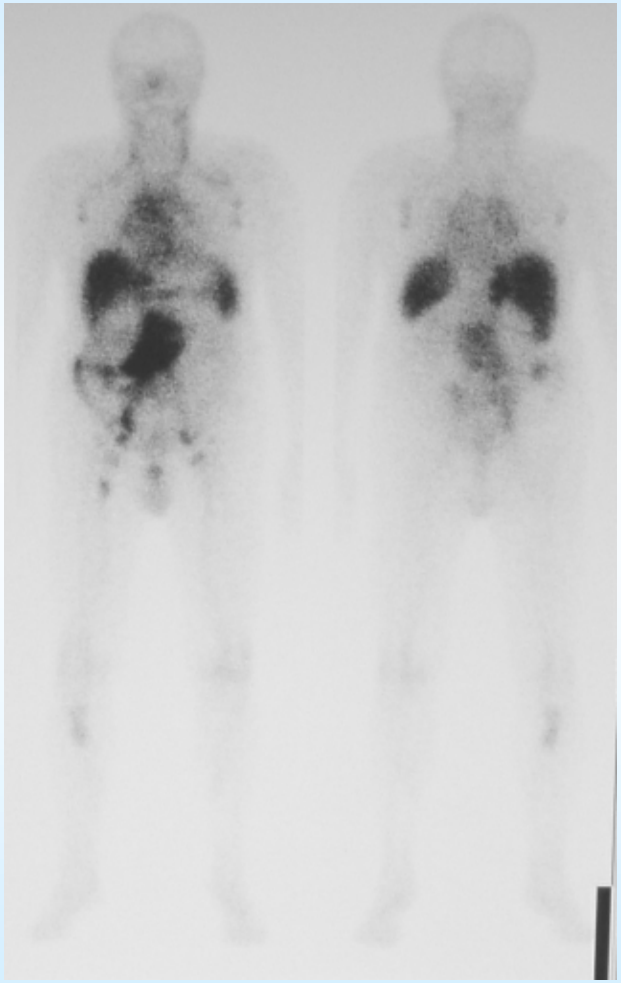
Dosimetry in Nuclear Medicine Therapies



F. Forrer
Institut of Nuclear Medicine
University Hospital Basel

Universitätsspital Basel

Nuclear Medicine

Therapies

- Radioiodine
- Phosphonates
- Metabolites (e.g. ^{131}I-mIBG)
- Radiopeptides
- Radioimmunotherapy
- Radiosynoviothesis
- Intracavitary Therapy

Background

- In comparison to conventional pharmaceuticals, radiopharmaceuticals suite for relatively simple quantification
- The first treatment with radioiodine was described in 1942
- In radioiodine therapy pretherapeutic dosimetry is demanded by law
- Most often the “Marinelli Formula” is used
- This formula was first described 1948[1]

[1]Marinelli et al. *Am J Roentgenol* 1948; 59: 260-81.

Marinelli Formula

Used in radioiodine therapy for benign thyroid disorder

$$\text{Activity} = K * \frac{\text{Absorbed Dose} * \text{Volume}}{\text{Max. Uptake (\%)} * \text{eff. Half-life}}$$

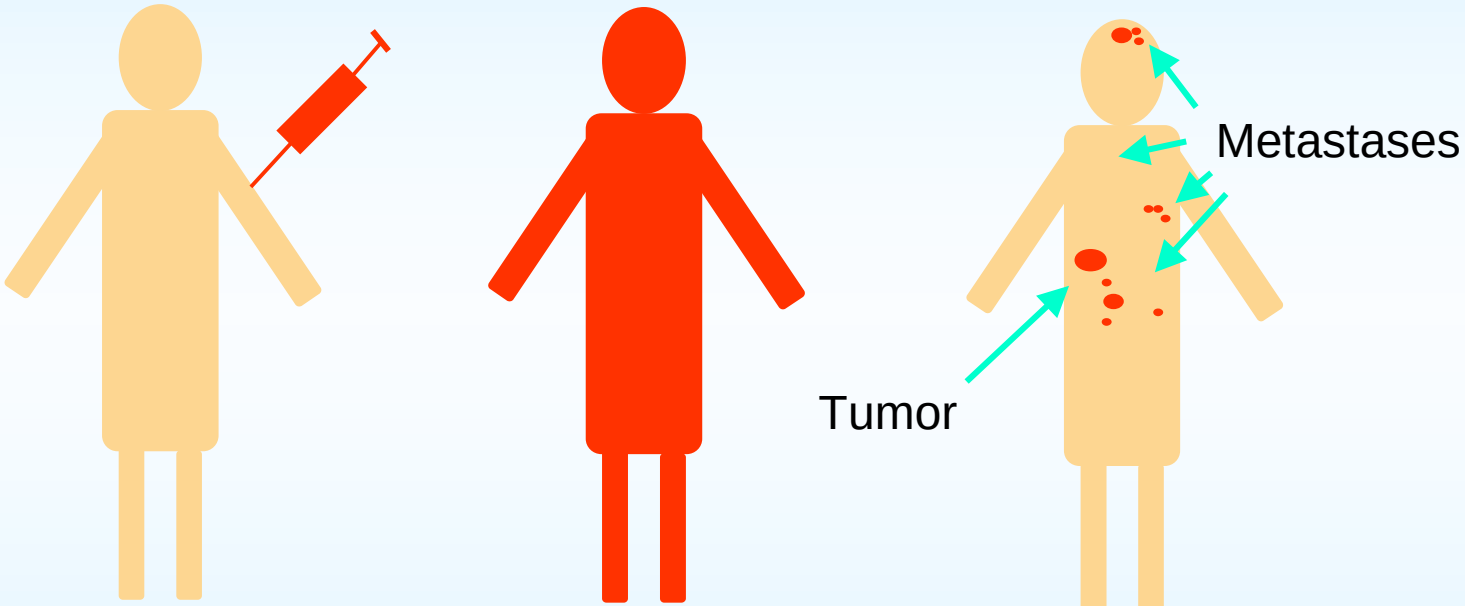
Radiopeptides

- Many new peptides are in preclinical studies
- The options for diagnostic and therapy with radiopeptides will increase
- In therapy the dose limiting toxicity is usually sever and has to be avoided
- Therefore, a safe but effective activity has to be defined
- Individual pretherapeutic dosimetry is desirable

DOTATOC

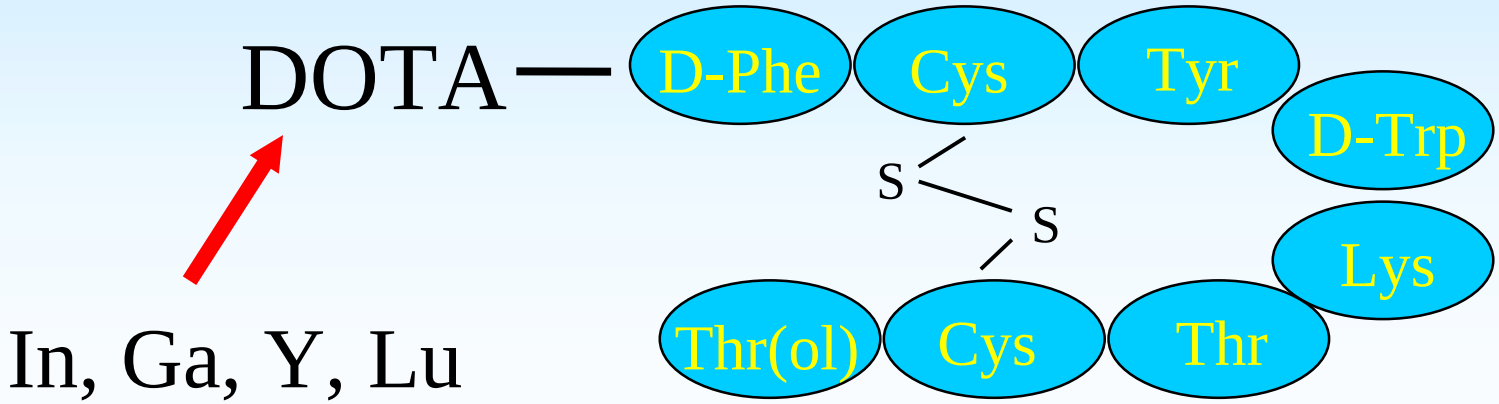
- Somatostatin analogue
- A high density of somatostatin receptors is found on many tumors, mainly neuroendocrine tumors
- Therapies with Y-90 labelled DOTATOC were started in Basel in 1996
- More than 700 patients are treated so far

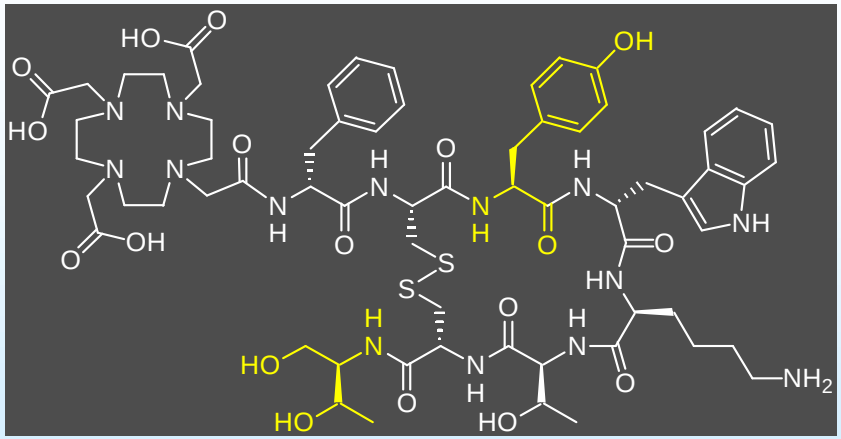
Magic Bullet Approach



Application Distribution Accumulation

DOTATOC

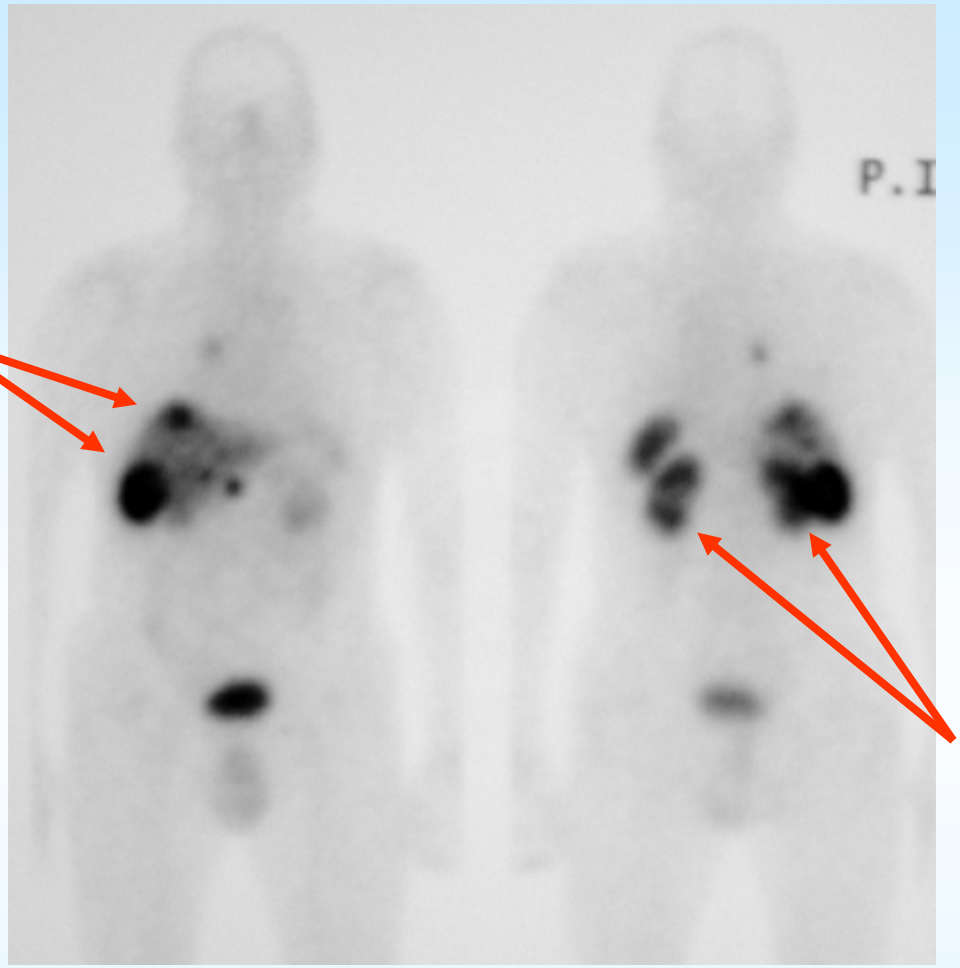




Results

Complete remission	5	89 %
Partial remission	26	
Stable disease	72	
Progressive disease	13	11 %

Metastases

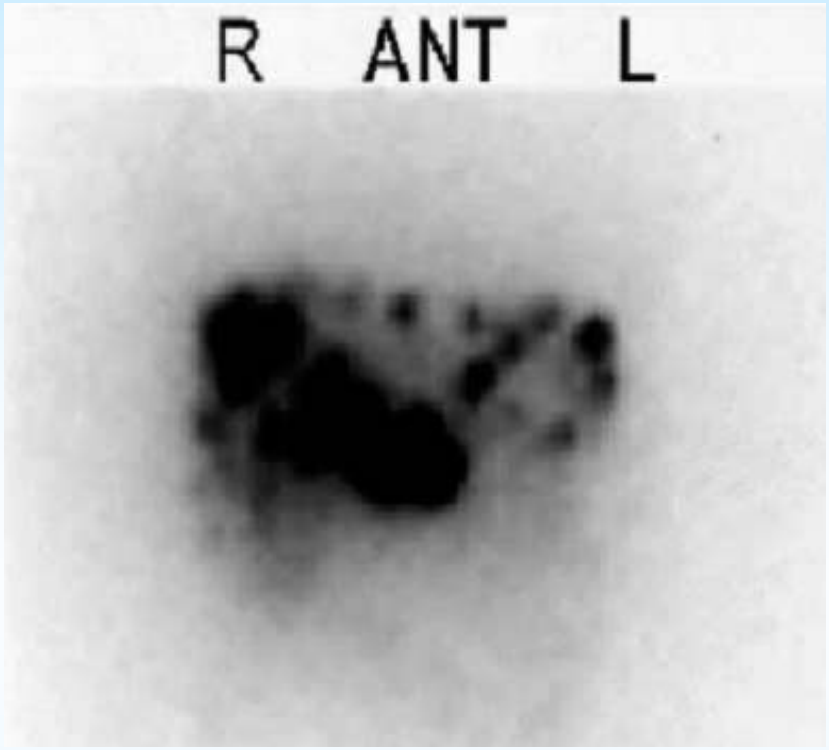


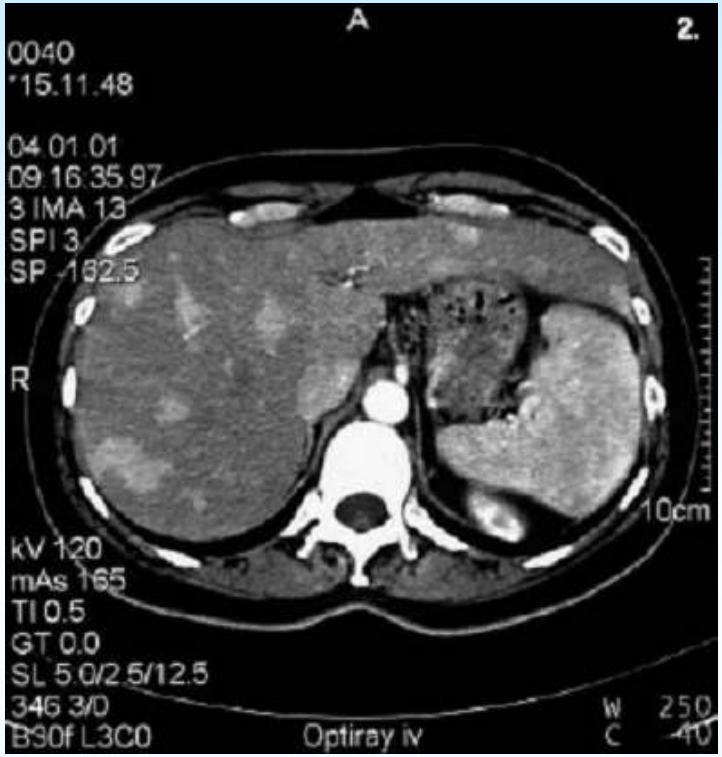
Kidneys!

20h p.i.; 7400 MBq ^{90}Y-DOTATOC
Neuroendocrine tumor of the pancreas

Universitätsspital Basel

Nuclear Medicine





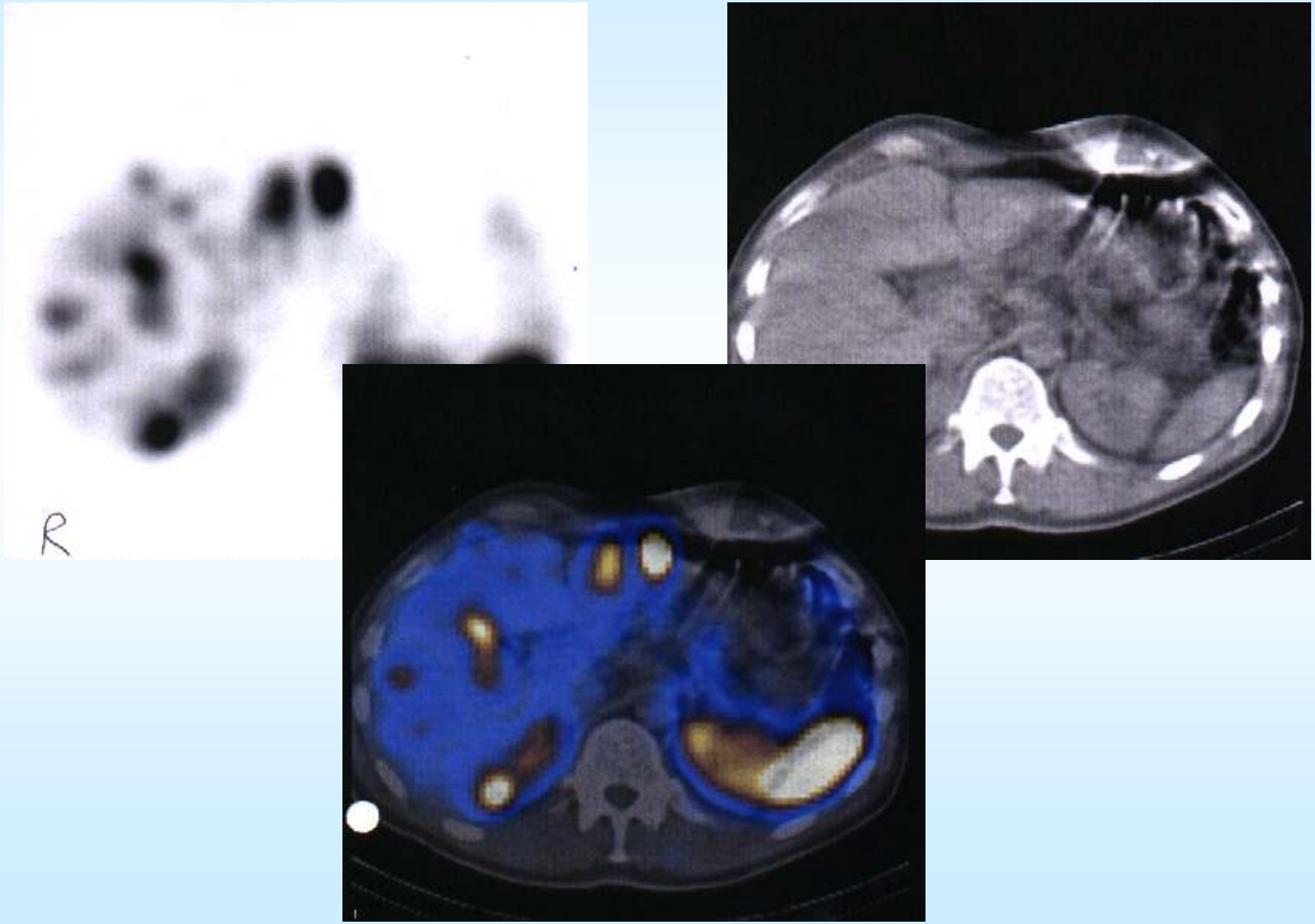
20h p.i.; 7400 MBq ^{90}Y-DOTATOC
Neuroendocrine tumour of the pancreas

Correlating CT-scan

Universitätsspital Basel

Nuclear Medicine

SPECT / CT mit ^{111}In-Octreotide

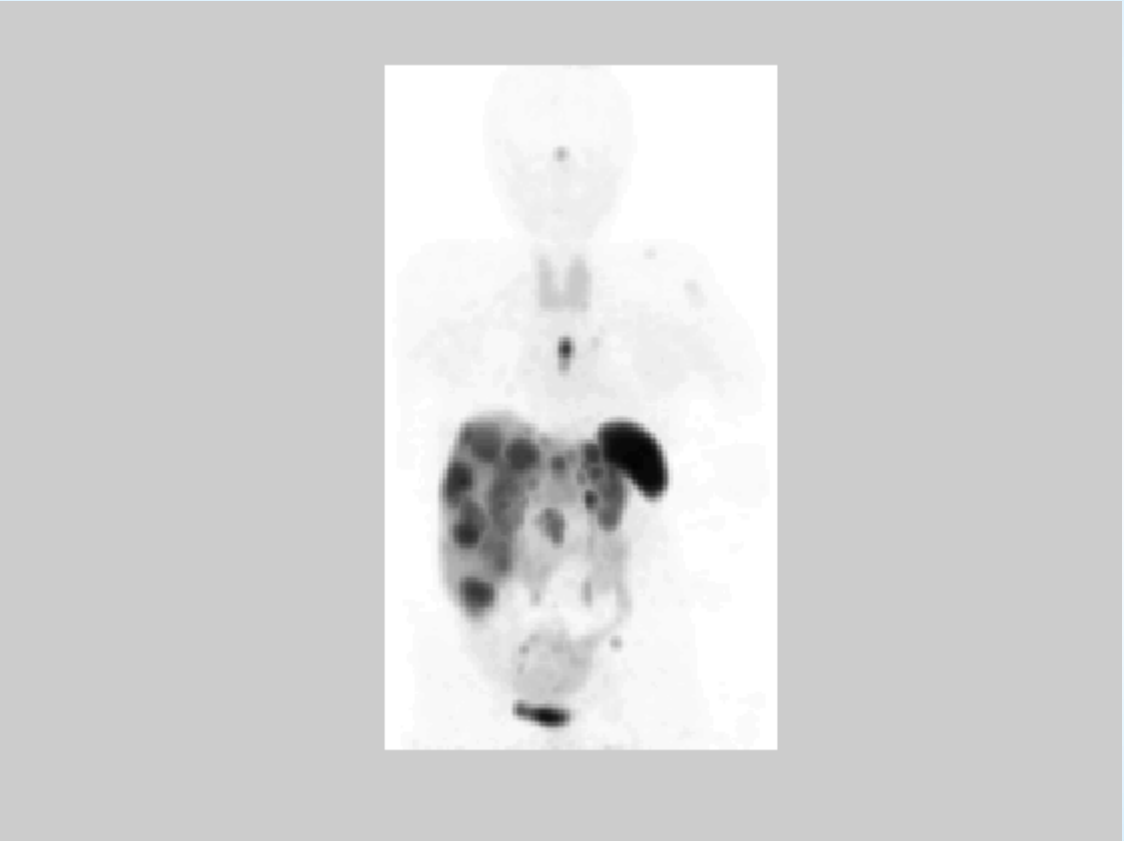


^{68}Ga-DOTATOC-PET

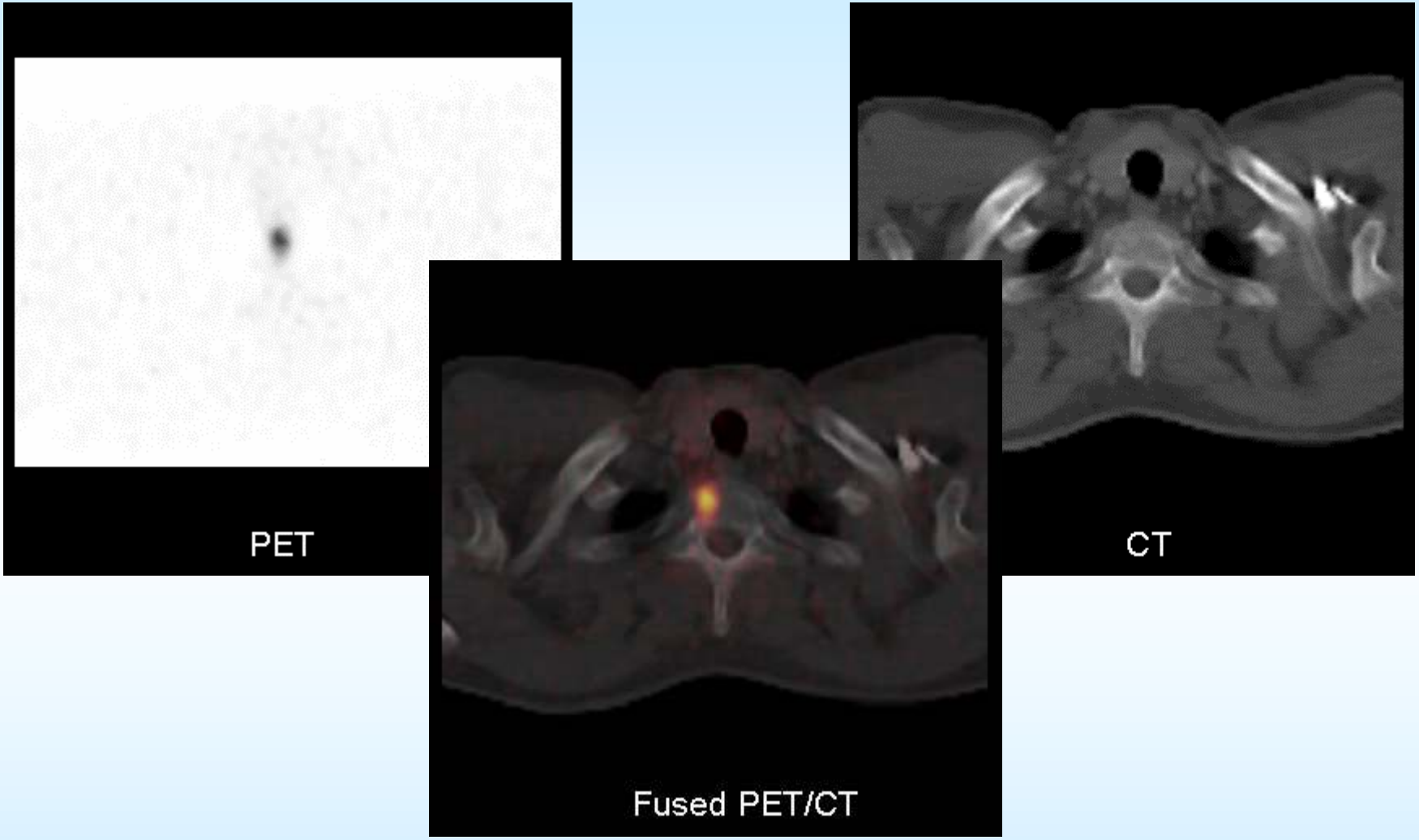
- Highly specific for visualisation of somatostatin receptor positive tumor tissue
- Anatomic localisation is difficult in certain cases

➡ PET-CT

^{68}Ga-DOTATOC-PET



Freundlicherweise zur Verfügung gestellt von Dr. M. Hofmann, Inselspital Bern



Universitätsspital Basel

Nuclear Medicine

A Comparison of ^{111}In-DOTATOC and ^{111}In-DOTATATE: Biodistribution and Dosimetry in the Identical Patients with Metastatic Neuroendocrine Tumors

F. Forrer [1], H. Uusijärvi [2], M. Cremonesi [3], C. Waldherr [1], P. Bernhardt [2], J. Müller-Brand [1], H. Mäcke [4]

[1] Institute of Nuclear Medcine, University Hospital Basel, Switzerland

[2] Department of Radiation Physics, Göteborg, Sweden

[3] Divisione di Medicina Nucleare, Istituto Europeo di Oncologia, Milano, Italia

[4] Division of Radiological Chemistry, University Hospital Basel, Switzerland

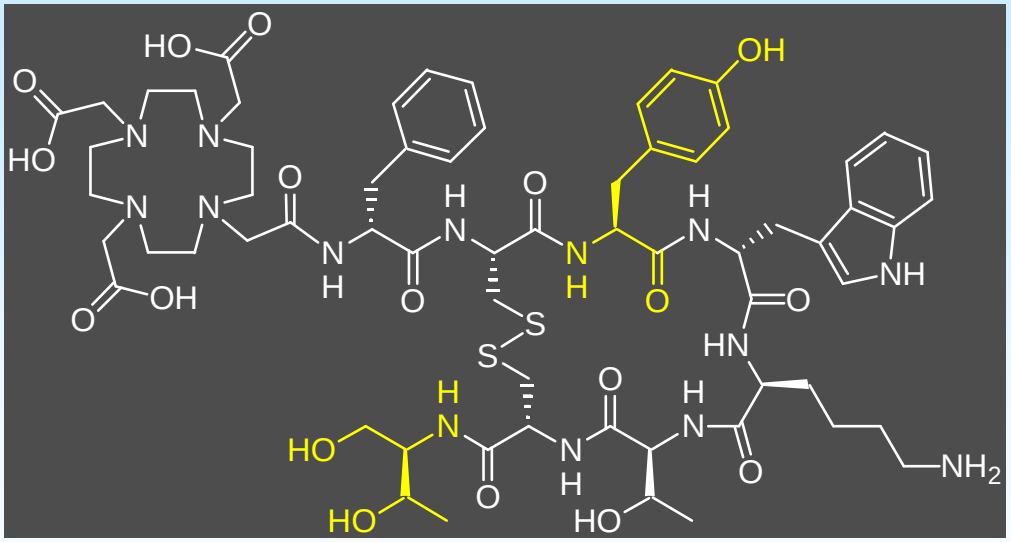
Universitätsspital Basel

Nuclear Medicine

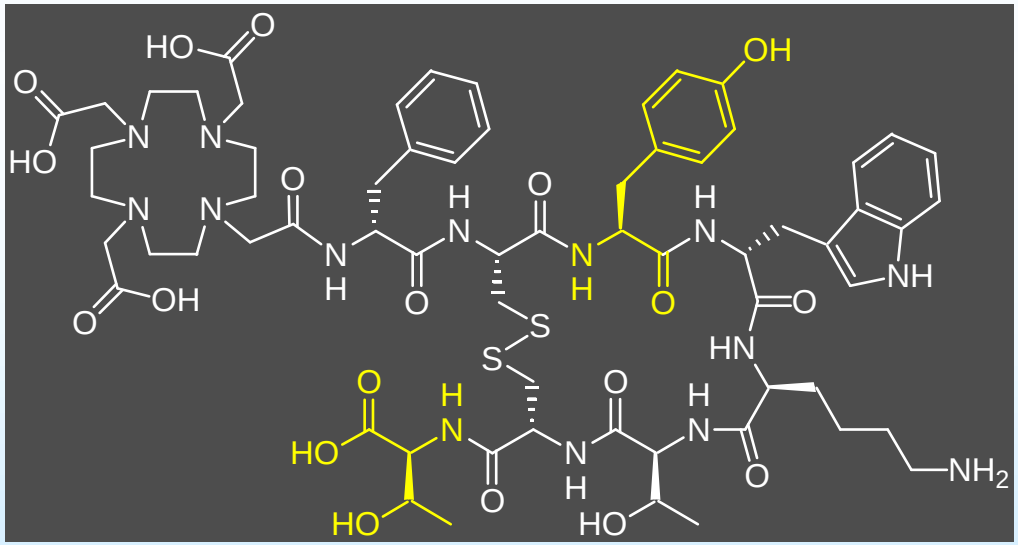
Background

- Both, ^{177}Lu-DOTATATE (DOTA-Tyr^{3}-Thr^{8}-Octreotide) and ^{90}Y-DOTATOC (DOTA-Tyr^{3}-Octreotide), are used for Peptide Receptor Mediated Radionuclide Therapy (PRMRT) in patients with metastatic neuroendocrine tumours.

- No direct comparison of biodistribution and dosimetry in patients has been performed with those two compounds.



DOTA-TOC
DOTA-Tyr^3-Octreotide



DOTA-TATE
DOTA-Tyr^3-Thr^8-Octreotide

Universitätsspital Basel

Nuclear Medicine

Methods

- 5 male patients (50-74 years) with known metastatic neuroendocrine tumours.
- All Patients were pretreated with ^{90}Y-DOTATOC. Time since treatment 14 - 25 months.

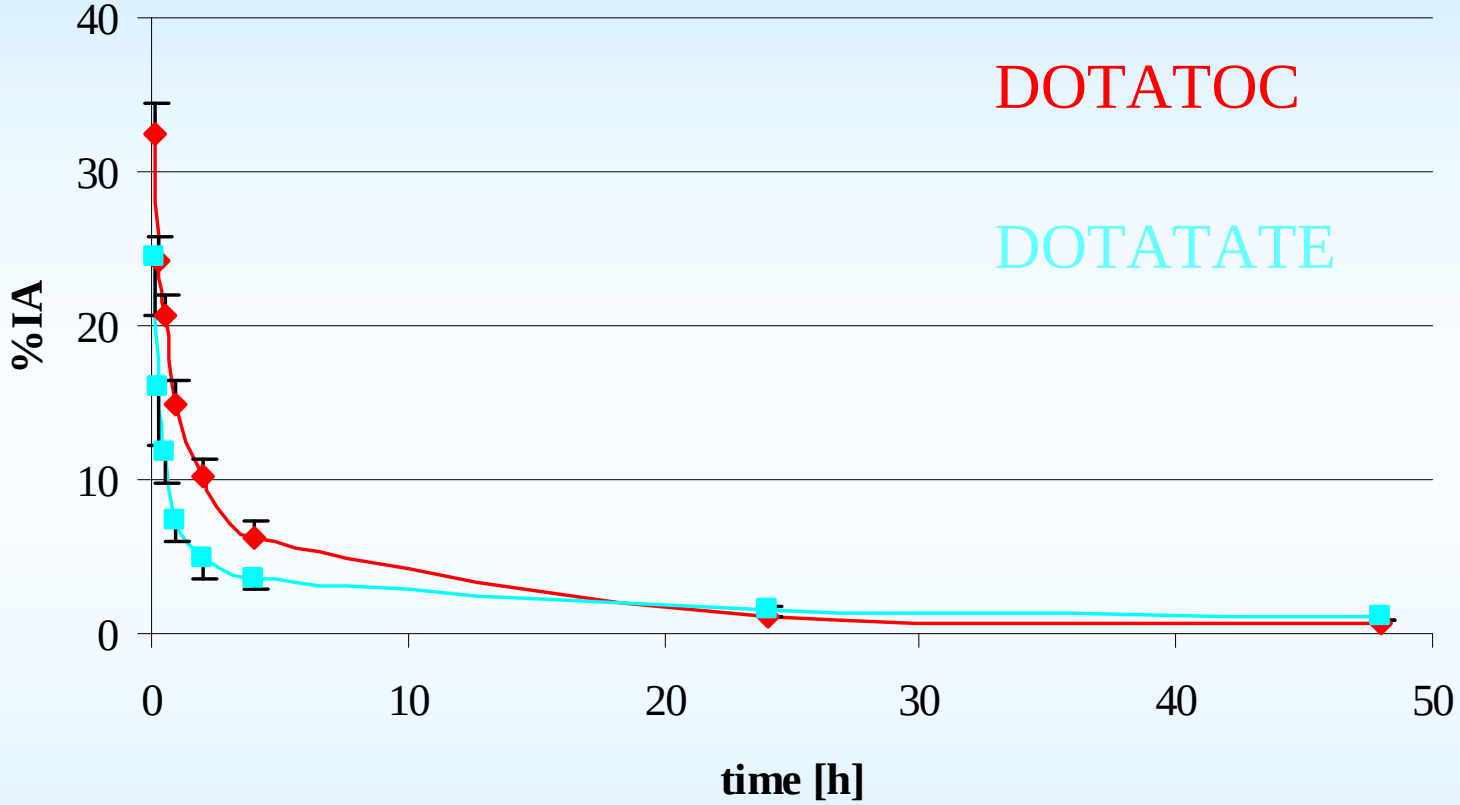
Methods

- Injection of 222 MBq ^{111}In-DOTATOC and 222 MBq ^{111}In-DOTATATE respectively in an interval of 2 weeks.
- Whole body scans were performed immediately, 1, 2, 4, 24 and 48 hours after injection with a dual head camera.
- Blood samples were drawn 10, 20, 30 and 60 minutes and 2, 4, 24 and 48 hours after injection.
- Urine was collected up to 48h p.i. (0-2 h, 2-4 h, 4-24 h, 24-48 h).

Methods

- We used ^{111}In as a surrogate for ^{90}Y.
- The dose for the whole body, the liver, the spleen, the kidneys and the clearly visible tumours were calculated with ROI-Technique and MIRDOSE 3.0.
- The dose to the red marrow was calculated from the activity in the blood.
- We used a compartment-model a described by *Cremonesi et al. (EJNM, August 1999).*

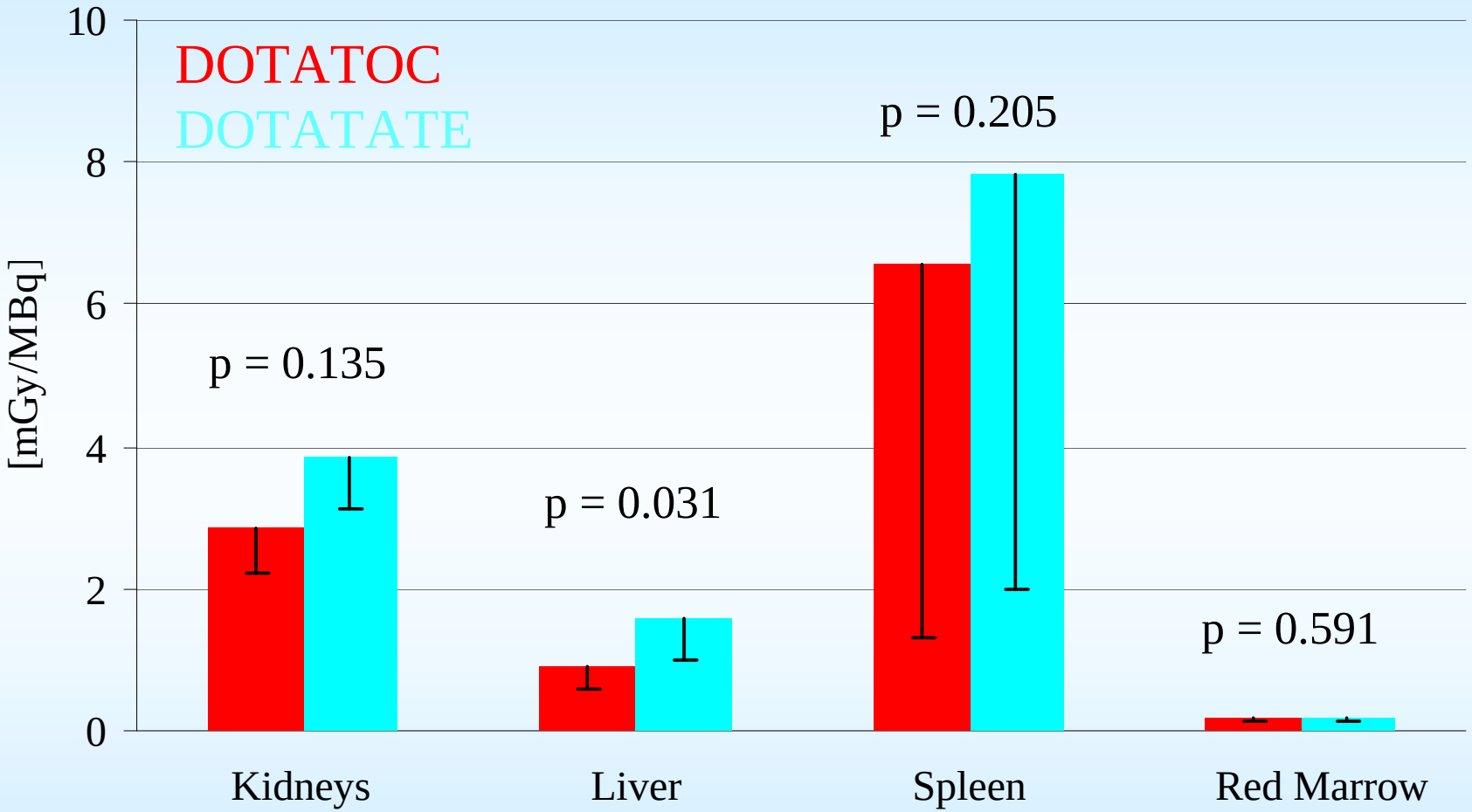
Bloodclearance



Universitätsspital Basel

Nuclear Medicine

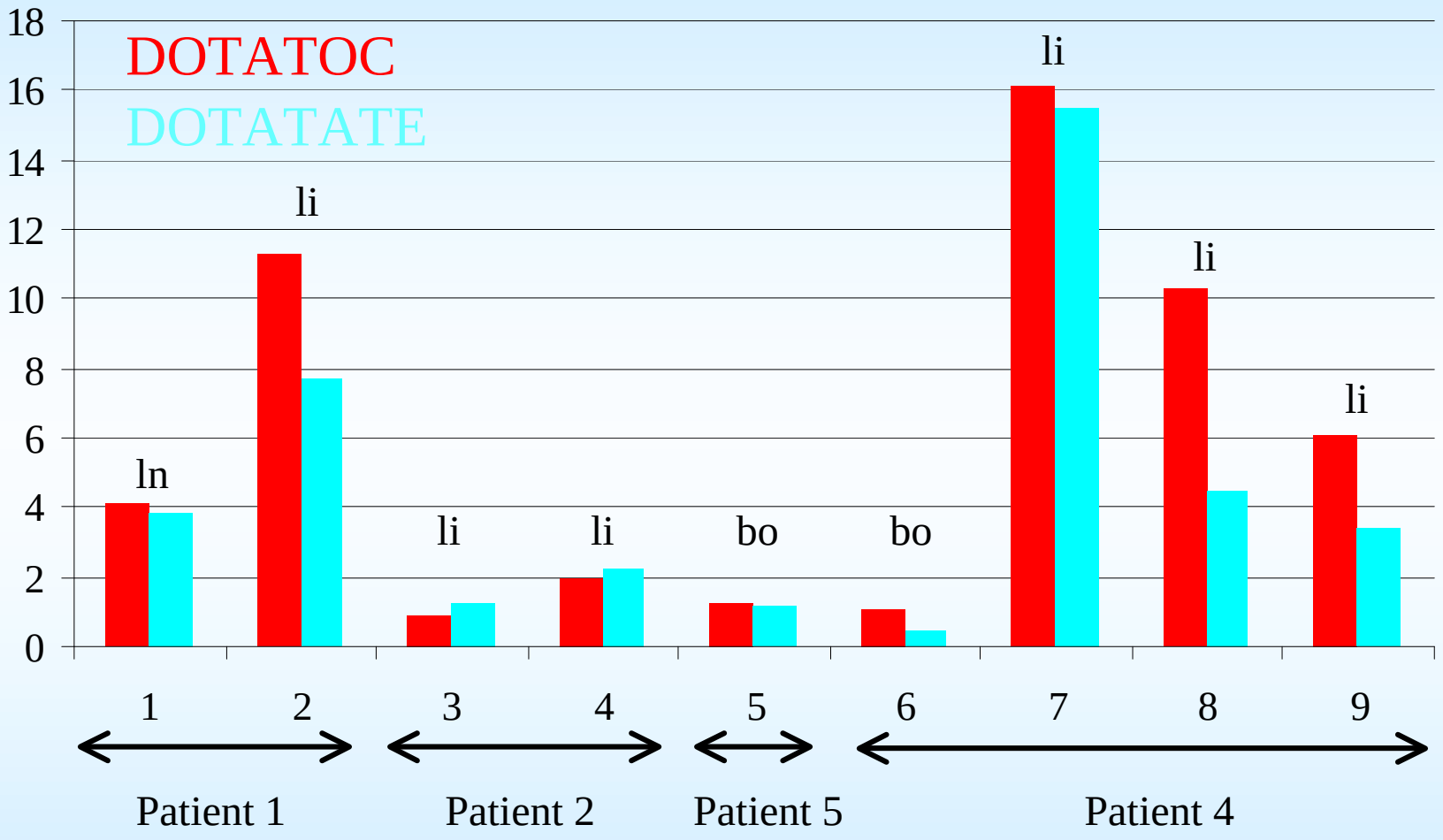
Absorbed Doses



Universitätsspital Basel

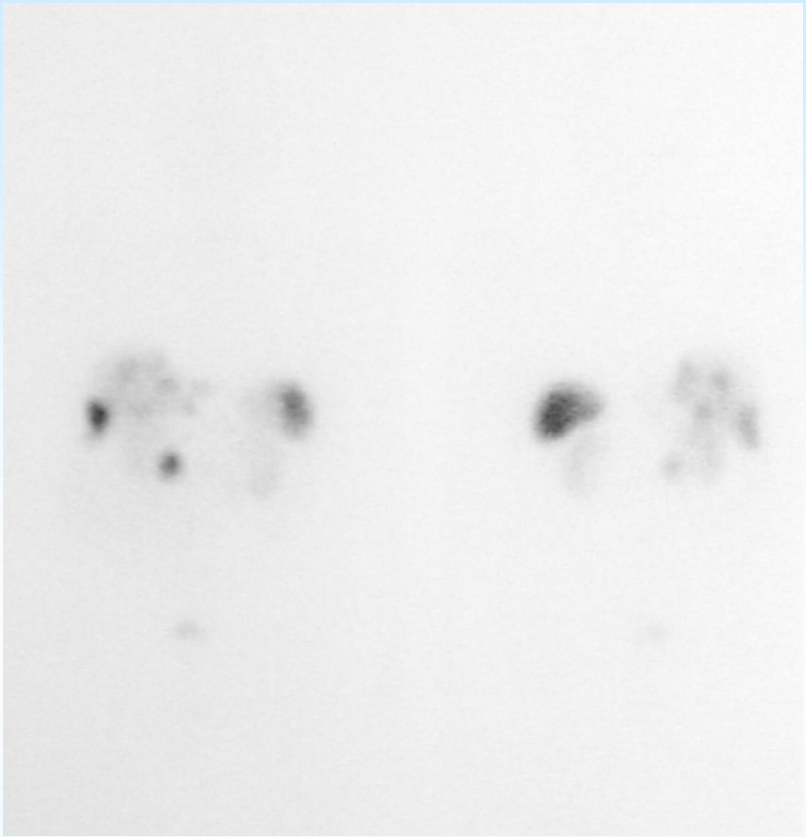
Nuclear Medicine

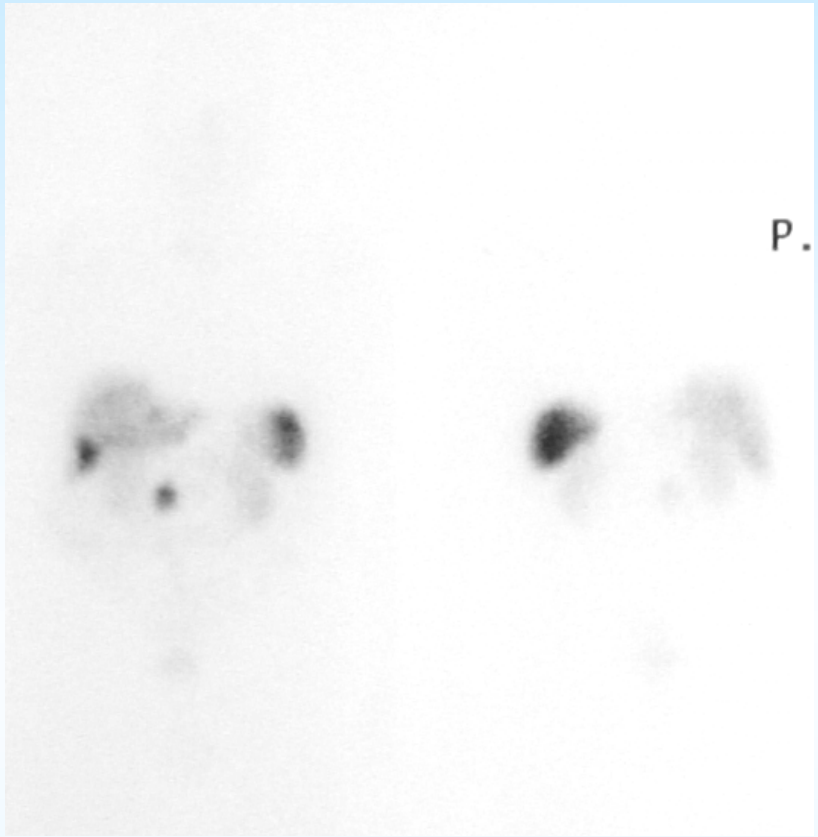
Tumour-to-Kidney-Ratio



Universitätsspital Basel

Nuclear Medicine





222 MBq
^{111}In- DOTATOC

24h p.i.

222 MBq
^{111}In- DOTATATE

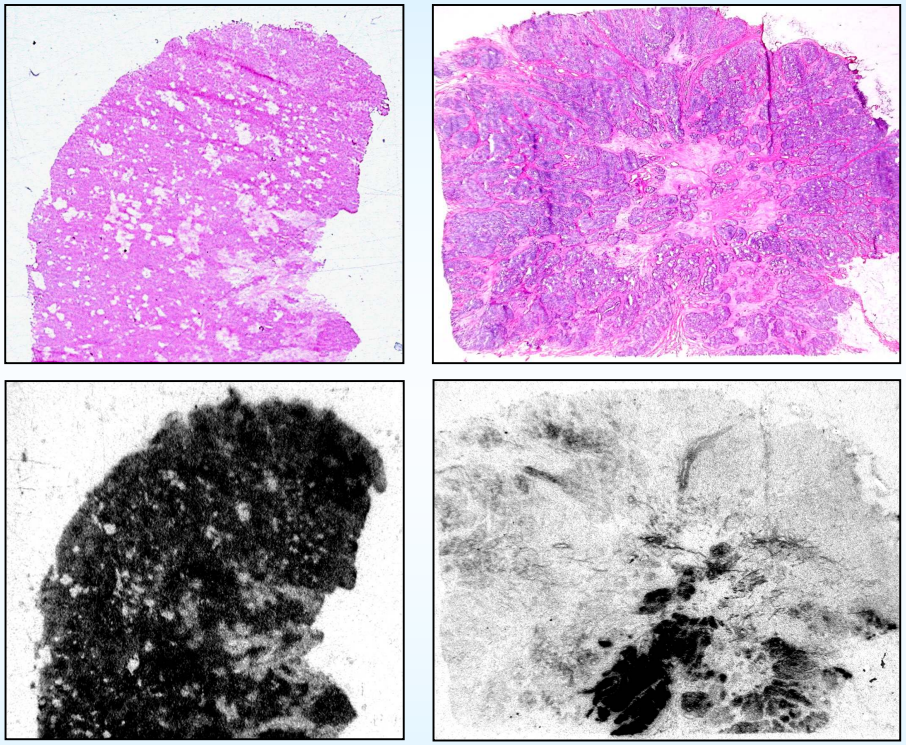
Universitätsspital Basel

Nuclear Medicine

Comparison of Absorbed Doses

	Forrer et al.	Cremonesi et al.	Förster et al.	Krenning et al.
derived from	^{111}In-DOTATOC	^{111}In-DOTATOC	^{86}Y-DOTATOC	^{86}Y-DOTATOC
Kidney	2.84 (±0.64)	3.31 (±2.22)	2.73 (±1.41)	2.1 (±0.78)
Liver	0.92 (±0.35)	0.72 (±0.57)	0.66 (±0.15)	-
Spleen	6.57 (±5.25)	7.62 (±6.30)	2.32 (±1.97)	1.83 (±1.45)
Red marrow	0.17 ±0.02)	0.03 (±0.01)	0.049 (±0.002)	0.11 (±0.06)

Variability in receptor homogeneity



Patho
Universität Bern

Radioimmunotherapy

- Radioimmunotherapy (RIT) showed convincing results with ^{90}Y and ^{131}I labelled antibodies in treatment of B-cell lymphoma
- The monoclonal antibody Rituximab is widely used for treatment of malignant lymphoma
- We are performing a clinical phase I/II study with ^{177}Lu-DOTA-Rituximab

Radioimmunotherapy with Lutetium-177-DOTA-Rituximab A Phase I/II - Study in Patients with Follicular and Mantle Cell Lymphoma

F. Forrer[1], A. Lohri[2], H. Uusijärvi[3], G. Moldenhauer[4], J. Chen[1], M. Dobbie[5], P. Schmid[5], R.Herrmann[5], H. Mäcke[1], J. Müller-Brand[1]

[1] Nuclear Medicine, University Hospital Basel, Switzerland

[2] Medical University Clinic, Oncology, Kantonsspital Liestal, Switzerland

[3] Department of Radiation Physics, University of Göteborg, Sweden

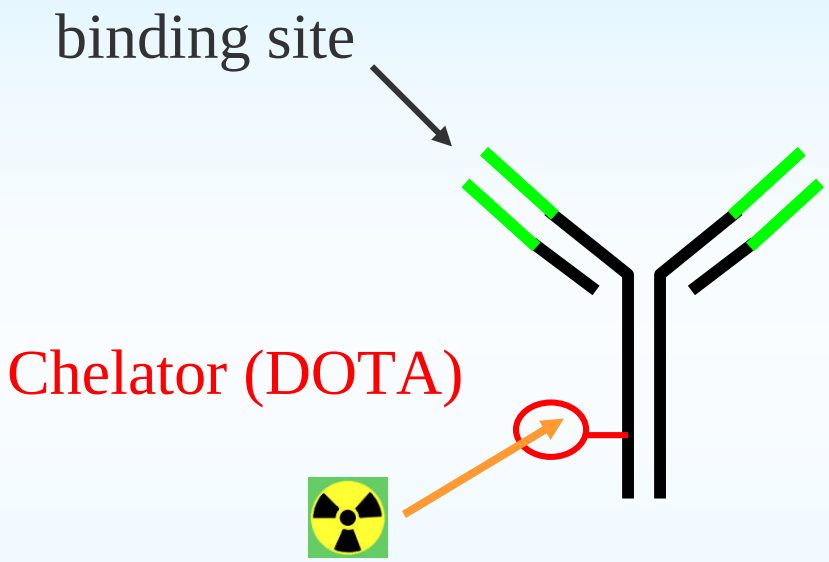
[4] Division of Molecular Immunology, German Cancer Research Center, Heidelberg, Germany

[5] Medical Oncology, University Hospital Basel, Switzerland

Universitätsspital Basel

Nuclear Medicine

Chimeric Radiolabelled Antibody



F_v = variable fragment

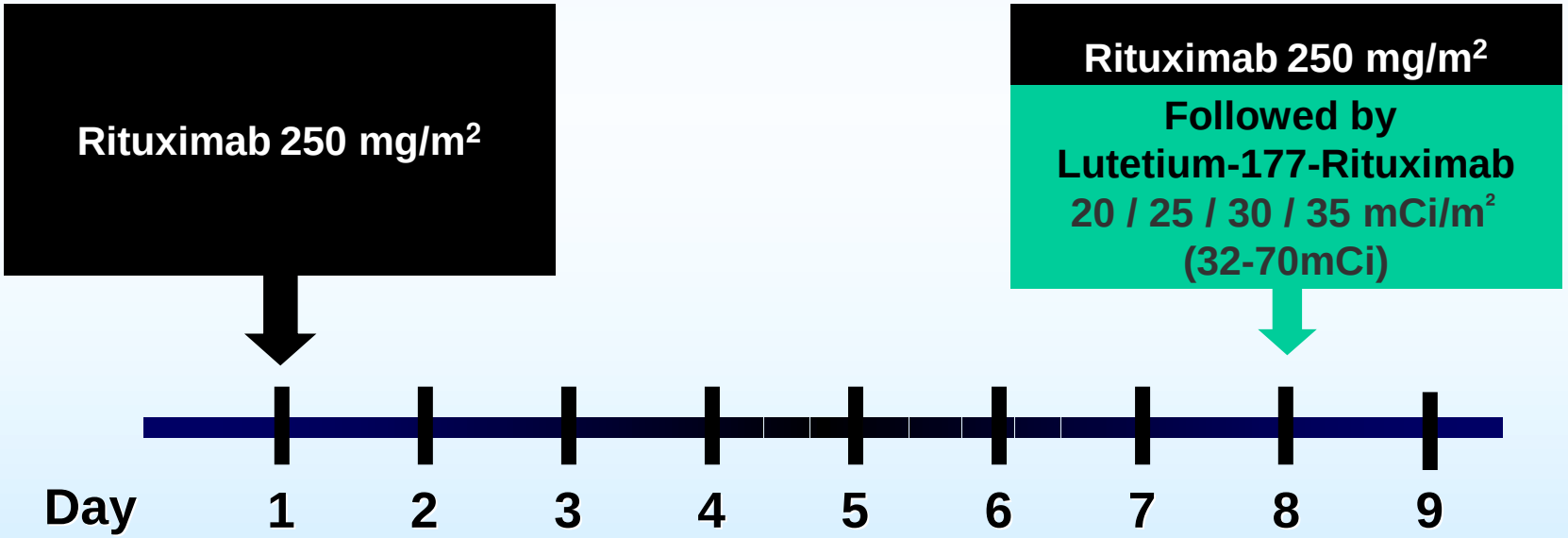
murine part

F_c = constant fragment

human part

Protocol ^{177}Lu-DOTA-Rituximab

- Staging: [^{18}F] FDG-PET, CT, bone marrow biopsy, blood counts, chemistry incl. creatinine



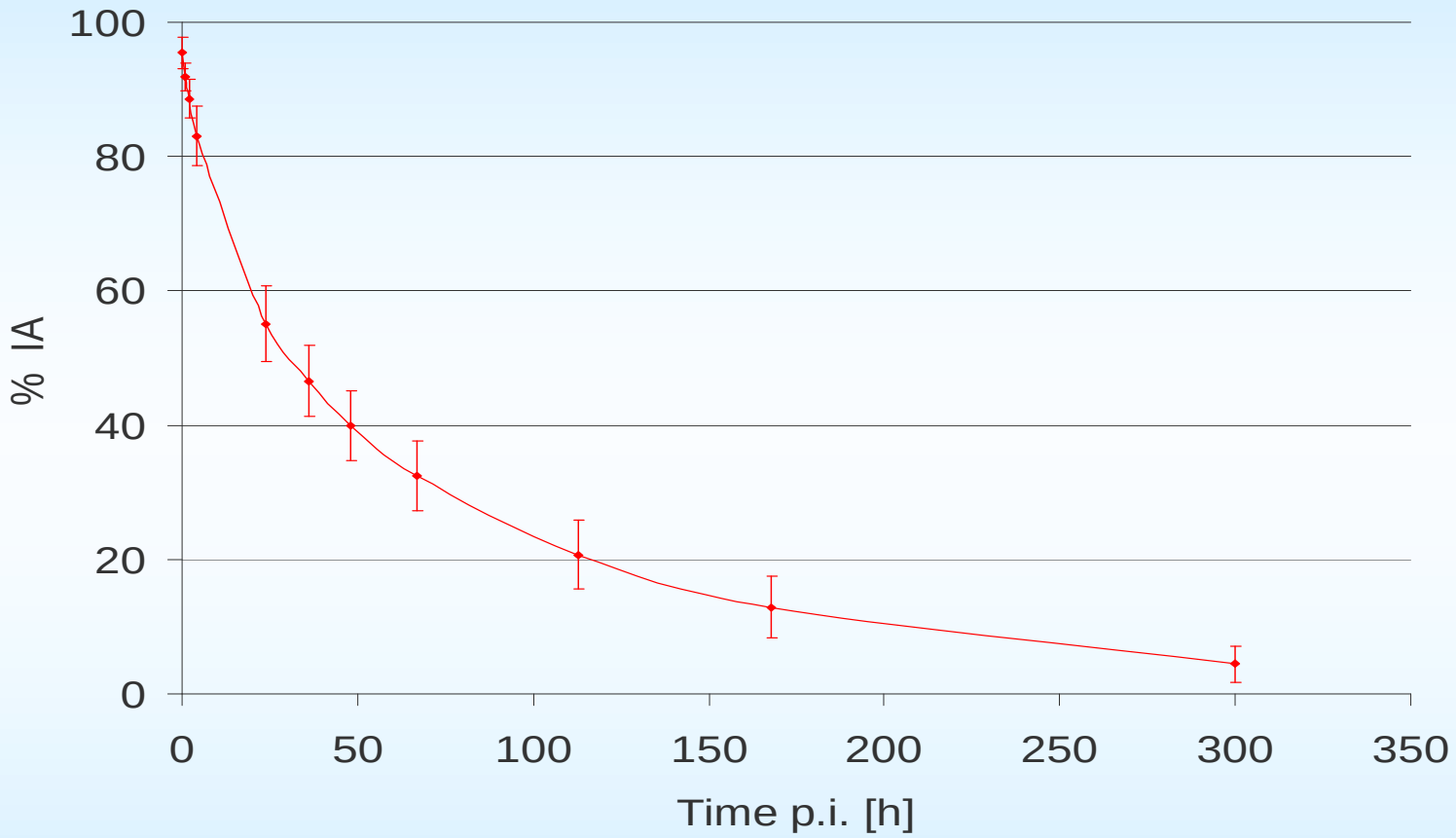
Universitätsspital Basel

Nuclear Medicine

Protocol ^{177}Lu-DOTA-Rituximab

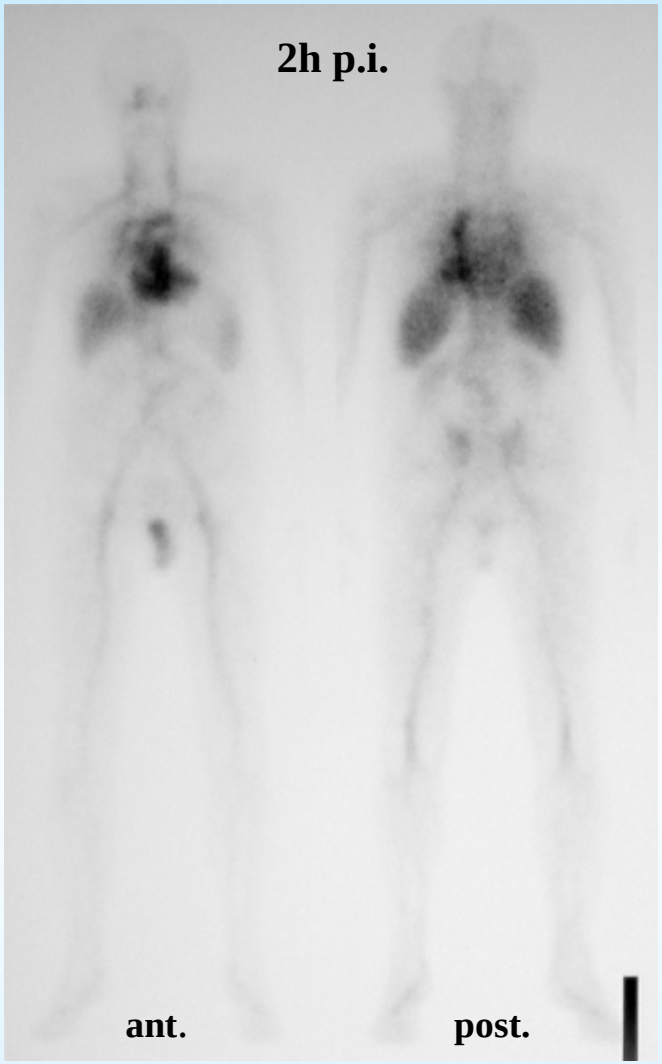
- Scintigraphic images, blood and urine samples up to 15 days p.i.
- Weekly blood counts and chemistry to week 8 or after resolution of nadir, then monthly
- Restaging after 2 month

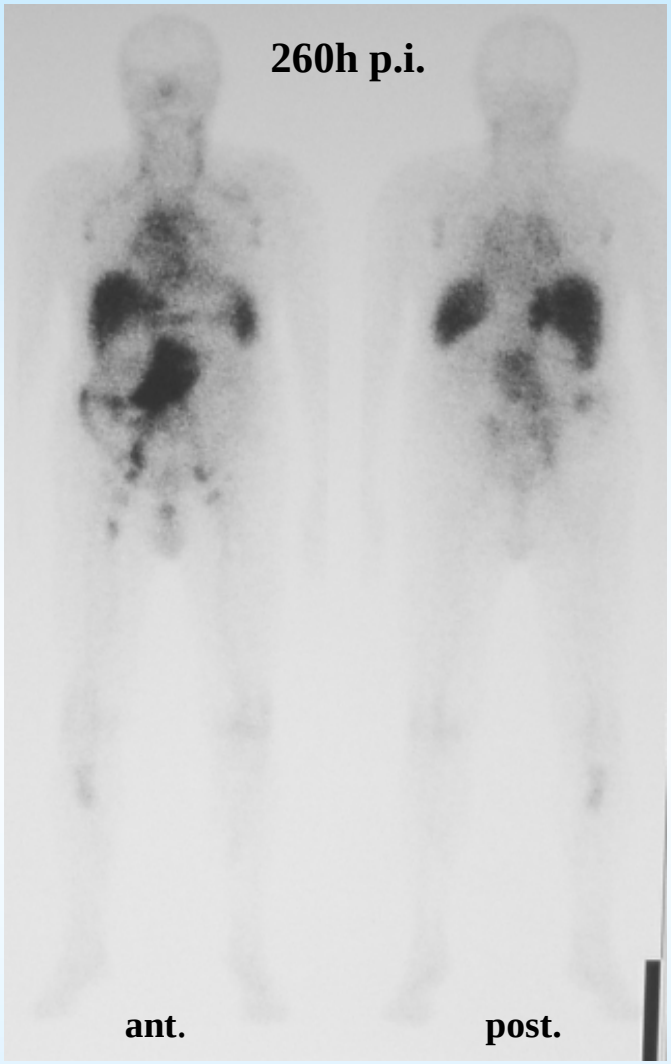
Blood Clearance



Universitätsspital Basel

Nuclear Medicine





2035 MBq (55 mCi) ^{177}Lu-DOTA-Rituximab

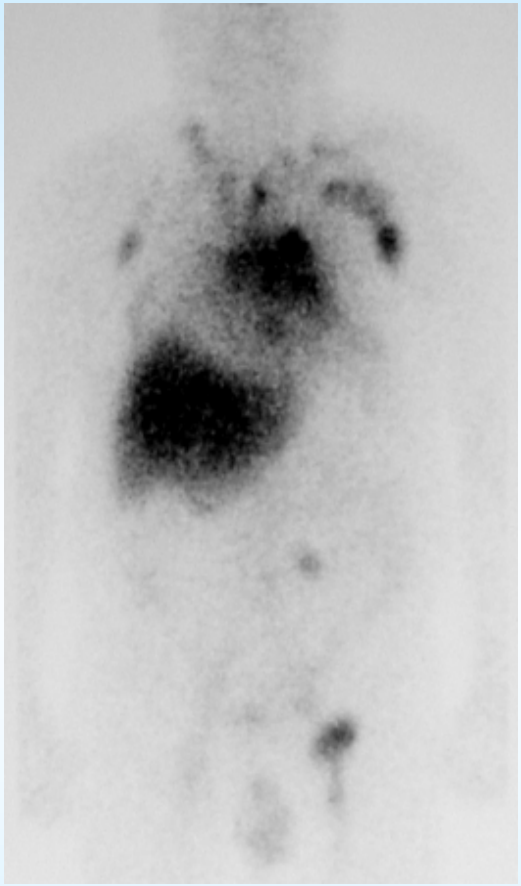
Universitätsspital Basel

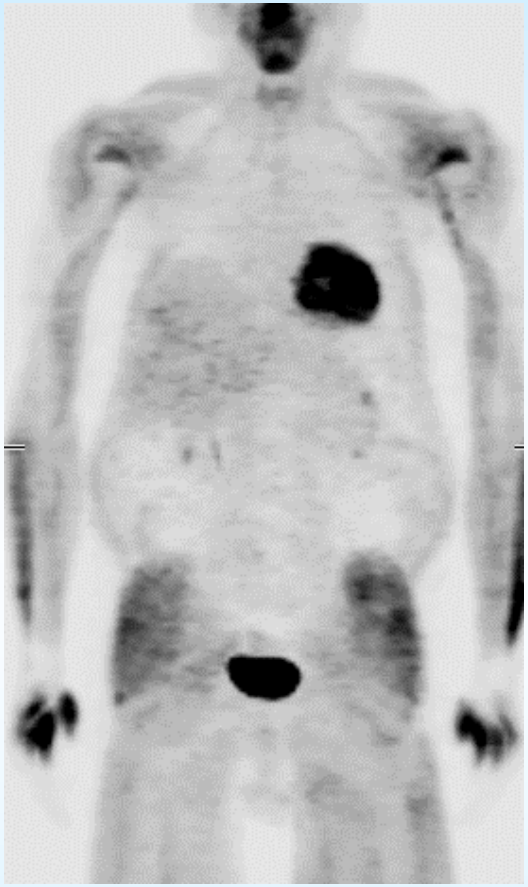
Nuclear Medicine

FDG-PET

^{177}Lu-DOTA-Rituximab

FDG-PET





Pre

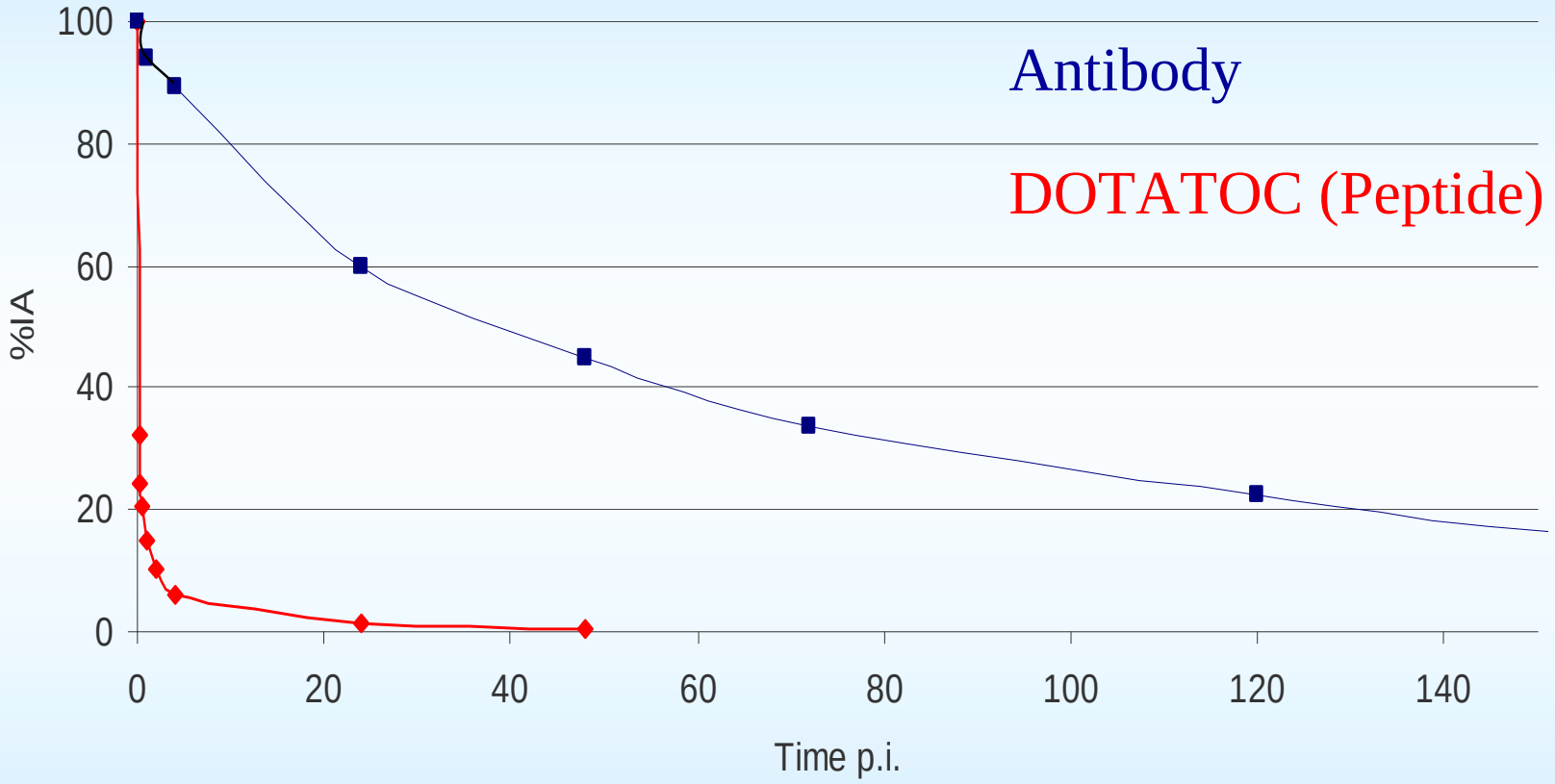
4d p.i.

Post

Universitätsspital Basel

Nuclear Medicine

Blood Clearance



Universitätsspital Basel

Nuclear Medicine

State of the art dosimetry in Nuclear Medicine

- In treatment of benign thyroid disorders obligatory
- Malignant thyroid tumors: fixed doses
- Phosphonates: fixed dose
- Radiopeptide: most often adapted to body surface
- Radioimmunotherapy: adapted to body weight / body surface

Conclusions

- Dosimetry in Nuclear Medicine therapy is not well established
- Accurate dosimetry could probably decrease toxicity
- New methods like SPECT-CT and PET-CT will help to simplify dosimetry
- In routine treatments a simple, accurate way of dosimetry is needed!

Conclusions

- To define a maximum tolerated injected activity, the maximum tolerated dose of normal tissue has to be known
- Not enough data are existing for low-dose-rate radiation
- Inhomogeneous distribution of activity causes problems in dosimetry

Thanks for your attention

fforrer@uhbs.ch