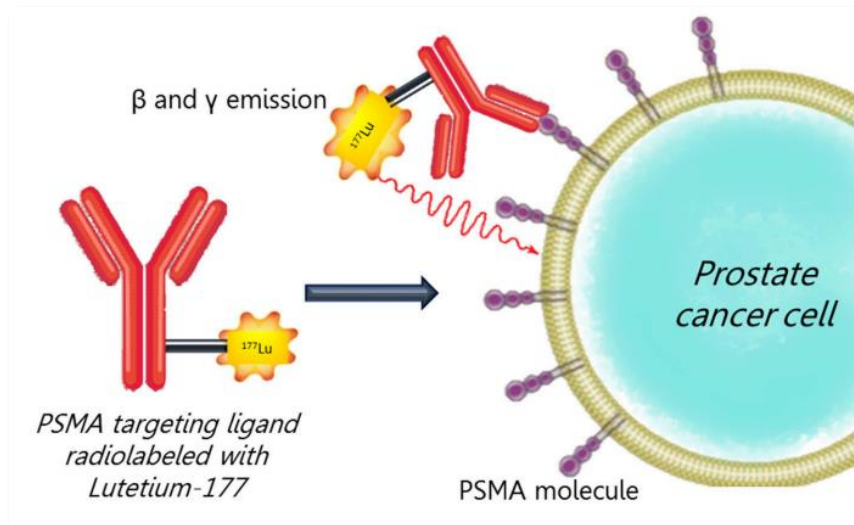
Targeted radionuclide therapy (radioligand therapy with Lu-177 PSMA)

Metastatic Castration Resistant Prostate Cancer (mCRPC) patients

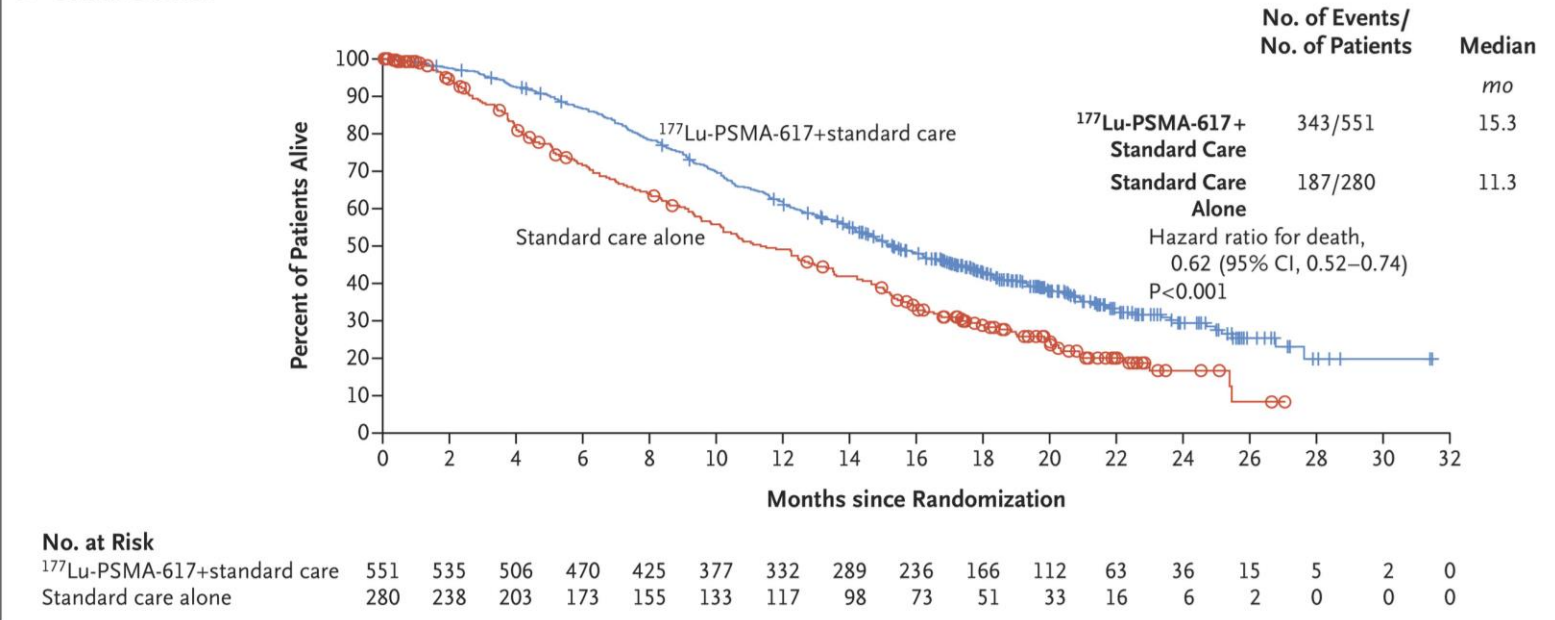
Metastatic sites → primarily bone metastases

Prostate cancer overexpress prostate-specific membrane antigen (PSMA)

Treatment with ^{177}Lu -PSMA (prostate specific membrane antigen)



B Overall Survival

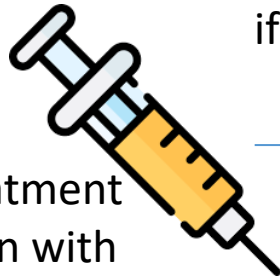


Targeted radionuclide therapy (radioligand therapy with Lu-177 PSMA)

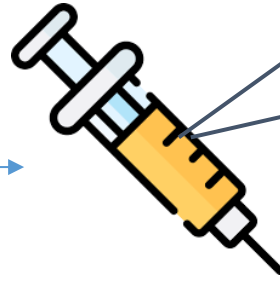
mCRPC



Pre-treatment
PET scan with
 ^{68}Ga PSMA
(diagnostics)



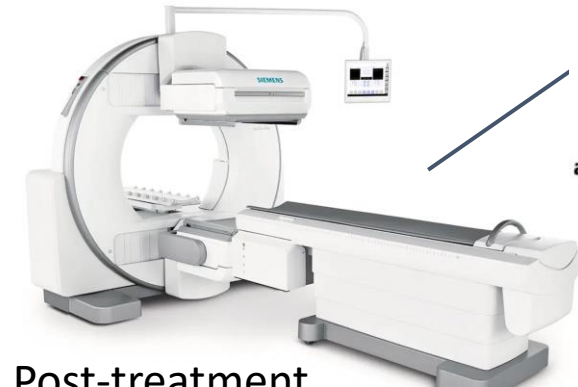
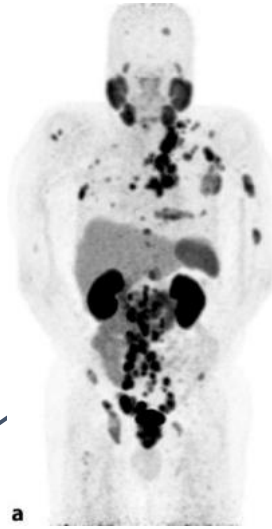
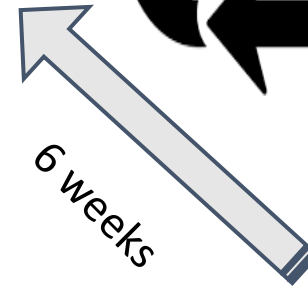
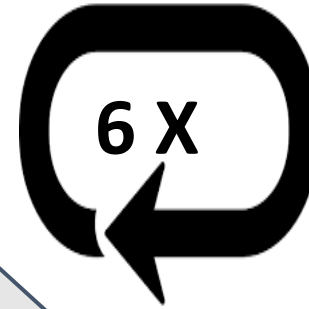
if eligible for
therapy



7.4 GBq of
 ^{177}Lu PSMA
(therapy)



Radioligand



Post-treatment
SPECT scan of
 ^{177}Lu PSMA



a

Targeted radionuclide therapy (radioligand therapy with Lu-177 PSMA)

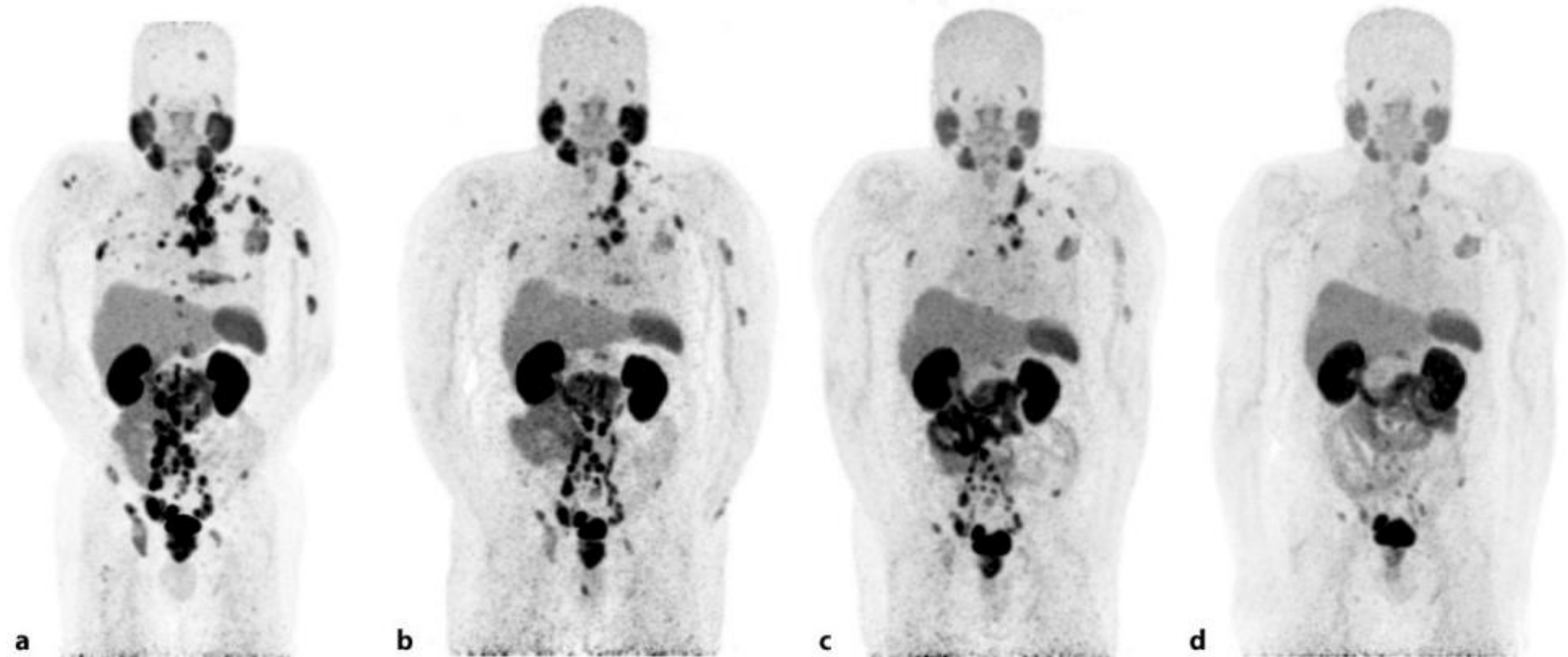


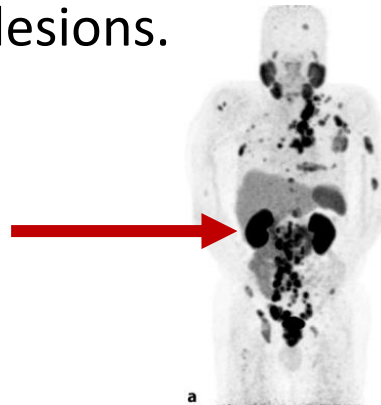
Fig. 1 Baseline (a) and follow-up (b after 2 cycles; c after 4 cycles; d after 6 cycles) [^{68}Ga]Ga-PSMA PET/CT of a patient with mCRPC, who was treated with 6.0 GBq [^{177}Lu]Lu-PSMA-617 (Novartis, Basel, Switzerland). Prostate-specific

antigen (PSA) response was as follows: 100 ng/ml (baseline), 190 ng/ml (after 2 cycles), 52 ng/ml (after 4 cycles) and 19 ng/ml (after 6 cycles)

Targeted radionuclide therapy

(radioligand therapy with Lu-177 PSMA)

- Theranostic pair : Ga-68 (diagnostics) and Lu-177 (therapy)
- Pre-therapy scan with Ga-68 to ensure eligibility to therapy and for assessing response to therapy in next treatment cycles.
- At present, a fixed amount of activity (200 mCi = 7.4 GBq) is generally prescribed to the patients (reduced activities in case of pre-existing renal dysfunction)
- Post-treatment image(s) can be acquired to ensure expected uptake of Lu-177 in lesions.
- Limiting organ (radiotoxicity) for Lu-177-based therapies ? → kidneys
- A generally accepted value for kidney toxicity → 23 Gy
 - Where does it come from? → external beam radiotherapy!
 - Same dose, but different delivery pattern : can we really expect the same degree of toxicity in nuclear medicine?

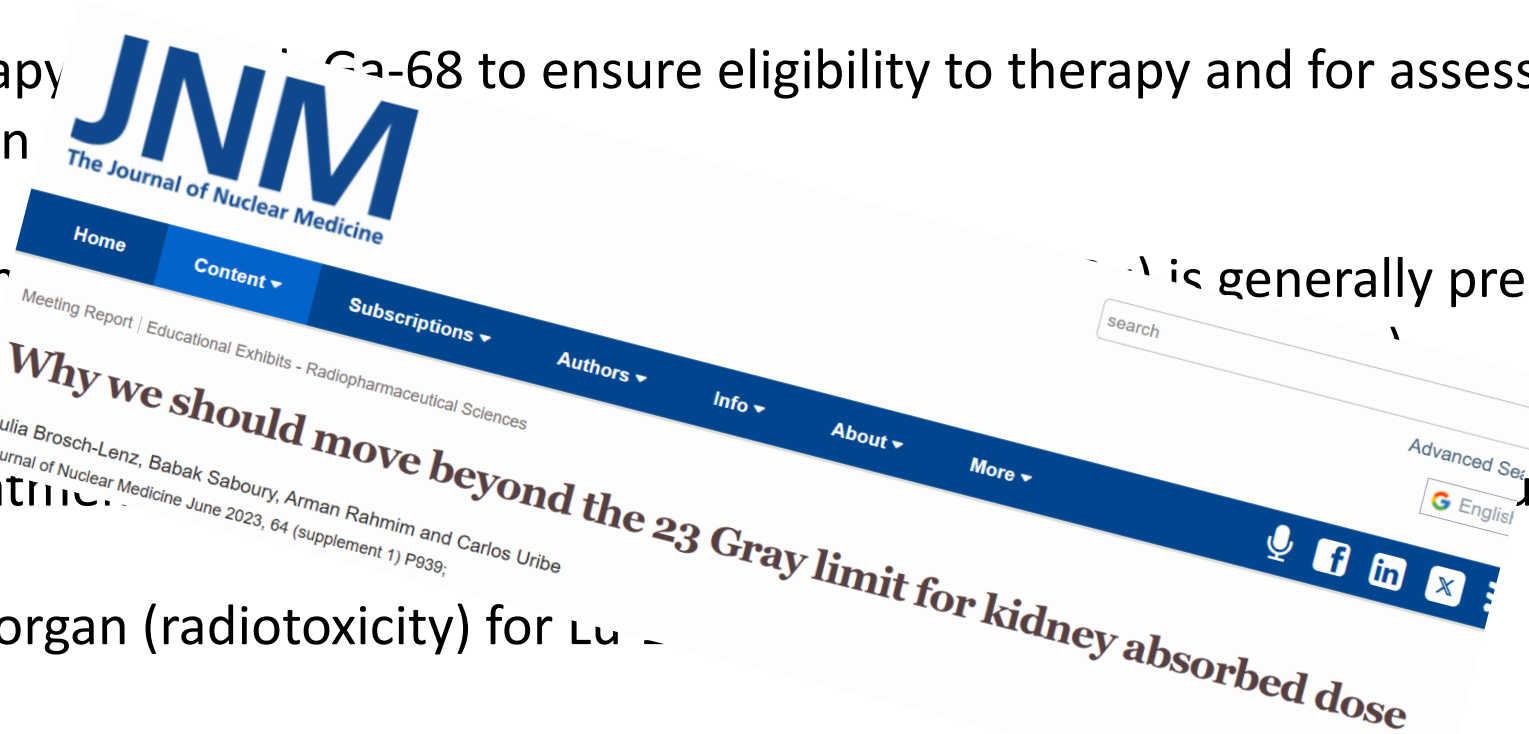


a

Targeted radionuclide therapy

(radioligand therapy with Lu-177 PSMA)

- Theranostic pair : Ga-68 (diagnostics) and Lu-177 (therapy)
- Pre-therapy Ga-68 to ensure eligibility to therapy and for assessing response to therapy in
- At preser patients
- Post-treatment
- Limiting organ (radiotoxicity) for Lu -
- A generally accepted value for kidney toxicity → 23 Gy
 - Where does it come from? → external beam radiotherapy!
 - Same dose, but different delivery pattern : can we really expect the same degree of toxicity in nuclear medicine?



Lu-177 is generally prescribed to the patients with Lu-177 in lesions.



Targeted radionuclide therapy

(radioligand therapy with Lu-177 PSMA : Dose–Response relationships)

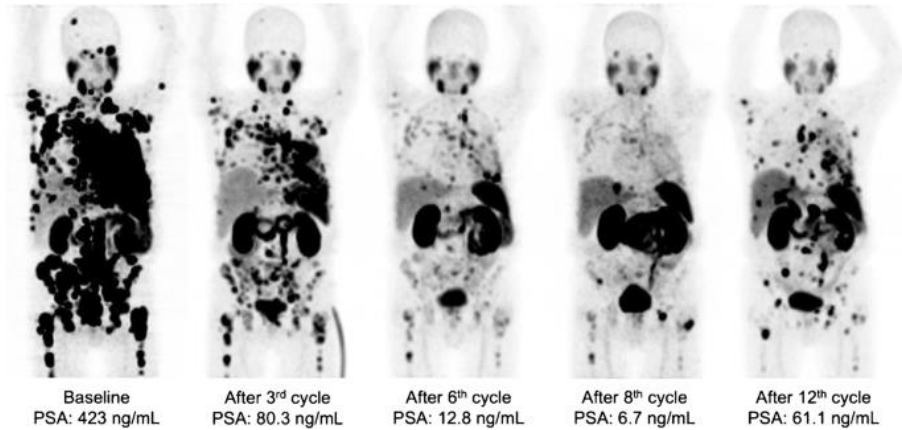
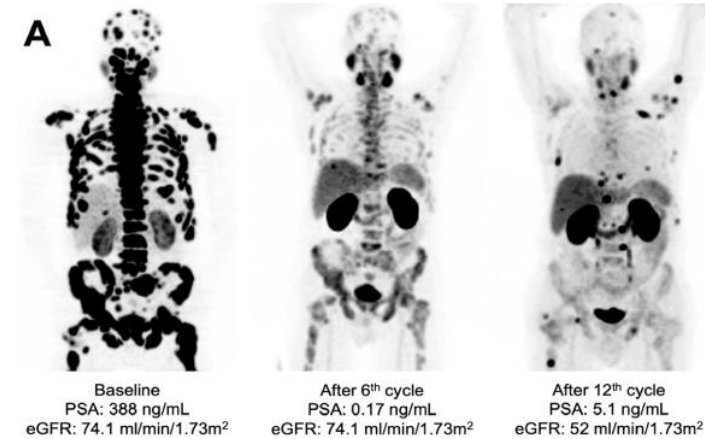
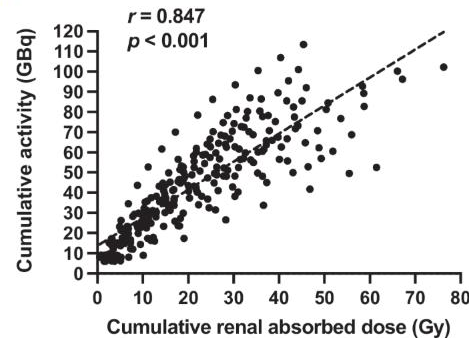
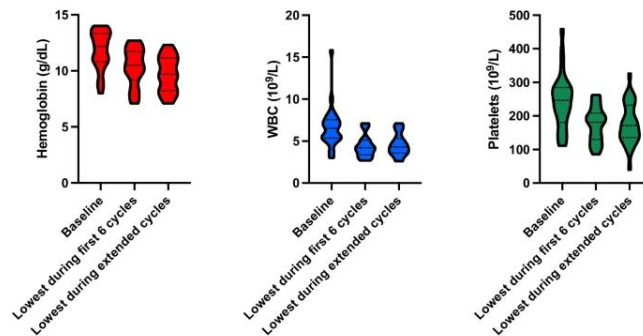


Fig. 7



eGFR (*estimated glomerular filtration rate*) is used as an indicator of **kidney function**

Fig. 6



Extended radioligand therapy is a feasible beyond 6 cycles of [177Lu]Lu-PSMA-617. Improved survival and acceptable safety justify more investigation on additional cycles / increased activity per cycle in selected patients.

Targeted radionuclide therapy (radioligand therapy with Lu-177 DOTA)

- Another type of radionuclide therapy with radioligands, that selectively targets **somatostatin receptors**.
- Somatostatin is a peptide hormone, typically overexpressed in neuroendocrine tumors (NET).
- NET : cancers form neuroendocrine cells, that have common characteristics with nerve cells (neurons) and endocrine cells (that secrete hormones). They are found in organs such as lungs, gastrointestinal tract, pancreas.
- This therapy is sometimes referred to as «peptide reception radionuclide therapy» (PRRT).

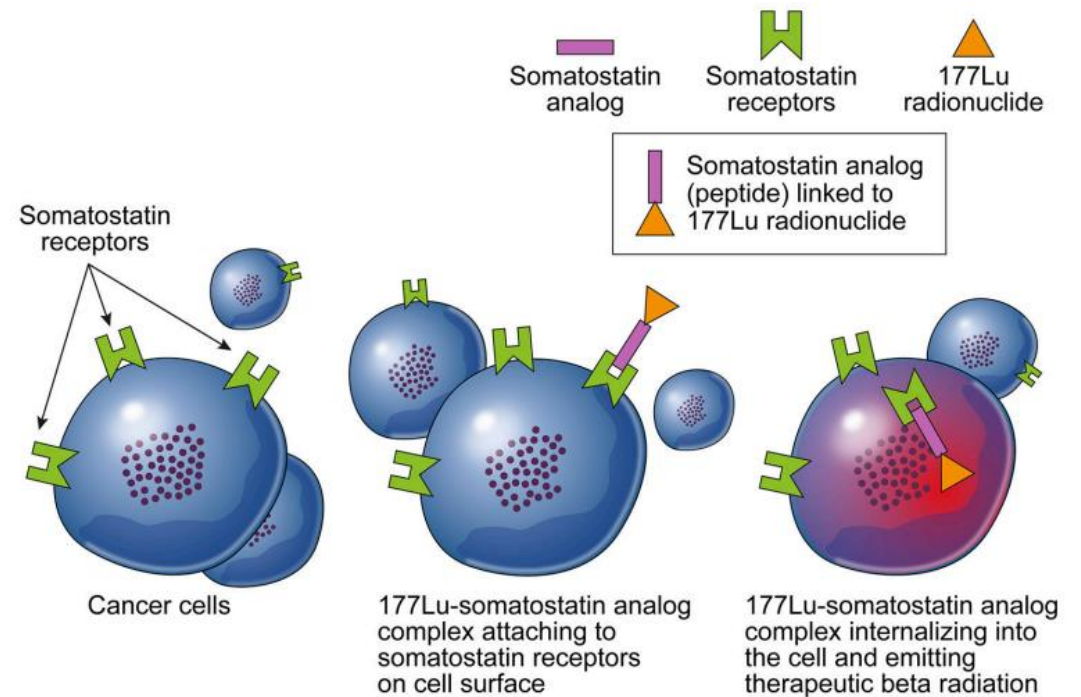
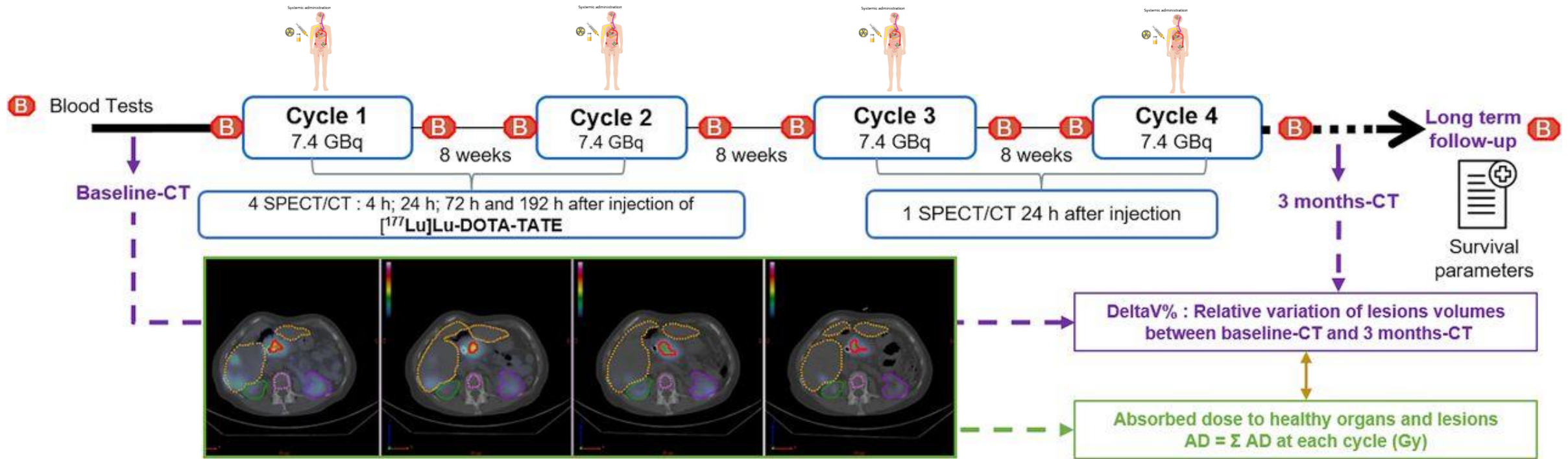


FIGURE 2 | Simplistic overview illustrating the ¹⁷⁷Lu-Dotatate peptide receptor radionuclide therapy - PRRT for somatostatin-receptor-positive neuroendocrine tumors. Illustration: (Steven D. Orwoll – Mayo Clinic Media).

Targeted radionuclide therapy (radioligand therapy with Lu-177 DOTA)



Why 7.4 GBq/cycle? \rightarrow (200 mCi)

As for Lu-177 PSMA : kidney toxicity from EBRT is set to 23 Gy

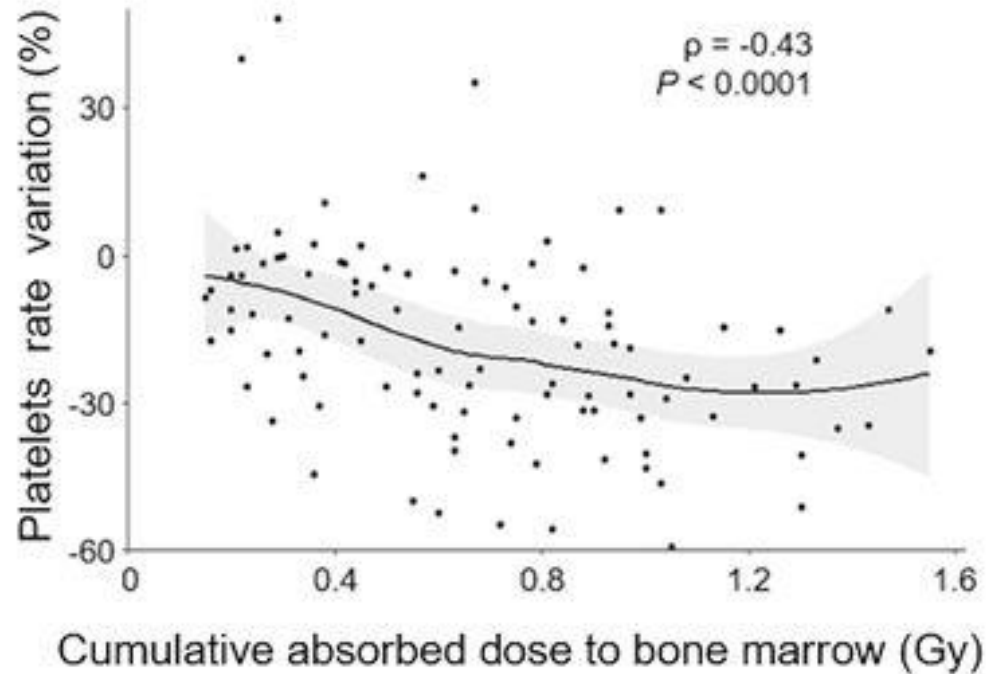
Potentially important margins for optimization

- Activity per cycle
- Number of cycles

Targeted radionuclide therapy

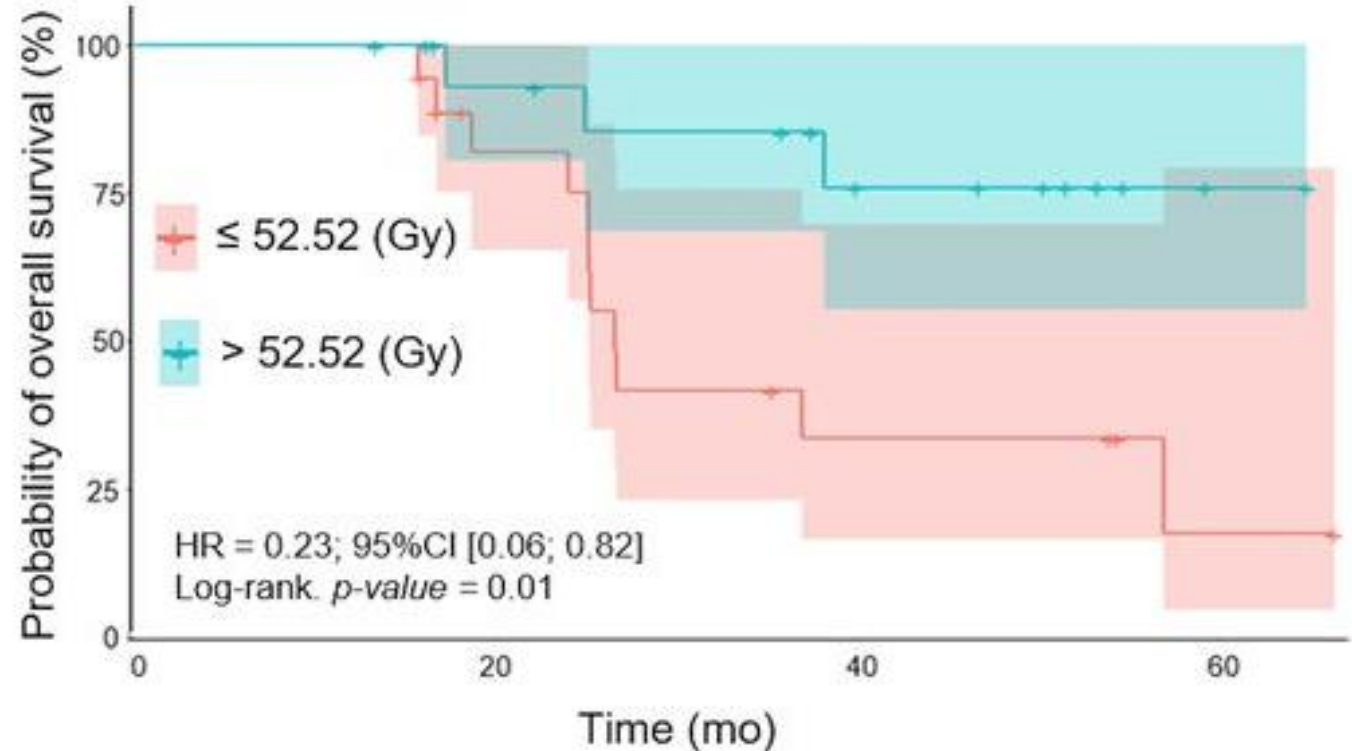
(radioligand therapy with Lu-177 DOTA : **Dose–Response relationships**)

Platelets rate variation versus cumulative absorbed dose to bone marrow



«The absorbed dose by the bone marrow was negatively and significantly ($P < 0.0001$) correlated with variations, compared with baseline values, of neutrophil, lymphocyte, leukocyte, and platelet counts.»

Overall survival related to minimum total absorbed dose to lesions



« Kaplan–Meier estimates of overall survival are shown as function of lowest total absorbed dose in each patient’s course of treatment ($n = 35$). »

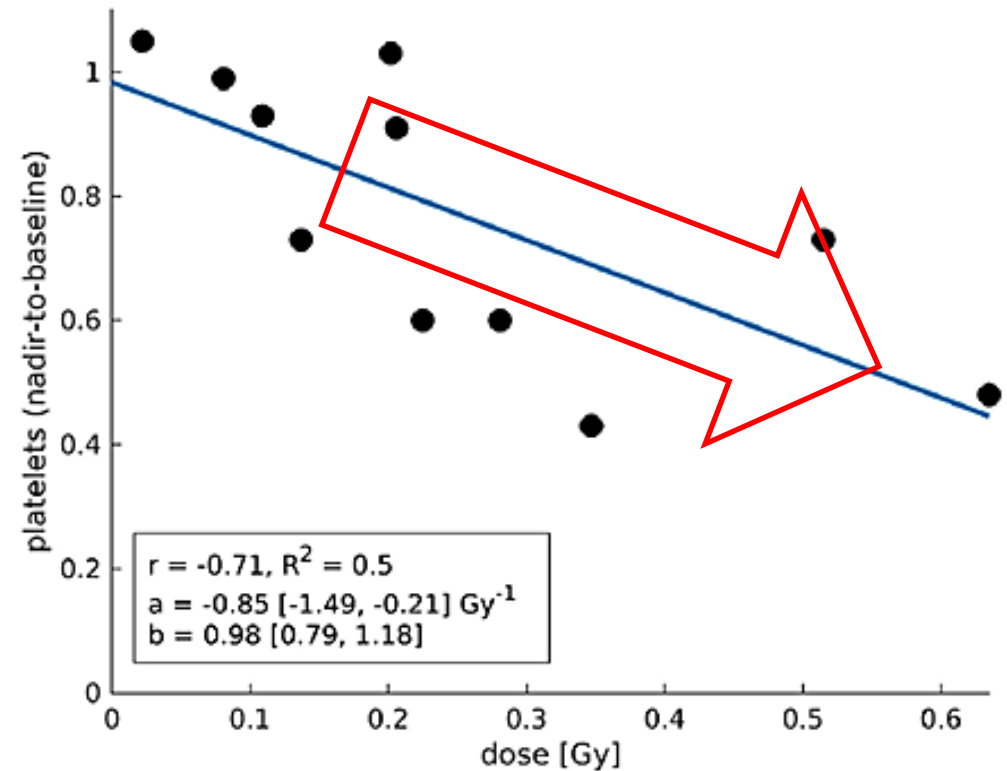
Targeted radionuclide therapy with Lu-177

(Dose–Response relationships : toxicity)

Haematologic toxicity

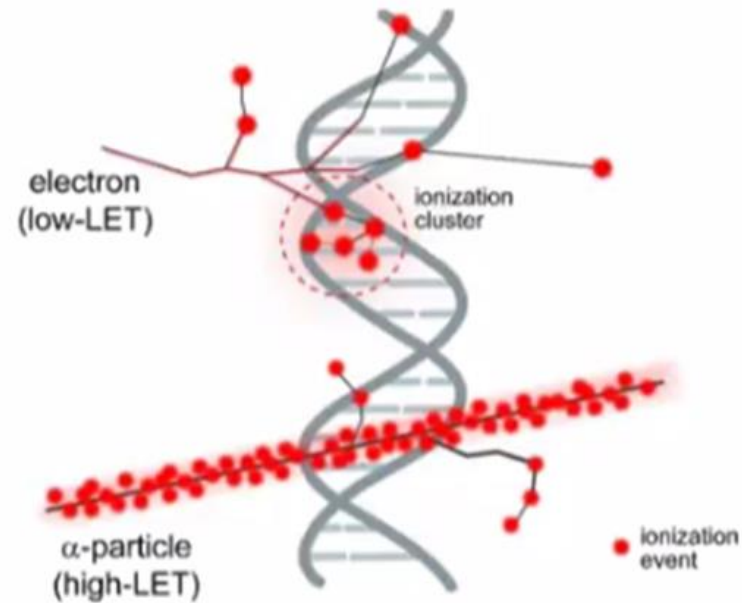
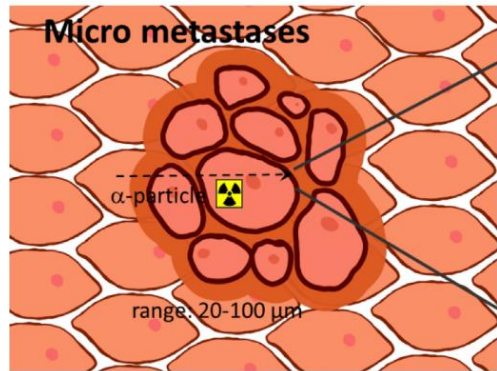
- Grade 3–4 toxicity, most often thrombocytopenia, has been observed in 10–15% of patients treated with [177Lu]Lu-DOTA and in approximately 10% of those treated with [177Lu]Lu-PSMA.
- The occurrence of secondary myelodysplastic syndrome or acute leukaemia has been observed several years after treatment with [177Lu]Lu-DOTA.

3D Monte Carlo bone marrow dosimetry in Lu-PSMA therapy and platelets counts



Targeted alpha therapy (TAT) (potential)

- Offer **high linear energy transfer (LET) radiation with short path length**
- Ideal for micrometastases - opening up new potential for therapies
- However, dosimetry remains complex

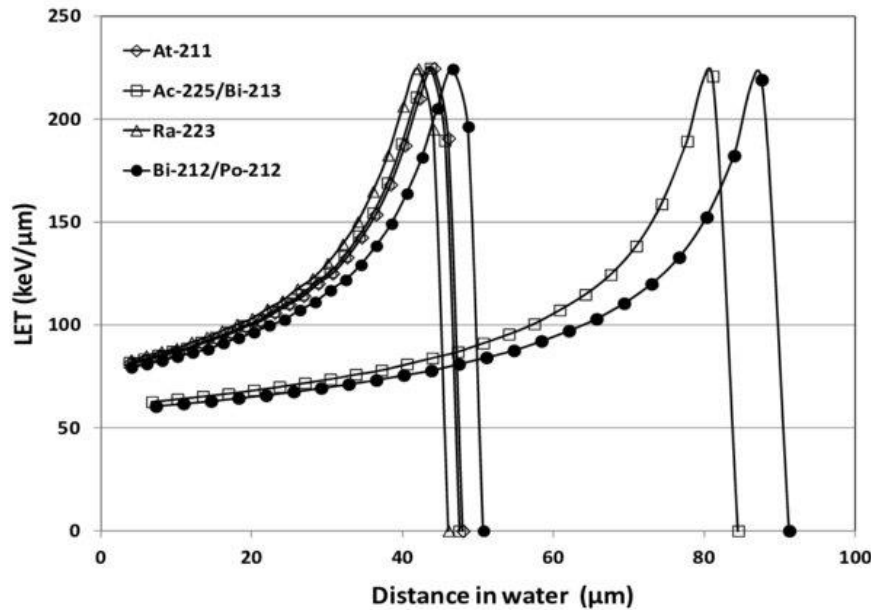
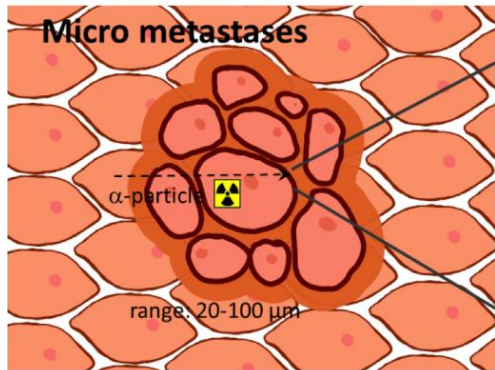


Iliakis et al., *Cancers* 2019

Decay type LET (keV/mm)	Therapeutic isotope	Half-life	$E_{\text{mean/max}}$ (MeV)	R_{max} (mm)	R_{90} (mm)
β^- LET~0.1–2	Y-90	2.7 d	0.94/2.28	11	5.5
	I-131	8 d	0.18/0.6	2	0.9
	Lu-177	6.7 d	0.13/0.5	1.5	0.6
α LET ~50-300	At-211	7.2 h	7.5	70	~ R_{max}
	Bi-213	46 min	8.4	85	~ R_{max}
	Ac-225	9 d	5.9	47	~ R_{max}

Targeted alpha therapy (TAT) (potential)

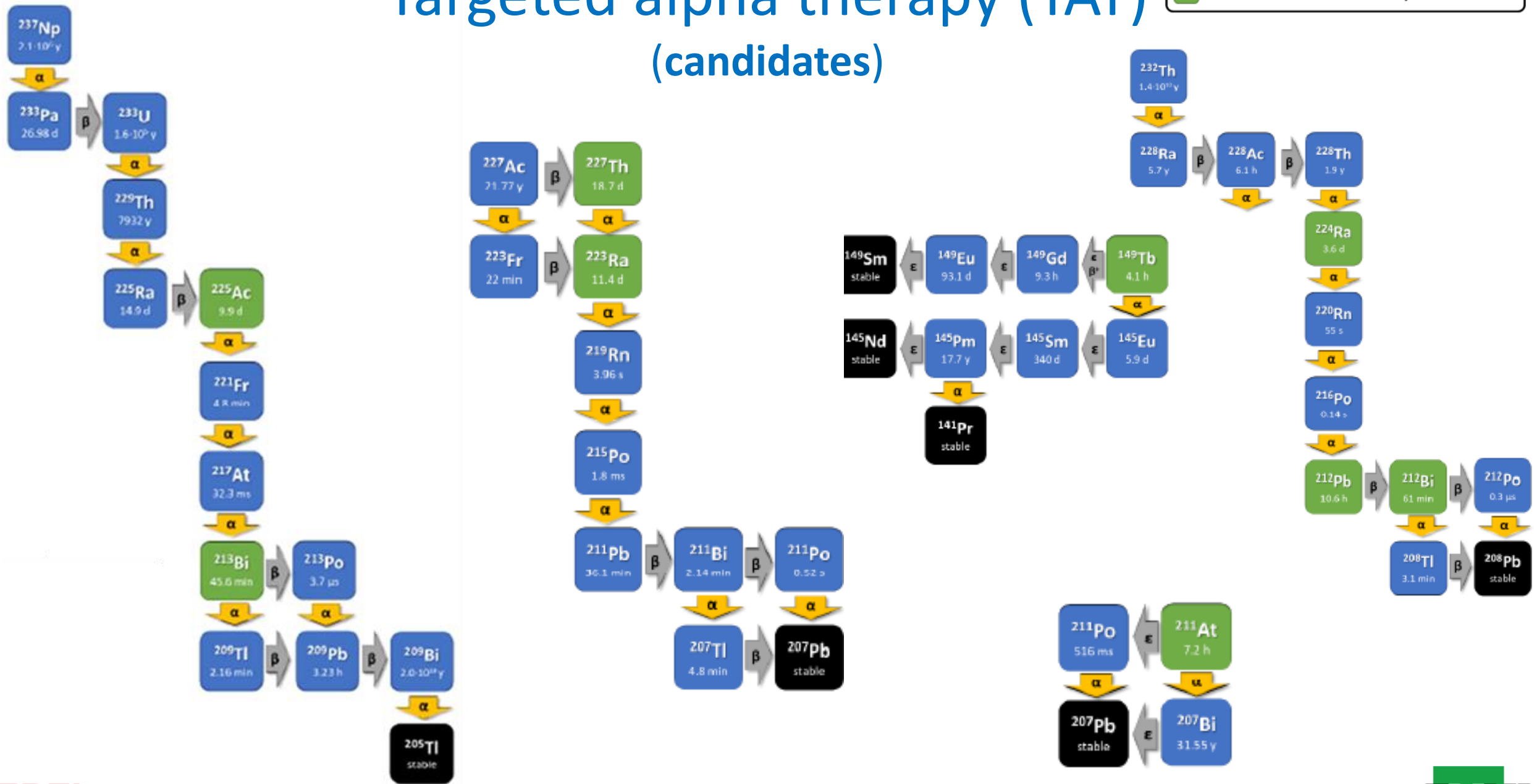
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	Ac-225	9 d	5.9	47	~ R_{max}

Targeted alpha therapy (TAT) (candidates)

■ radionuclides commonly used for TAT



Targeted alpha therapy (TAT) (imaging challenges)

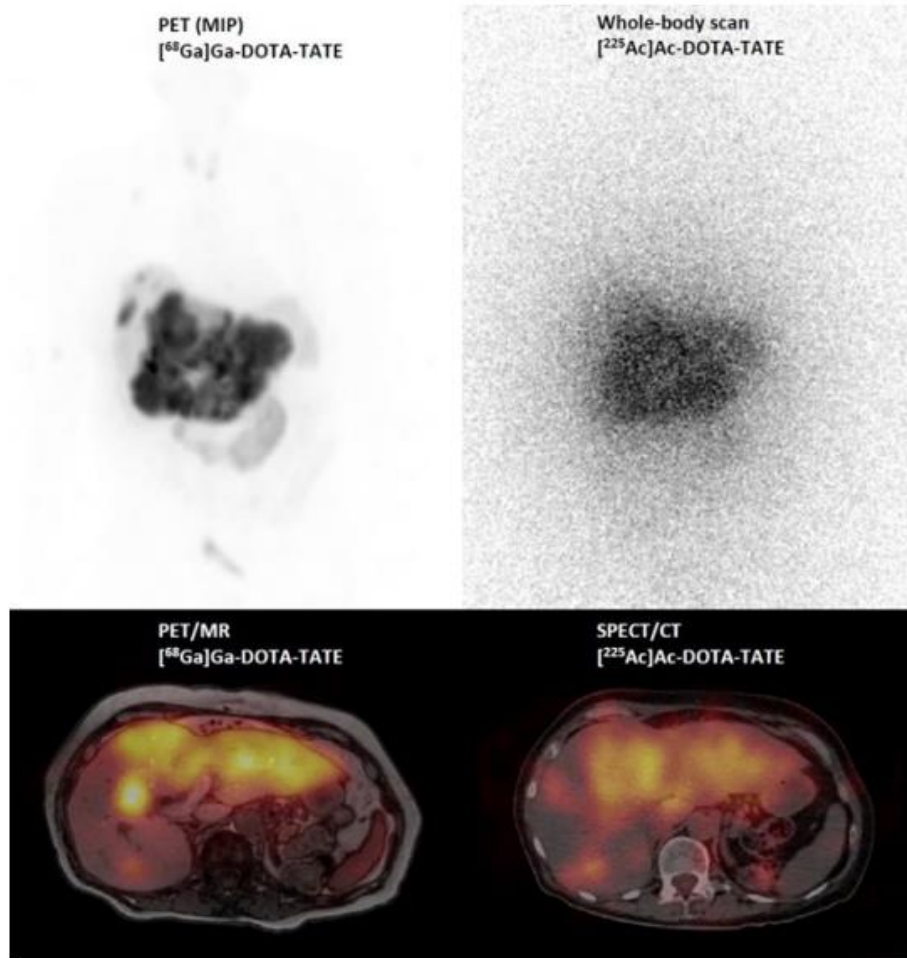


Figure 6. $[^{68}\text{Ga}]\text{Ga-DOA-TATE}$ PET/MR (maximum intensity projection (MIP) and PET/MR fusion image) and post-therapy scintigraphic imaging (whole body and SPECT/CT fusion image) 24 h after injection of 6.5 MBq $[^{225}\text{Ac}]\text{Ac-DOA-TATE}$ in a patient with a G3 neuroendocrine tumor.

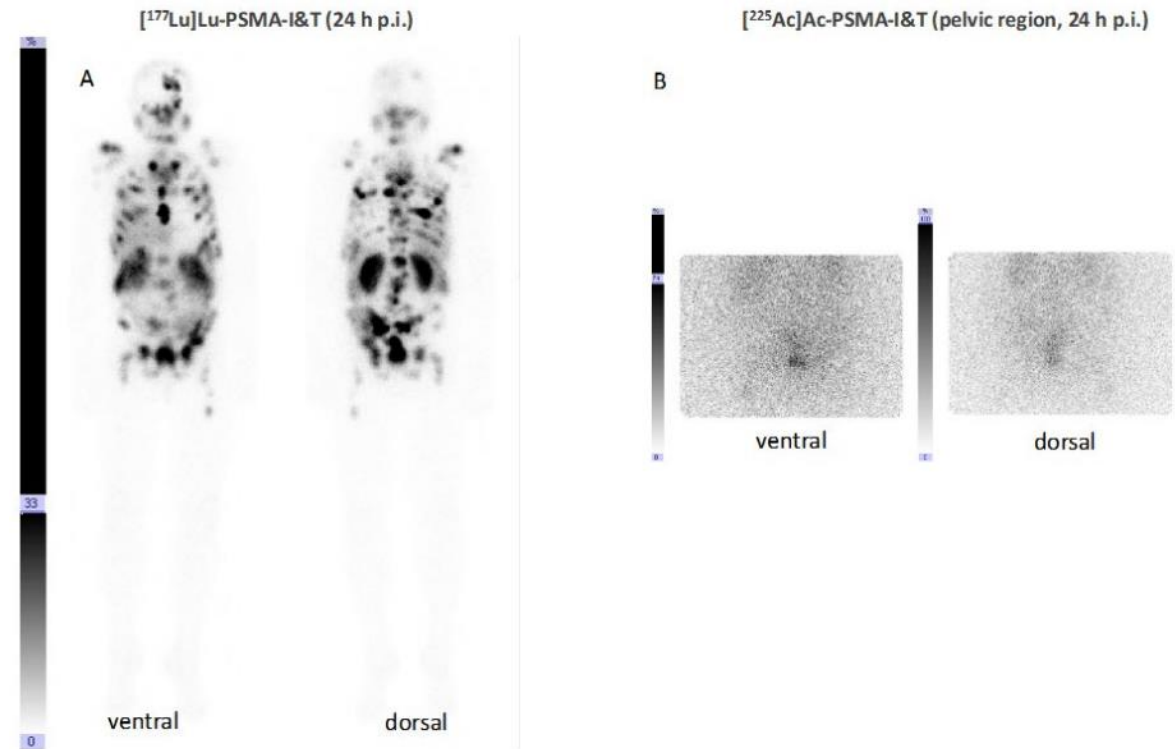


Figure 8. Anterior and posterior scintigraphic imaging of a patient treated with 5 GBq $[^{177}\text{Lu}]\text{Lu-PSMA-I\&T}$ (A) and subsequently—due to rising PSA levels combined with reduced bone marrow reserve—with 8 MBq $[^{225}\text{Ac}]\text{Ac-PSMA-I\&T}$ 6 months afterwards (B).

Targeted alpha therapy (TAT) (dosimetry challenges)

Dosimetry for α emitters is challenging:

- Low gamma yield
- Long chains, several radionuclides at equilibrium
- The daughters may detach from the radiopharmaceutical vector and follow their own biokinetics inside the body!
→ potential toxicity
- Possible to use Lu-177 PSMA to predict the activity distribution (and thus the dose) of Ac-225 PSMA

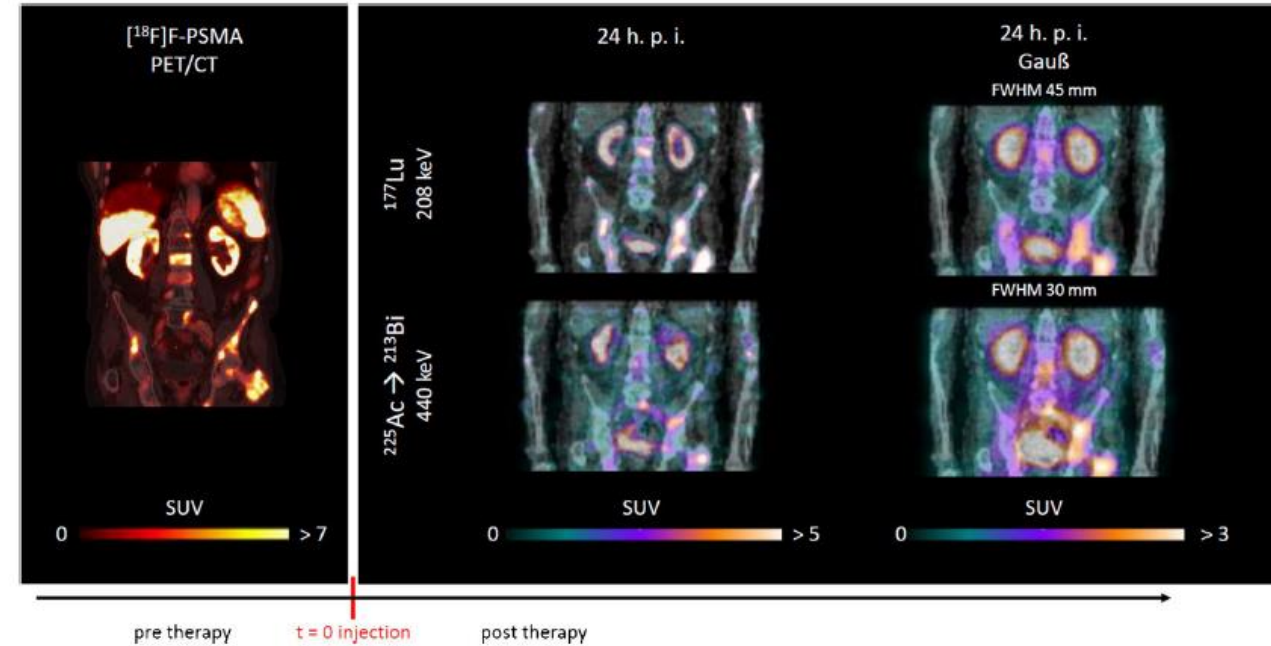
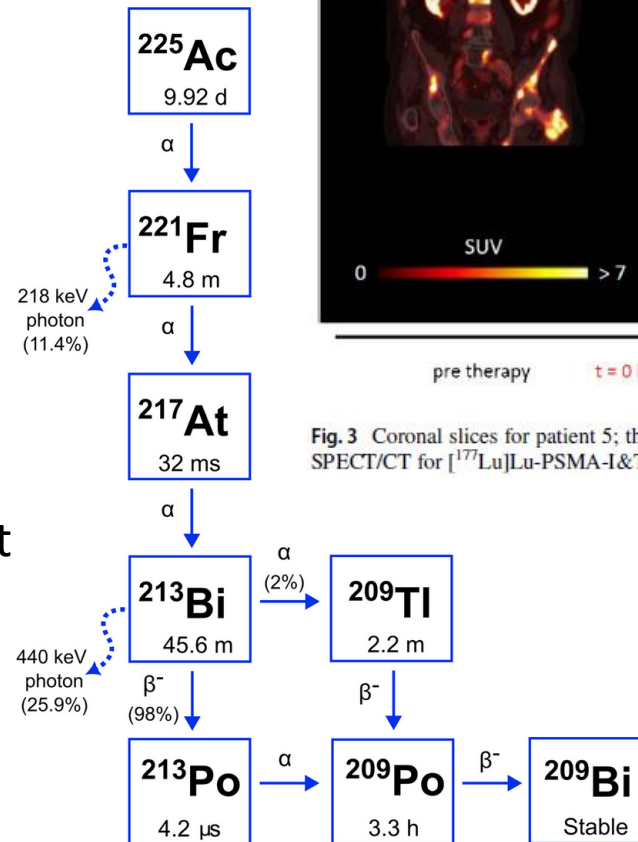
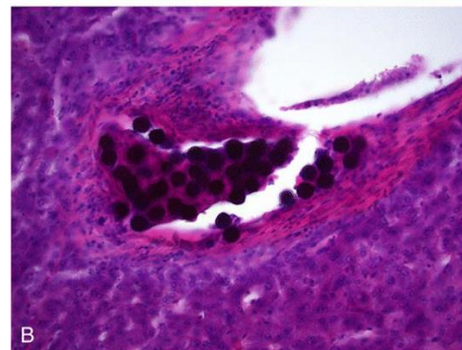
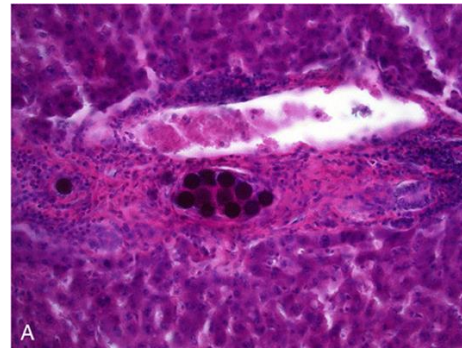
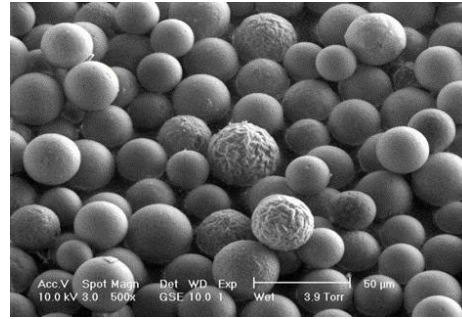
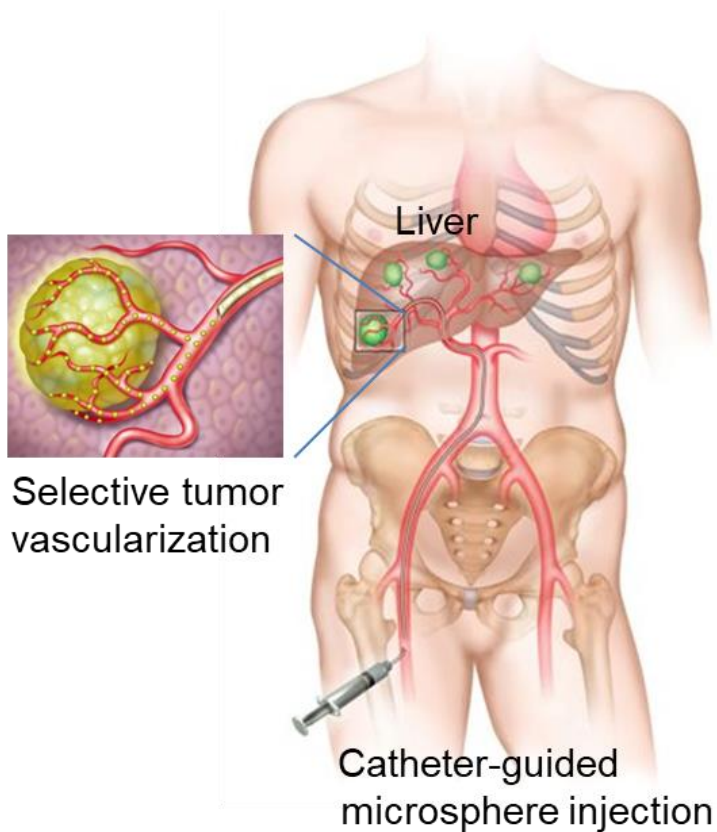


Fig. 3 Coronal slices for patient 5; the pre-therapeutic PSMA PET/CT is shown together with the filtered and unfiltered therapeutic quantitative SPECT/CT for ^{177}Lu]Lu-PSMA-I&T and ^{225}Ac]Ac-PSMA-I&T at 24 h p. i

Selective Internal Radiation Therapy (SIRT) (transarterial radioembolization)



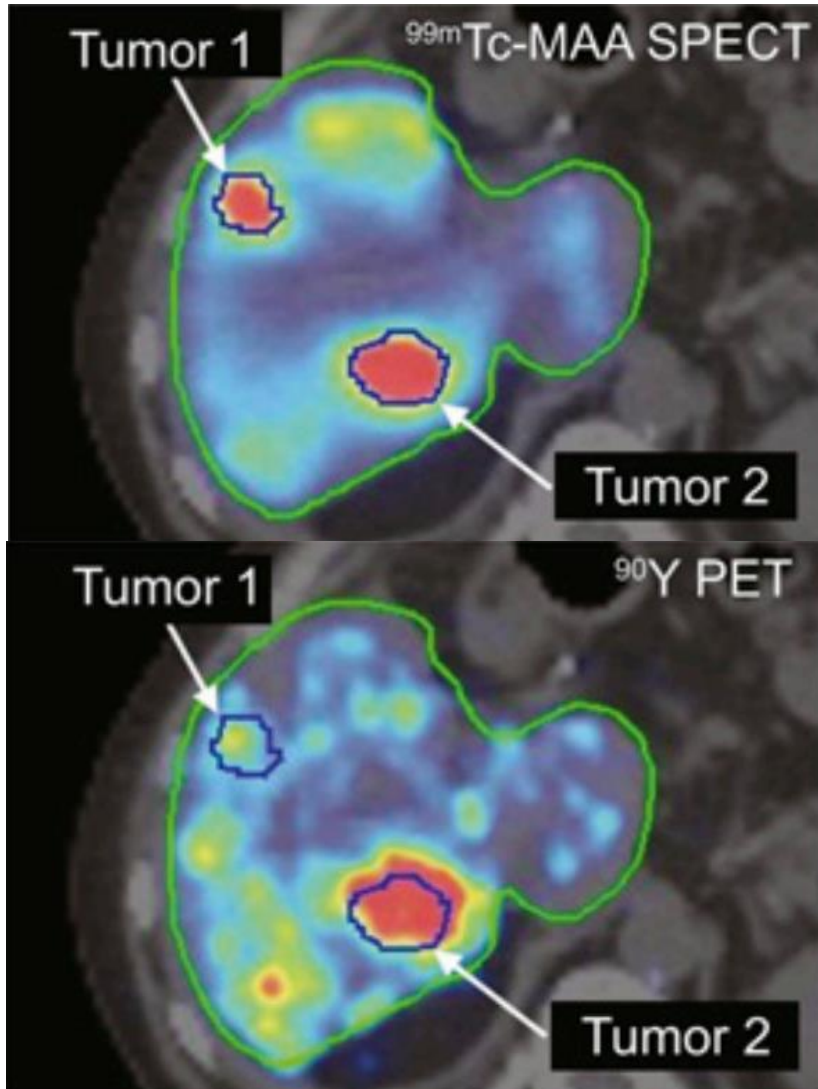
Yttrium-90 microsphere radioembolization is a valuable therapeutic option in unresectable hepatocellular carcinoma (HCC) and hepatic metastases.

It is based on the selective vascularization of the liver : tumor (mainly hepatic artery) vs. non tumor (mainly portal vein).

The spheres (~30 μm) are implanted in the liver as medical devices (no biokinetic behavior).

Radioactivity thus follows the physical decay of Y-90 (β^-).

Selective Internal Radiation Therapy (SIRT) (transarterial radioembolization)

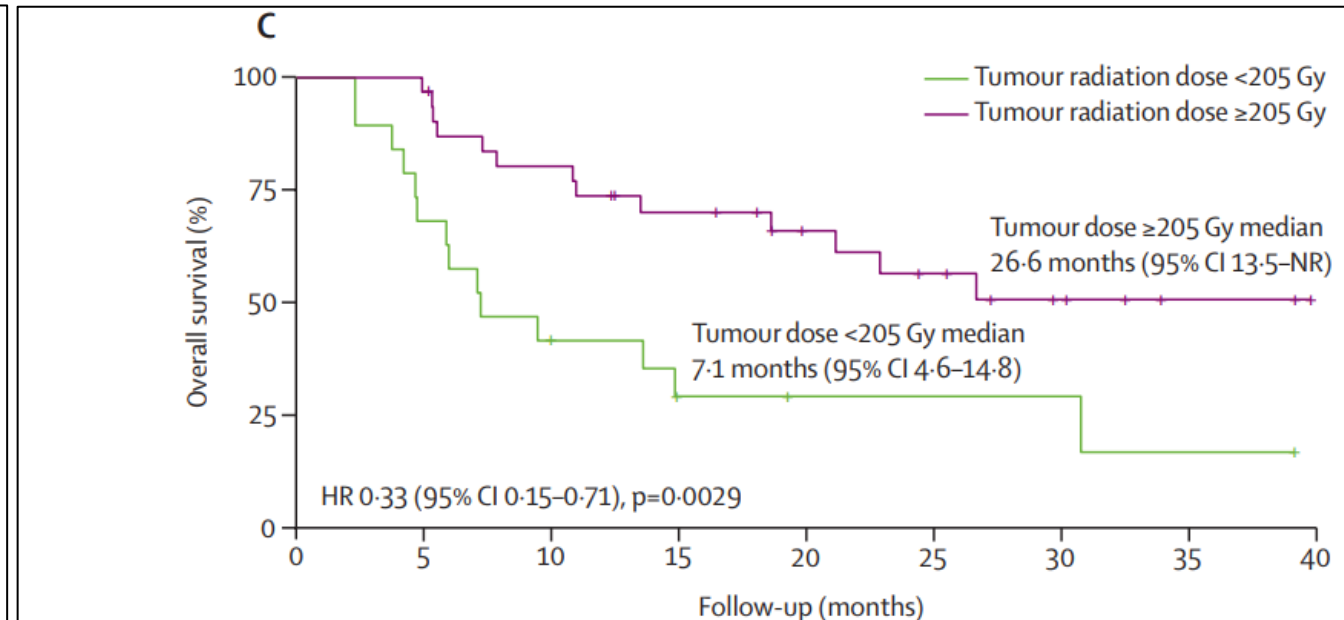
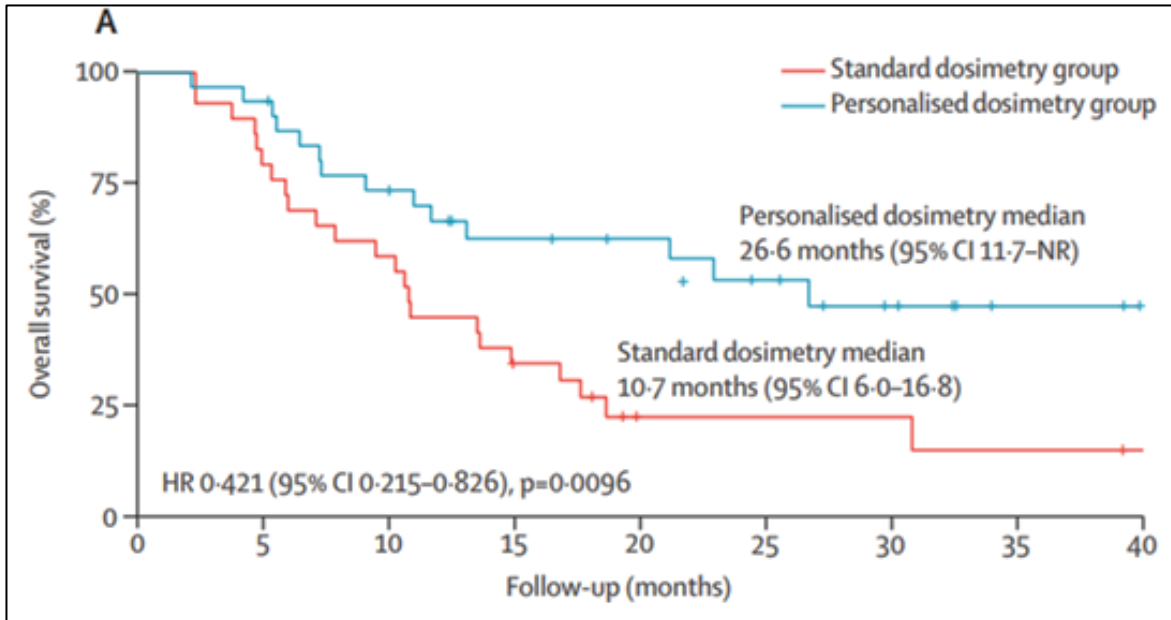


Dose planning can be performed using Tc-99m-labelled macro aggregated albumin (MAA):

1. Fluoroscopically-guided pre-therapy (Tc-99m MAA).
2. The predictive dosimetry based on the Tc-99m SPECT.
3. Single-time point dosimetry is done, allowing to determine patient-specific activity administration of Y-90 microspheres.
4. Fluoroscopically-guided therapy (Y-90).
5. Post-treatment verification (e.g. with Y-90 PET)

Selective Internal Radiation Therapy (SIRT) (dose-response relationship)

Study on ~30 patients per category



European Journal of Nuclear Medicine and Molecular Imaging (2021) 48:1570–1584
<https://doi.org/10.1007/s00259-020-05163-5>

GUIDELINES



International recommendations for personalised selective internal radiation therapy of primary and metastatic liver diseases with yttrium-90 resin microspheres

Hugo Levillain¹ · Oreste Bagni² · Christophe M. Deroose³ · Arnaud Dieudonné⁴ · Silvano Gnesin⁵ · Oliver S. Grosser⁶ · S. Cheenu Kappadath⁷ · Andrew Kennedy⁸ · Nima Kokabi⁹ · David M. Liu¹⁰ · David C. Madoff¹¹ · Armeen Mahvash¹² · Antonio Martínez de la Cuesta¹³ · David C. E. Ng¹⁴ · Philipp M. Paprottka¹⁵ · Cinzia Pettinato¹⁶ · Macarena Rodríguez-Fraile¹³ · Riad Salem¹⁷ · Bruno Sangro¹³ · Lidia Strigari¹⁸ · Daniel Y. Sze¹⁹ · Berlinda J. de Wit van der veen²⁰ · Patrick Flamen¹

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Source: [https://doi.org/10.1016/S2468-1253\(20\)30290-9](https://doi.org/10.1016/S2468-1253(20)30290-9)

European Journal of Nuclear Medicine and Molecular Imaging (2022) 49:1682–1699
<https://doi.org/10.1007/s00259-021-05600-z>

GUIDELINES



EANM procedure guideline for the treatment of liver cancer and liver metastases with intra-arterial radioactive compounds

M. Weber¹ · M. Lam² · C. Chiesa³ · M. Konijnenberg⁴ · M. Cremonesi⁵ · P. Flamen⁶ · S. Gnesin⁷ · L. Bodei⁸ · T. Kracmerova⁹ · M. Luster¹⁰ · E. Garin¹¹ · K. Herrmann¹

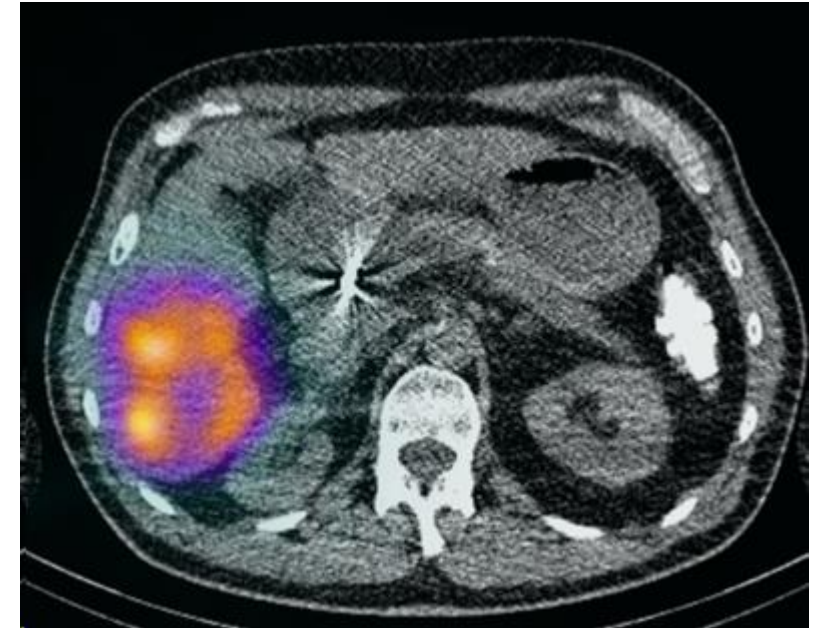
Received: 9 September 2021 / Accepted: 19 October 2021 / Published online: 11 February 2022
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Selective Internal Radiation Therapy (SIRT)

(oversimplified calculation / orders of magnitude) *

- Compute the activity of Y-90 microspheres to be administered to a HCC patient:
 - Tumor target dose = 210 Gy
 - Tumor volume = 1 kg
 - Y-90 physical half-life = 64.1 h
 - Mean β - energy = 0.93 MeV



Hint : start computing the number of decays of Y-90 for 1 GBq

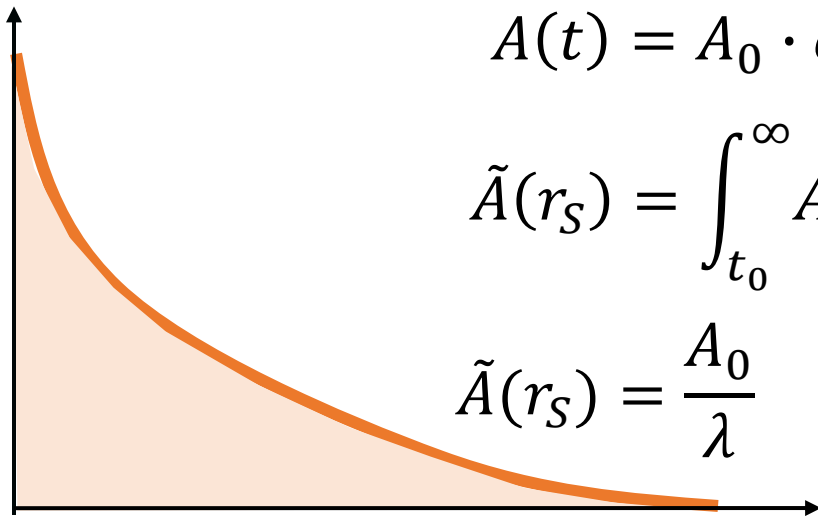
Reminder : $A(t) = A_0 \cdot e^{-\lambda t}$ where $\lambda = \ln(2) / T_{\text{half life}}$

*not clinically pertinent, just an exercice

Selective Internal Radiation Therapy (SIRT)

(oversimplified calculation / orders of magnitude)

- Compute the activity of Y-90 microspheres to be administered to a HCC patient:



$$A(t) = A_0 \cdot e^{-\lambda t}$$

$$\tilde{A}(r_S) = \int_{t_0}^{\infty} A(t) dt = \int_{t_0}^{\infty} A_0 \cdot e^{-\lambda t} dt$$

$$\tilde{A}(r_S) = \frac{A_0}{\lambda}$$



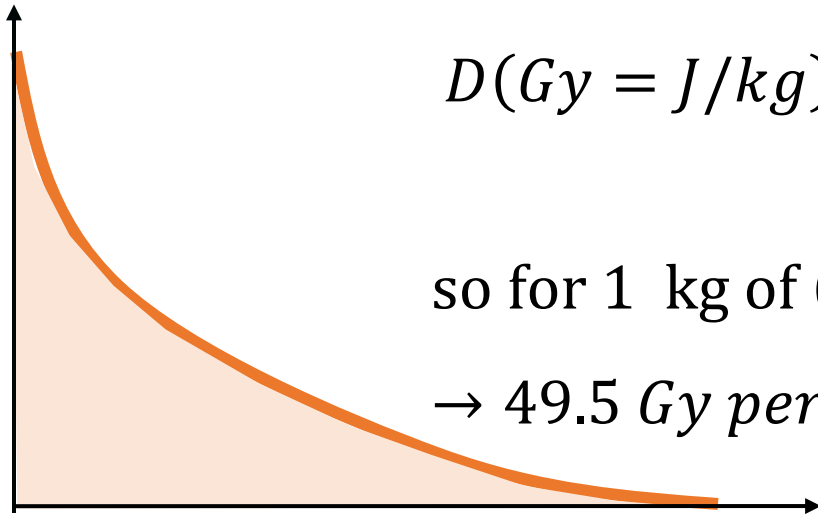
$$\tilde{A}(r_S) = \frac{A_0}{\lambda} = \frac{10^9 \text{ Bq}}{3 \cdot 10^{-6} \text{ s}^{-1}} = 3.3 \cdot 10^{14} \text{ decays}$$

$$E(J) = 3.3 \cdot 10^{14} \text{ decays} \cdot 0.93 \cdot 10^6 \text{ eV} \cdot 1.6 \cdot 10^{-19} \text{ J/eV} = 49.5 \text{ J}$$

Selective Internal Radiation Therapy (SIRT)

(oversimplified calculation / orders of magnitude)

- Compute the activity of Y-90 microspheres to be administered to a HCC patient:



$$D(Gy = J/kg) = 49.5 Gy$$

so for 1 kg of (tumor) tissue

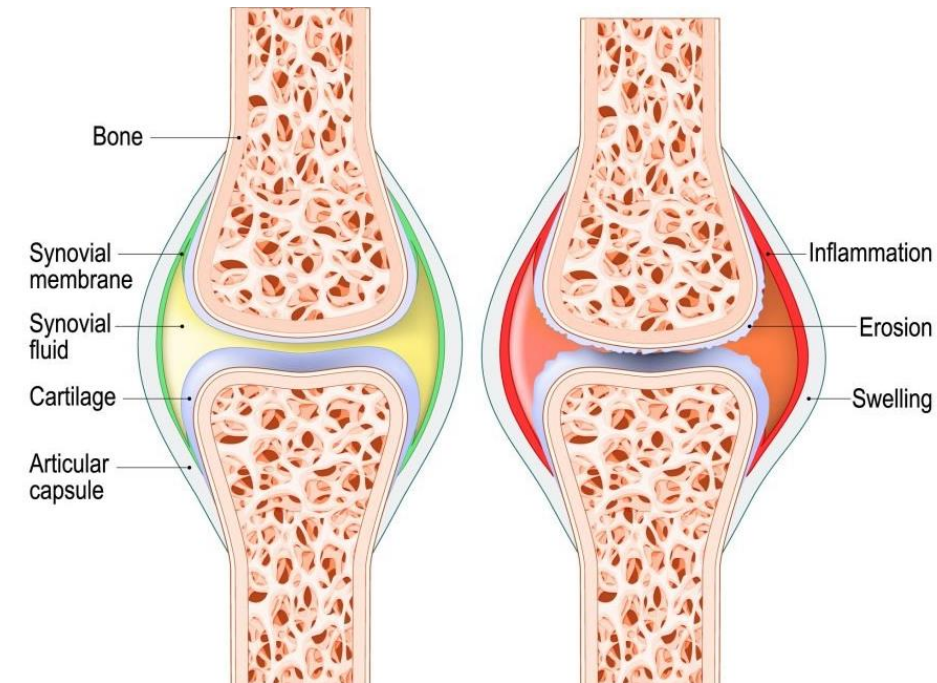
→ 49.5 Gy per GBq



to reach 210 Gy → 4.2 GBq

Radiosynoviorthesis (joint pain)

- Joint pain may result from synovitis (i.e. inflammation of the synovial membrane).
- Synovitis may appear in case of osteoarthritis, rheumatoid arthritis, hemophilic arthropathy.
- β - emitters are injected in the joint cavity.
- Radiopharmaceuticals are phagocytized by the macrophages of the synovial membrane.
- Radiation induces fibrosis and sclerosis in the synovial membrane.
- Reduce of inflammation and thus joint pain, quality of life improvement.



European Journal of Nuclear Medicine and Molecular Imaging (2021) 49:681–708
<https://doi.org/10.1007/s00259-021-05541-7>

GUIDELINES



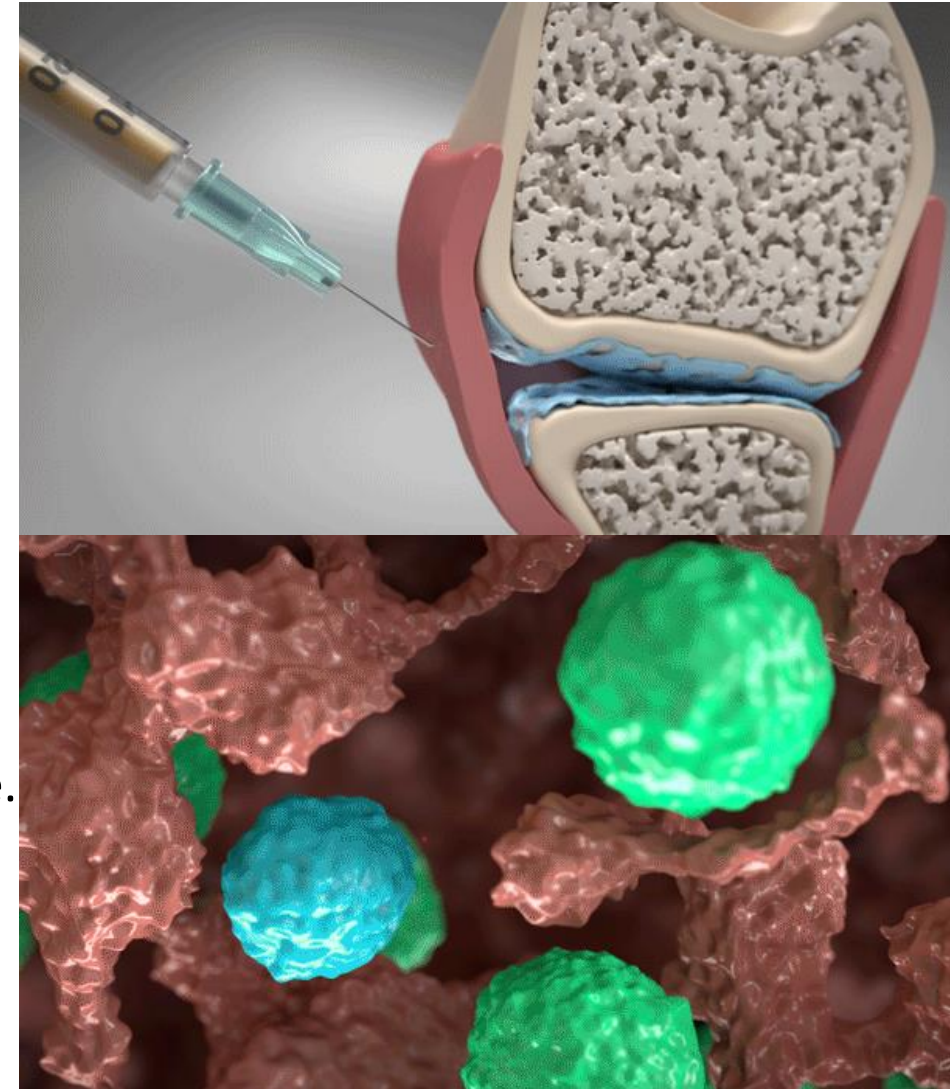
The EANM guideline for radiosynoviorthesis

W.U. Kampen¹ · B. Boddenberg-Pätzold² · M. Fischer³ · M. Gabriel⁴ · R. Klett⁵ · M. Konijnenberg⁶ · E. Kresnik⁷ · H. Lellouche^{8,9} · F. Paycha¹⁰ · L. Terslev¹¹ · C. Turkmen¹² · F. van der Zant¹³ · L. Antunovic¹⁴ · E. Panagiotidis¹⁵ · G. Gnanasegaran¹⁶ · T. Kuwert¹⁷ · T. Van den Wyngaert^{18,19} on behalf of the EANM Bone & Joint Committee, the Dosimetry Committee, the Oncology & Theranostics Committee

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Radiosynoviorthesis (joint pain)

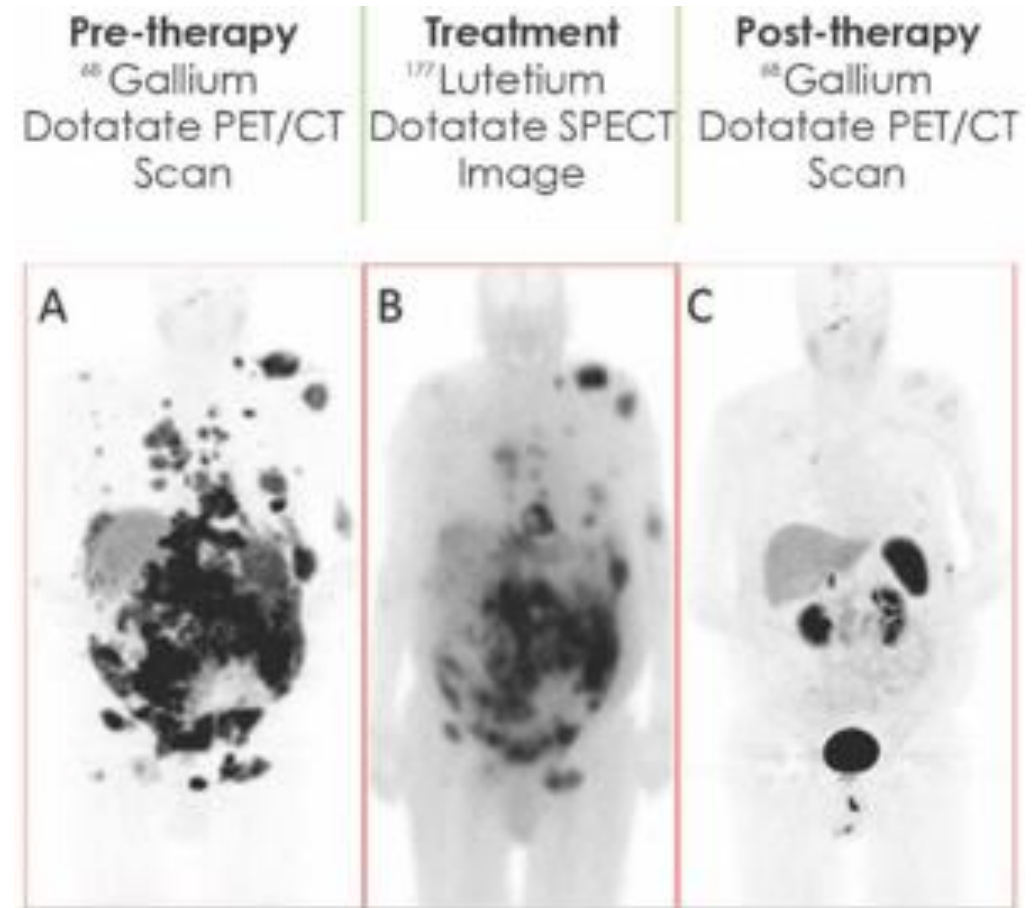
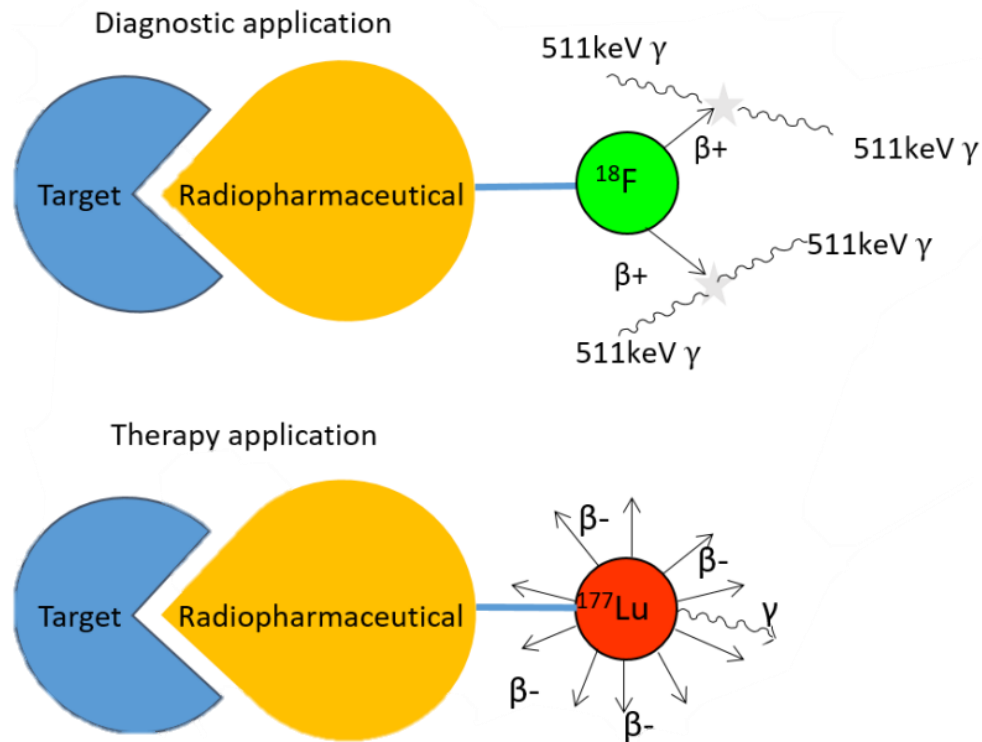
- Joint pain may result from synovitis (i.e. inflammation of the synovial membrane).
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- β - emitters are injected in the joint cavity.
- Radiopharmaceuticals are phagocytized by the macrophages of the synovial membrane.
- Radiation induces fibrosis and sclerosis in the synovial membrane.
- Reduce of inflammation and thus joint pain, quality of life improvement.



Theranostics

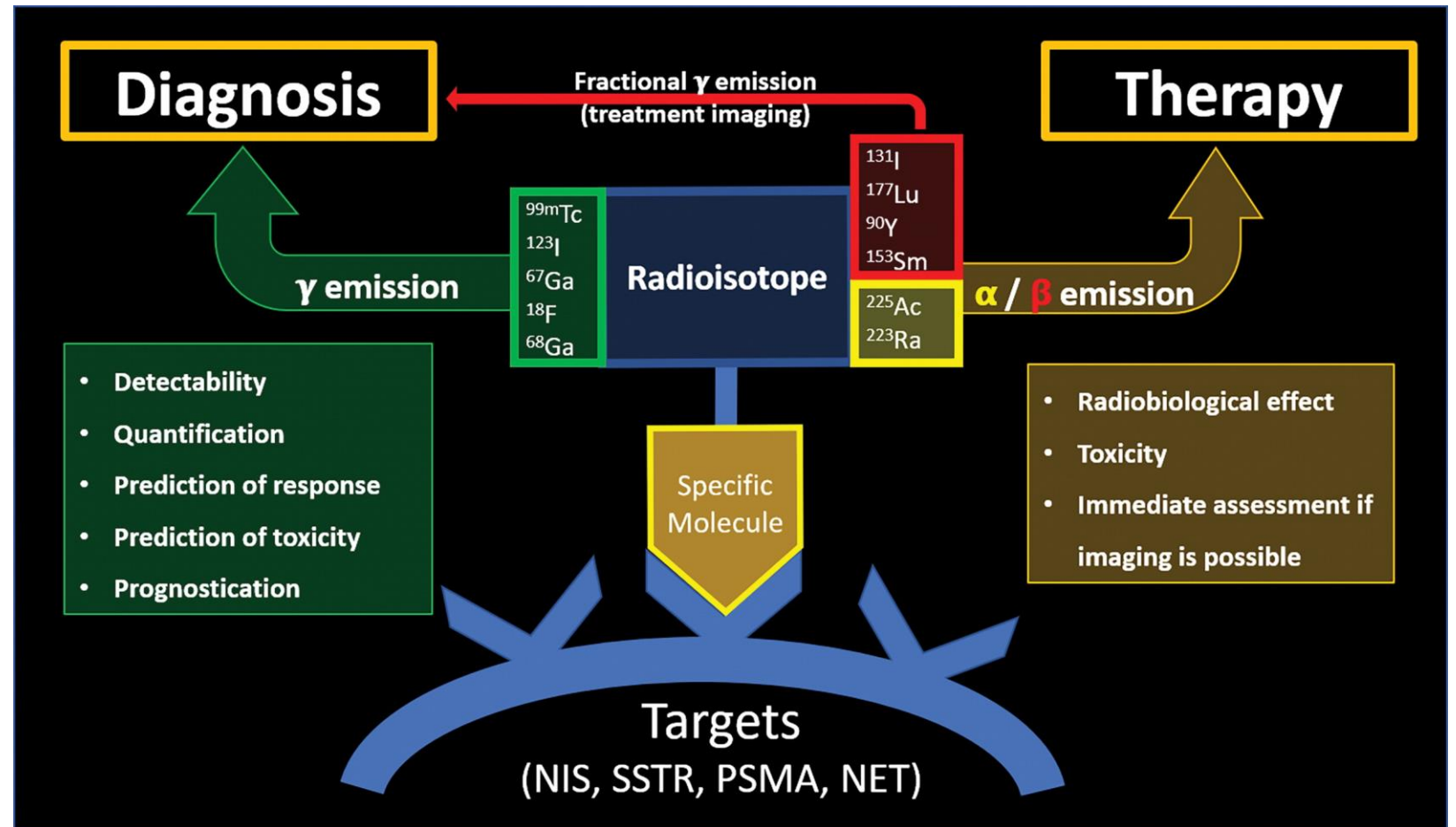
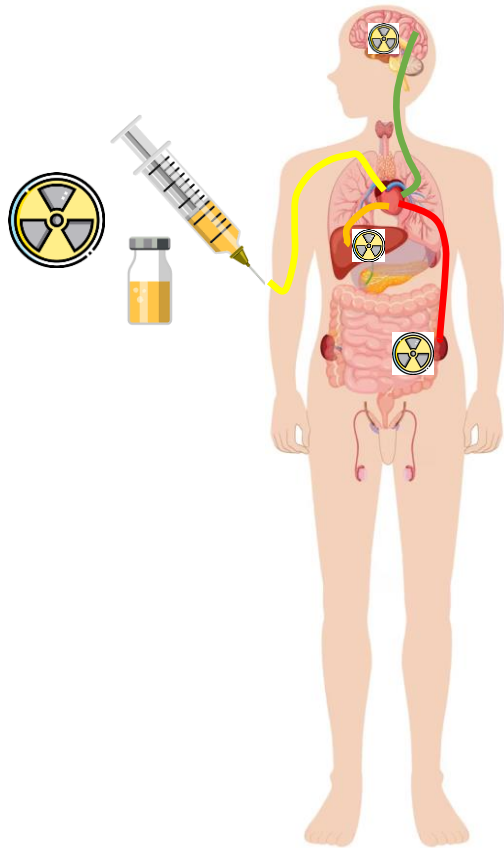
Recap from lecture 6:

Same vector (i.e. biodistribution) but different radionuclide (i.e. dose delivery)!



Theranostic pairs

Assuming comparable biokinetic → Use of diagnostic isotopes (e.g., Ga-68) with therapeutic analogs (e.g., Lu-177) enables **individualized therapy planning**.



Theranostic pairs

Therapeutic Application	RP for Dosimetry	RP for Therapy	Activity Typically Administered
Thyroid cancer	^{123}I , ^{124}I , ^{131}I	^{131}I	1.1 to 5.5 GBq (thyroid remnant ablation) 5.5–11 GBq (treatment of metastases) single administration [23]
Neuroblastoma	$(^{131}\text{I})\text{mIBG}$	$(^{131}\text{I})\text{mIBG}$	3.7–11.2 GBq per cycle; multiple cycles [24]
PRRT for NET and other somatostatin receptor expressing tumors	^{111}In -DOTATOC	^{90}Y -DOTATOC *	2.8–3.7 GBq per cycle; 4 cycles [25]
	^{177}Lu -DOTATATE	^{177}Lu -DOTATATE	7.4 GBq per cycle; 4 cycles [6]
Radioembolization of primary and secondary liver tumors	$^{99\text{m}}\text{Tc}$ -MAA, ^{90}Y microspheres	^{90}Y resin or glass microspheres	2–4 GBq (resin) 3–20 GBq (glass) single administration [26]
	^{166}Ho microspheres	^{166}Ho poly-L-lactic acid microspheres	3.8 GBq/kg (liver weight) single administration [27]
Radioimmunotherapy for hematologic malignancies (leukemia, MDS, myeloma, lymphoma)	^{111}In -MoAbs	^{90}Y -MoAbs (Zevalin [®])	11–14 MBq/kg (body weight) single administration [28]
	^{131}I -MoAbs	^{131}I -MoAbs (Bexxar [®])	2.2–5.7 GBq single administration [29]
Prostate cancer	^{177}Lu -PSMA	^{177}Lu -PSMA	3.7–9.3 GBq; 2 to six cycles [30]
	imaging not possible, extrapolation from ^{177}Lu -PSMA data	^{225}Ac -PSMA *	4–13.4 MBq per cycle; 2–6 cycles [31]
Bone metastases from breast and prostate cancers	^{223}Ra	^{223}Ra	55 kBq/kg (body weight) per cycle; 6 cycles [32]



Therapy – Dosimetry : opportunities

Theranostic pairs and personalized dosimetry

- Combining diagnostic isotopes (e.g., Ga-68) with therapeutic analogs (e.g., Lu-177) enables personalized treatment planning to maximize efficacy and minimize toxicity.

Dose–Response Relationships

- Evidence shows absorbed dose correlates with tumor control and toxicity (kidneys, bone marrow), supporting rational, dose-guided therapy.

Alpha Emitters

- Isotopes like Ac-225 and Bi-213 deliver high LET radiation with short range, ideal for micrometastases and potentially curative approaches, though imaging and dosimetry remain challenging.

Artificial Intelligence & Automation

- AI supports automated segmentation, rapid image processing, and predictive modelling for individualized treatment planning.

Advanced Imaging Techniques

- Improved SPECT/CT and PET/CT allow better activity quantification and spatial resolution for accurate dose estimation.

Advanced dosimetry techniques

- Development of methods to take into account for dose inhomogeneities and prediction of biological response.

Therapy – Dosimetry : challenges

Time & Data & Resource Constraints

- Full dosimetry requires multiple imaging sessions over several days, making it burdensome for patients and clinics. Many centers lack specialized software, skilled personnel, and comprehensive datasets for validation.

Biological Uncertainty

- Variability in tumor uptake, clearance, and radiosensitivity reduces outcome predictability, even with precise dose calculations.

Alpha Particle Dosimetry Limitations

- Extremely difficult due to short range and high toxicity; current imaging methods often cannot track alpha emitters effectively.

Regulatory Inertia

- Standardized dosimetry-based prescribing is not mandated, slowing widespread adoption.

Dose Constraints for Critical Organs

- Kidneys, liver, and bone marrow remain dose-limiting; thresholds are debated and lack personalization.

Lack of Standardization

- No universal protocols for dose calculation, imaging time points, or quantification methods, leading to variability across centers.

Quantification Issues

- Errors from partial volume effects, organ motion, and calibration compromise dose accuracy.

Summary

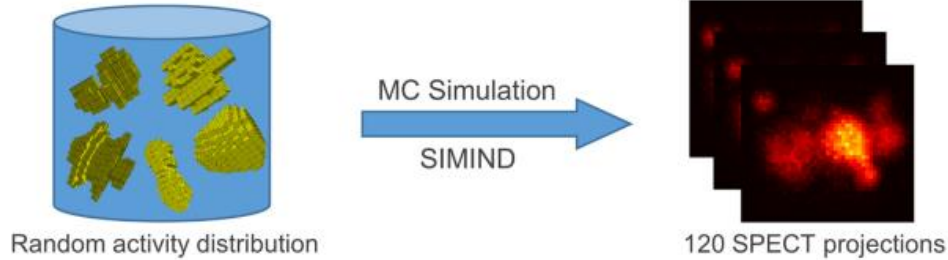
- Briefly describe the **most promising advanced techniques** in nuclear medicine
- Describe the different **therapeutic applications** of nuclear medicine and **theranostics**
- Explain the **workflow** required to perform **dosimetry** in nuclear medicine

Additional slides

New trends in SPECT (AI examples)

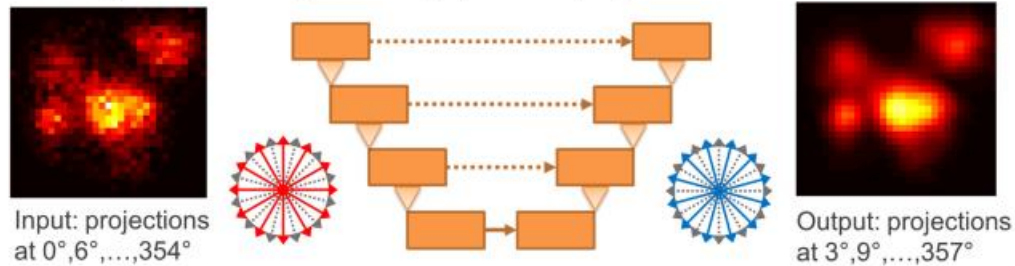
fast SPECT using AI-generated synthetic projections

1 Generation of a large simulated SPECT dataset



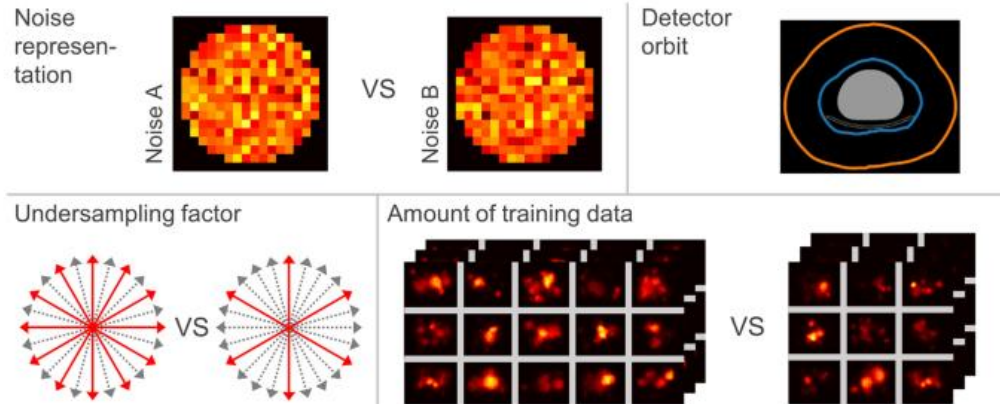
Create (with Monte Carlo) a comprehensive database of projections

2 Training of u-nets for generating synthetic projections



Train a deep learning algorithm to generate missing projections

3 Performance analysis based on different u-nets



potential for **accelerating** SPECT/CT imaging
(only acquire a sub-sample of the original data)

Theranostic pairs (advantages)

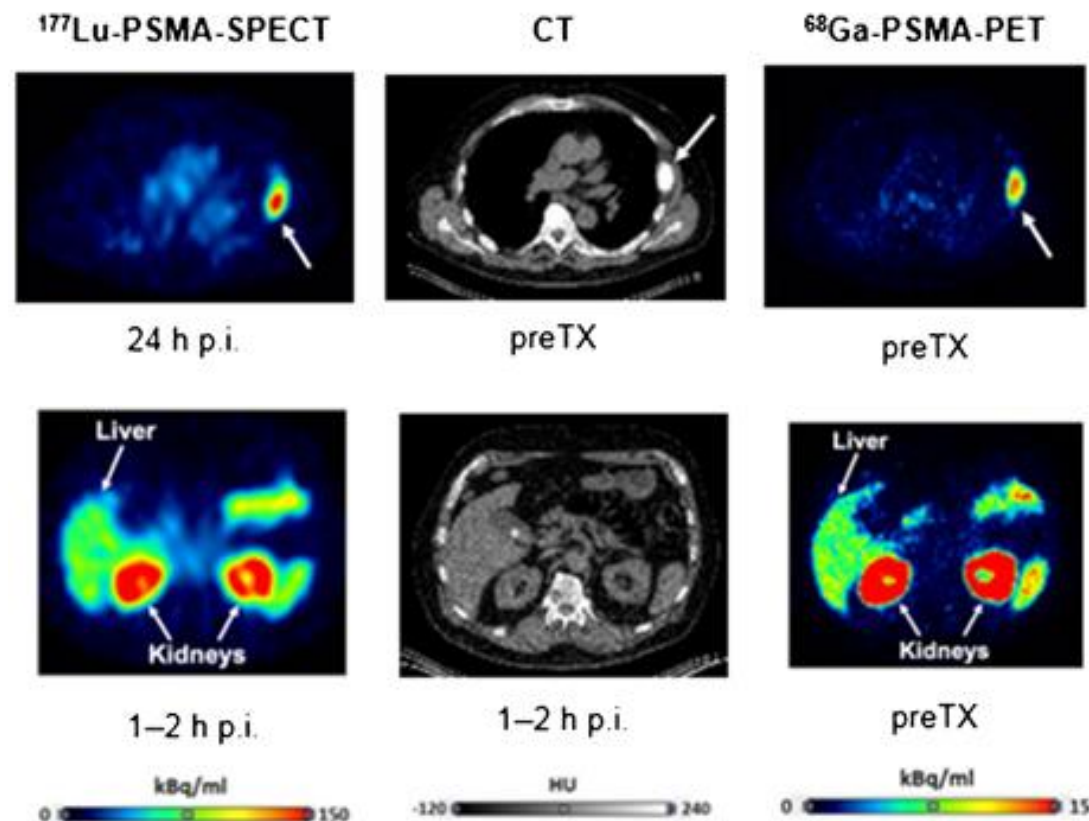
Assuming comparable biokinetic

→ Use of diagnostic isotopes (e.g., Ga-68) with therapeutic analogs (e.g., Lu-177) enables **individualized therapy planning**.

A single time point [68Ga]Ga-PSMA-PET used to predict the absorbed dose of [177Lu]Lu-PSMA therapy to organs, and (to a limited extent) to lesions.

Simple treatment planning for personalization of [177Lu]Lu-PSMA therapy.

- **~10% accuracy in normal organs**
 - More predictable biokinetic behavior
 - More consistent anatomical segmentation
- **~30% accuracy in lesions**
 - More variable biokinetic behavior
 - Segmentation challenging (PVE)



Theranostic pairs

(disadvantages)

Diagnostic/therapeutic radiometal are used

Not identical biological properties or binding affinities to the same chelator.

→ differences in biodistribution between the diagnostic vs therapeutic compounds

The typically short half-life of diagnostic vs therapeutic radionuclides

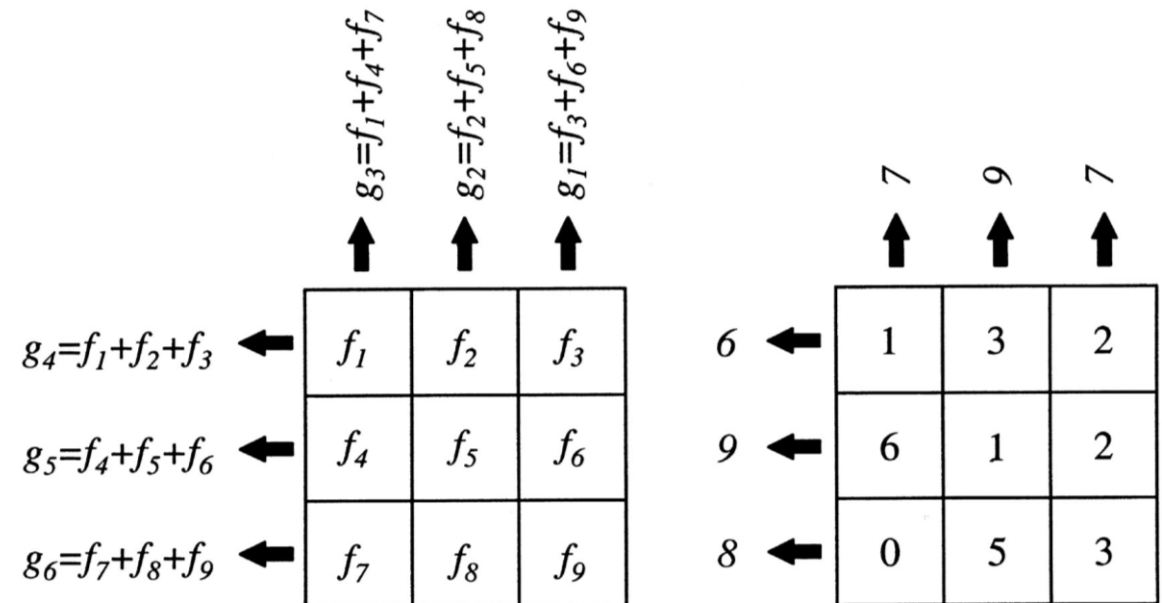
ex. Ga-68 (~1h) vs Lu-177 (160h)

- diagnostic information for only few hours post-injection
- Difficult /suboptimal extrapolation to therapeutic relevant times (days)
- Challenging predictive dosimetry from diagnostic compound

Some questions

- **Back-projection vs. forward projection.**
- The operations g_1 to g_6 are forward projections : find projections starting from pixel values (easy, if we know the pixel values = the activity distribution inside our object/patient).
- In reality, in SPECT or PET, we only have access to the ensemble of measured (finite) projections themselves, under the form of sinograms. We thus we have to find mathematical solutions (backprojection, filtered-backprojections and iterative reconstruction algorithms) to «reconstruct back» the «real» activity distribution inside our object/patient.

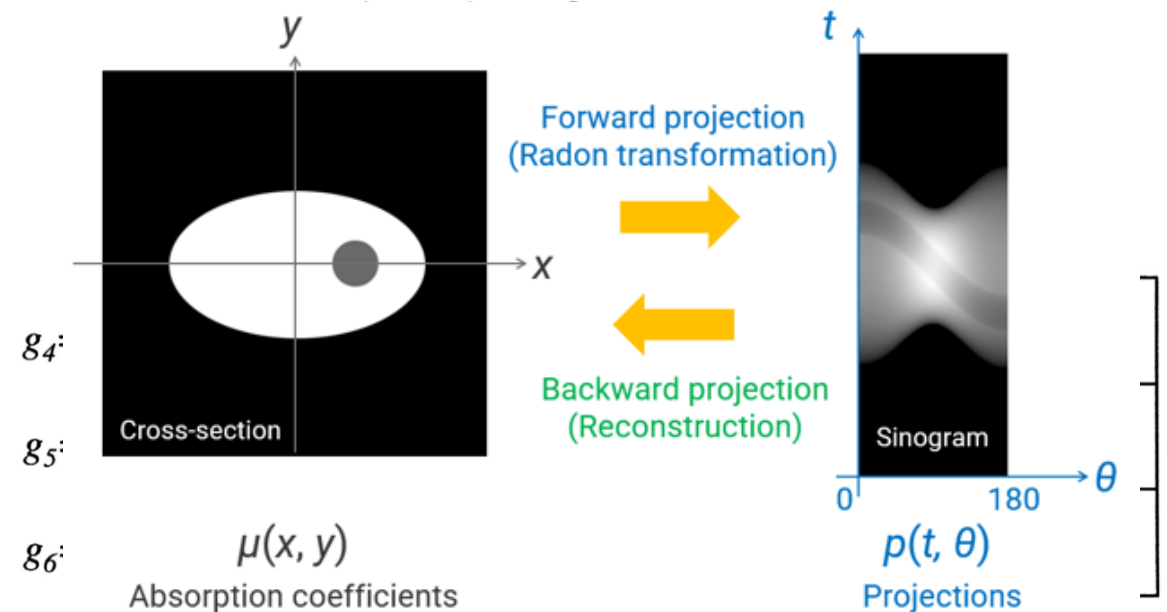
- Forward projections are used in iterative reconstruction algorithms to generate a sinogram starting from an initial «guess» image. The sinogram generated from forward projection is compared in an iterative process with the (real) measured one, until convergence criteria are met.



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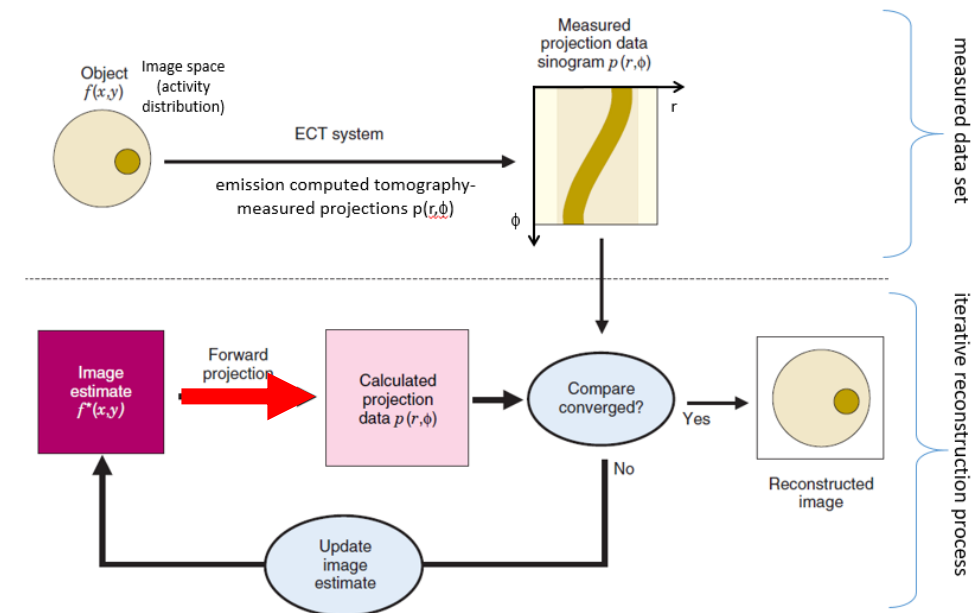
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Some questions

- The collimators in the gamma camera

The collimator is a “weak link” for the performance of a gamma camera system, as indeed it is in any nuclear medicine imaging system employing the principles of *absorptive collimation*. *Collimator efficiency*, defined as the fraction of γ rays striking the collimator that actually pass through it to project the γ -ray image onto the detector, is typically only a few percent or less. *Collimator resolution*, which refers to the sharpness or detail of the γ -ray image projected onto the detector, also is rather poor, generally worse than the intrinsic resolution of the camera detector and electronics.

Collimators are necessary, as indeed, they are fundamental for event localisation in the gamma camera.

However, the fact of adding them (independently on their shape) worsen the spatial resolution that could be achievable intrinsically (by the detector and electronics alone). In fact, we add geometric limitations (hole size, length, septa thickness)

Intrinsic resolution is better than extrinsic, BUT we need the collimators for event localization.

The big disadvantage is on the efficiency (absorptive collimation results in a huge loss of photons)!

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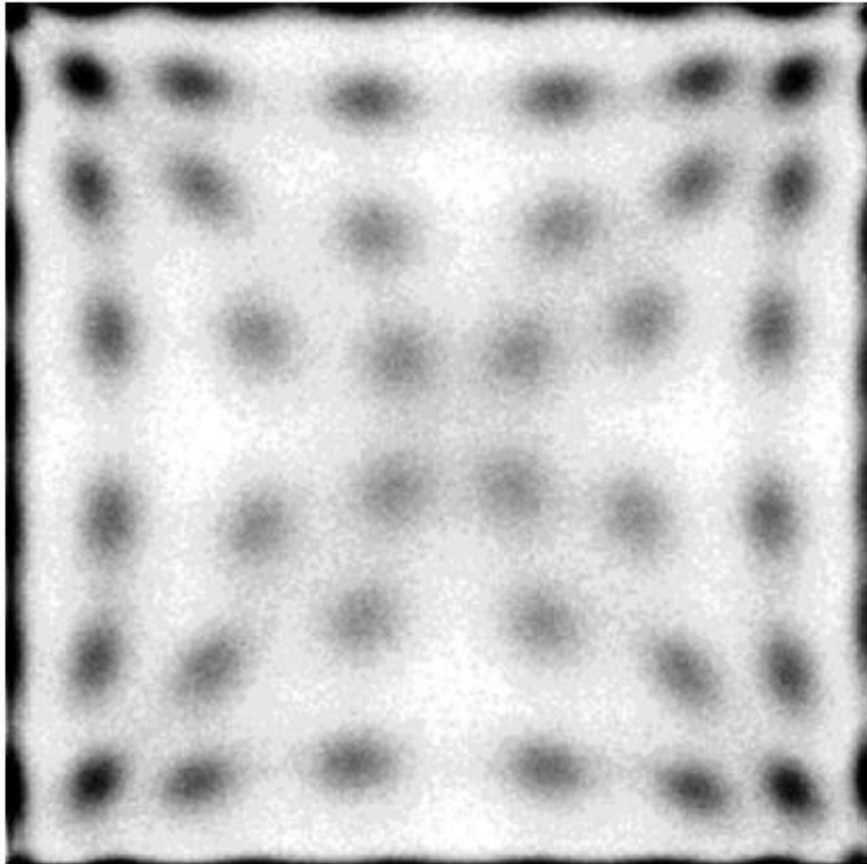


FIGURE 18-15 Flood-field image obtained by uniformly irradiating a block detector with 511-keV annihilation photons. Individual block detector elements appear as distinct “blobs” in the image, allowing separation of events recorded within individual detector elements.

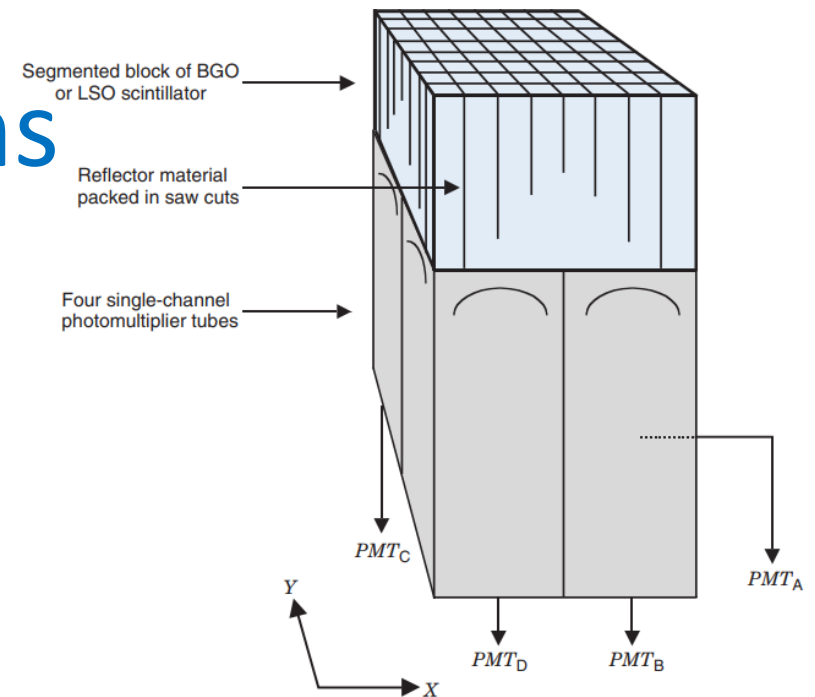


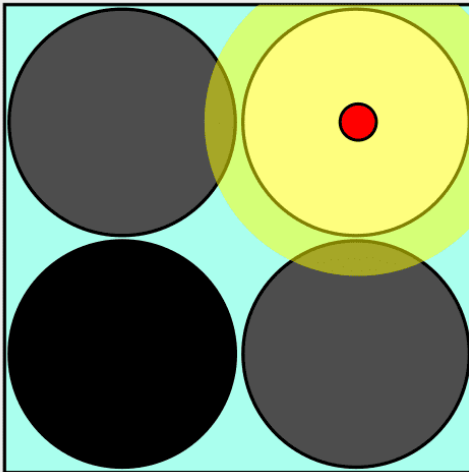
FIGURE 18-14 Block detector commonly used in clinical PET scanners. A piece of BGO or LSO scintillator is cut into an array of smaller elements that are read out using four single-channel photomultiplier tubes (PMTs). The cuts in the material are filled with an opaque reflective material that, along with the depths of the cuts, helps control the distribution of scintillation light reaching the PMTs.

Figure 18-15 shows the image obtained from uniform irradiation of a block detector. The image is not uniform. Rather, the calculated locations for recorded events are clustered in small localized areas corresponding to the individual detector elements. There is a small amount of overlap, but the individual elements are clearly resolved. Although the array pattern is nonlinear, the separation is sufficiently clear to allow each (x,y) location in the image to be assigned to a specific detector element in the array, for example, by using a look-up table.

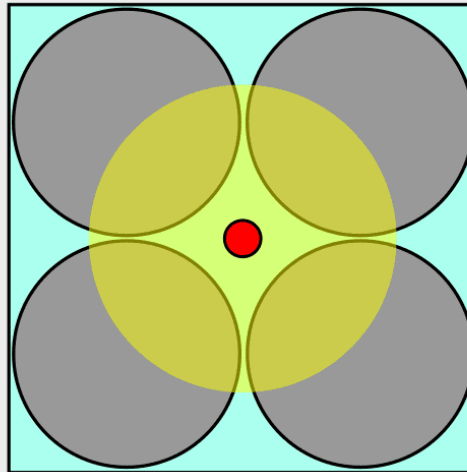
Some questions

Positional Logic

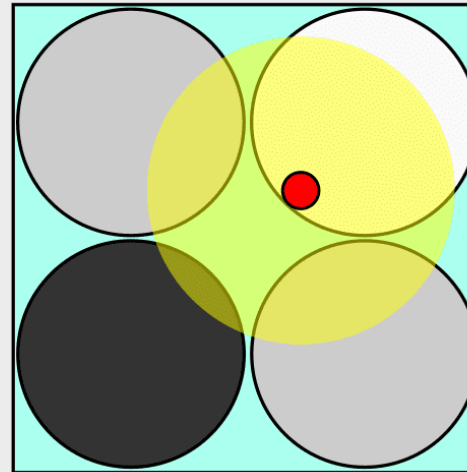
- Site of Scintillation
- Scintillation Light Spread
- Low PMT Signal
- High PMT Signal



Scintillation Over PMT

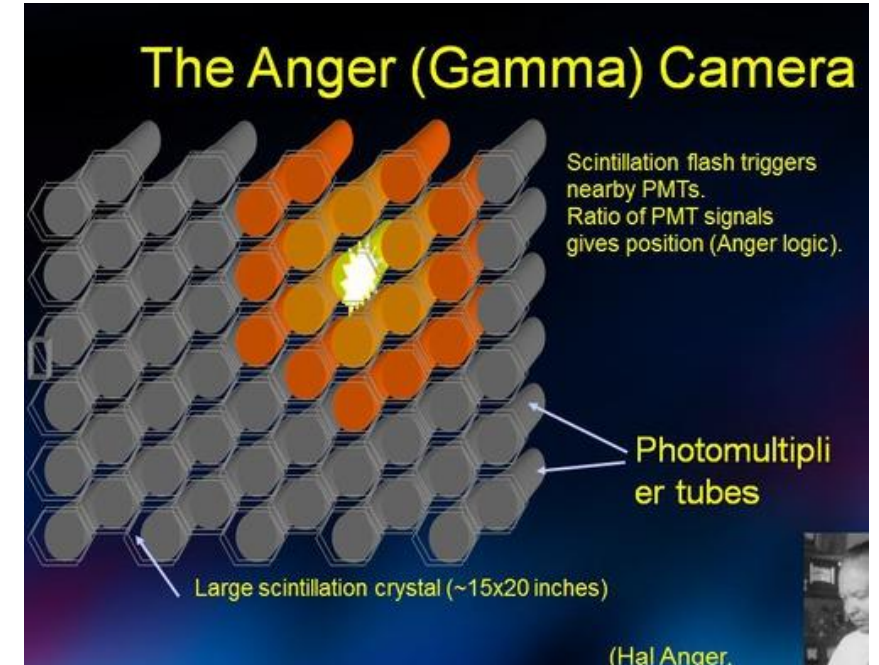


Scintillation Between PMTs



Offset Scintillation

ONCOLOGYMEDICALPHYSICS.COM



Some questions

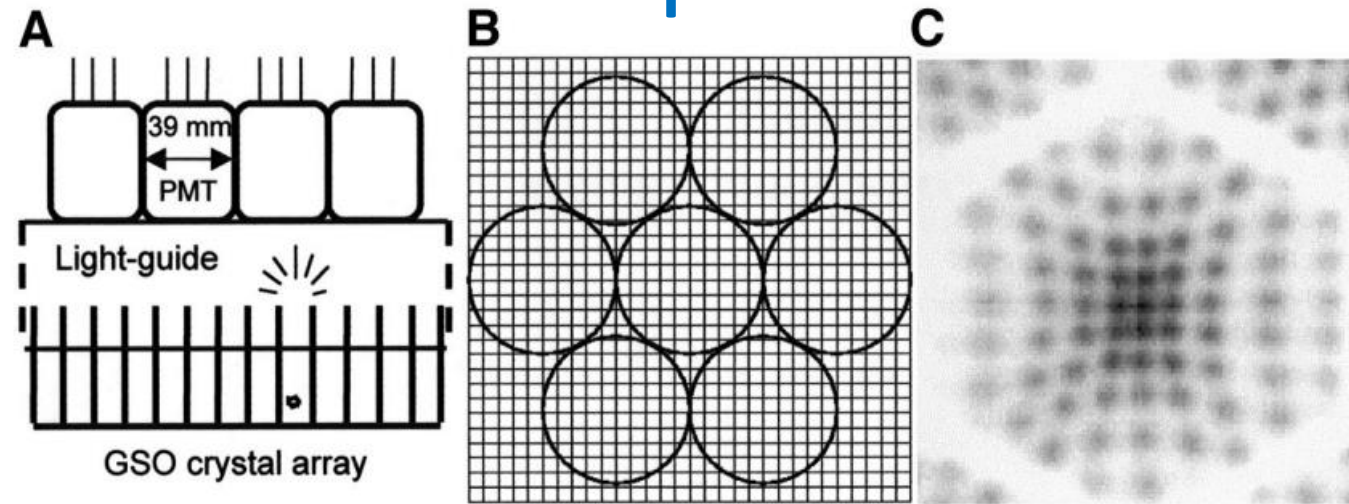


FIGURE 1. GSO Anger-logic detector. (A) Cross-sectional schematic of detector, showing GSO crystal array, annular light-guide, and PMT array. Crystal dimensions are $4 \times 4 \times 10 \text{ mm}^3$, PMTs are 39-mm diameter in hexagonal grid, and light-guide thickness (including slots) is 19 mm. (B) View of one 7-PMT cluster of continuous hexagonal PMT array (other PMTs not shown) overlaying crystal grid. Each PMT sees many crystals, and local 7-PMT cluster is used to determine energy and position of interaction. (C) Flood image with coarse position sampling. Image is linearly distorted with gaps between PMT regions due to use of Anger logic for position determination, but crystals are well discriminated.

Figure 1C shows a flood image for 1 PMT region (with part of adjacent PMT regions seen in the corners). Very good crystal discrimination is obtained. The gaps that appear between PMTs are due to the nonlinear behavior of the local centroid algorithm in positioning an event near the boundary of a PMT, because in this region the position calculation is sensitive to which PMT cluster is chosen for the event

Source; Performance of a Brain PET Camera Based on Anger-Logic Gadolinium Oxyorthosilicate Detectors

Joel S. Karp, Suleman Surti, Margaret E. Daube-Witherspoon, Richard Freifelder, Christopher A. Cardi, Lars-Eric Adam, Kilian Bilger and Gerd Muehllehner
Journal of Nuclear Medicine August 2003, 44 (8) 1340-1349;