The Abdus Salam International Centre for Theoretical Physics

United Nations Educational, Scientific and Cultural Organization

IAEA International Atomic Energy Agency

2484-10

ICTP-IAEA Joint Workshop on Nuclear Data for Science and Technology: Medical Applications

30 September - 4 October, 2013

The radionuclides and their particles: their origin, character, and fate

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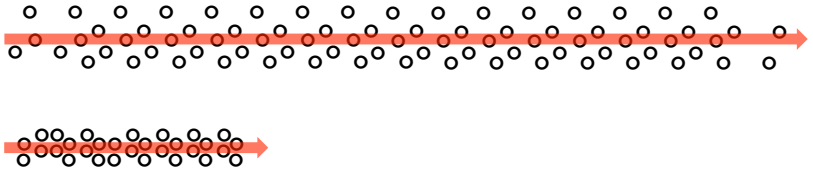
The radionuclides and their particles: their origin, character, and fate

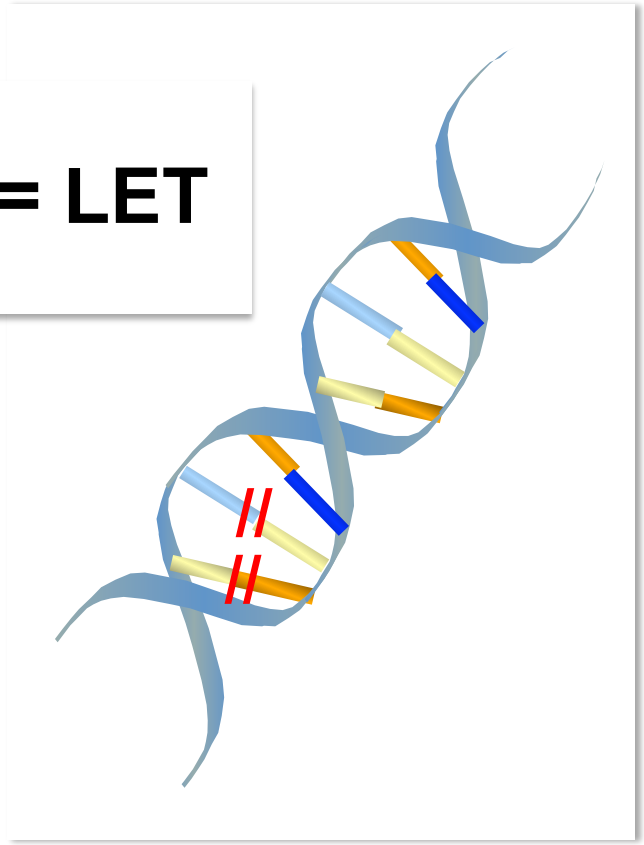
Their fate:

1. PARTICLE INTERACTION WITH MATTER (WATER)

2. IONIZATING WATER MOLECULES,
   THERBY CREATING REACTIVE RADICALS:
   H_2O ->->->-> OH°, H°, etc.



$$\frac{\text{energy}}{\text{distance}} = \textbf{LET}$$

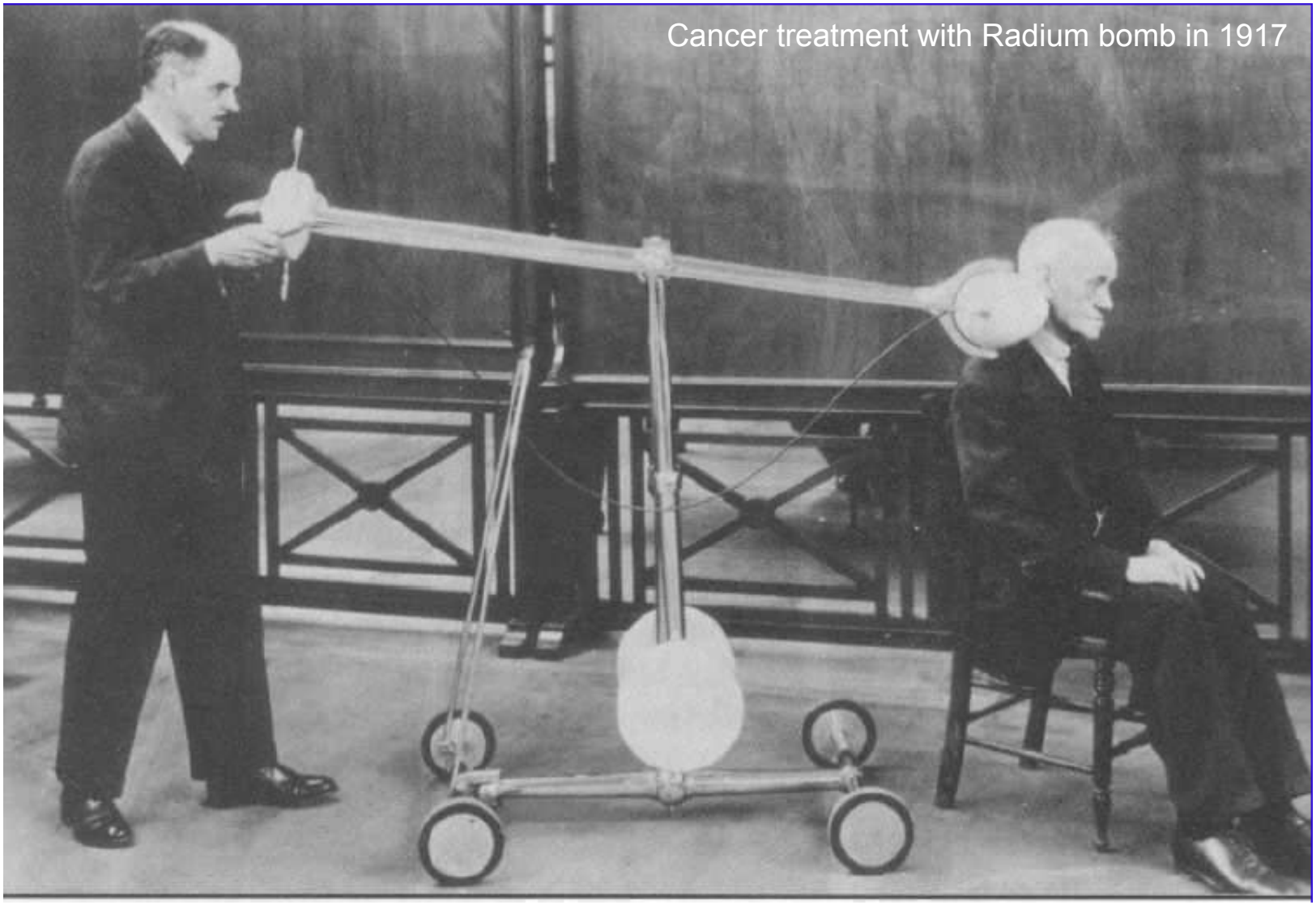


3. DNA DOUBLE-BOND BREAKS

4. RADIATION DOSE PER VOLUME IN GY

5. RADIATION DOSE ≈ THERAPY RESPONSE“

therapeutic radiation dose: EXTERNAL IRRADIATION



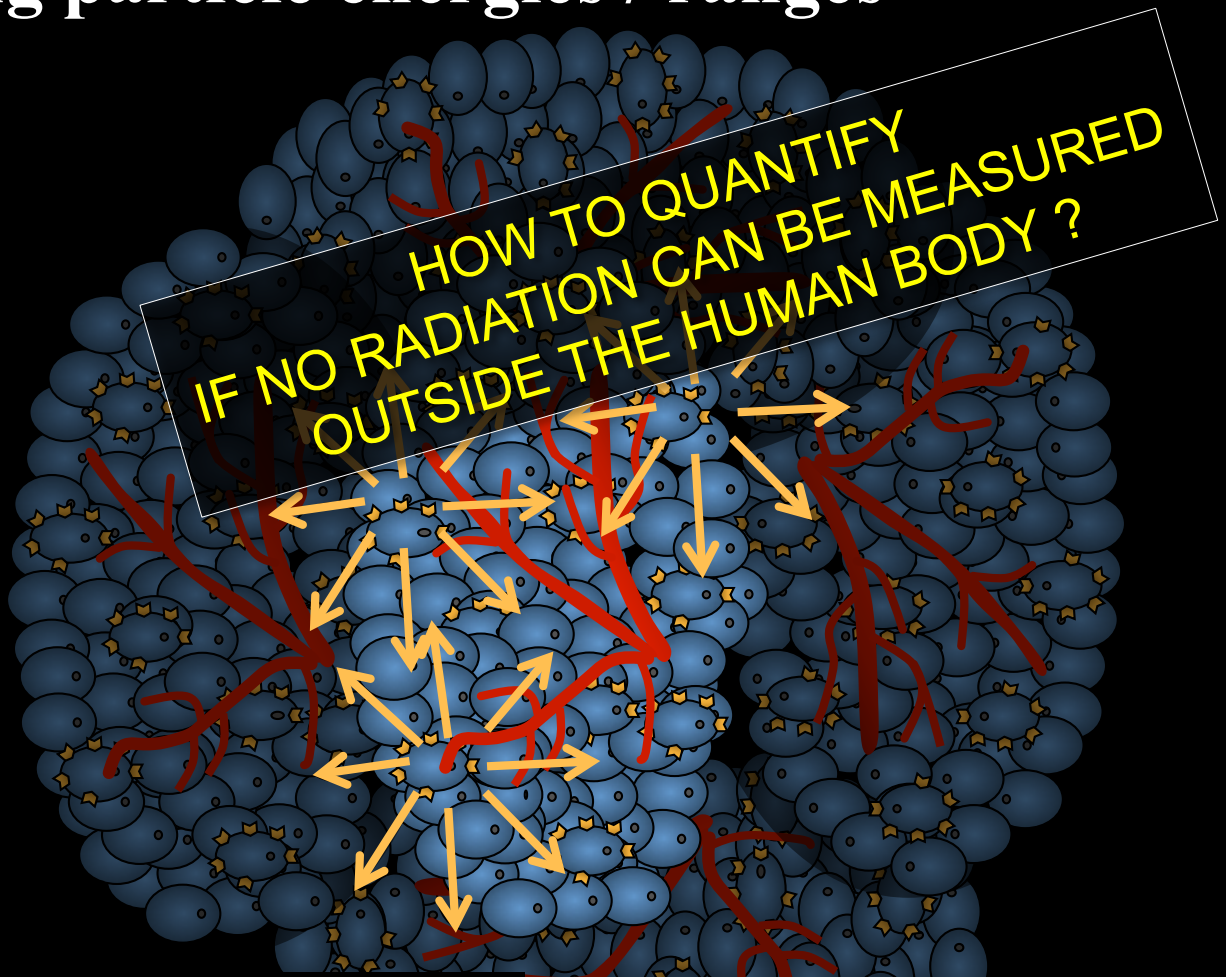
therapeutic radiation dose: INTERNAL IRRADIATION

	factors	influenced by
1	how long is	radiopharmacology $^{BIOL}t_{1/2}$
2	the target organ (tumour)	source (s) and target (t) organ
3	exposed to what absolute radioactivity A	
4	of a certain radionuclide	
5	of physical-half-life $^{PHYS}t_{1/2}$	
6	of radiation characteristics	MIRD S-factors

time integral of the activity

HOW TO QUANTIFY IN VIVO ?

Radionuclides of different kinds of particle emission and varying particle energies / ranges



3.

… delivery of therapeutic doses of ionizing radiation to the malignant cells

but not to surrounding healthy cells

quantification of radiation doses *in vivo*

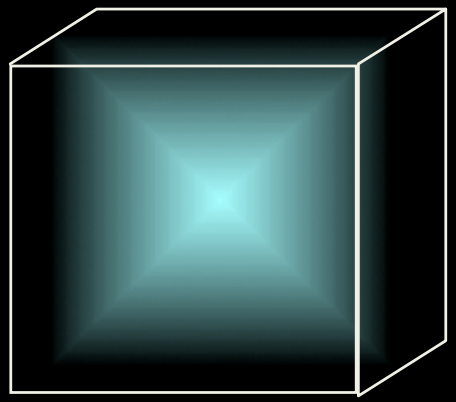
HOW TO QUANTIFY
IF NO RADIATION CAN BE MEASURED
OUTSIDE THE HUMAN BODY ?

ERT

^{90}Y / ^{177}Lu / …

particle emission (α, β^-, Ae^-)

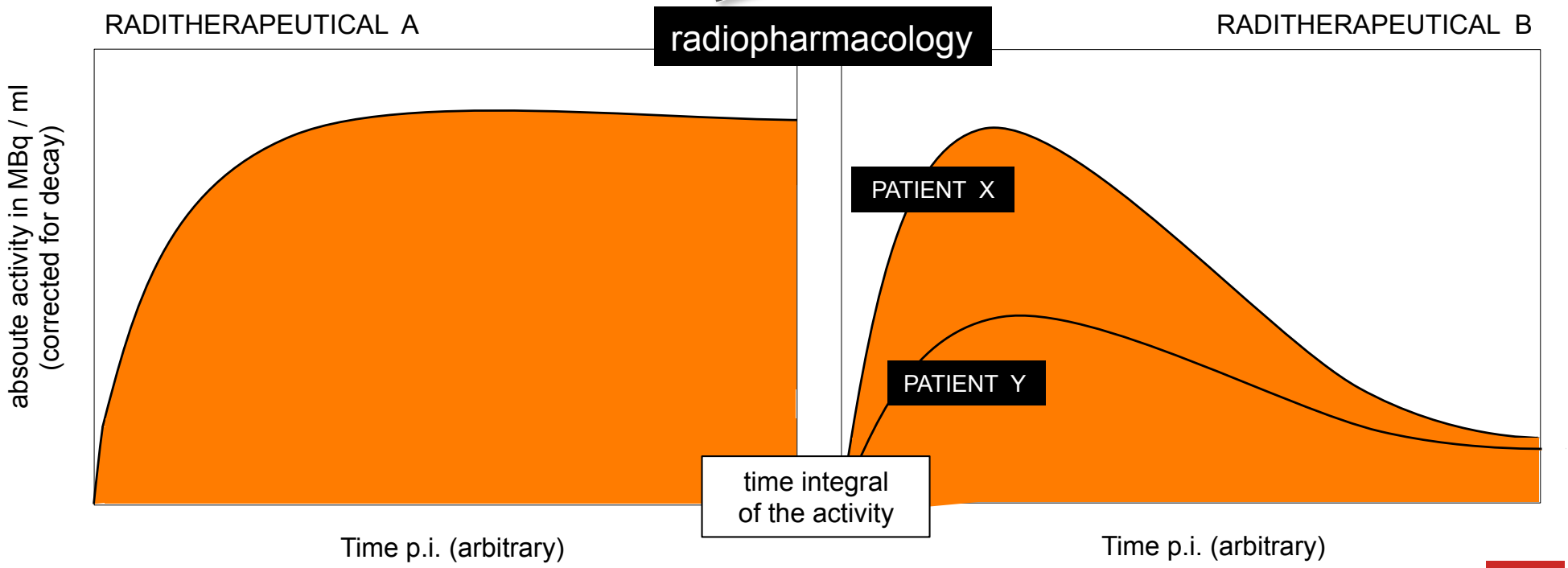
(without) γ-component



“BLACK BOX”

quantification of radiation doses *in vivo*

HOW TO QUANTIFY
IF NO RADIATION CAN BE MEASURED
OUTSIDE THE HUMAN BODY ?



(pre-therapeutic) determination of radiation doses: The impact of PECT / CT

$\bar{D}$:	mean absorbed dose	
$\bar{D}_{t \leftarrow s} = S_{t \leftarrow s} \tilde{A}_s$	source (s) and target (t) organ	
S-values:	mean absorbed dose in unit t per cumulated activity in s	
$\tilde{A}$:	cumulated activity	$\tilde{A} = \int A(t)\, dt$
		$\tilde{A}_s = \int A_s \exp-(\lambda_{phys} + \lambda_{biol})t\, dt$

time integral of the activity

$\lambda_{phys} = \ln 2 / t_{1/2}$

$$\bar{D}_{t \leftarrow s} = S_{t \leftarrow s} \int A_s \exp-(\lambda_{phys} + \lambda_{biol})t\, dt$$

MIRD:
→ S factors
→ $t_{1/2}$

PET:
absolute activity in source organ
→ (Bq / ml)

PET:
uptake kinetics
→ (Bq / ml / min)

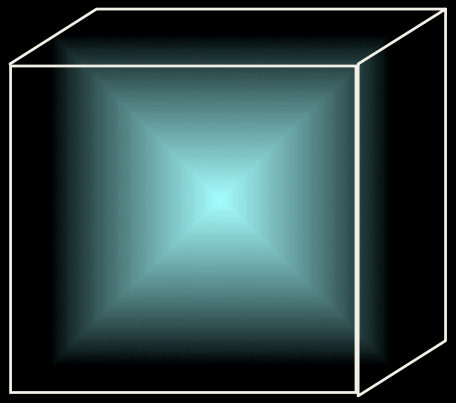
quantification of radiation doses *in vivo*

ERT

^{90}Y / ^{177}Lu / …

particle emission (α, β^-, Ae^-)

(without) γ-component

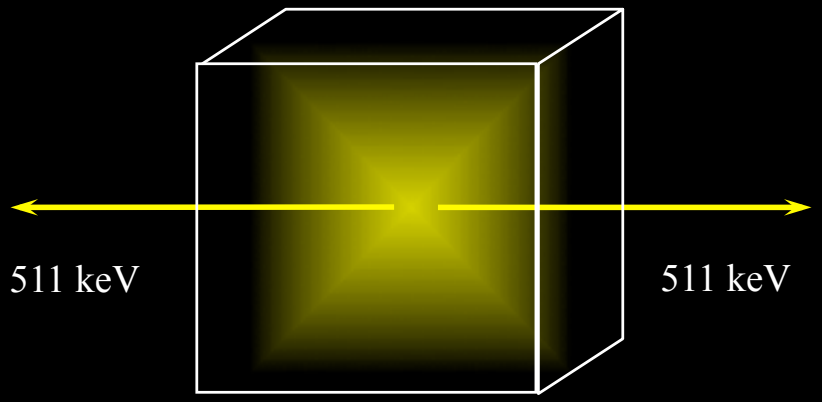


“BLACK BOX”

PET

***Me^{III}**

β^+ decay ⇨ annihilation



LOCALIZATION (2 mm)
and
QUANTIFICATION

(pre-therapeutic) determination of radiation doses: The impact of PECT / CT

WANTED:

1. Molecules = targeting vectors
2. An adequate therapeutic nuclide
3. A corresponding positron emitter

Supposed:
A promising TV is
labelled with a promising radionuclide …

What is the radiation dose
delivered to a certain person ?

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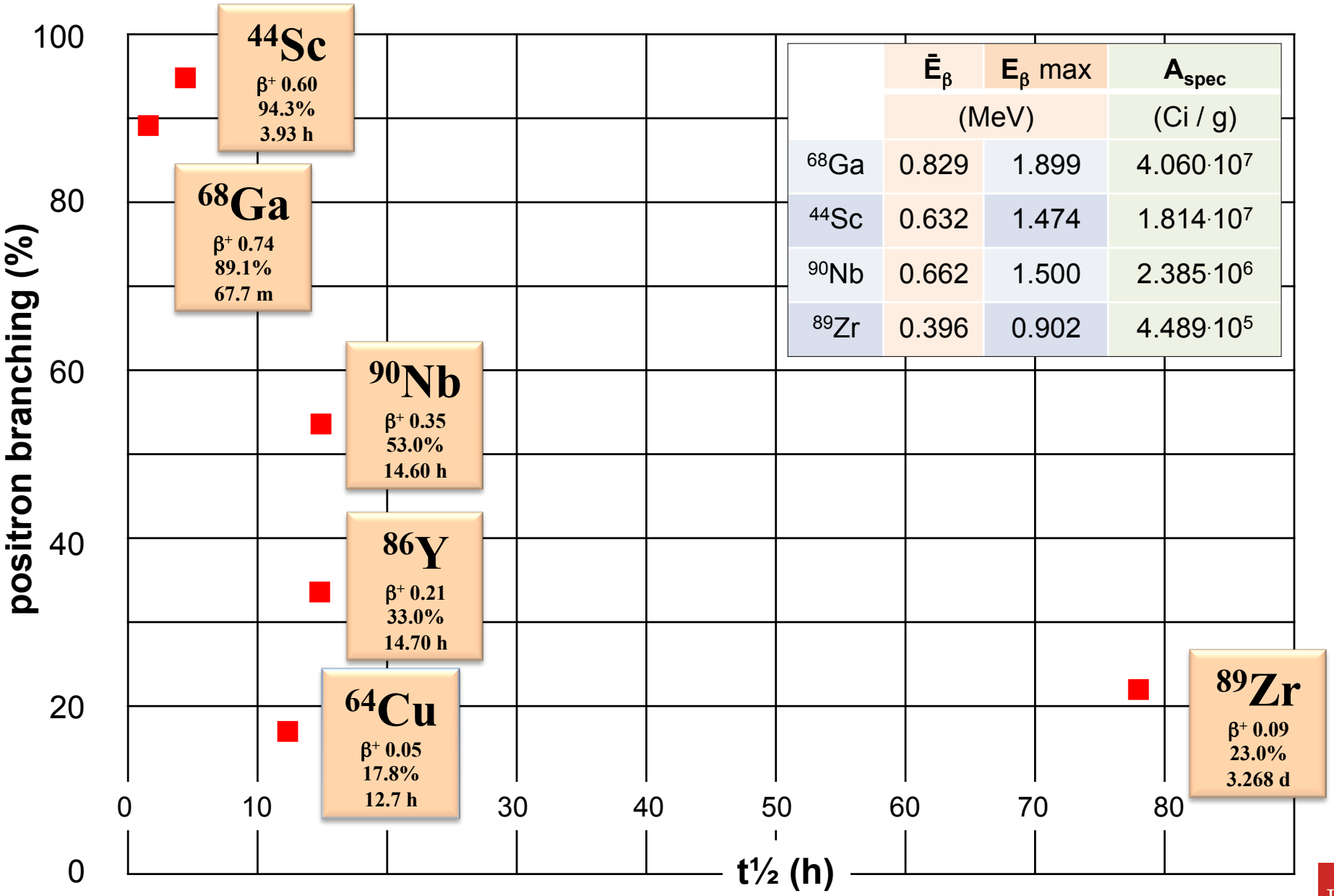
Choice of PET nuclide: t½ vs. positron branching (%)



	$\bar{E}_\beta$	E_β max	A_{spec}
	(MeV)		(Ci / g)
^{68}Ga	0.829	1.899	$4.060 \cdot 10^7$
^{44}Sc	0.632	1.474	$1.814 \cdot 10^7$
^{90}Nb	0.662	1.500	$2.385 \cdot 10^6$
^{89}Zr	0.396	0.902	$4.489 \cdot 10^5$

http://www.nndc.bnl.gov/chart

Browne E, Firestone RB. Table of Radioactive Isotopes, Shirley VS, Editor, Wiley 1986,

(pre-therapeutic) determination of radiation doses

	PRE-therapeutic organ and tumor dosimetry		Targeting vectors
	Choice of positron emitter: match physical half-life t½ with biological half-life of tumor targeting vector	^{68}Ga	„small“ molecules: peptides, amino acids, inorganic ligands
		^{44}Sc	
		^{90}Nb, ^{86}Y, ^{64}Cu	antibody fragments micro-bodies
		^{89}Zr, ^{124}I	monoclonal antibodies, nano-particles drug carriers
		^{68}Ga, ^{18}F PRE-TARGETING	
+	POST-therapeutic evaluation *via* PET/CT		
=	individual treatment of a patient („personalized medicine“)		

^{68}Ga
β⁺ 0.74
67.7 m

^{44}Sc
β⁺ 0.60
3.92 h

^{86}Y
β⁺ 0.21
33.0%
14.70 h

^{90}Nb
β⁺ 0.35
53.0%
14.60 h

^{89}Zr
β⁺ 0.09
23.0%
3.268 d

^{18}F
β⁺ 0.6
96.0%
110 min

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(pre-therapeutic) determination of radiation doses

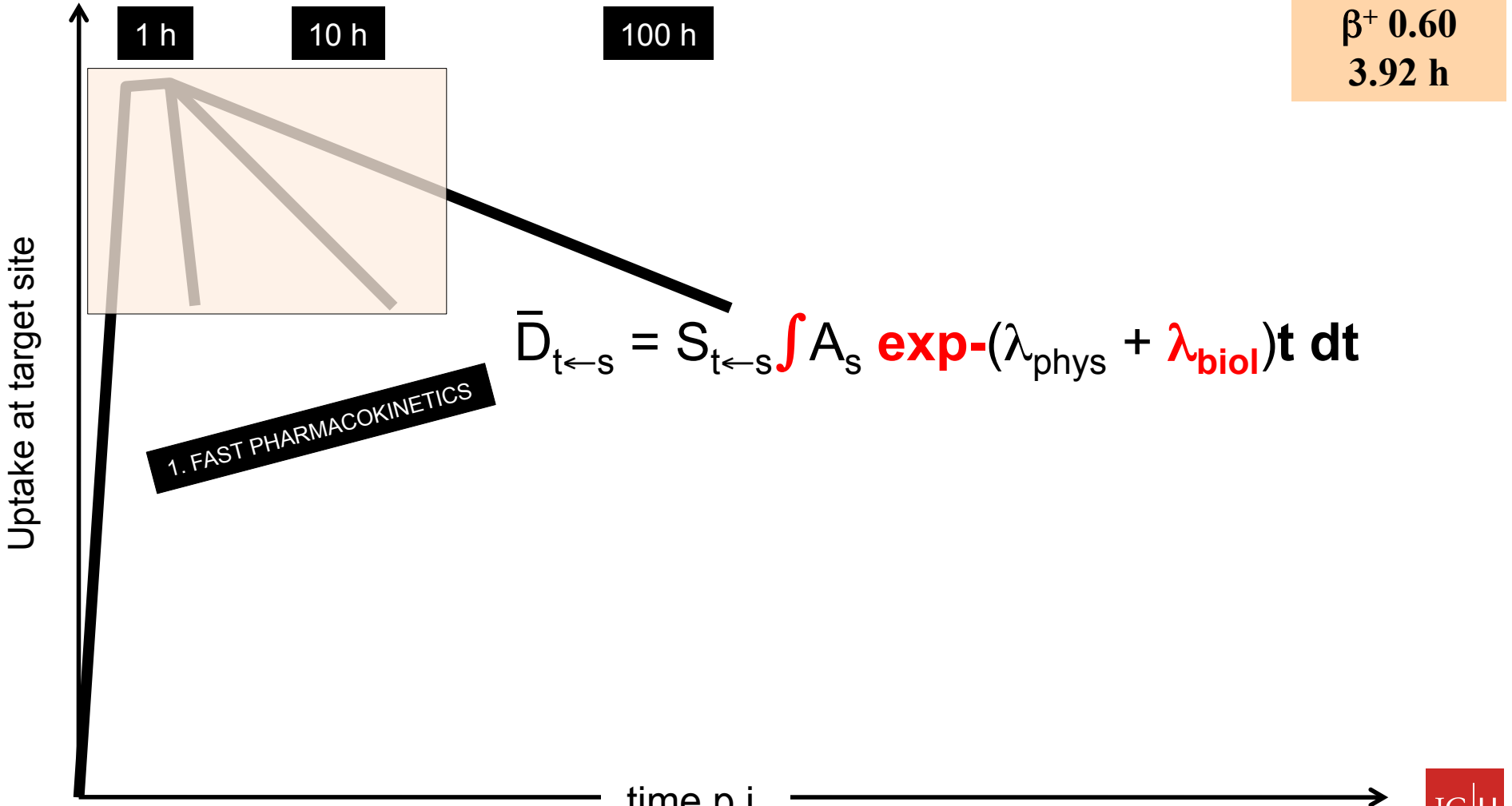
^{223}Bi	^{90}Y	^{177}Lu	^{225}Ac
α 5.87 … β⁻ 1.4 … 45.6 min	β⁻ 2.3 … . 64.1 h	β⁻ 0.6 … . 6.71 d	α 5.83 … . 10.0 d

DIAGNOSTIC $^{M}_{III}$

= THERAPEUTIC $^{M}_{III}$

^{68}Ga
β⁺ 0.74
67.7 m

^{44}Sc
β⁺ 0.60
3.92 h



$$\bar{D}_{t\leftarrow s} = S_{t\leftarrow s} \int A_s \; \mathbf{exp}^{-}(\lambda_{phys} + \lambda_{biol})t \; dt$$

(pre-therapeutic) determination of radiation doses:

The ideal situation

^{86}Y β^+ 0.21 33.0% 14.70 h	^{90}Y β^- 2.3 MeV 64.1 h	^{68}Ga β^+ 0.74 89.1% 67.7 m	^{67}Ga AE 68.1 h
^{64}Cu β^+ 0.05 17.8% 12.7 h	^{67}Cu β^- 61.9 h		

$$\bar{D}_{t \leftarrow s} = S_{t \leftarrow s} \int A_s \, \exp-(\lambda_{phys} + \lambda_{biol})t \, dt$$

PET-ICAL λ_{biol} = THERAPEUTICAL λ_{biol}

PET vs. ERT: homologous couplings

ERT		PET	
^{89}Sr	(50.4 d)	^{83}Sr	(1.35 d, 24% β^+)
^{90}Y	(3.19 d)	^{86}Y	(14.7 h, 33% β^+)
^{153}Sm	(1.95 d)	^{142}Sm	(72 min, 5.7% β^+)
		^{142}Pm	(0.6 min, 78% β^+)
^{131}I	(8.02 d)	^{124}I	(4.18 d, 63% β^+)
		^{120}I	(1.35 h, 46% β^+)

Individual Radiation Dosimetry: The Concept of THERANOSTICS:

Biological target: Bone metastases

how to quantify organ radiation doses of ^{90}Y-radiotherapeutics *in vivo* using ^{86}Y-surrogates ?

1. „bone affine“ radiometals (Ca-analogues)

[^{90}Y]citrate vs. [^{90}Y]EDTMP

≈ 80% of patients with prostatic carcinoma develop metastatic bone disease

≈ 50% of them experience bone pain

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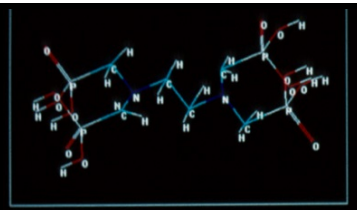
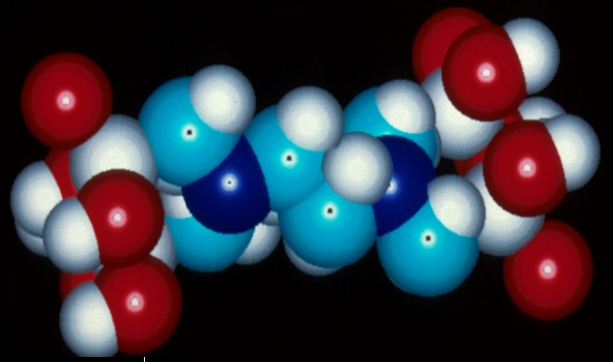
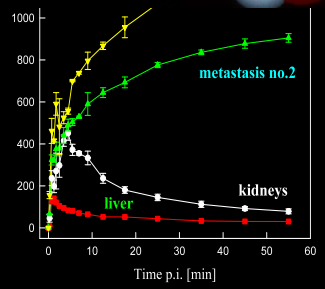
[^{86}Y]EDTMP-PET: imaging of bone metastases

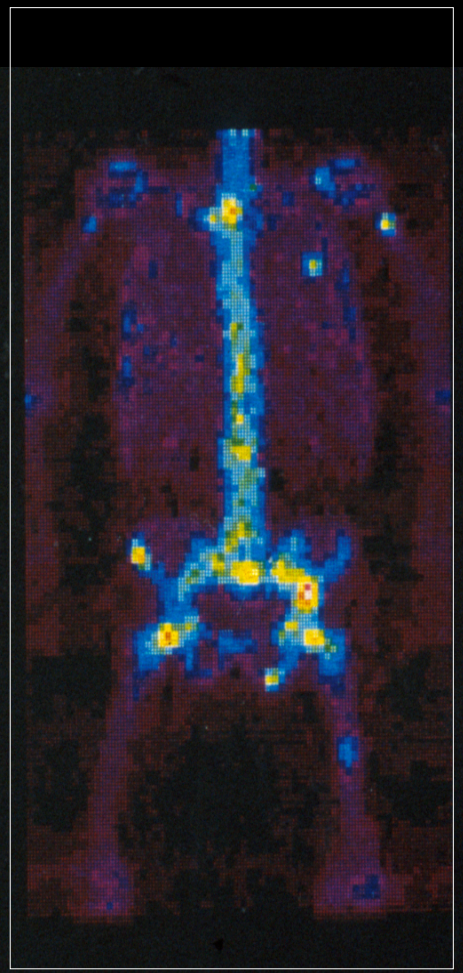


EDTMP

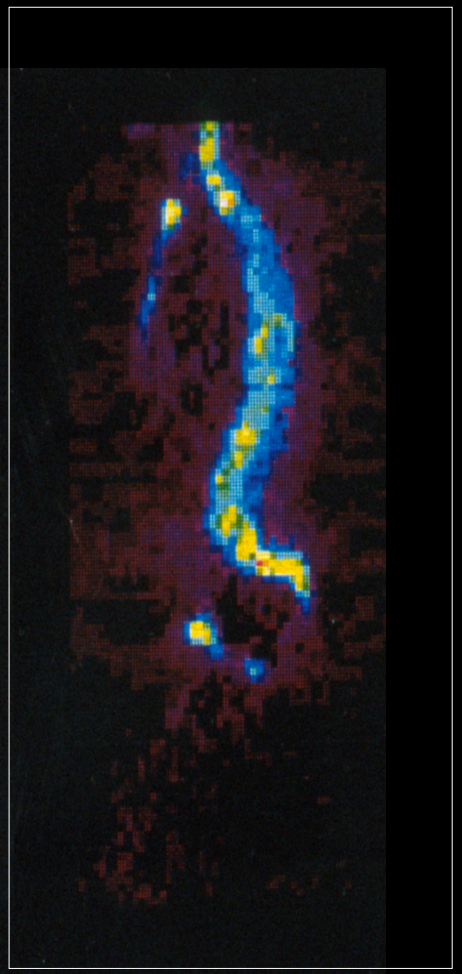
(Ethylenediamine tetramethylene phosphonic acid)





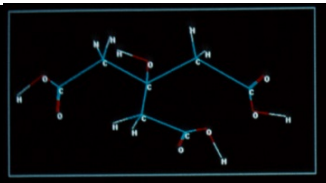


anterior view



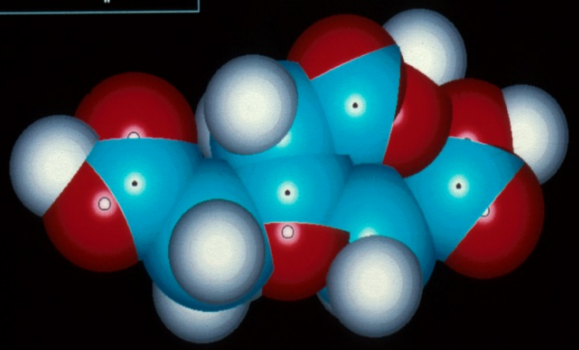
median section

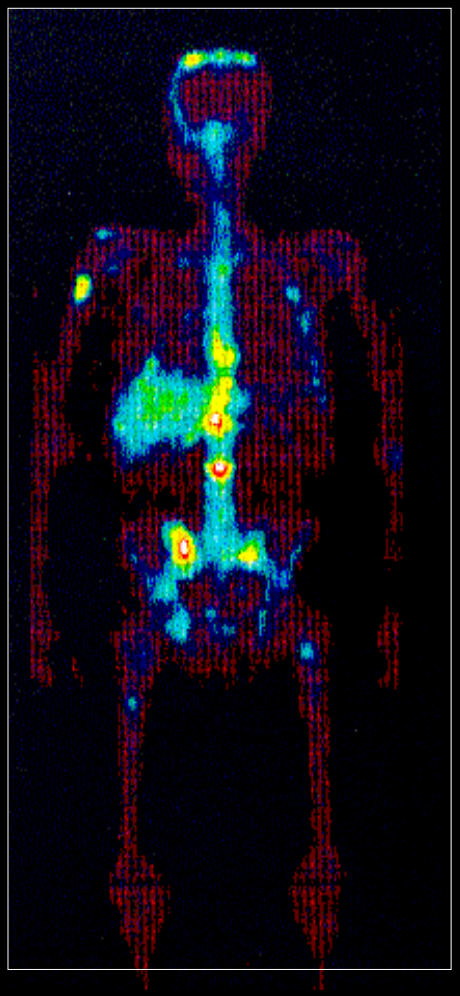
[^{86}Y]Citrate-PET: imaging of bone metastases

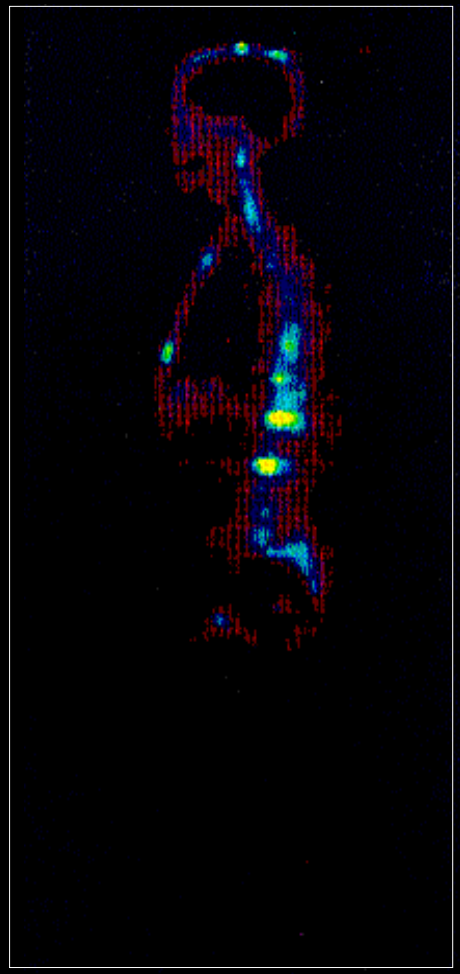


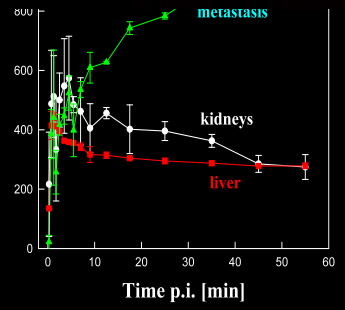
CITRATE

(2-Hydroxipropane tricarbonic acid)





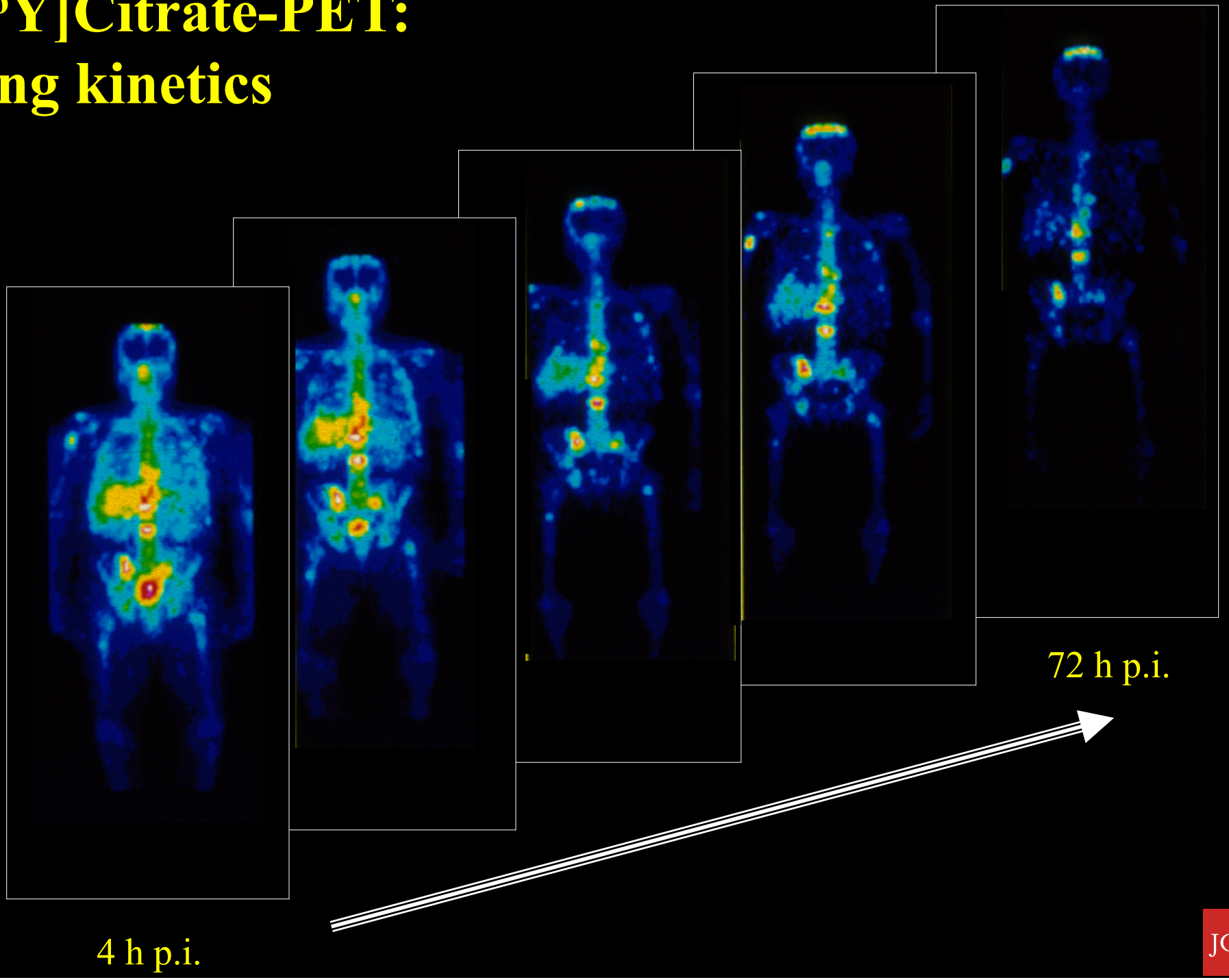




anterior view (6 mm)

median section

[^{86}Y]Citrate-PET: long kinetics



[^{90}Y]Citrate vs. [^{90}Y]EDTMP
mean radiation doses (n = 5)
[mGy / MBq ^{90}Y injected]

^{90}Y complex	bone metastases (per cc)	red bone marrow (total)	liver (total)
Citrate	25.5 $^{10.6}$	2.5 $^{0.4}$	1.8 $^{0.3}$
EDTMP	17.8 $^{1.7}$	1.8 $^{0.6}$	-

Individual Radiation Dosimetry: The Concept of THERANOSTICS:

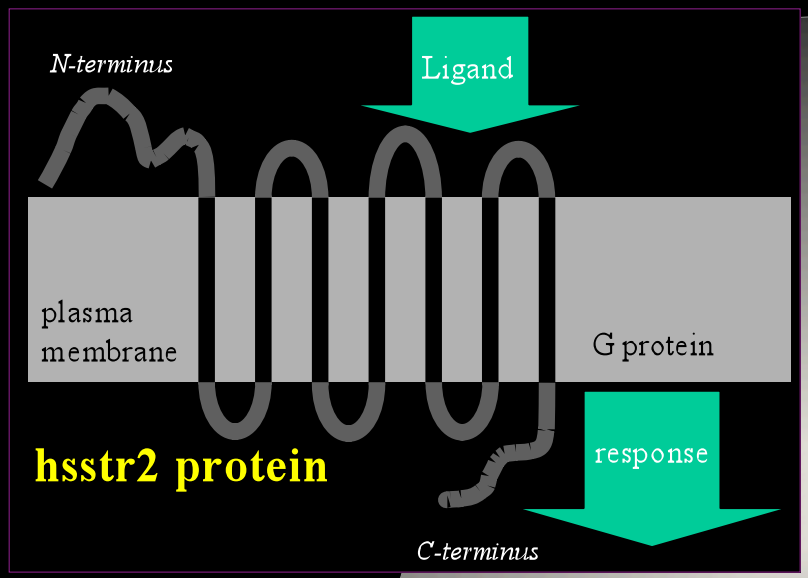
Biological target: Neuroendocrine tumours

Somatostatin receptor expressing tumors

Somatostatin receptor

octreotide (SMS 201-995)
human SRIF-receptor subtypes

^{68}Ga-DOTATOC



hSSTR1 > 1000 nmol / L
hSSTR2 0.32 nmol / L
hSSTR3 31.6 nmol / L
hSSTR4 > 1000 nmol / L
hSSTR5 7.3 nmol / L

Neuroendocrine tumors
Pituitary adenomas / islet cell tumors / carcinoids / MTC / SCLC

Tumors of the nervous system
Astrocytoma / meningioma / neuroblastoma

Renal cell carcinoma
Malignant lymphoma
Breast cancer

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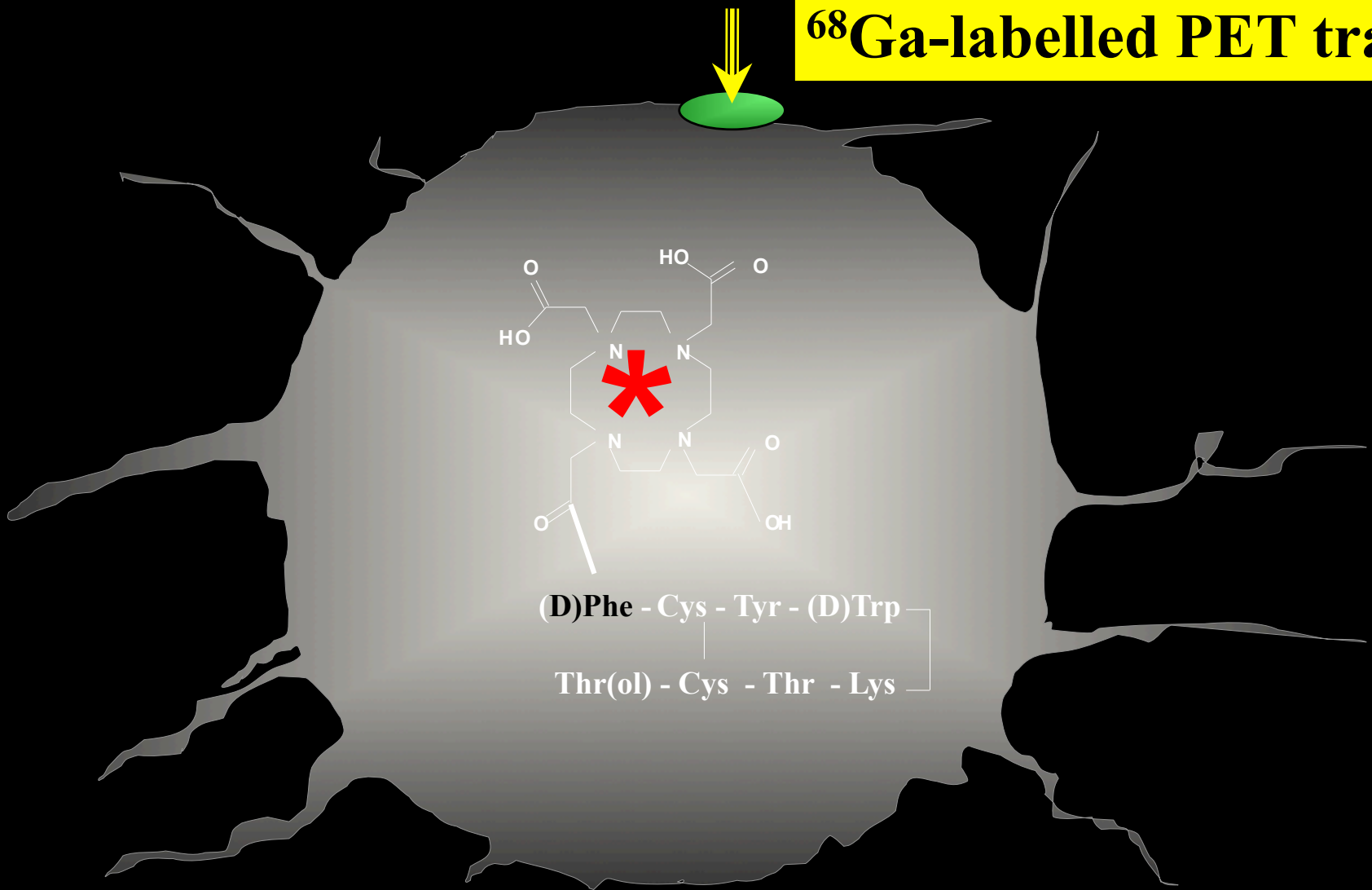
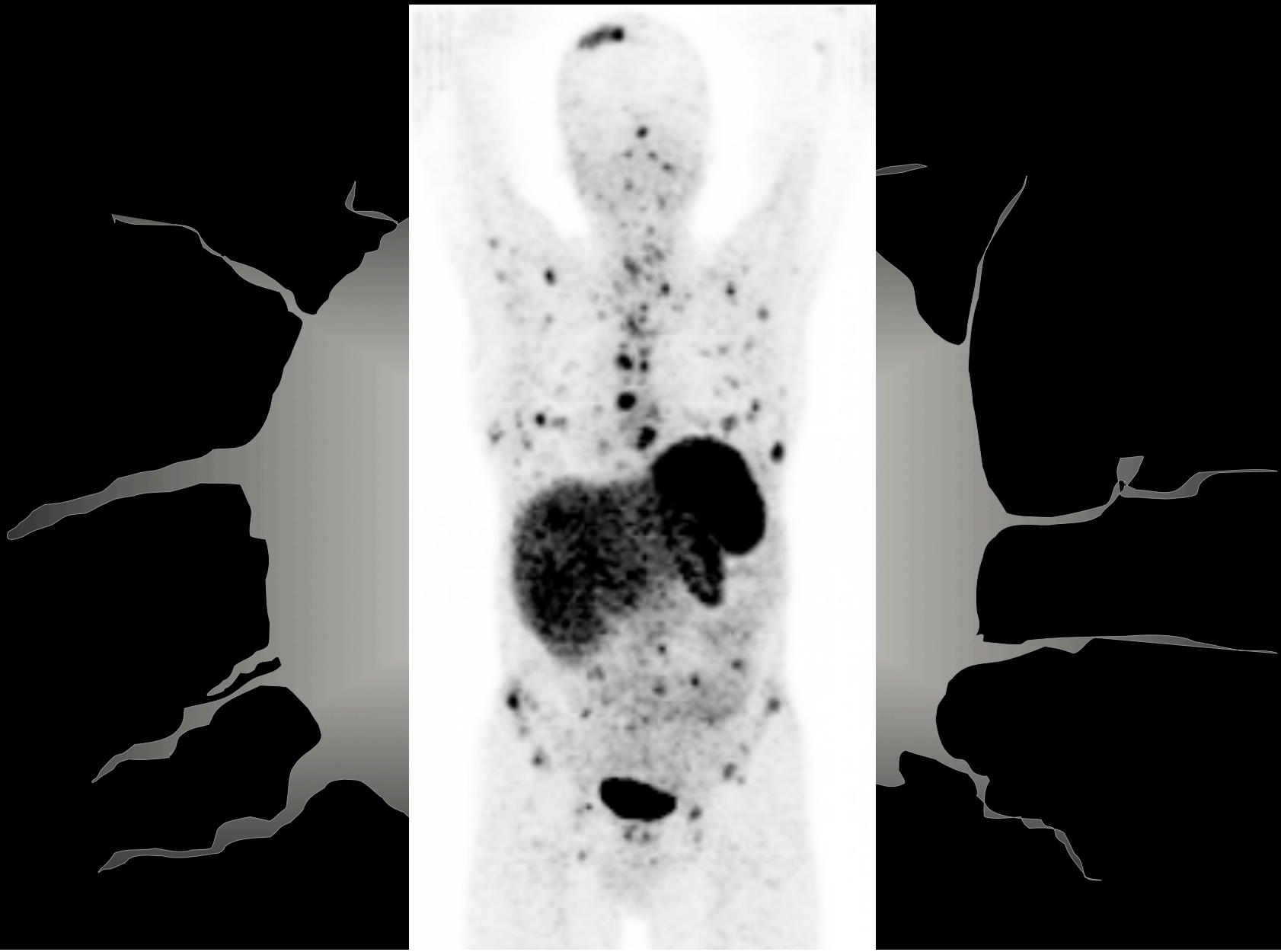
Somatostatin: tumor membrane receptors
receptor ligand: octreotide analogues

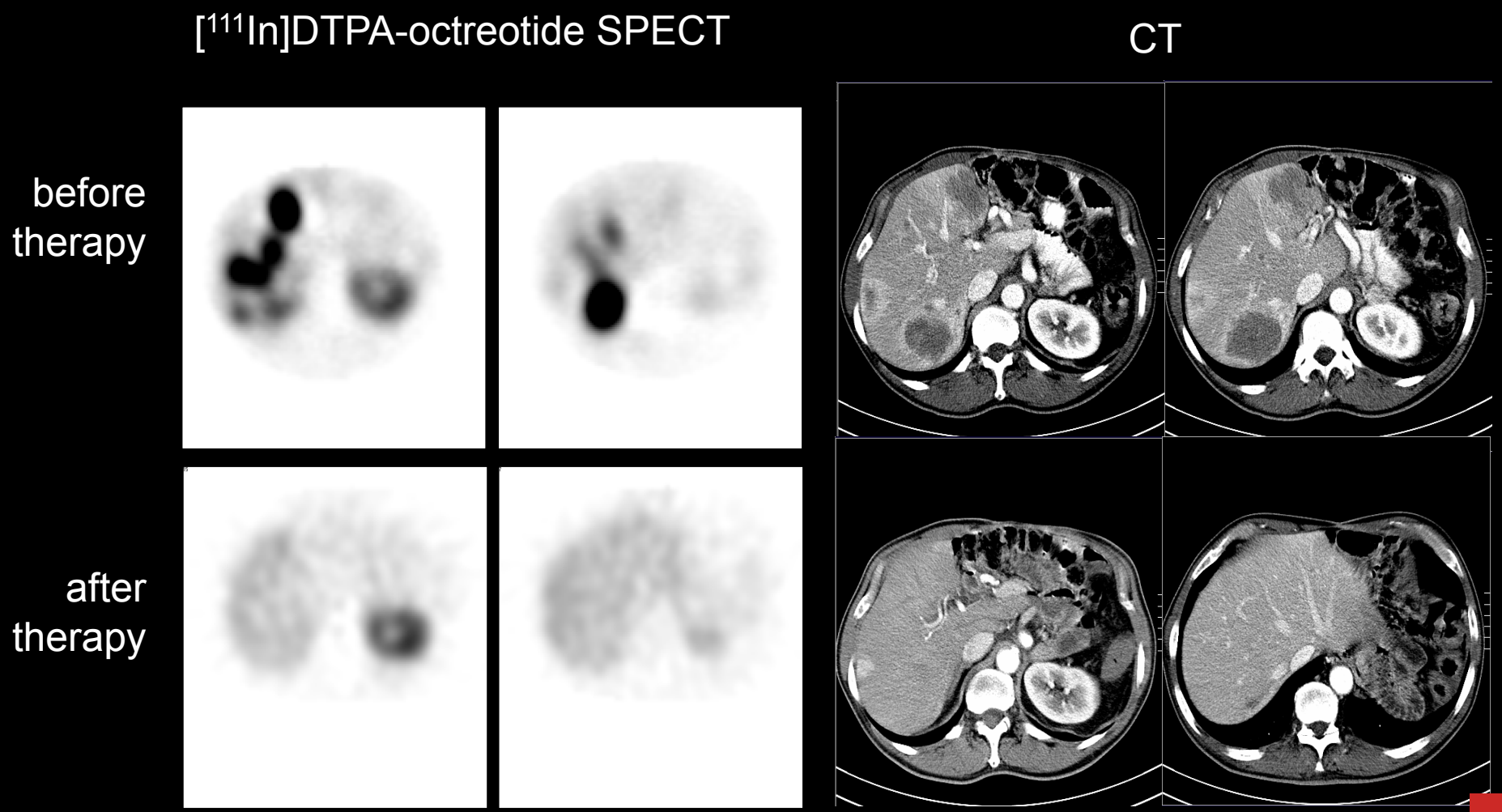
^{68}Ga-labelled PET tracer



Somatostatin: tumor membrane receptors
receptor ligand: octreotide analogues



Peptide receptor radionuclide therapy
with the somatostatin analogue
[^{90}Y]DOTATOC in neuroendocrine tumours



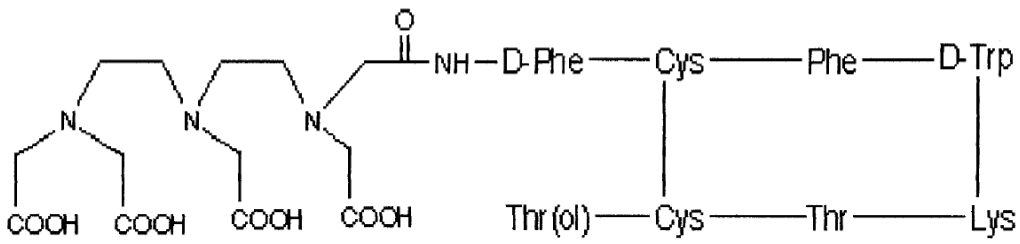
[^{86}Y]DOTA-DPhe^{1}-Tyr^{3}-octreotide in patients

[^{90}Y]**DOTATOC** used for treatment of patients with neuroendocrine tumors
- usually with standard doses -

an accurate pretherapeutic dosimetry would allow
for an individual planning of the optimal therapeutic strategy

compare the biodistribution and resulting dosimetric calculations
for therapeutical exposure of normal tissue and tumor masses based on

- **[^{86}Y]DOTATOC-PET**
- **[^{111}In]DTPA-octreotide SPECT**



OctreoScan

Departments of Nuclear Medicine
Endocrinology and Metabolism
Institute of Nuclear Chemistry

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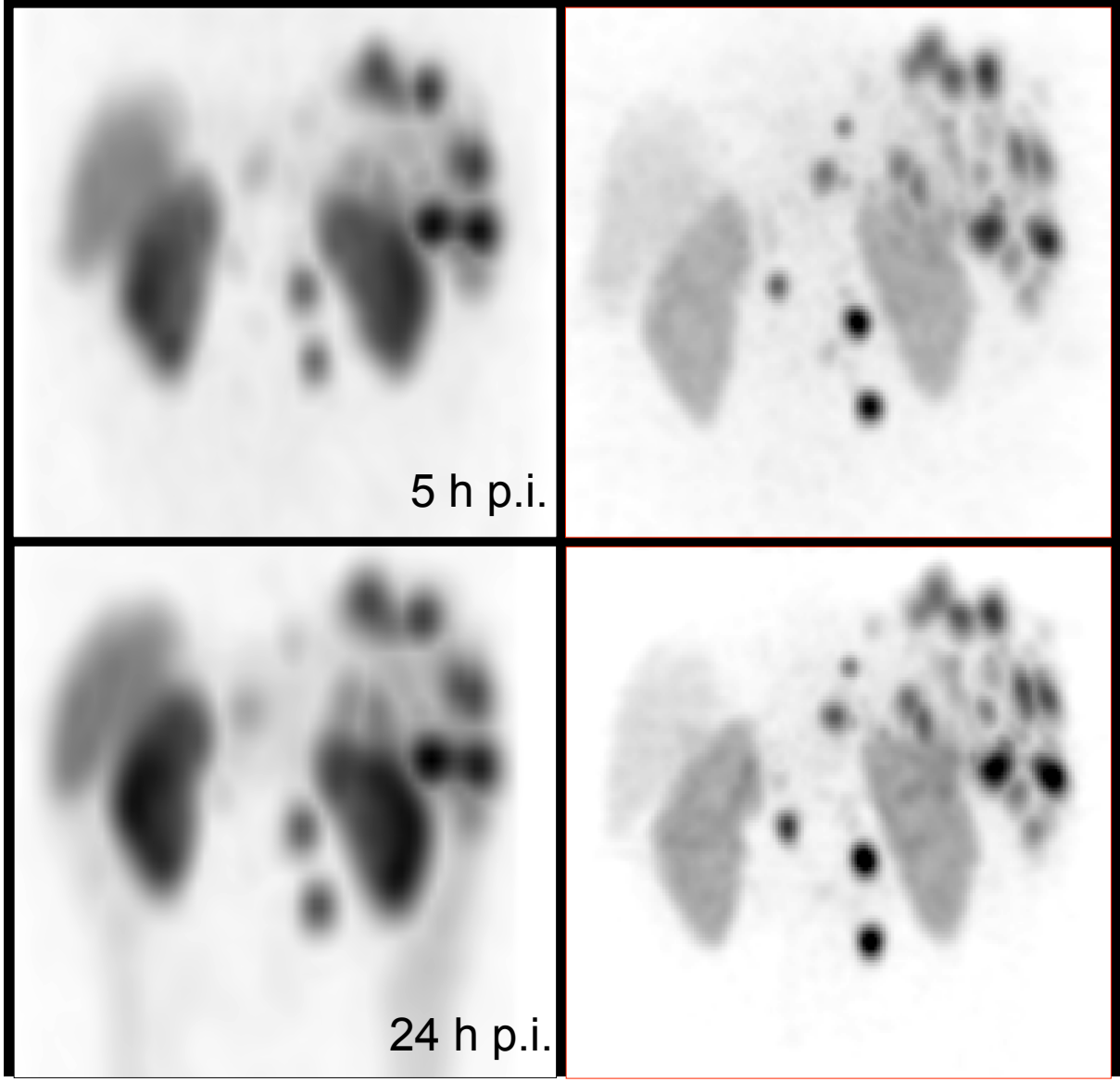
[^{86}Y]DOTA-DPhe^{1}-Tyr^{3}-octreotide in patients

[^{111}In]DTPA-octreotide SPECT

[^{86}Y]DOTA-DPhe^{1}-Tyr^{3}-octreotide PET

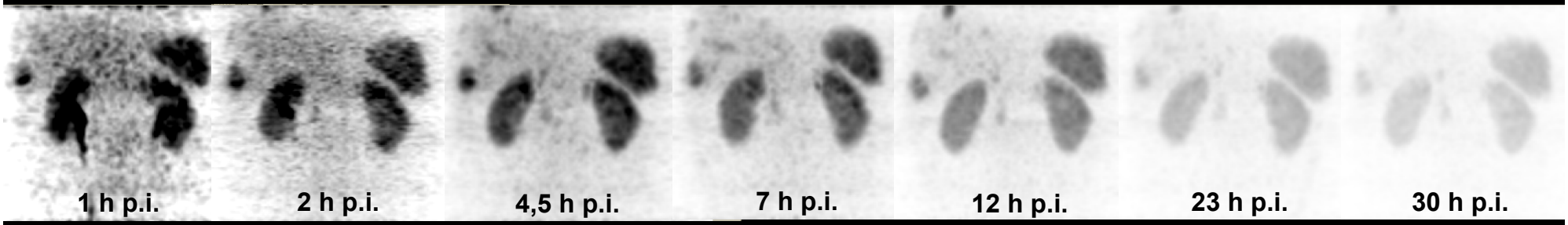


Scintigraphic abdominal images acquired 24 h after injection affected by carcinoid with extensive hepatic and paraaortal metastases.

Patients:

- 3 patients with metastases of carcinoid tumor (histologically confirmed)
- No therapy with unlabeled somatostatin > 4 weeks
- Age: 46 – 67 years, male
- All were candidates for a possible ^{90}Y-DOTATOC therapy

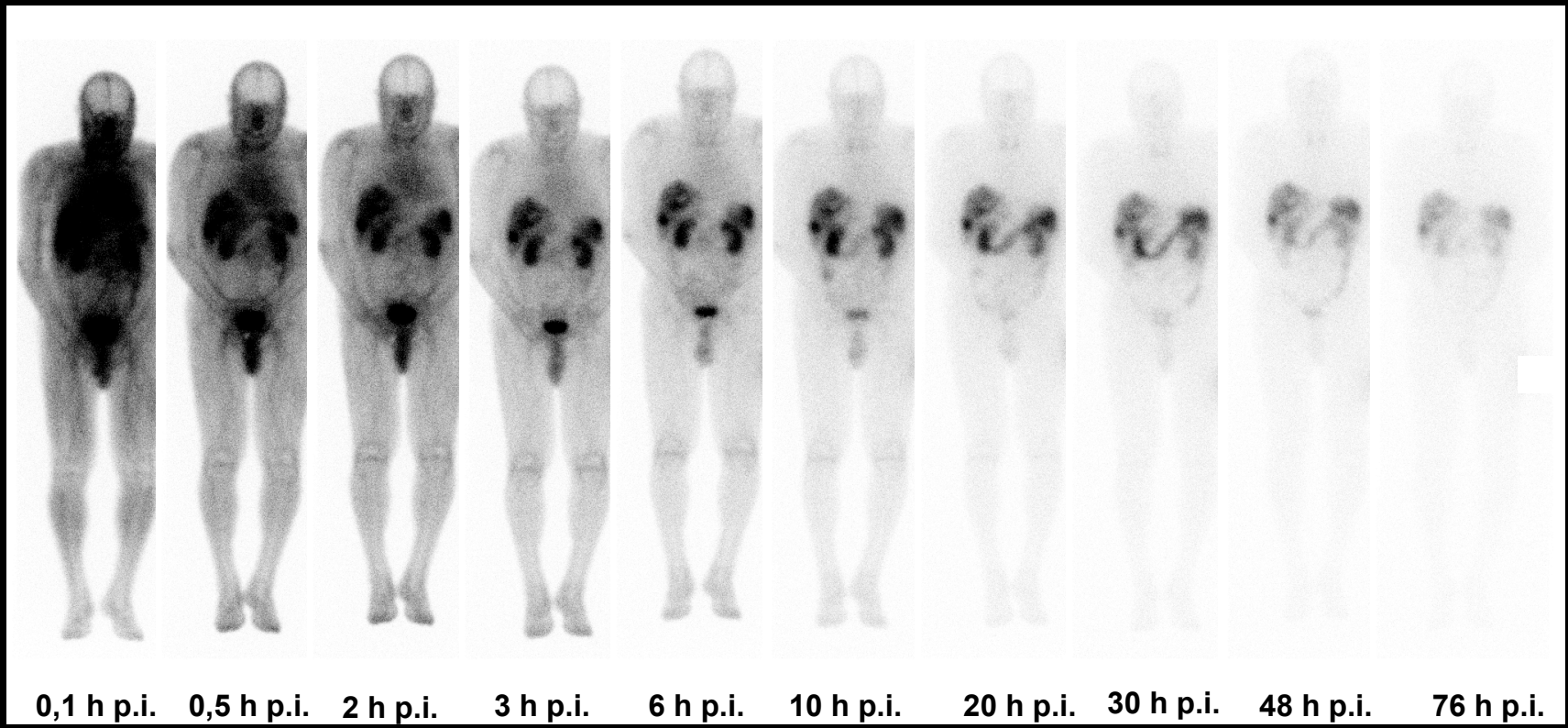
^{86}Y-DOTATOC-PET



(max. pixel projection)

^{111}In-DTPA-octreotide-SPECT

Patient 3

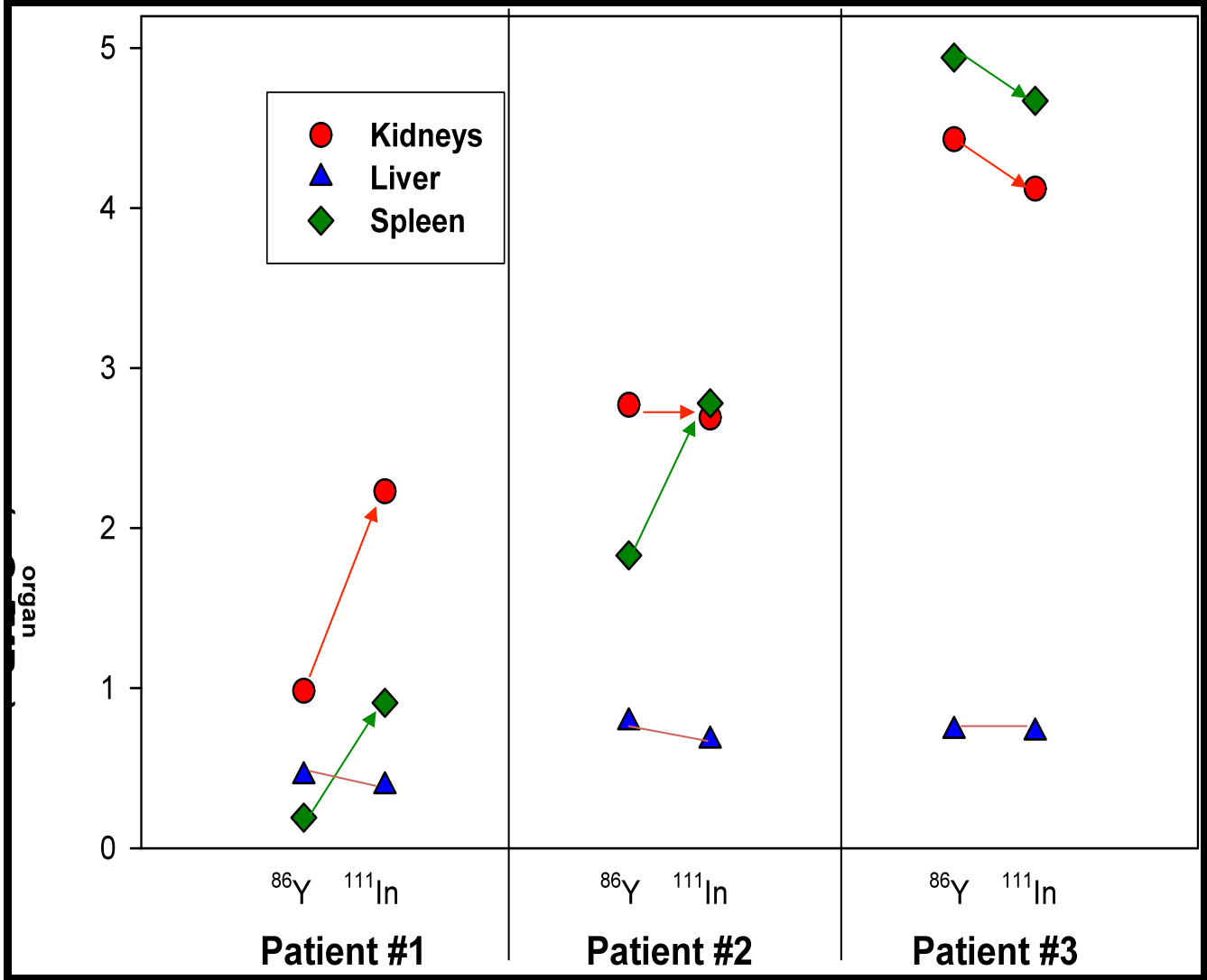


estimated organ doses for ^{90}Y-DOTATOC

Source/Target organs	t_{organ}(h)	D_{organ}(mGy/MBq)	t_{organ}(h)	D_{organ}(mGy/MBq)
	based on ^{111}In-DTPA-octreotide		based on ^{86}Y-DOTATOC	
Intestine wall	0.47±0.1	0.62±0.43	-	0.05±0.002
Kidneys	1.67±0.45	3.01±0.81	1.51±0.78	2.73±1.41
Liver	2.11±0.53	0.59±0.15	2.33±0.53	0.66±0.15
Other tissue	-	0.04±0.01	-	0.05±0.002
Red marrow	0.04±0.01	0.04±0.01	0.04±0.01	0.05±0.002
Spleen	0.95±0.52	2.79±1.54	0.79±0.67	2.32±1.97
Urinary bladder wall	0.87±0.004	0.76±0.5	0.78±0.17	1.03±0.23
Remainder of the body	5.39±1.05	-	6.36±0.21	-
Total body	-	0.09±0.01	-	0.08±0.01
Effective Dose (mSv/MBq)		0.35±0.17		0.22±0.07

Estimated organ doses for [^{90}Y]DOTATOC therapy

(based on [^{86}Y]DOTATOC-PET)



- Serum kinetics and urinary excretion:
  no relevant differences.

- Dose estimation for organs:
  differences of 10.5 – 20.1%
  depending on the tracer.

- Large across subject variability in the kinetics of normal tissue
- Residence times
- liver: 1.59 – 2.79 h
- spleen: 0.07 – 1.68 h
- kidneys: 0.55 – 2.46 h

estimated organ doses for kidneys, liver, spleen: comparable for both approaches

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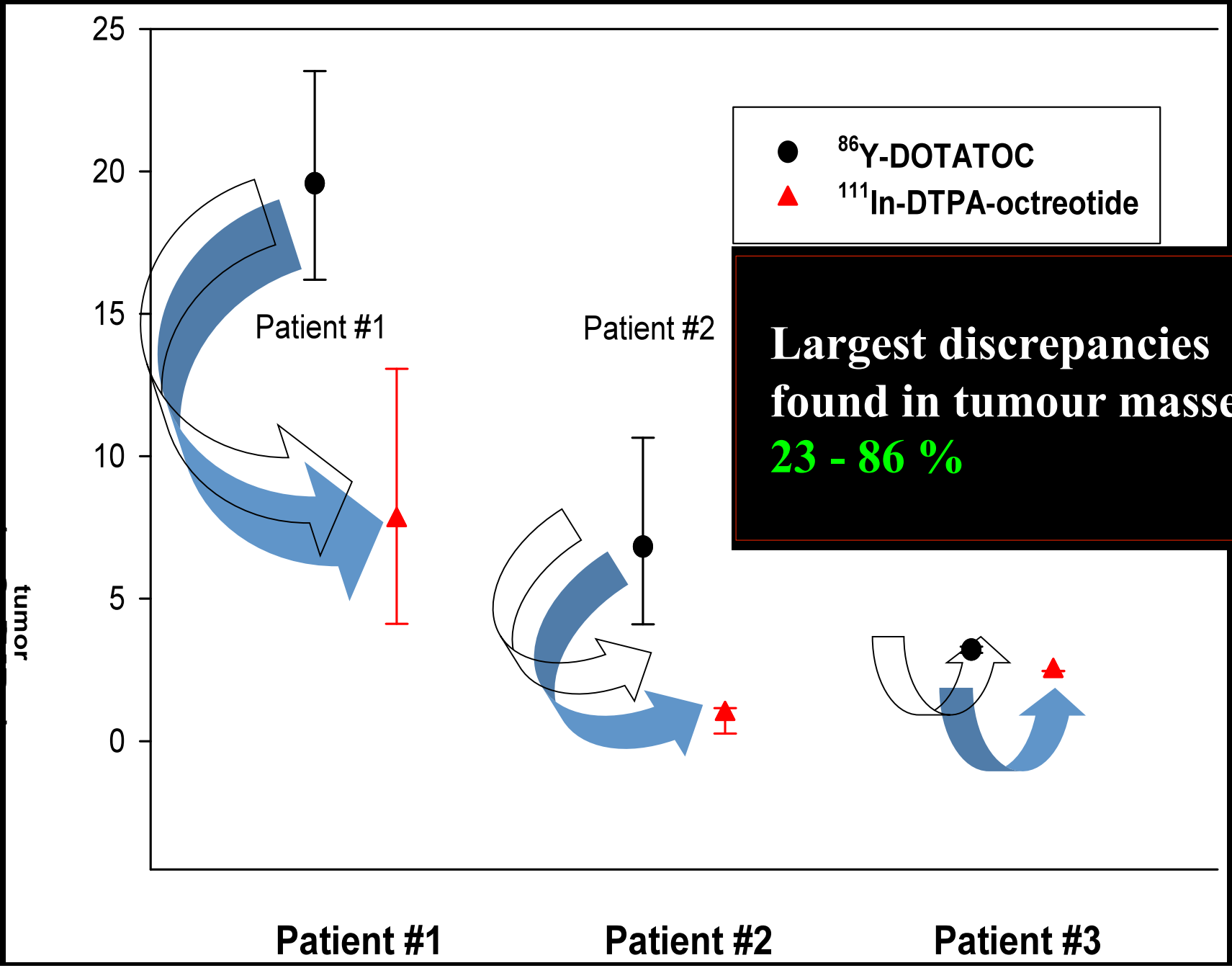
Estimated tumour doses for [^{90}Y]DOTATOC therapy



Individual Radiation Dosimetry: The Concept of THERANOSTICS:

Biological target: Neuroendocrine tumours

(pre-therapeutic) determination of radiation doses:

The non-ideal situation

^{68}Ga	^{44}Sc	^{177}Lu	^{90}Y
β^+ 0.74 89.1% 67.7 m	β^+ 0.60 94.3% 3.93 h	β^- 6.71 d	β^- 2.3 MeV 64.1 h

(pre-therapeutic) determination of radiation doses:

The non-ideal situation and a solution ...

^{68}Ga	^{44}Sc	^{177}Lu	^{90}Y
β^+ 0.74	β^+ 0.60	β^-	β^- 2.3 MeV
89.1%	94.3%	6.71 d	64.1 h
67.7 m	3.93 h		

$$\bar{D}_{THERAPEUTICAL} = \kappa \, S \, \bar{D}_{PET\text{-}ICAL}$$

κ
CORRECT
FOR DEVIATIONS
IN PHARMACOLOGY

$$\bar{D}_{t \leftarrow s} = S_{t \leftarrow s} \int A_s \exp-(\lambda_{phys} + \lambda_{biol})t \, dt$$

MIRD:
→ S factors
→ t½

PET:
absolute activity in source organ
→ (Bq / ml)

PET:
uptake kinetics
→ (Bq / ml / min)

^{68}Ga-BFC+targeting vector

DIAGNOSTIC M^{III}

= THERAPEUTIC M^{III}

^{68}Ga

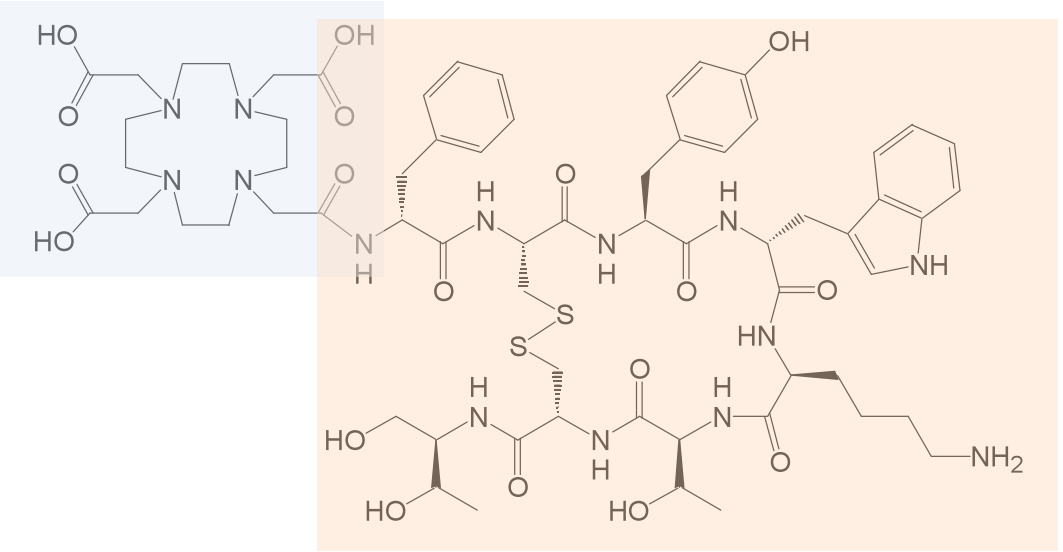
β^+ 0.74

67.7 m

^{44}Sc

β^+ 0.60

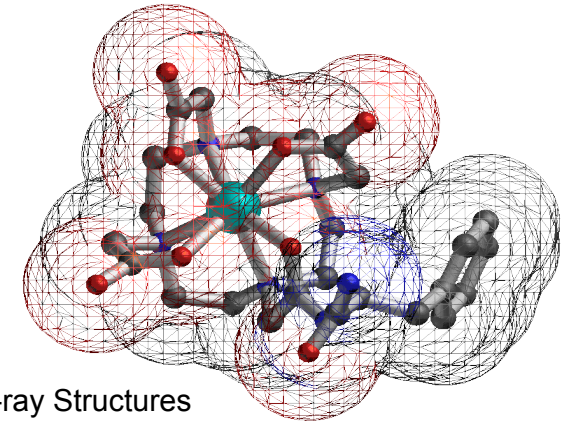
3.92 h



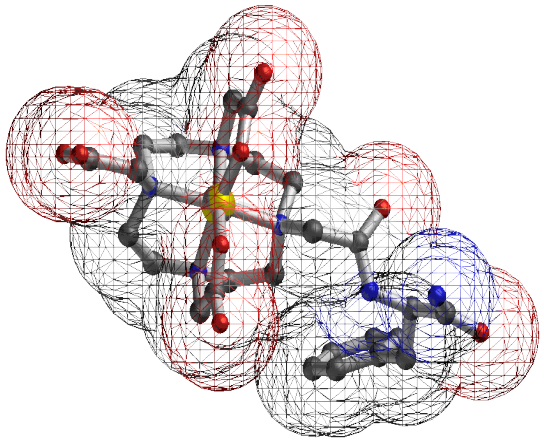
Me(III)-DOTA-Tyr^3-octreotides

^{68}Ga
β^+ 0.74
67.7 m

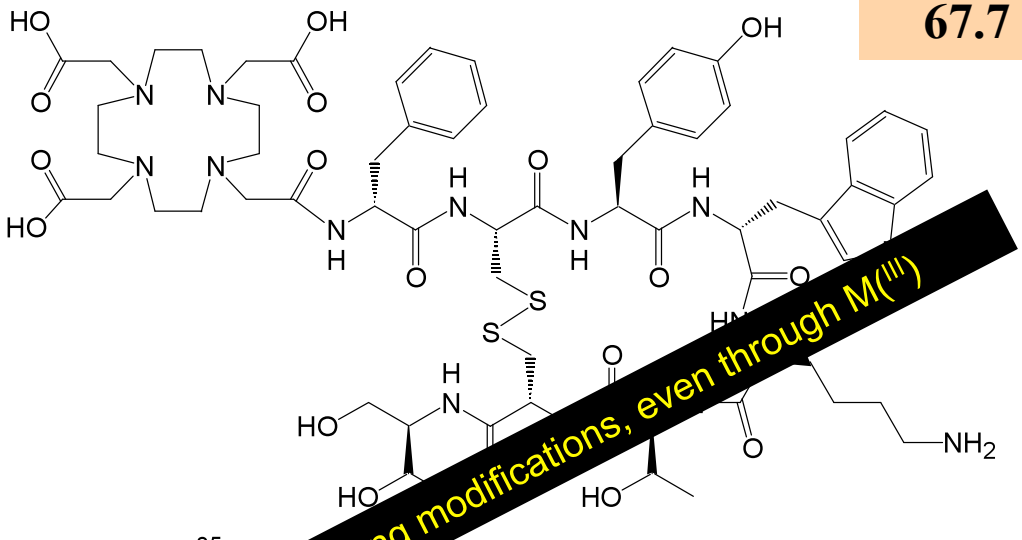
^{111}In: SPECT
^{90}Y, ^{177}Lu: ERT



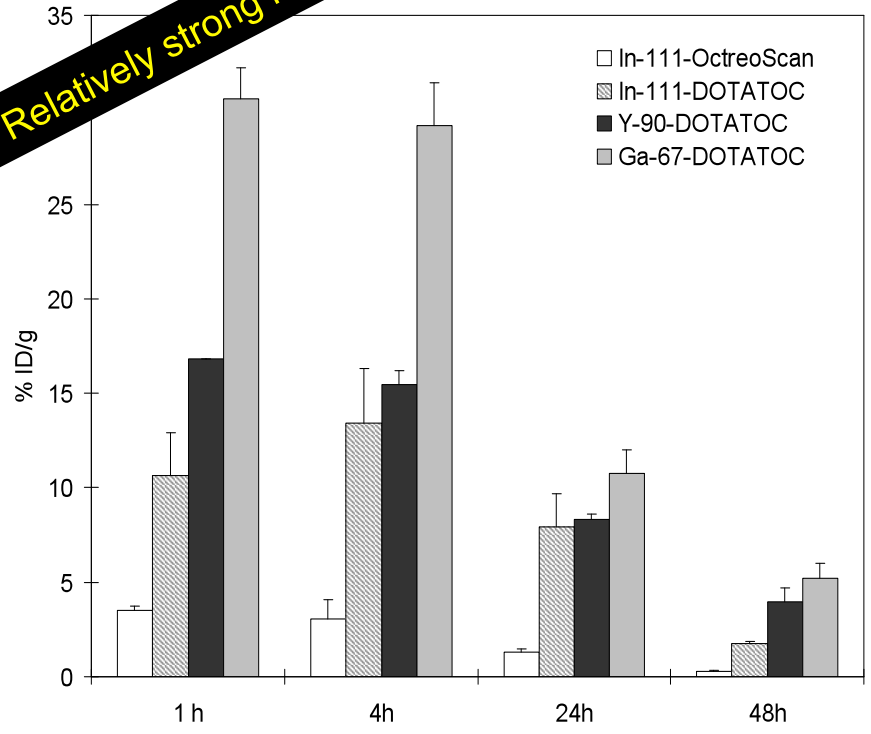
X-ray Structures
Y-DOTA-D-PheNH$_2$ distorted square antiprismatic geometry
Ga-DOTA-D-PheNH$_2$ *cis*-pseudooctahedral geometry



A. Heppeler, H.R. Mäcke et al., Chem. Eur. J. 1999, 5, 1974-1981



Relatively strong modifications, even through M(III)



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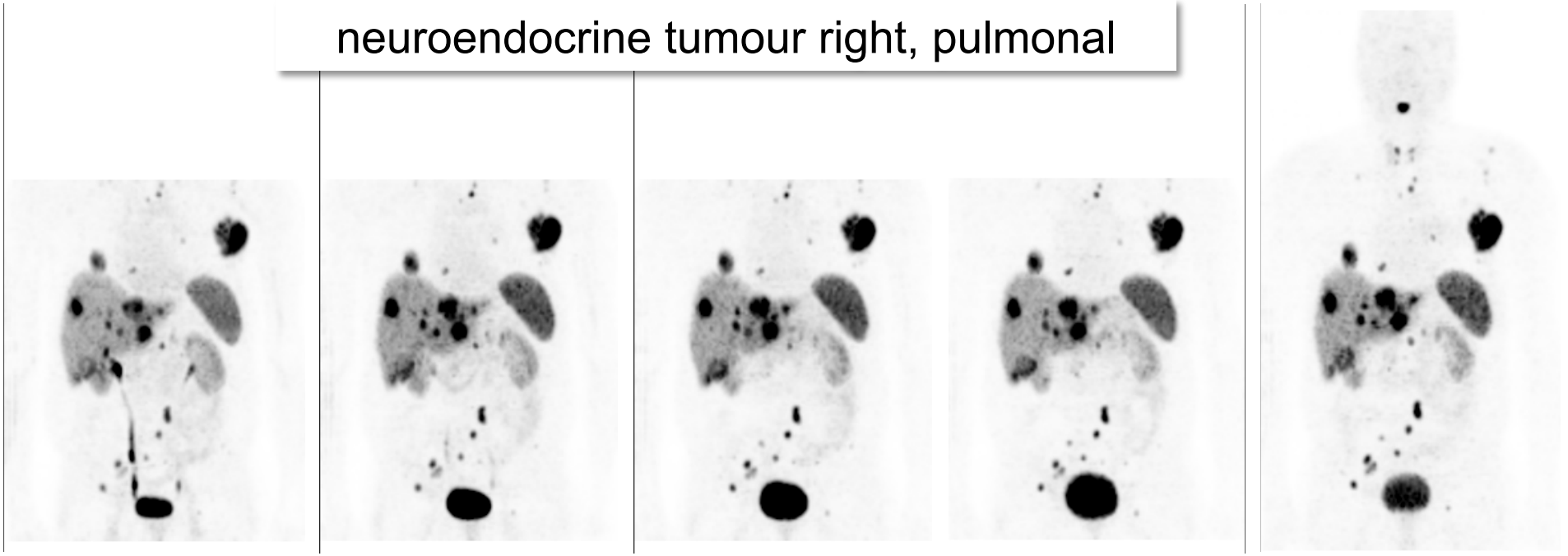
^{68}Ga-DOTA-Tyr^3-octreotides

Uptake kinetics

^{68}Ga
β^+ 0.74
67.7 m

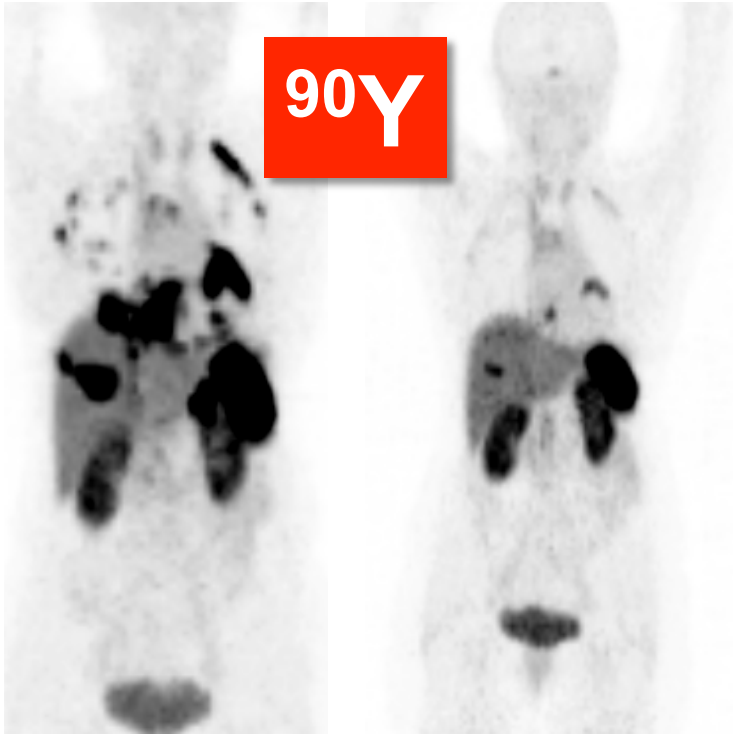


already at 20 min. p.i. all tumours localised,
at 40 min. p.i. any disturbing activity in the urea tubes

^{68}Ga-DOTA-Tyr^3-octreotides vs. PRRT

^{68}Ga
β^+ 0.74
67.7 m

^{68}Ga SUV$_{max}$ and therapy response



before PRRT-1
4 GBq Y-90
SUV 15.8

3-mo after
PRRT-1
SUV 8.4

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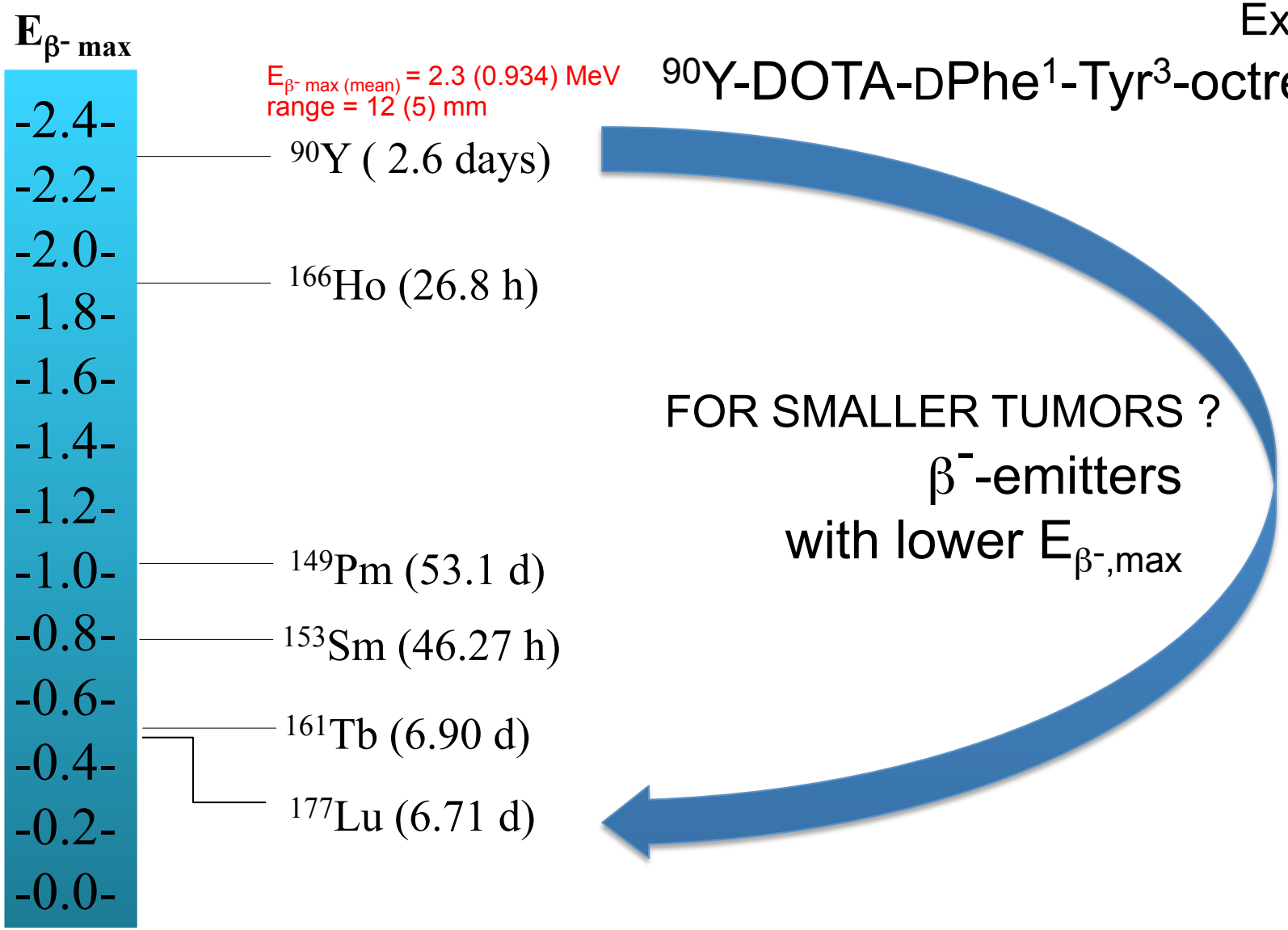
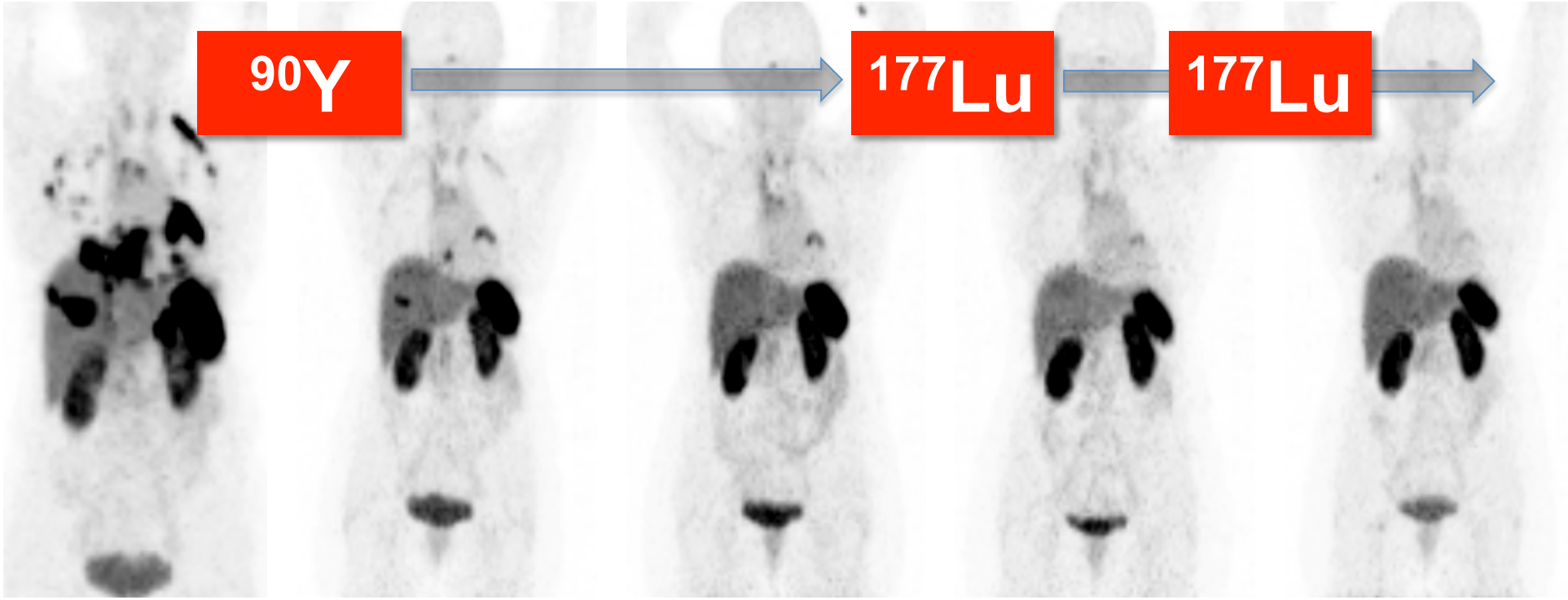
Radiolanthanides for Therapy



^{68}Ga-DOTA-Tyr^3-octreotides vs. PRRT

^{68}Ga
β^+ 0.74
67.7 m

^{68}Ga SUV$_{max}$ and therapy response



before PRRT-1	3-mo after	before PRRT-2	before PRRT-3	18-mo after
4 GBq Y-90	PRRT-1	4.5 GBq Lu-177	5.5 GBq Lu-177	PRRT-3
SUV 15.8	SUV 8.4	SUV 9.3	SUV 6.9	SUV 3.4

Persisting Complete Remission!

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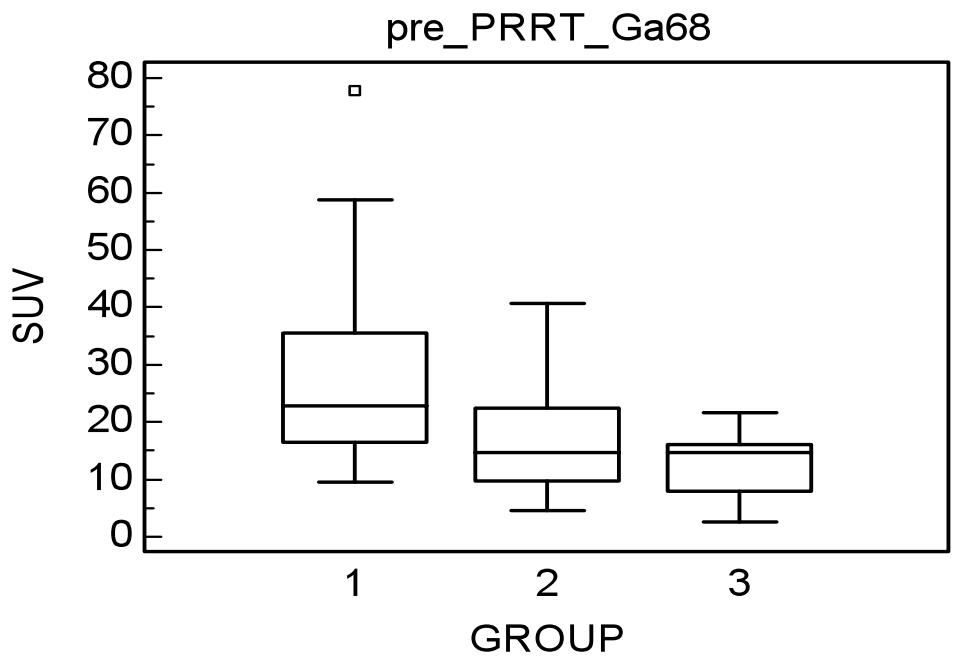
^{68}Ga-DOTA-Tyr^3-octreotides vs. PRRT

^{68}Ga
β^+ 0.74
67.7 m

^{68}Ga SUV_{max} and therapy response

			SUVmax_Ga		
			Pre_PRRT	Post_PRRT	*p*
			Mean ± SD (Median)	Mean ± SD (Median)	
Ga	PR + MR	45	27.2 ± 14.8 (22.9)*	16.4 ± 9.6 (14.1)	<0.0001
	SD	22	17.6 ± 9.9 (14.6)*	16.9 ± 9.5 (14.1)	n.s.
	PD	10	12.9 ± 5.6 (14.6) *	19.9 ± 7.5 (22.3)	0,002



1) PR + MR n=45; 27.2 ± 14.8

2) SD n=22; 17.6 ± 9.9

3) PD n=10; 12.9 ± 5.6

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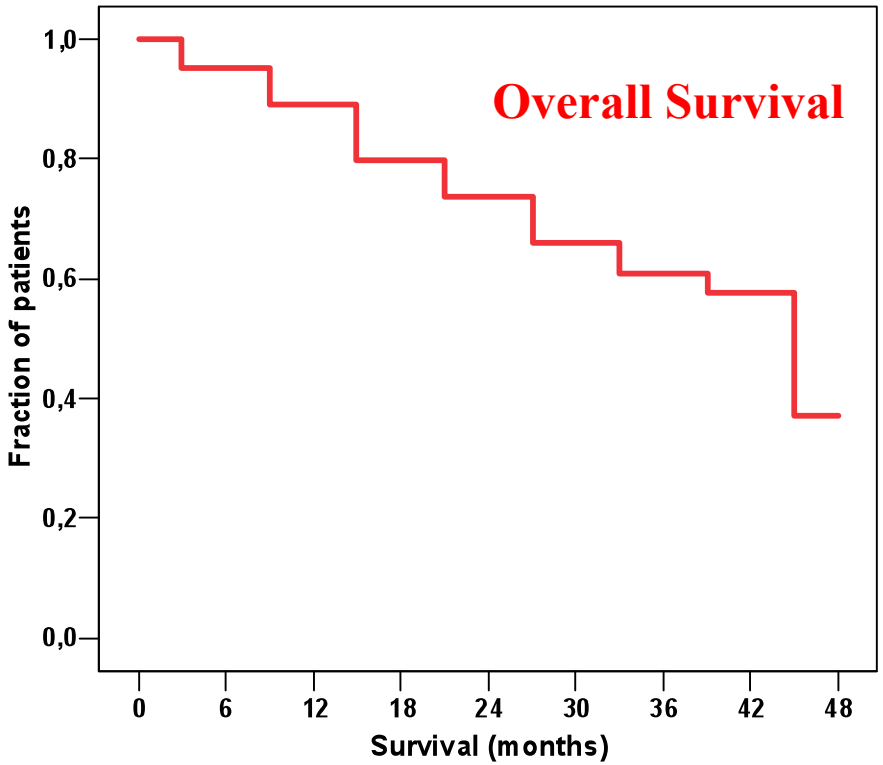
Peptide Receptor Radionuclide Therapy

Treatment With the Radiolabeled Somatostatin Analog [^{177}Lu-DOTA^{0},Tyr^{3}]Octreotate: Toxicity, Efficacy, and Survival

Dik J. Kwekkeboom, Wouter W. de Herder, Boen L. Kam, Casper H. van Eijck, Martijn van Essen, Peter P. Kooij, Richard A. Feelders, Maarten O. van Aken, and Eric P. Krenning

VOLUME 26 · NUMBER 13 · MAY 1 2008

JOURNAL OF CLINICAL ONCOLOGY

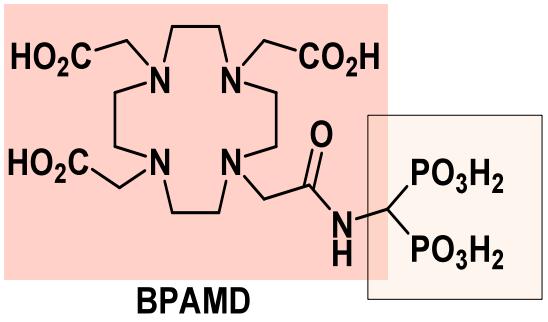


Median OS from diagnosis was 128 months.
Compared with historical controls, there was a survival benefit of 40 to 72 months.

predictors of success: uptake of Octreoscan
(and Karnofsky index)

^{68}Ga-DOTA-non-peptides

Target: bone metastases
Vector: DOTA-conjugated bisphosphonates



BPAMD

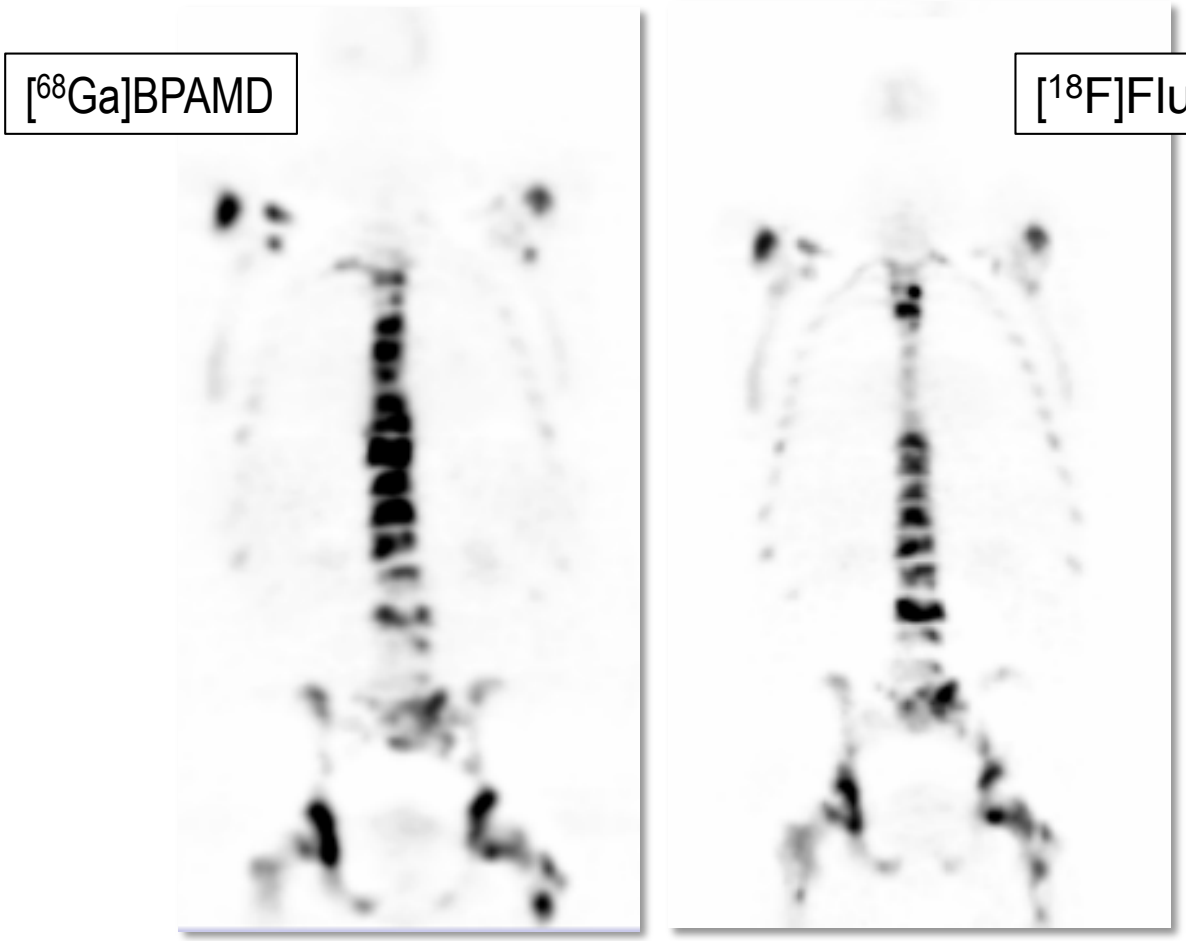
^{68}Ga
β^+ 0.74
67.7 m

^{68}Ga SUV$_{max}$ and therapy response

SUVmax values

10th thoracic vertebra
[^{68}Ga]BPAMD **77.1** / ^{18}F$^-$ 39.1
L2 vertebra
[^{68}Ga]BPAMD **62.1** / ^{18}F$^-$ 39.2

Different uptake mechanisms



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Fellner M, Baum RP, Peters JA, Lukes I, Hermann P, Prasad V, Rösch F.
PET/CT imaging of osteoblastic bone metastases with ^{68}Ga-bosphosphonates– first human study. Eur J Nucl Med Mol Imag 37/4 (2010) 834; 37:834

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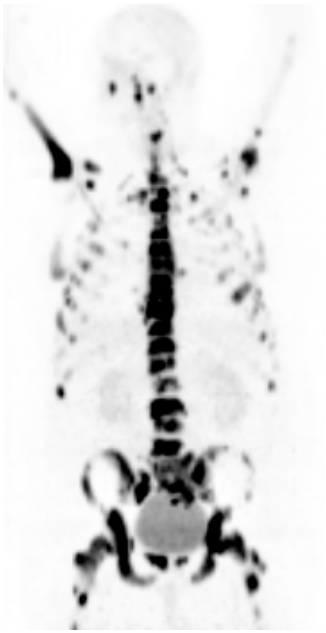
^{68}Ga-DOTA-bisphosphonates

Target: bone metastases
Vector: DOTA-conjugated bisphosphonates

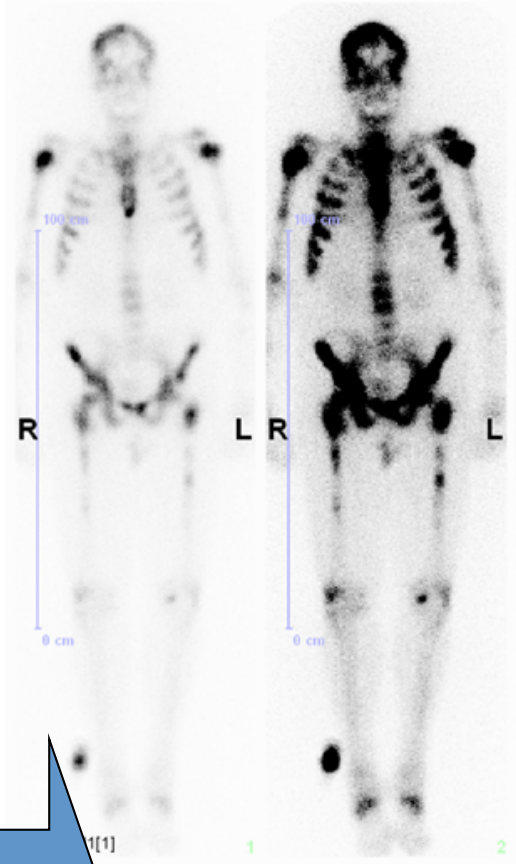
^{68}Ga SUV$_{max}$ and therapy response

^{68}Ga
β^+ 0.74
67.7 m



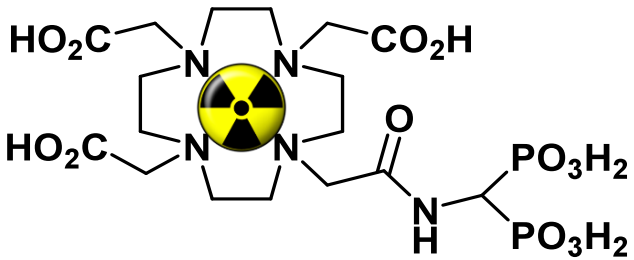
THERANOSTICS:
Same compound used for
Diagnoses
Dosimetry
Treatment

PET/CT-diagnoses (^{68}Ga)
AND
therapy (^{177}Lu)



PET/CT-diagnoses

^{68}Ga



BPAMD

^{177}Lu

therapy

Rösch F, Baum RP. Generator-based PET radiopharmaceuticals for molecular imaging of tumours: On the way to THERANOSTICS. Dalton Transitions 40/23 (2011) 6104-6111

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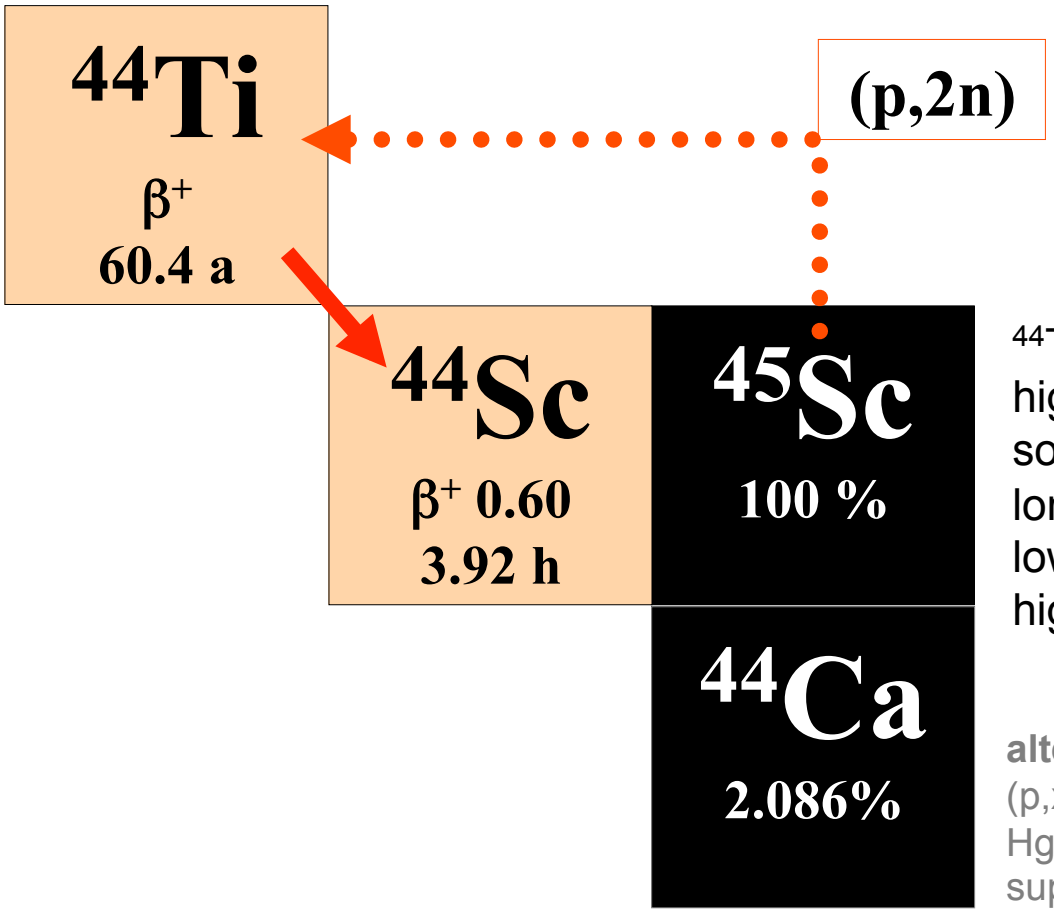
The $^{44}Ti/^{44}Sc$ generator

^{44}Sc
β^+ 0.60
3.92 h



^{44}Ti production:	(p,2n)
high p-flux	(> 0.1 mA)
sophisticated targetry	(< 10°)
long term	(> 10 d)
low yield,	
high costs	

alternatives
(p,xn) induced processes
Hg–EURISOL: 10 Bq/s
supernovea collapses

^{44}Ti/^{44}Sc generator: Post-processing

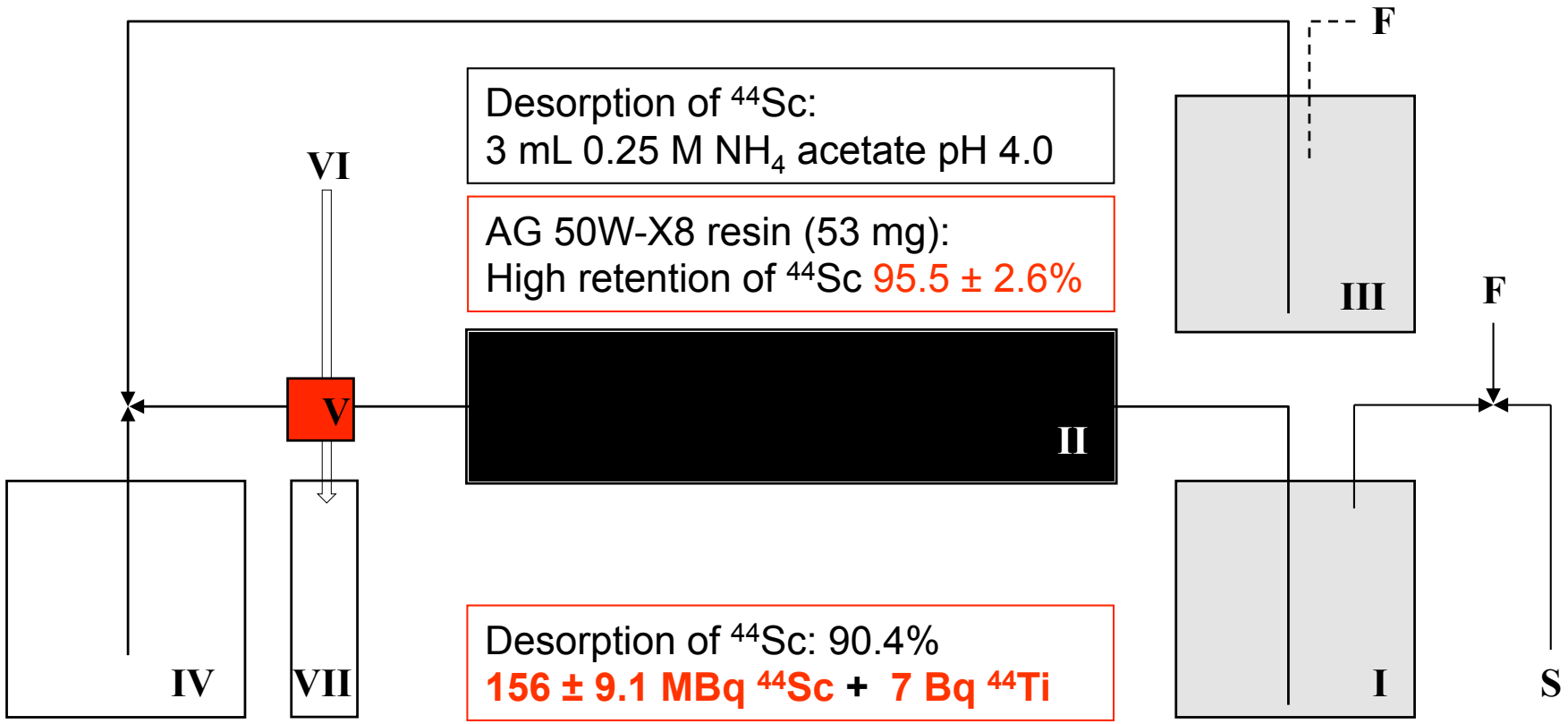
^{44}Sc
β^+ 0.60
3.92 h

Challange: many years stability !

Elution strategies: STANDARD: usual, uni-directional elution, vs
REVERSE: usual elution + backward after the elution using identic eluent

^{44}Sc yield: >90 % (160 MBq)
^{44}Ti breakthrough: < $1 \cdot 10^{-6}$ % (<10 Bq)

After 6 years of regular elution: performance stable, breakthrough of ^{44}Ti very low (<4.8×10^{-7})



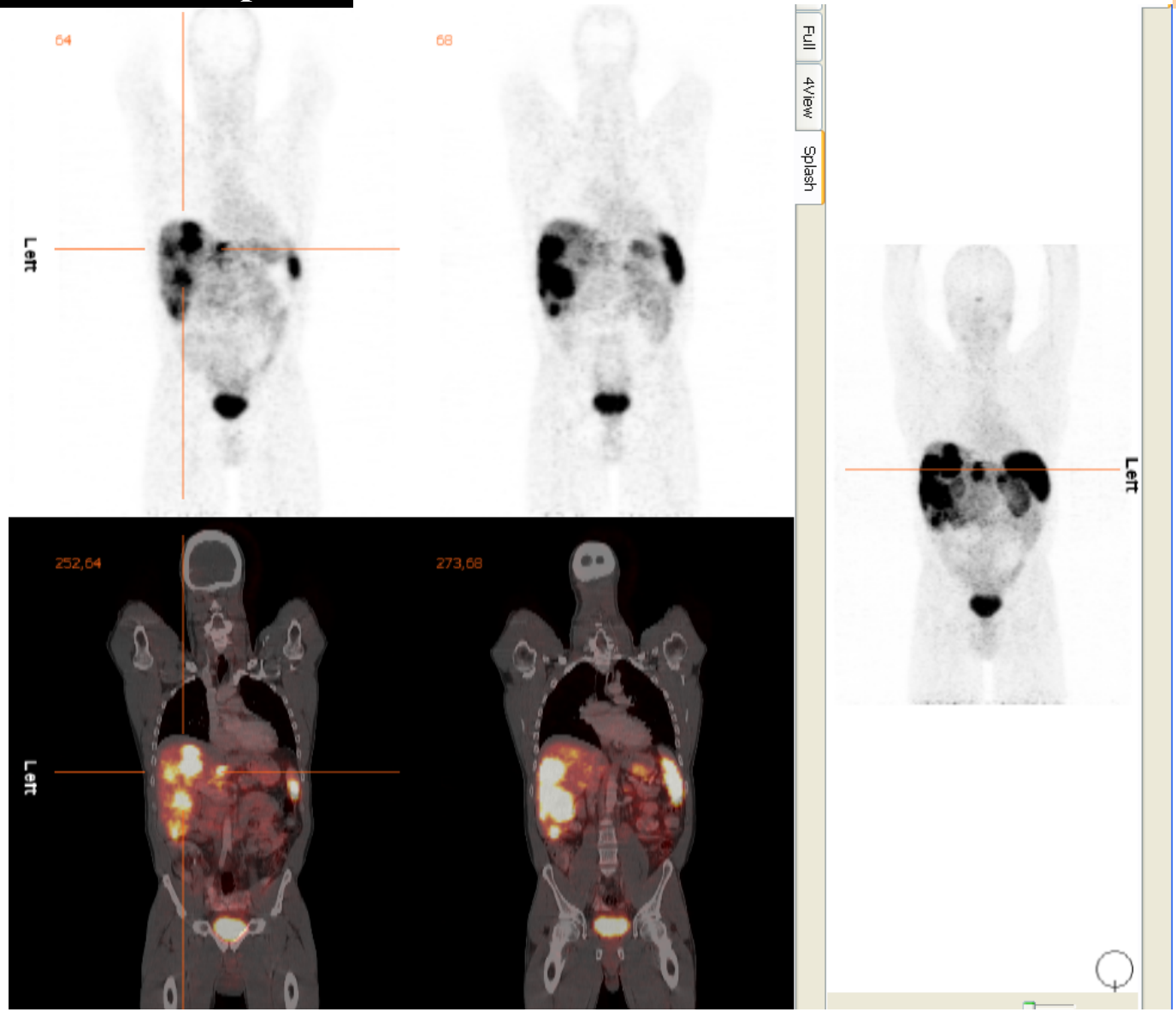
Pruszyynski M, Loktionova NS, Filosofov DV, Rösch F, Post-elution processing of ^{44}Ti/^{44}Sc generator-derived ^{44}Sc for clinical application. Appl Radiat Isot 68 (2010) 1636-1641

^{44}Sc-DOTA-Tyr^3-octreotides PET/CT vs. PRRT

^{44}Sc
β^+ 0.60
3.92 h

^{44}Sc-DOTA-TOC 40 min. p.i.

1 mCi injected



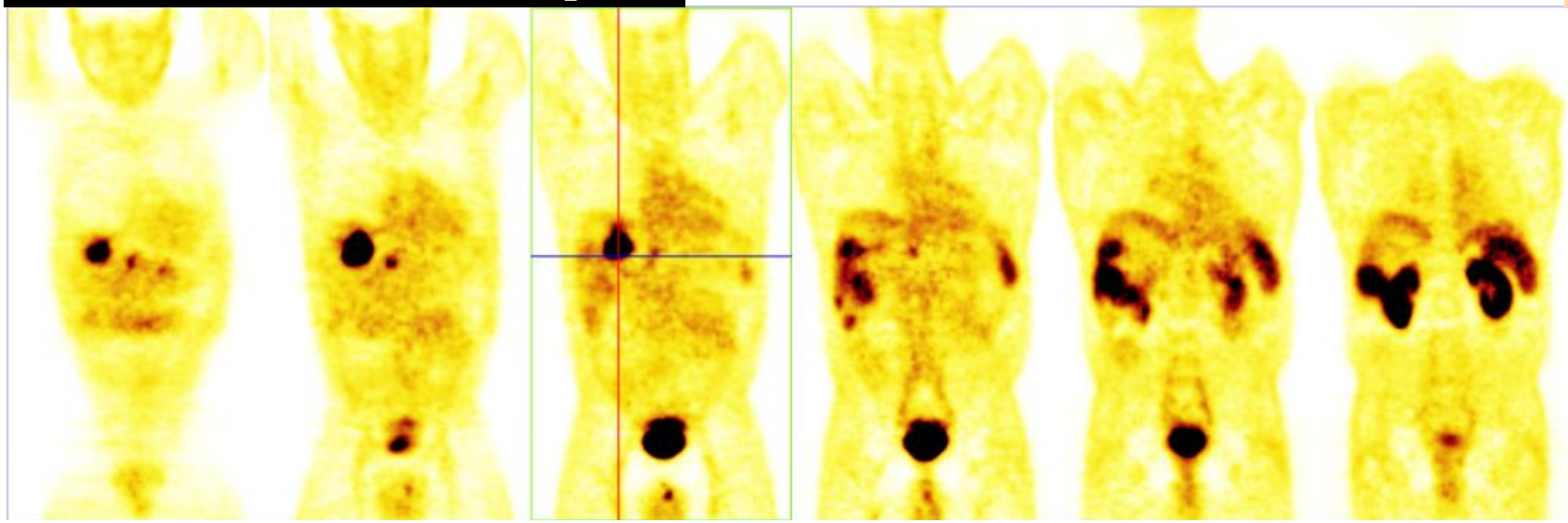
Baum RP. Dept. of Nuclear Medicine/P.E.T. Center, Zentralklinik Bad Berka

Rösch F, Baum RP. Generator-based PET radiopharmaceuticals for molecular imaging of tumours: On the way to THERANOSTICS. Dalton Transitions 40/23 (2011) 6104-6111

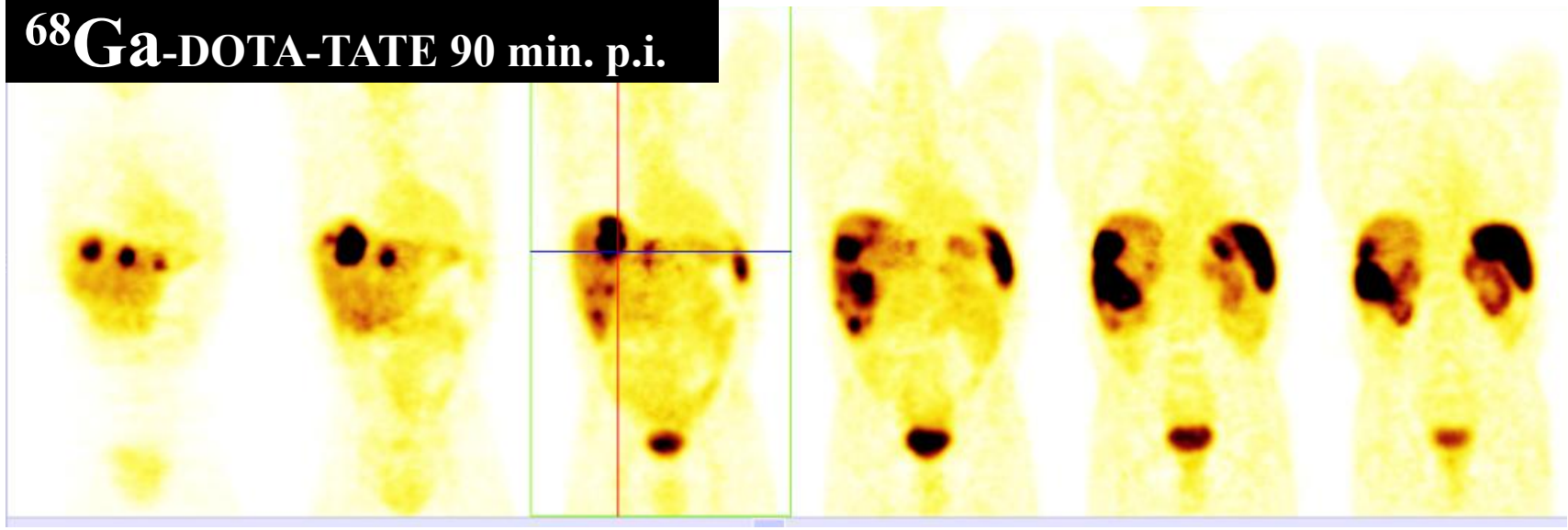
^{44}Sc-DOTA-Tyr^3-octreotides PET/CT vs. PRRT

^{44}Sc
β^+ 0.60
3.92 h

^{44}Sc-DOTA-TOC 40 min. p.i.



^{68}Ga-DOTA-TATE 90 min. p.i.



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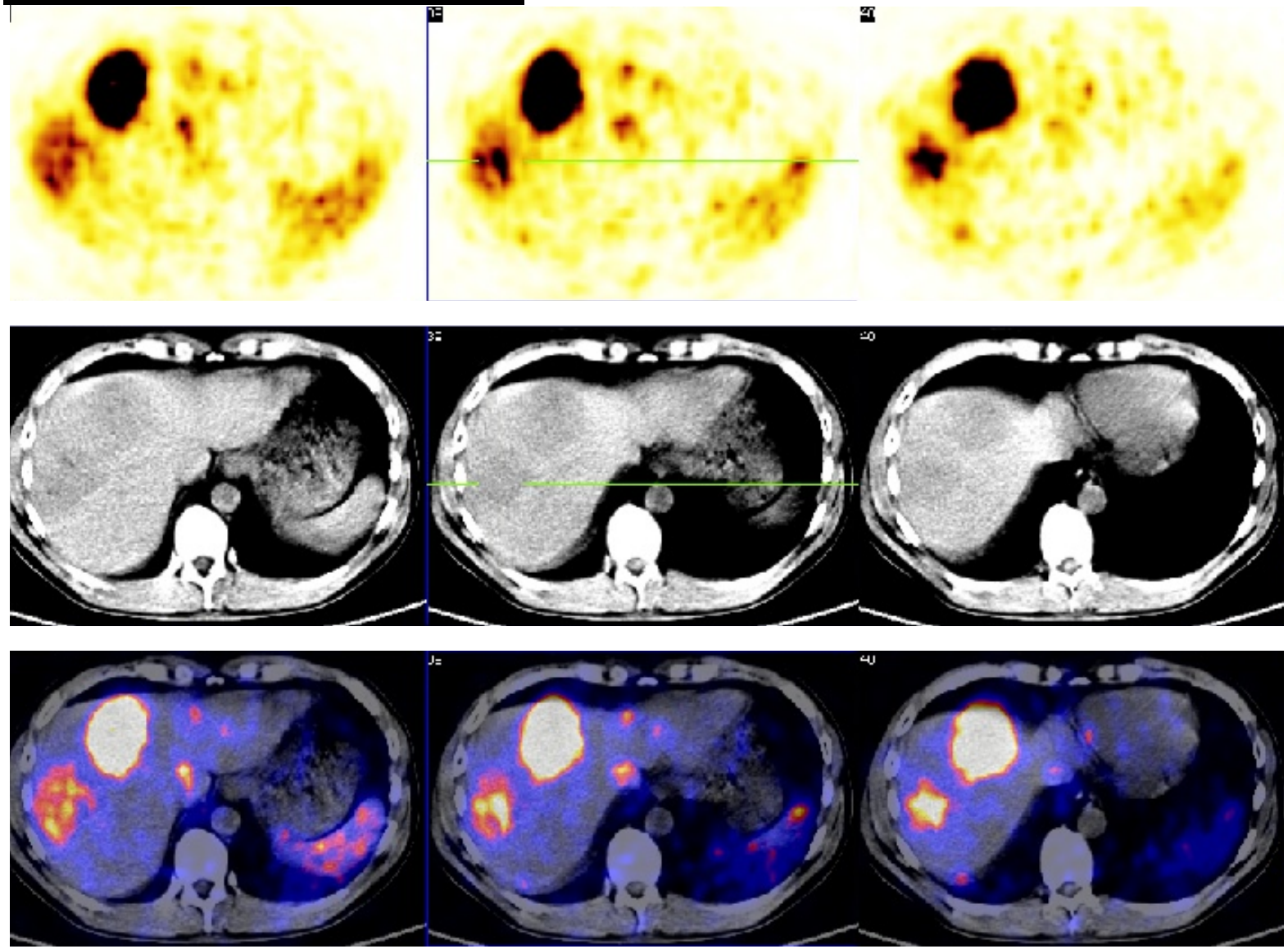
Rösch F, Baum RP. Generator-based PET radiopharmaceuticals for molecular imaging of tumours: On the way to THERANOSTICS. Dalton Transitions 40/23 (2011) 6104-6111

^{44}Sc-DOTA-Tyr^3-octreotides PET/CT vs. PRRT

^{44}Sc
β^+ 0.60
3.92 h

^{44}Sc-DOTA-TOC 18 h p.i.



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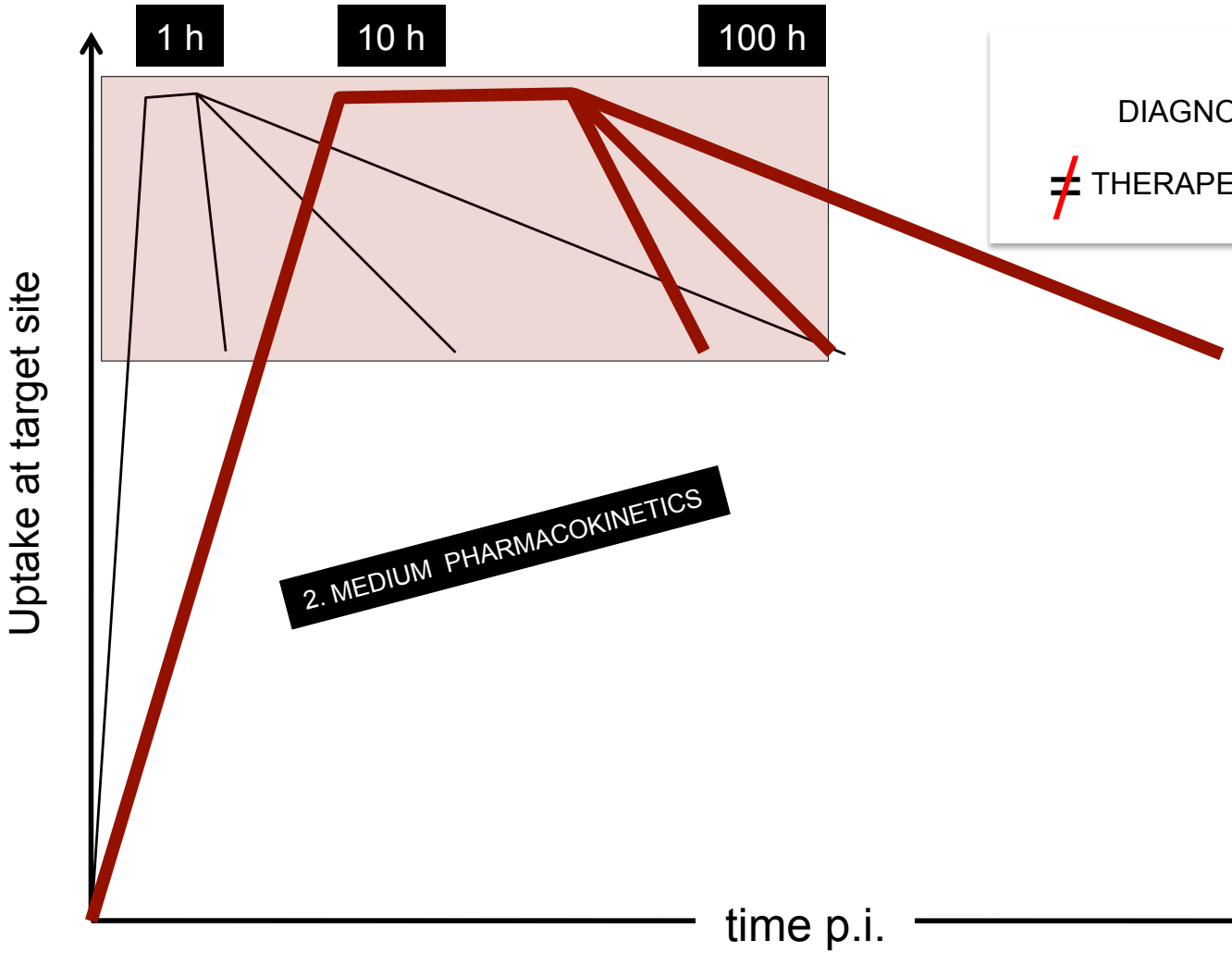
(pre-therapeutic) determination of radiation doses

^{90}Y	^{177}Lu	^{225}Ac
β^- 2.3 …	β^- 0.6 …	α 5.83 …
64.1 h	6.71 d	10.0 d

DIAGNOSTIC M_{III}
= THERAPEUTIC M_{III}

DIAGNOSTIC $M_{V, IV}$
≠ THERAPEUTIC M_{III}



^{86}Y
β^+ 0.21
33.0%
14.7 h

^{90}Nb
β^+ 0.35
51.0%
14.6 h

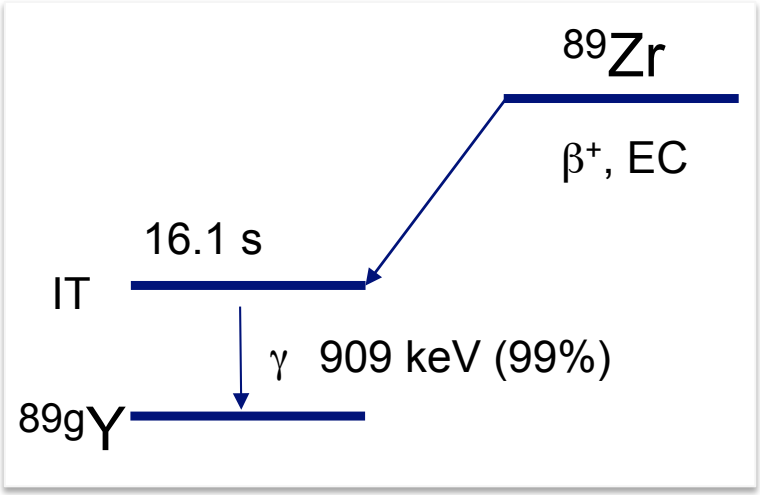
^{89}Zr
β^+ 0.09
23.0%
3.268 d

Production of ^{89}Zr

^{89}Zr
β^+ 0.09
23.0%
3.268 d

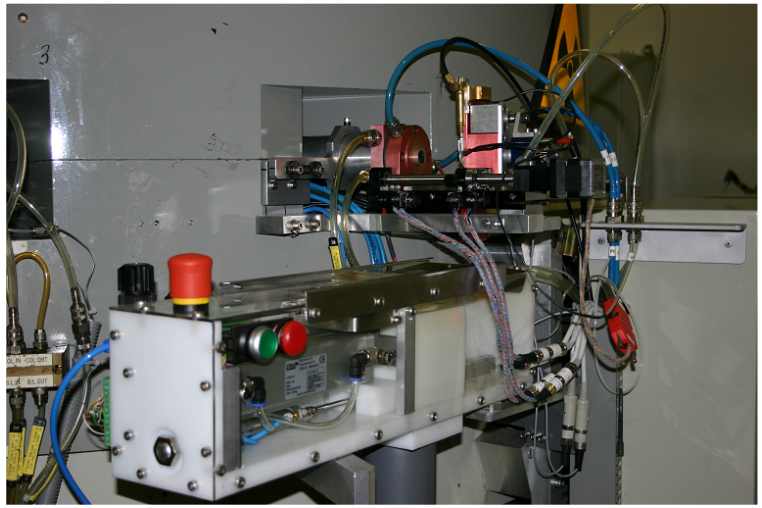
^{88}Zr 83.4 d	**^{89}Zr** 4.16 m 78.4 h
^{87}Y 13 h 80.3 h	**^{88}Y** 106.6 d

(p,n) → **^{89}Y** 100 %



IT= isomeric transition

- Nuclear reaction $^{89}Y(p,n)^{89}Zr$
- Target: ^{89}Y disk (mono-isotopic !)
- Separation: dissolve in 6 M HCl,
- affinity chromatography



Verel et al, J Nucl Med 2003, 44, 1271-1281.

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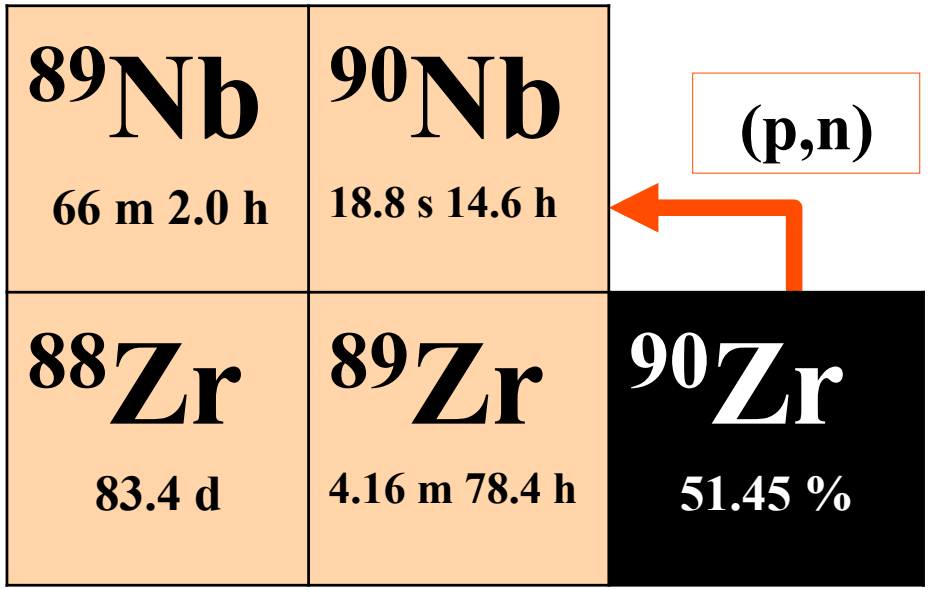
Production of ^{90}Nb

^{90}Nb
β^+ 0.35
51.0%
14.6 h



- Nuclear reaction ^{90}Zr (p,n) ^{90}Nb
- obtained as ^{90}Nb in Zirconium foil
- Work up: dissolve in conc. HF
- Multistep separation procedure (extraction + anion exchange)

Busse S, Rösch F, Qaim SM. Cross section data for the production of the positron emitting niobium isotope ^{90}Nb via the ^{90}Zr(p,n) reaction. Radiochim Acta 96 (2002) 1-5
Busse S, Brockmann J, Rösch F. Radiochemical separation of no-carrier-added radioniobium from zirconium targets for application of ^{90}Nb labelled compounds. Radiochim Acta 90 (2002) 411-415

Production and specifications of ^{90}Nb and ^{89}Zr

Parameters	Radionuclide	
	^{90}Nb	^{89}Zr
Production		
Energy (MeV)	17.5	<13
Beam current (μA)	Up to 10	Up to 50
Yield (MBq/μah)	~ 150 (290*)	38-42
Typical bombardment	1 h yield ~725 MBq	4-6 h yield ~6000 MBq
Purification (%)	76-81	95
Specifications		
Chemical form	Nb^{V} in 6 M HCl/0.01 M oxalic acid	Zr^{IV} in 1 M oxalic acid
Specific activity (MBq/g)	no carrier added $8.82 \cdot 10^{10}$	no carrier added $1.66 \cdot 10^{10}$
Radioactivity conc. (MBq/ml)		> 740
Radionuclide purity (%)	> 97	> 99.9
Availability	Testing batches (DKFZ Heidelberg)	Catalogue product (IBA Moleculare)

^{90}Nb
β^+ 0.35
51.0%
14.6 h

^{89}Zr
β^+ 0.09
23.0%
3.268 d

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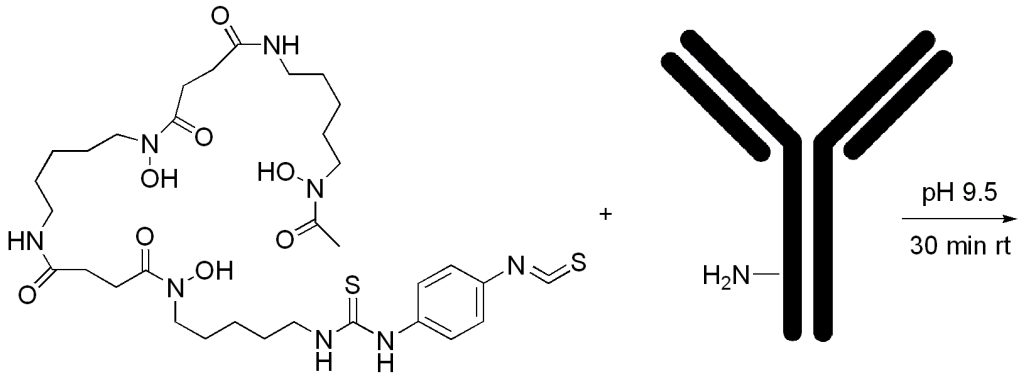
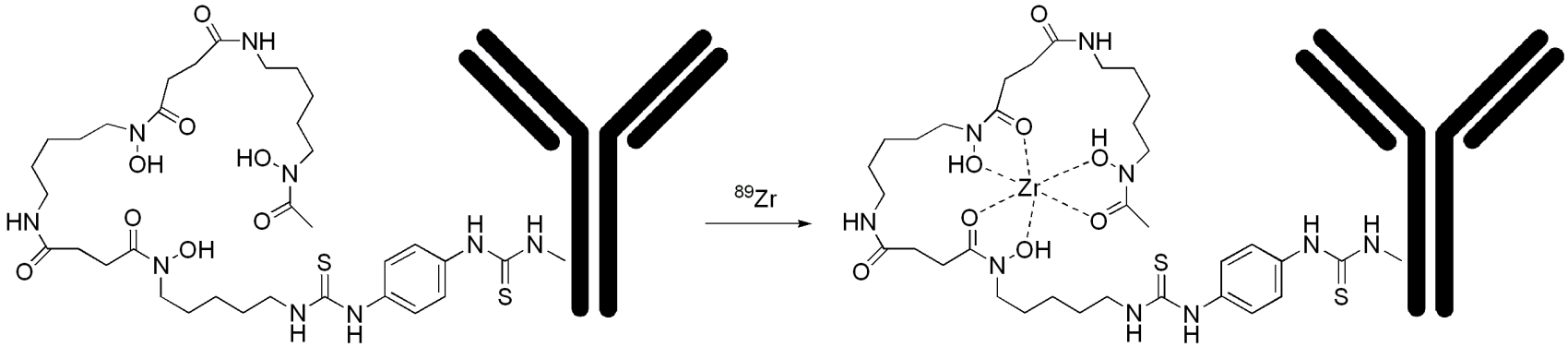
Nb(V) / Zr(IV)-Df-proteins

conjugation chemistry: NCS-Df

^{89}Zr
β^+ 0.09
23.0%
3.268 d



NCS-Df



3 eq. NCS-Df used = 1-1.5 Df per mAb

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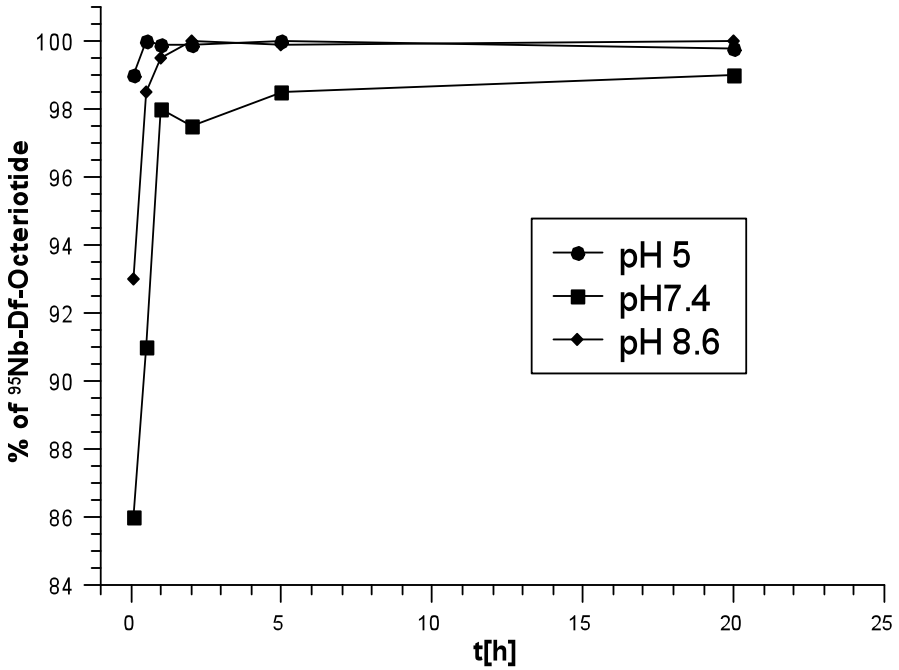
Perk et al, Eur J Nucl Med Mol Imaging 2010, 37, 250-259; Vosjan et al, Nature Protocols 2010, 5, 739-743.

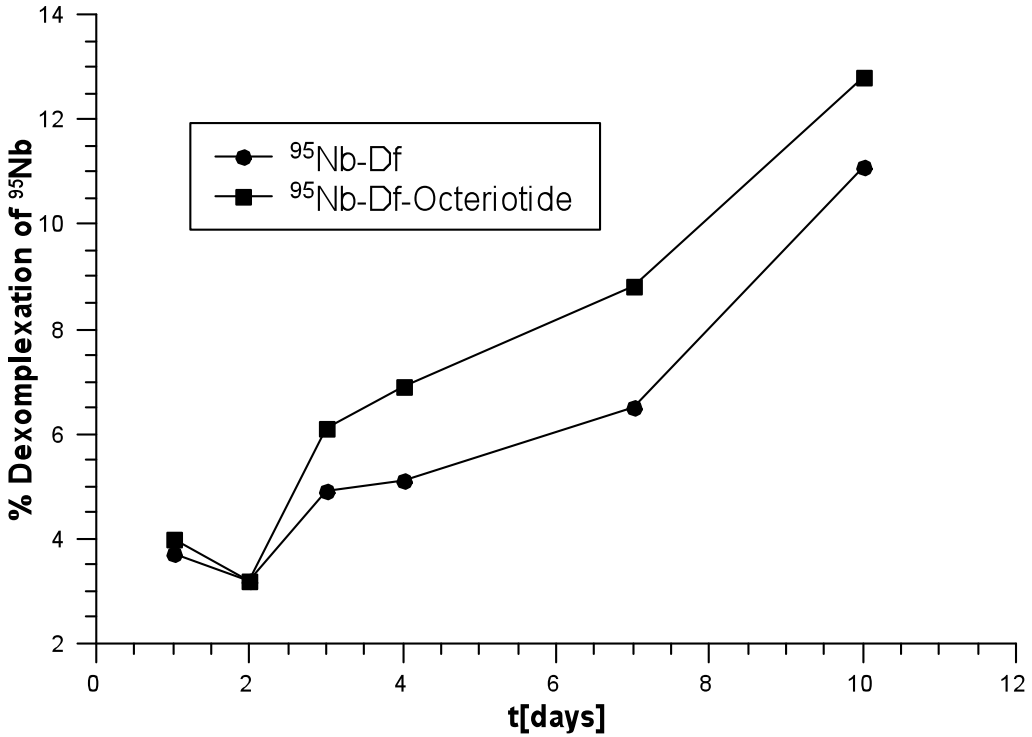
Nb(V) / Zr(IV)-Df-peptides

Proof-of-principle chemistry: Df-(D)Phe^{1}-Octreotide

^{90}Nb
β^+ 0.35
51.0%
14.6 h



^{95}Nb-Df-Octreotide complex formation at different pH values



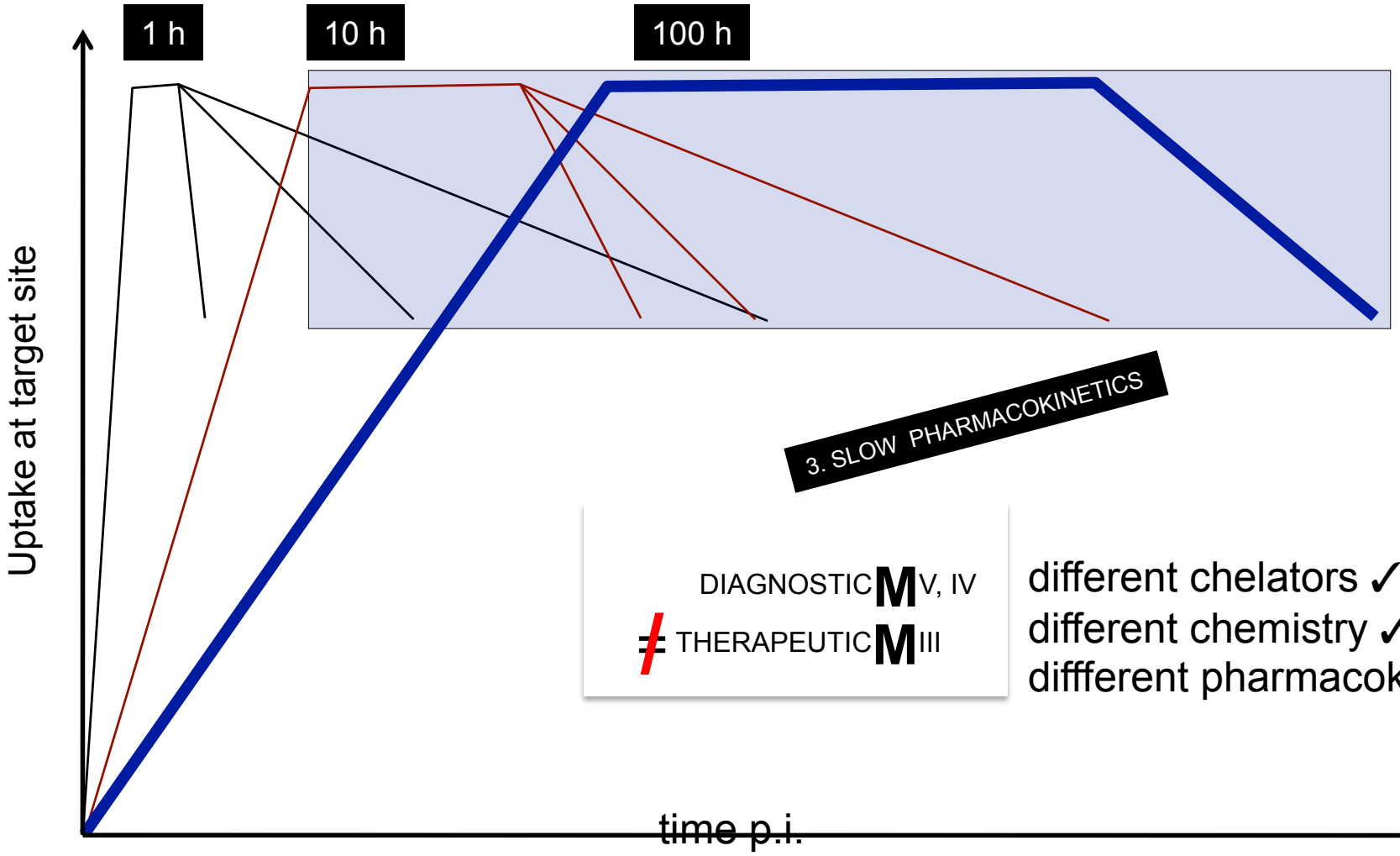
Serum stability of ^{95}Nb-Df and ^{95}Nb-Df-Octreotide

Busse S. PhD Thesis, 2000, University of Mainz

(pre-therapeutic) determination of radiation doses

^{90}Y	^{177}Lu	^{225}Ac
β^- 2.3 …	β^- 0.6 …	α 5.83 …
.	.	.
64.1 h	6.71 d	10.0 d

^{89}Zr
β^+ 0.09
23.0%
3.268 d

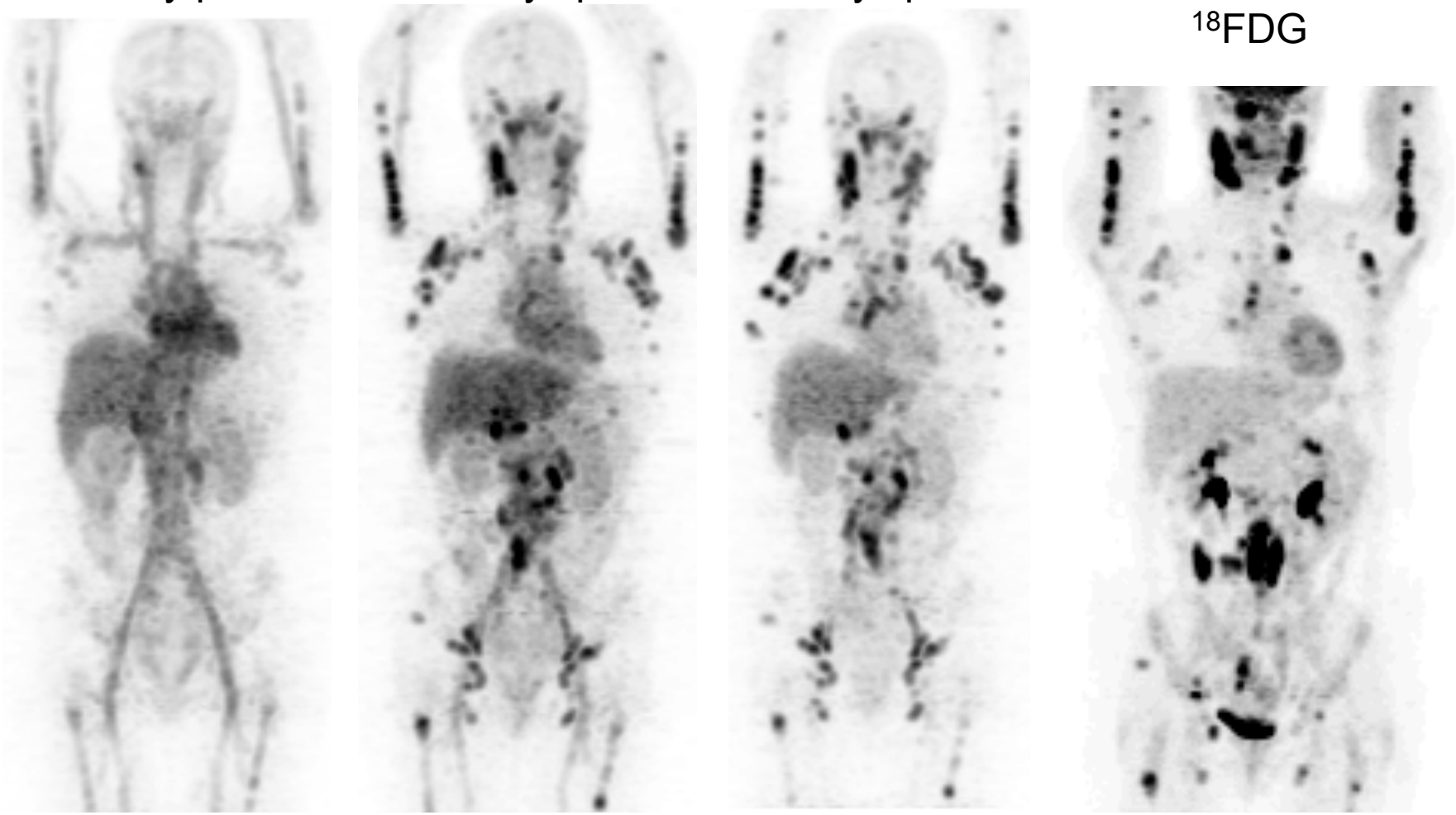


Immuno-PET:
Application of ^{89}Zr-labeled monoclonal antibodies

Confirmation lymphoma targeting with ^{89}Zr-N-suc-Df-rituximab

^{89}Zr
β^+ 0.09
23.0%
3.268 d

1 day p.i. | 3 days p.i. | 6 days p.i. | ^{18}FDG



Collaboration: Kristoff Muylle, Patrick Flamen, Brussels

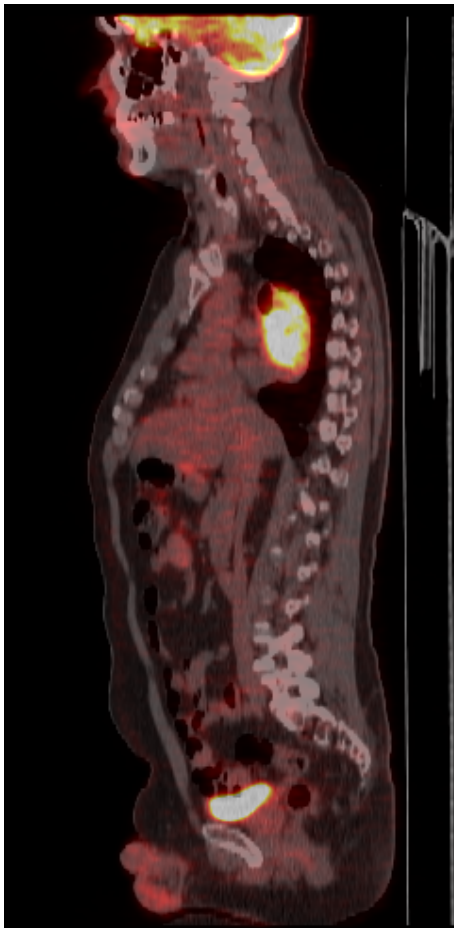
Danielle Vugts
Otolaryngology/Head and Neck Surgery,
Nuclear Medicine & PET research, VU University Medical Center, Amsterdam

Immuno-PET:
Application of ^{89}Zr-labeled monoclonal antibodies

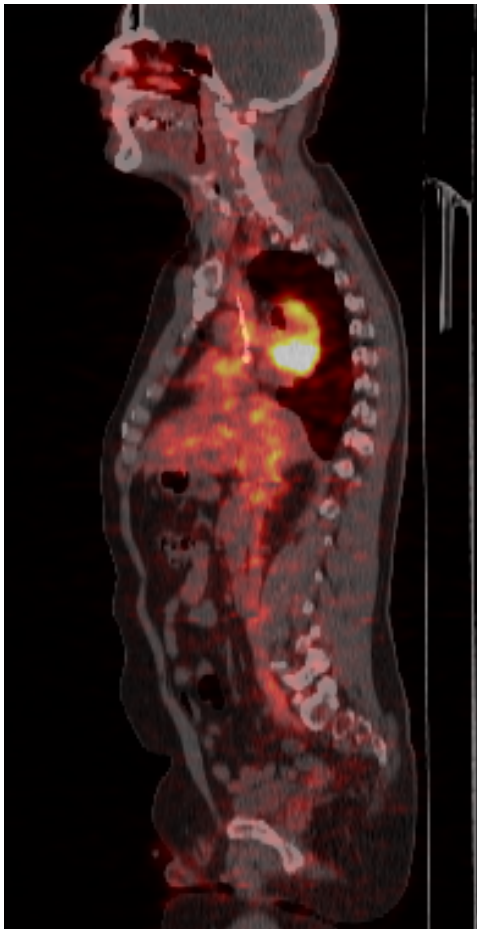
From 'one size fits all' to 'personalized therapy'

^{89}Zr
β^+ 0.09
23.0%
3.268 d

^{18}FDG PET-CT
before

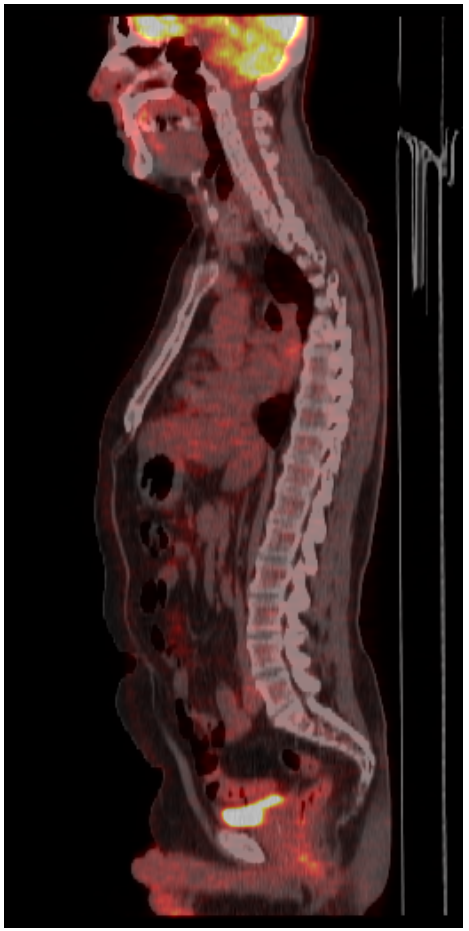


^{89}Zr-rituximab
before



^{90}Y-rituximab
treatment

^{18}FDG PET-CT
3 months after

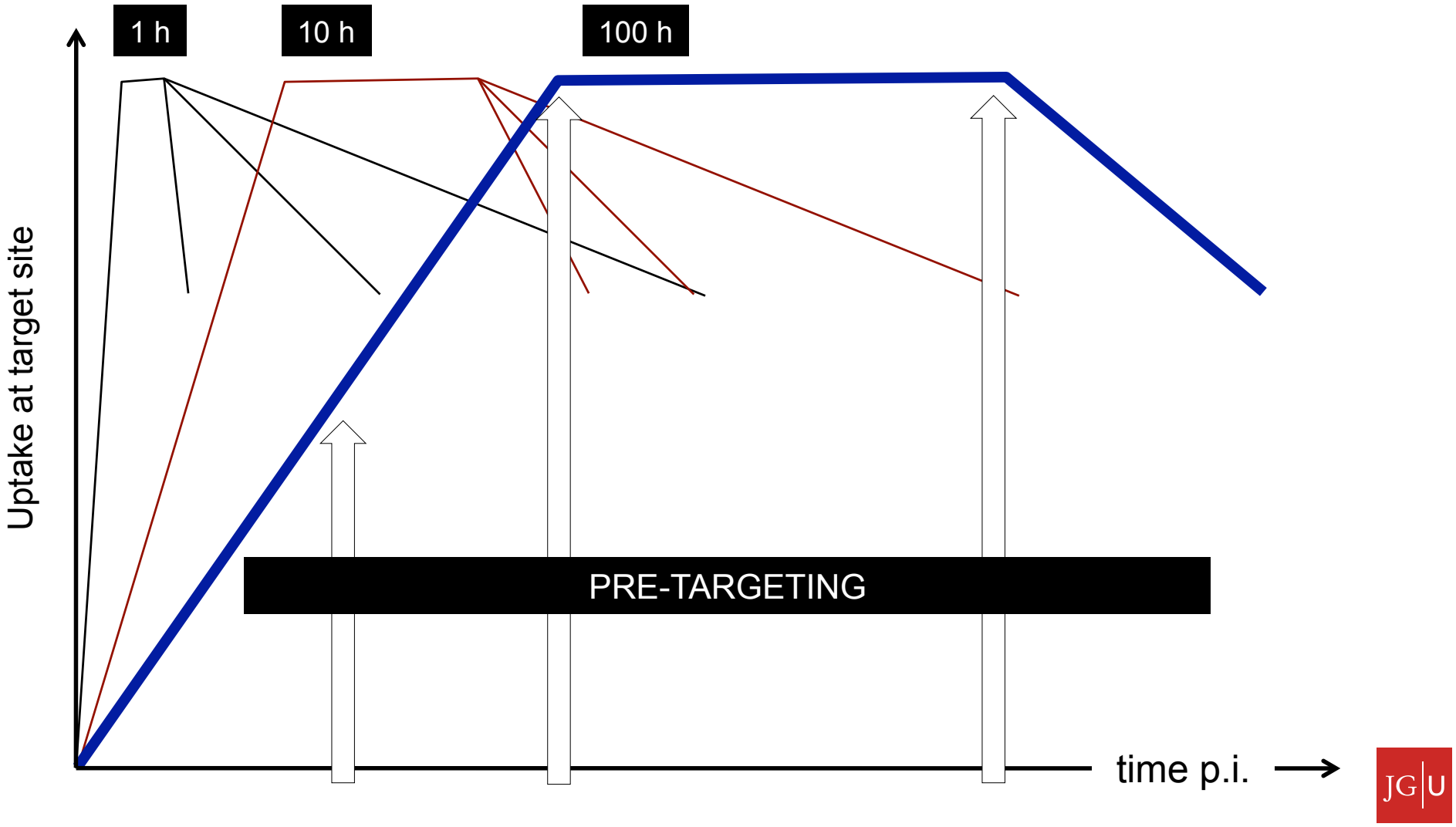


Danielle Vugts
Otolaryngology/Head and Neck Surgery,
Nuclear Medicine & PET research, VU University Medical Center, Amsterdam

Collaboration: Kristoff Muylle, Patrick Flamen, Brussels

(pre-therapeutic) determination of radiation doses

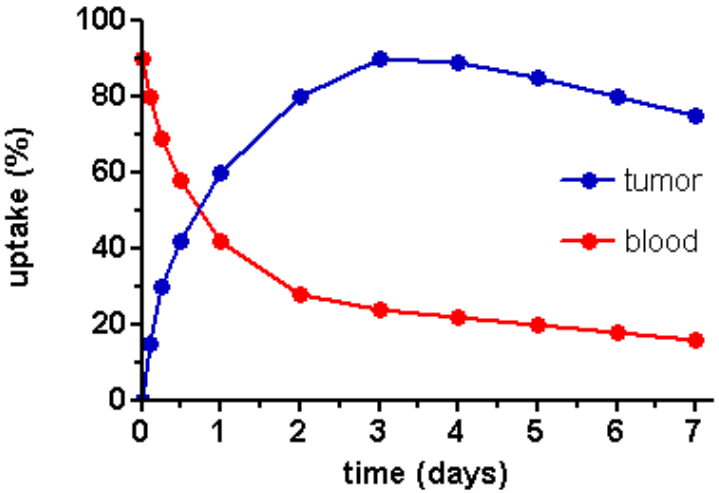
^{90}Y	^{177}Lu	^{225}Ac
β^- 2.3 …	β^- 0.6 …	α 5.83 …
64.1 h	6.71 d	10.0 d

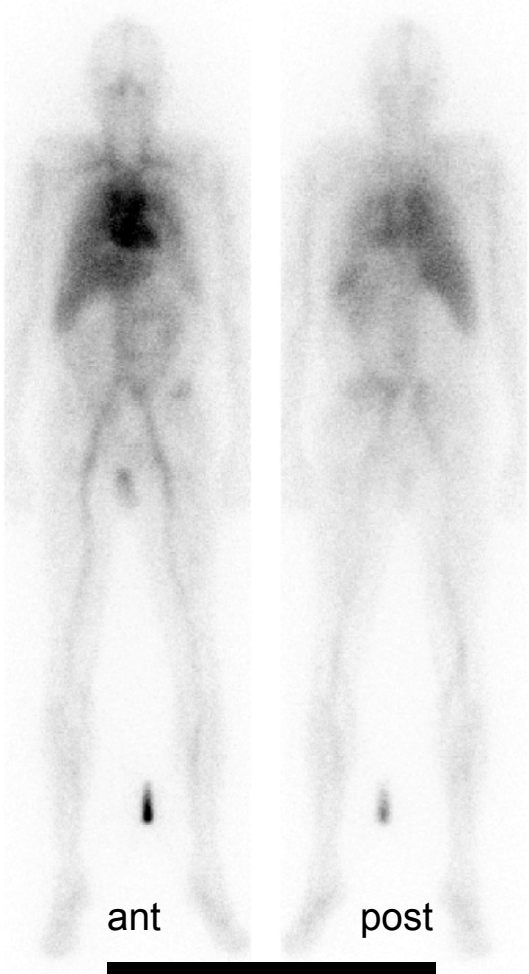


PRE-TARGETING

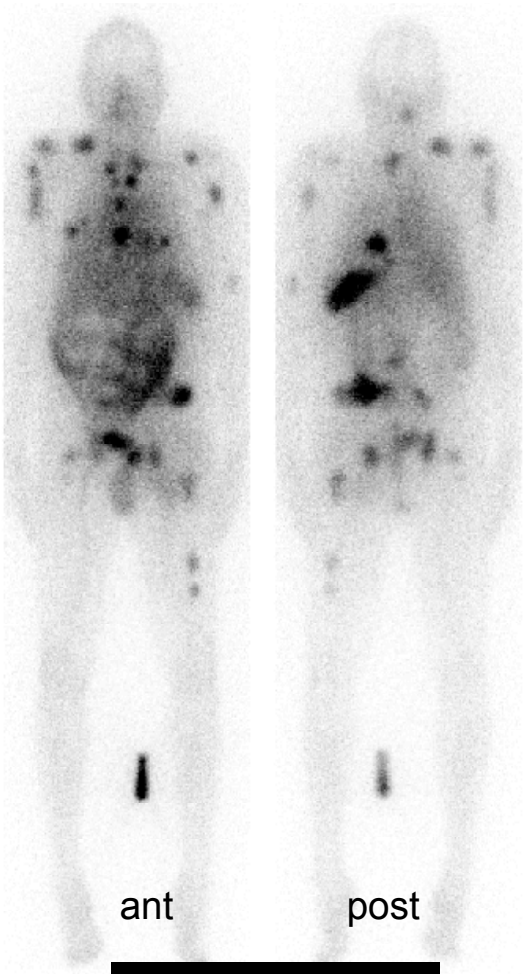
Radioimmunotargeting
with ^{131}I-cG250

Kinetics of antibody targeting





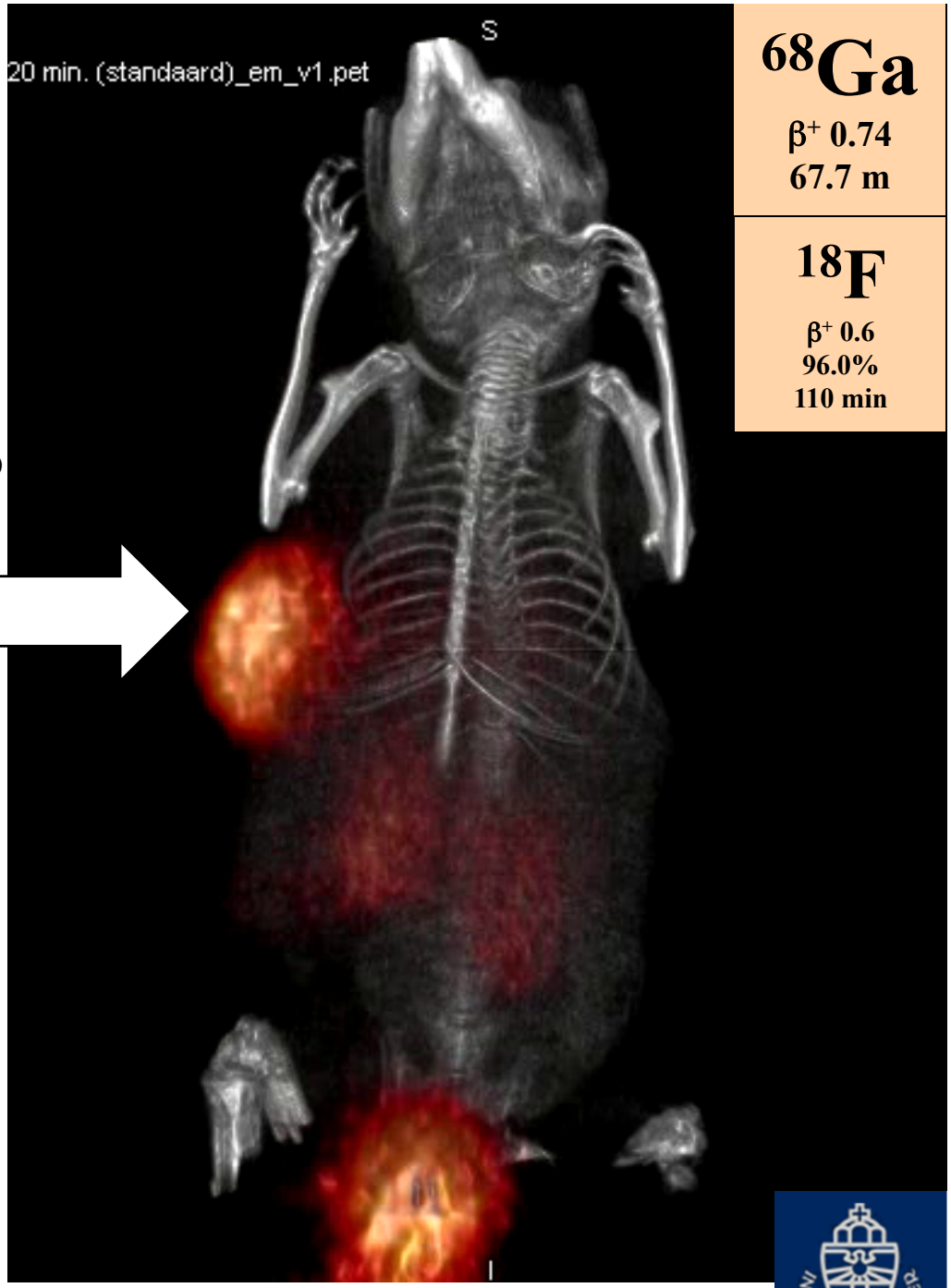
1 h p.i.



72 h p.i.

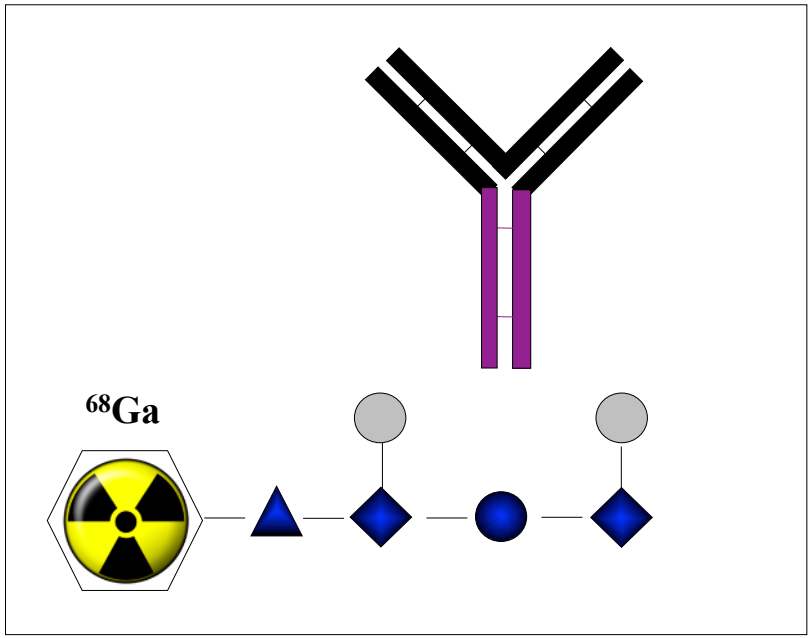
O C Boerman, R Schoffelen, G Franssen, W McBride, R M Sharkey, D M Goldenberg, W J Oyen
Radboud University Nijmegen Medical Center, The Netherlands / Immunomedics, Morris Plains, NJ / Garden State Cancer Center, Belleville, NJ

Pre-targeted ImmunoPET imaging of CEA-expressing tumors using a ^{68}Ga-labeled peptide



t = 0: trivalent bsAb, anti-CEA x anti-HSG bsAb

t = 16 h: ^{68}Ga-IMP-288



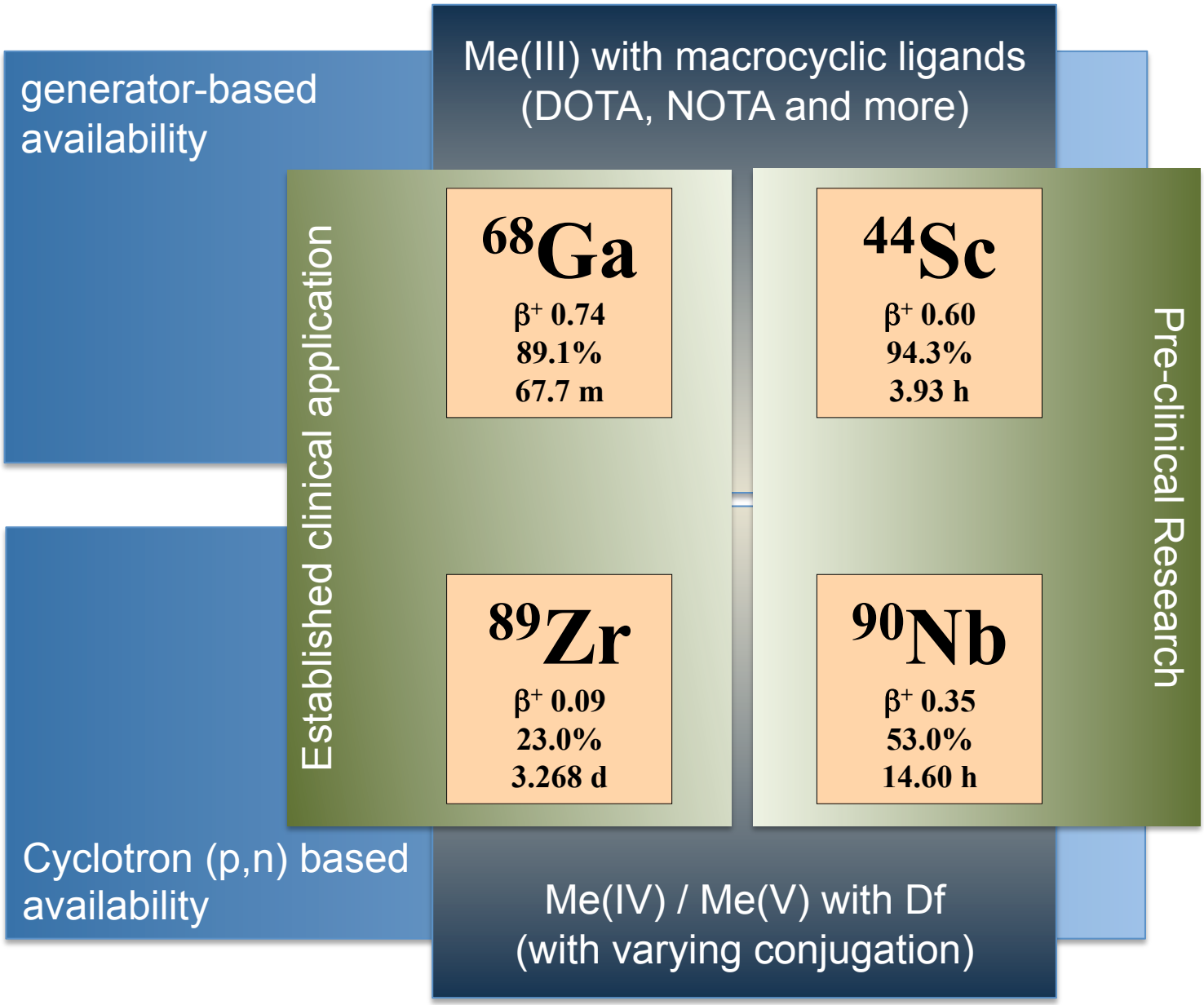
O C Boerman, R Schoffelen, G Franssen, W McBride, R M Sharkey, D M Goldenberg, W J Oyen
Radboud University Nijmegen Medical Center, The Netherlands / Immunomedics, Morris Plains, NJ / Garden State Cancer Center, Belleville, NJ

Conclusion

big brothers – little sisters

Short-lived generator-derived ^{68}Ga and ^{44}Sc and longer-lived cyclotron-produced ^{90}Nb and ^{89}Zr positron emitters:

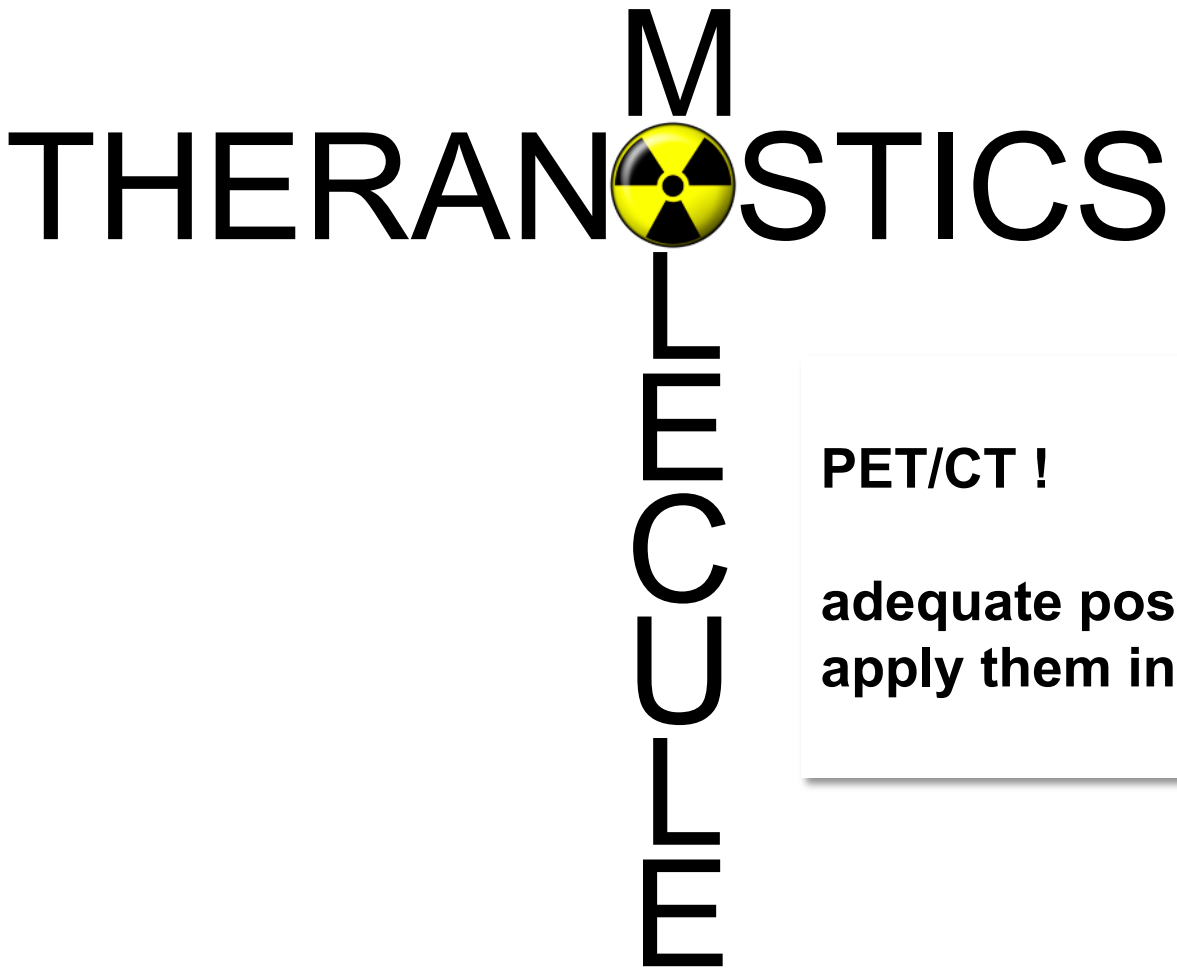
Availability, labelling and directions of applications



1. **PET/CT**

2. **For therapy**
Decicion-making
Dosimetry
Control

Summary:
(pre-therapeutic) determination of radiation doses



PET/CT !

adequate positron emitters available
apply them in clinical (routine)