Universitätsklinikum Würzburg

Dosimetry of Nuclear Medicine Treatments

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Klinik und Poliklinik für Nuklearmedizin
Direktor: Prof. Dr. A. Buck

Contents

Nuclear Medicine Dosimetry

Diagnostics	Therapy
Low activities ~<1GBq, short-lived nuclides, γ/β^+ emitters	High activities ~>1GBq, long-lived nuclides, α/β^- emitters
Stochastic risk	Deterministic damage and stochastic risk
Model-based dosimetry in a representative group of volunteers or patients	Patient-specific dosimetry
Optimize image quality	Maximize tumor absorbed doses
Minimizing radiation-associated risk	Minimize the absorbed doses to the organs-at-risk

Main List of Isotopes used for Therapy

Radio-nuclide	Halflife (h)	β_{max} (MeV)	γ (keV)	Max. range (mm)
I-131	192	0.61	364	2.0
Y-90*	64	2.3	-	12
Lu-177	161	0.50	208	1.5
Ra-223	274	5.8 (α) ≈ 28 (α)	81/84/95/ 144/154/269	0.05

* β^+-Emitter (emission probability: $63.8 \cdot 10^{-6}$)

Alpha emitting isotopes for potential therapeutic applications in nuclear medicine

Radionuclide	Half-Life	Max. Particle Energy*
At-211	7.2 hrs	6.0 MeV
Bi-213	46 min	6.0 MeV
Ra-223	11.4 days	5.8 MeV
Ac-225	10.0 days	5.9 MeV

* without progeny

Therapy Modalities

Metabolic active radiopharmaceuticals

- Radioiodine Therapy of Thyroid Diseases (benign/malignant)
- Bone Pain Palliative Treatment of Bone Metastases (Ra-223)

Specifically binding radiopharmaceuticals

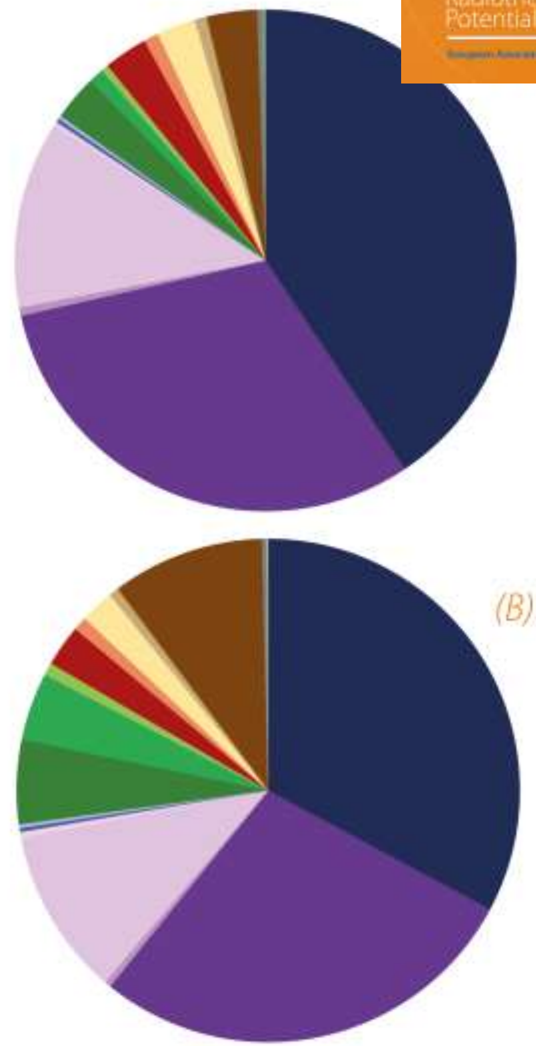
- Compounds addressing specific antigens or receptors
  - Dotatate or Dotatoc
  - MiBG
  - PSMA-labelling ligands
- Treatment of lymphoma using antibodies

Locoregional therapies

- Selective Internal radiotherapy
- Radiosynoviorthesis

Frequency of Treatments in Europe

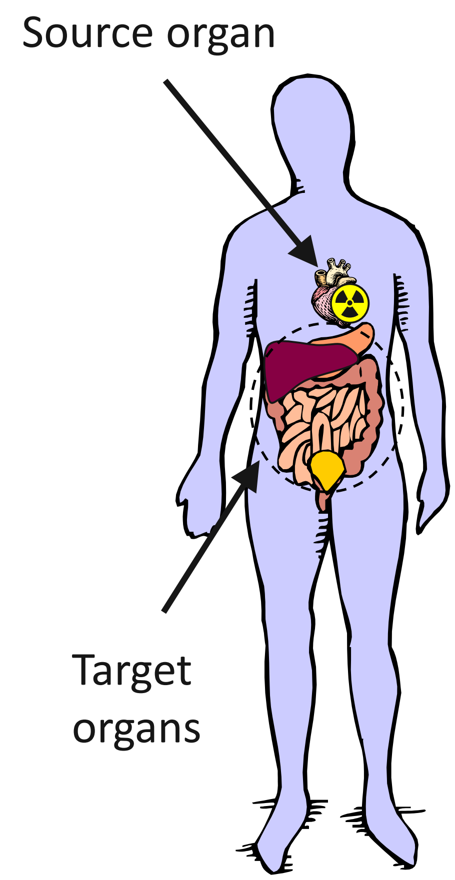
- ^{131}I-NaI for benign thyroid diseases
- ^{131}I-NaI for thyroid remnant ablation of adults
- ^{131}I-NaI for thyroid remnant ablation of children and young adults
- ^{131}I-NaI for thyroid cancer therapy for adults
- ^{131}I-NaI for thyroid cancer therapy for children and young adults
- ^{131}I-mIBG for neuroblastoma
- ^{131}I-mIBG for adult neuroendocrine tumours
- ^{177}Lu-somatostatin analogues for neuroendocrine tumours
- ^{90}Y-somatostatin analogues for neuroendocrine tumours
- ^{177}Lu-PSMA therapy of castration resistant prostate cancer
- ^{90}Y resin microspheres for intra-arterial treatments in the liver
- ^{90}Y glass microspheres for intra-arterial treatments in the liver
- Radiation synovectomy using ^{90}Y-, ^{186}Re- or ^{169}Er-colloids
- ^{153}Sm-EDTMP for bone metastases
- $^{89}SrCl_2$ (for bone metastases
- $^{223}RaCl_2$ for bone metastases
- ^{32}P sodium-phosphate ($Na_3{}^{32}PO_4$) for myeloproliferative disease
- ^{90}Y-ibritumomab-tiuxetan for B-cell lymphoma



Contents

Fundamentals of Nuclear Medicine Dosimetry

- The administered activity distributes in the body
- Based on cellular functions and physiology, it accumulates in individual organs in a different way (biodistribution and biokinetics)
- For assessing radiation-related risks, the absorbed dose in the individual organs needs to be calculated
- For calculating absorbed dose, a formalism called MIRD*-Scheme was developed in 1976 (summing over all organ contributions)



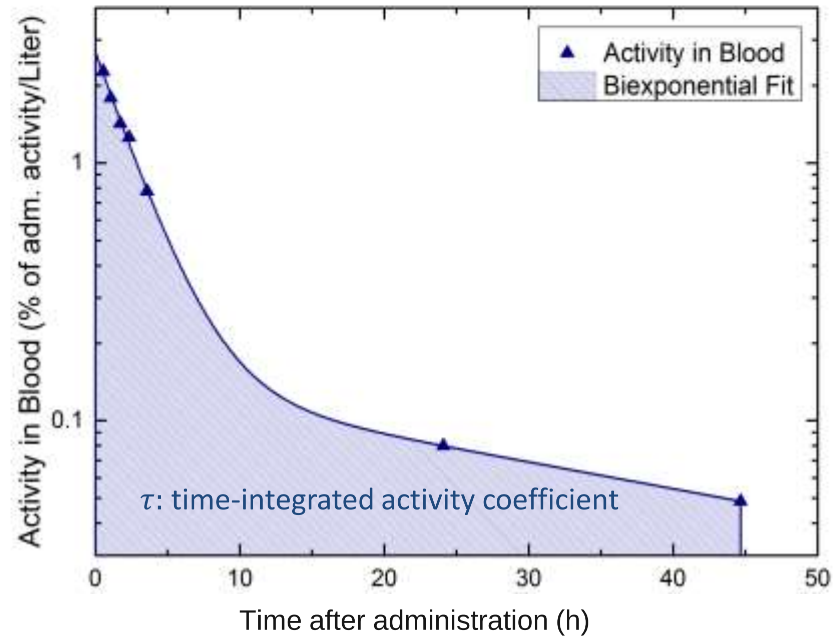
* *M*edical *I*nternal *R*adiation *D*ose - group of the Society of Nuclear Medicine, USA

MIRD Formalism*

- The mean absorbed dose D_T in the individual target organ T
- Assumption: activity is distributed uniformly in the organs

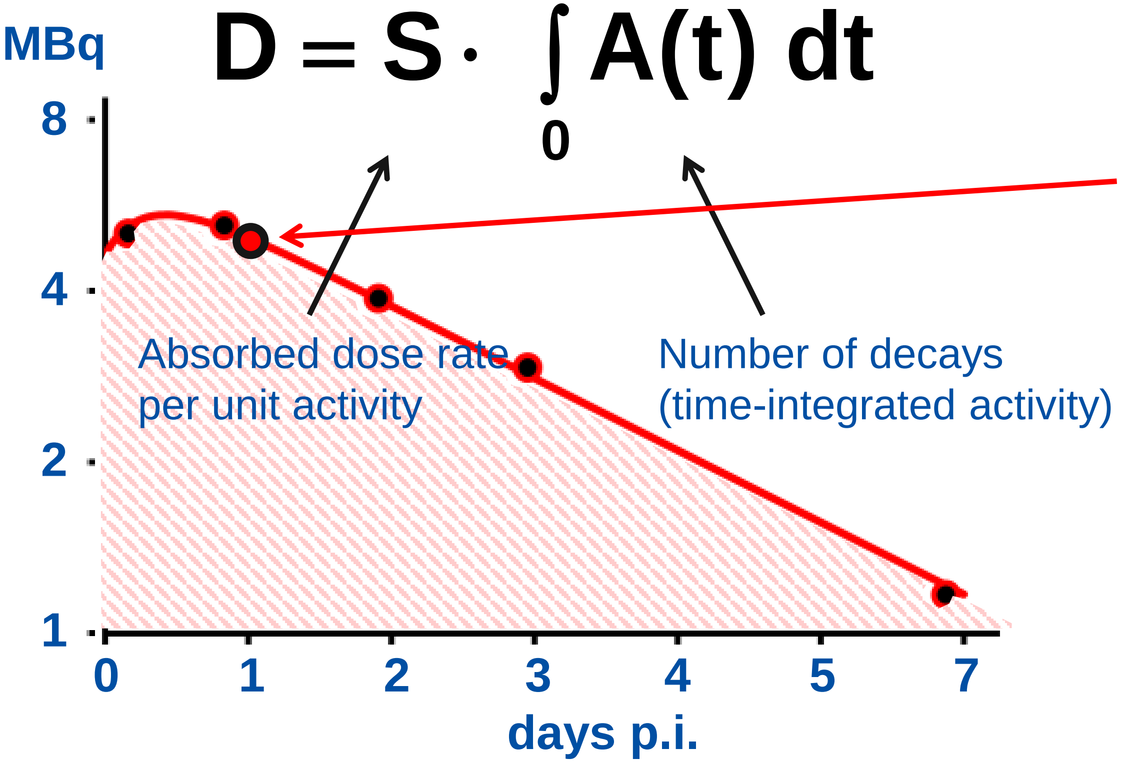
- $D_T = A_0 \cdot \sum_S \int_0^\infty A_S(t')\,dt' \cdot S_{T\leftarrow S} = A_0 \cdot \sum_S \tau_S \cdot S_{T\leftarrow S}$

  - A_0 : administered activity
  - $A_S(t')$: time activity curve of the source organ
  - τ: time-integrated activity coefficient
  - $S_{T\leftarrow S}$: mean absorbed dose per nuclear disintegration in the target organ
    - Nuclide specific
    - Geometry dependent



Dosimetry in Nuclear Medicine

$$D = S \cdot \int_0^\infty A(t)\, dt$$



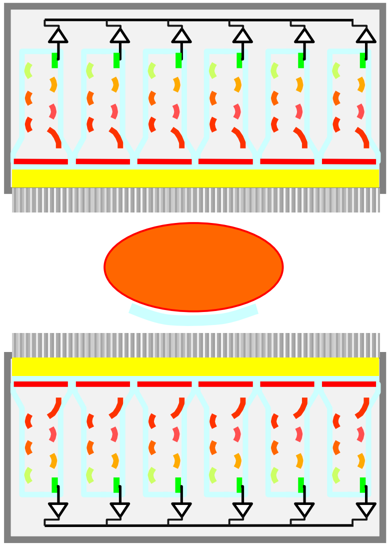
Absorbed Dose Limits for Organs-at-Risk

Bone Marrow:	2 Gy
Kidneys (Emami 1991):	23 Gy
Kidneys (Threshold, MIRD 20):	33 Gy BED
Salivary Glands (Buchali 1991):	20 Gy
Lacrimal Glands (Parsons 1996):	40 Gy
Nasal Mucuous Membrane (Yin 2010):	37 Gy

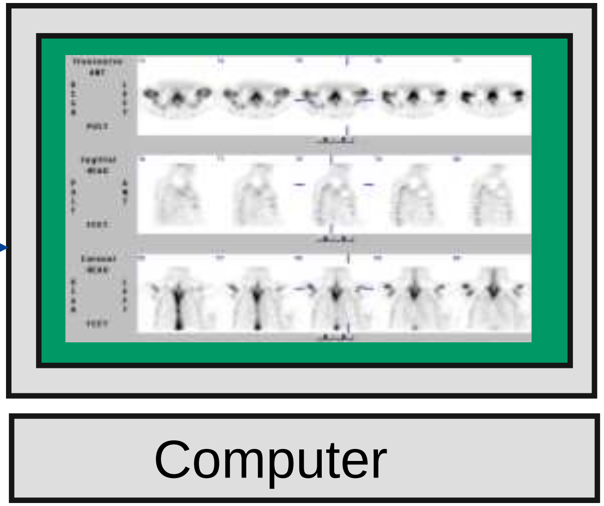
Three Steps to Calculate Absorbed Doses

I. Quantitative Imaging (multiple time-points)

Quantitative SPECT (Single Photon Emission Computer Tomography)



- Isotope
- Energy Resolution
- Collimator
- Electronics
- Spatial Resolution
- Calibration Source
- Attenuation
- Scatter
- Noise
- Reconstruction
- Partial Volume Effect



SPECT/CT

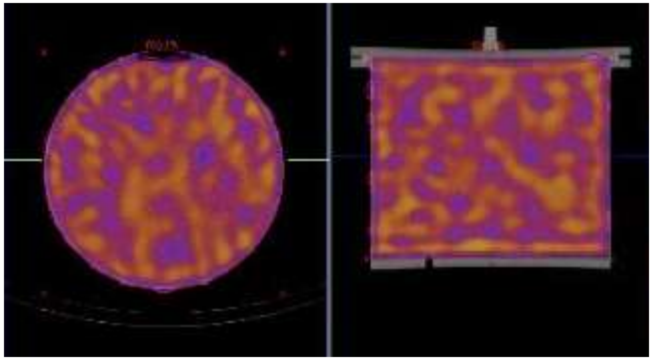
<u>integrated CT</u>

- morphologic correlation
- Measurement of the attenuation map
- Scatter correction by using triple window techniques
- quantitative Analysis

Validation of a SPECT/CT Quantification

<u>Calibration Experiment</u>

- ► Intevo Bold (0.95cm crystal)
- ► Jaszczak phantom (6.7 L)
  + Lu-177 solution (73.5 kBq/mL)
- ► SPECT-CT acquisition
  (MELP, 60×30s views, NCO)
- ► xSPECT Reconstruction
  (48 iterations, 1 subset, no filtering)
- ► VOI around entire phantom
  → Activity in Bq/mL



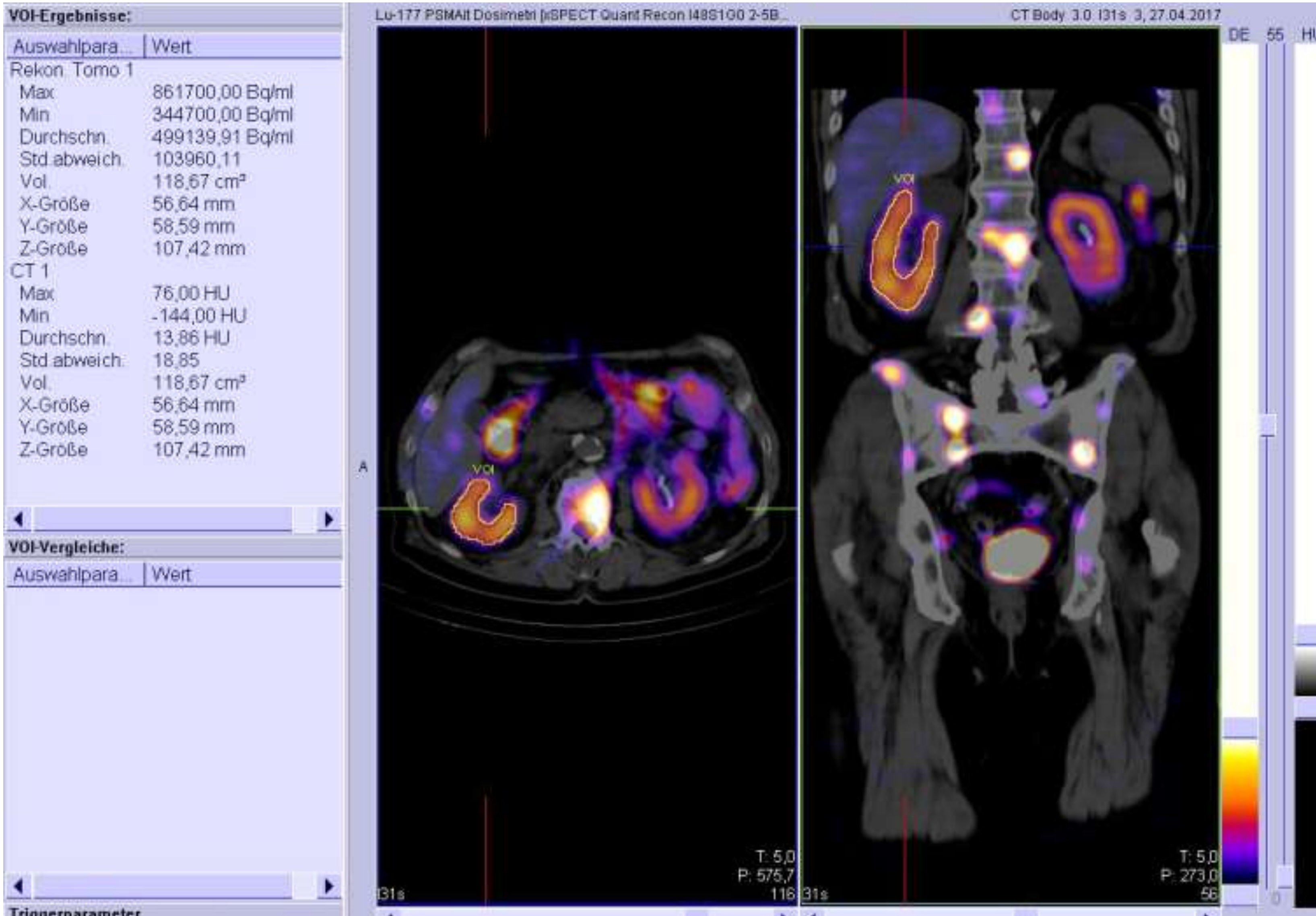
xSPECT Reconstruction

Dose Calibrator: 490.6 MBq

xSPECT Quant: 496.5 MBq

→ **Error of only 1.2%**

Methods: xSpect i48s1G0

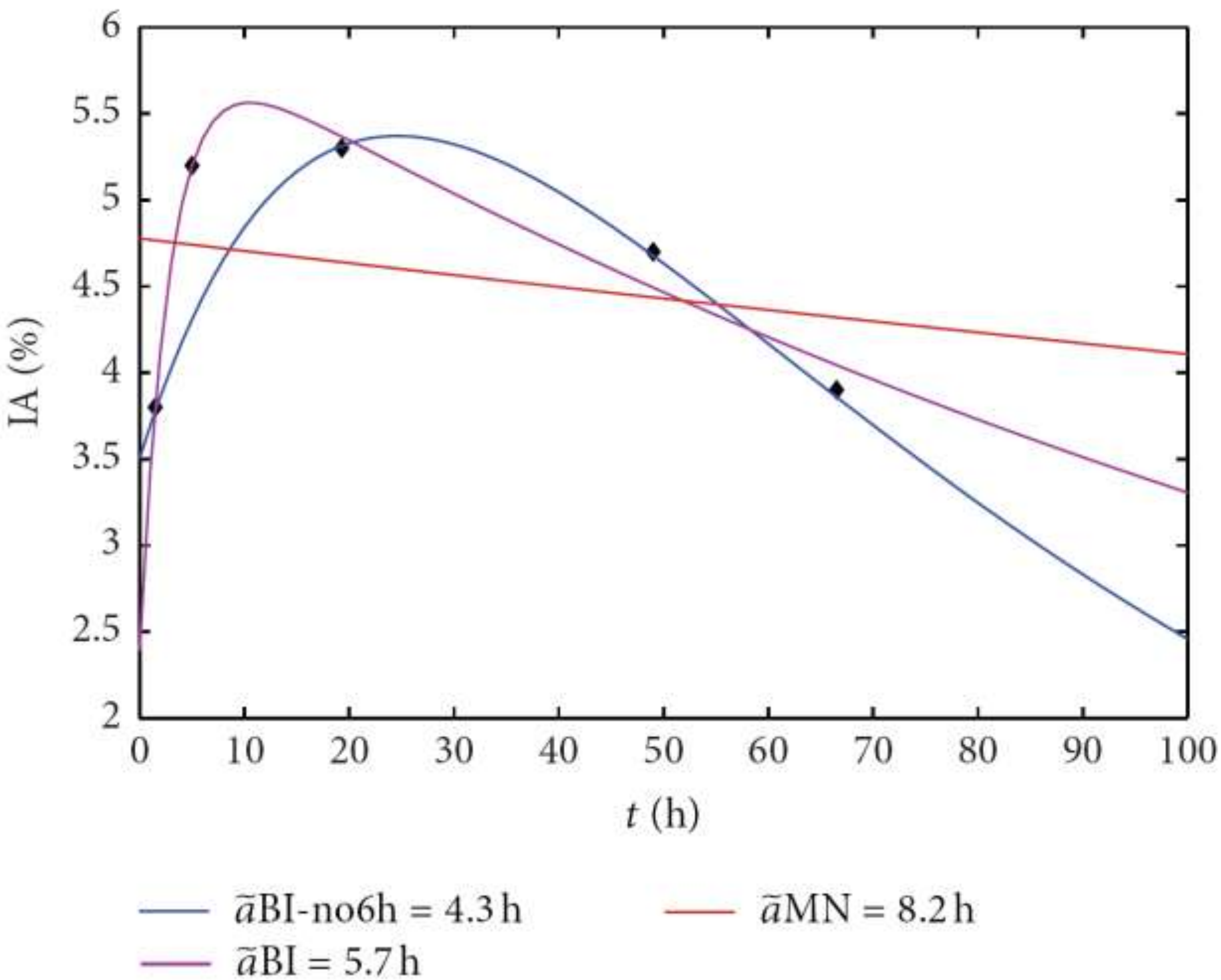


Three Steps to Calculate Absorbed Doses

I. Quantitative Imaging (multiple time-points)

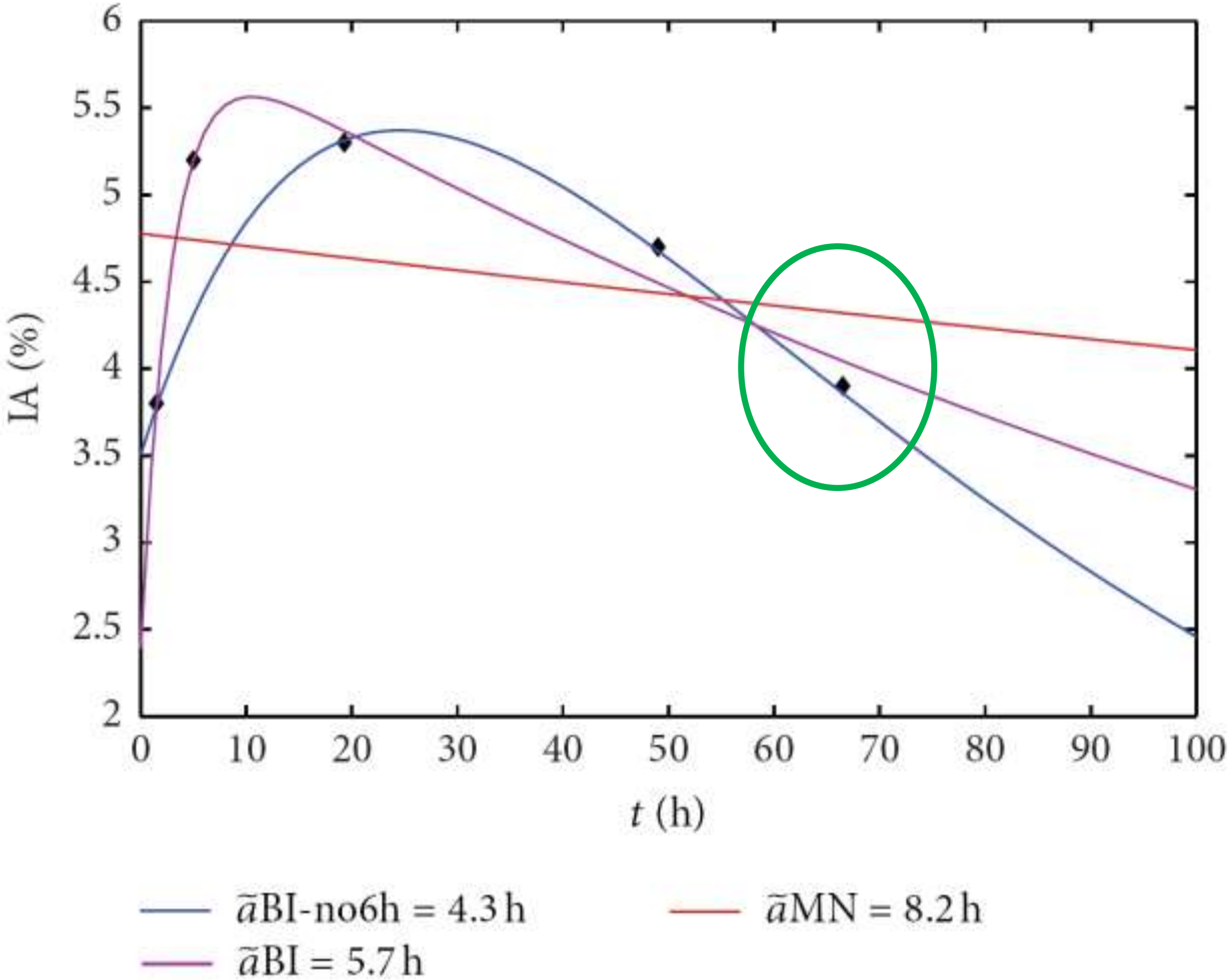
II. Integration of the Time-Activity Curve

Three Steps to Calculate Absorbed Doses
II Integration of the Time-Activity Curve



Guerriero et al. Kidney dosimetry in ^{177}Lu and ^{90}Y peptide receptor radionuclide therapy: influence of image timing, time-activity integration method, and risk factors. Biomed Res Int. 2013;2013:935351.

Three Steps to Calculate Absorbed Doses
II Integration of the Time-Activity Curve



Guerriero et al. Kidney dosimetry in ^{177}Lu and ^{90}Y peptide receptor radionuclide therapy: influence of image timing, time-activity integration method, and risk factors. Biomed Res Int. 2013;2013:935351.

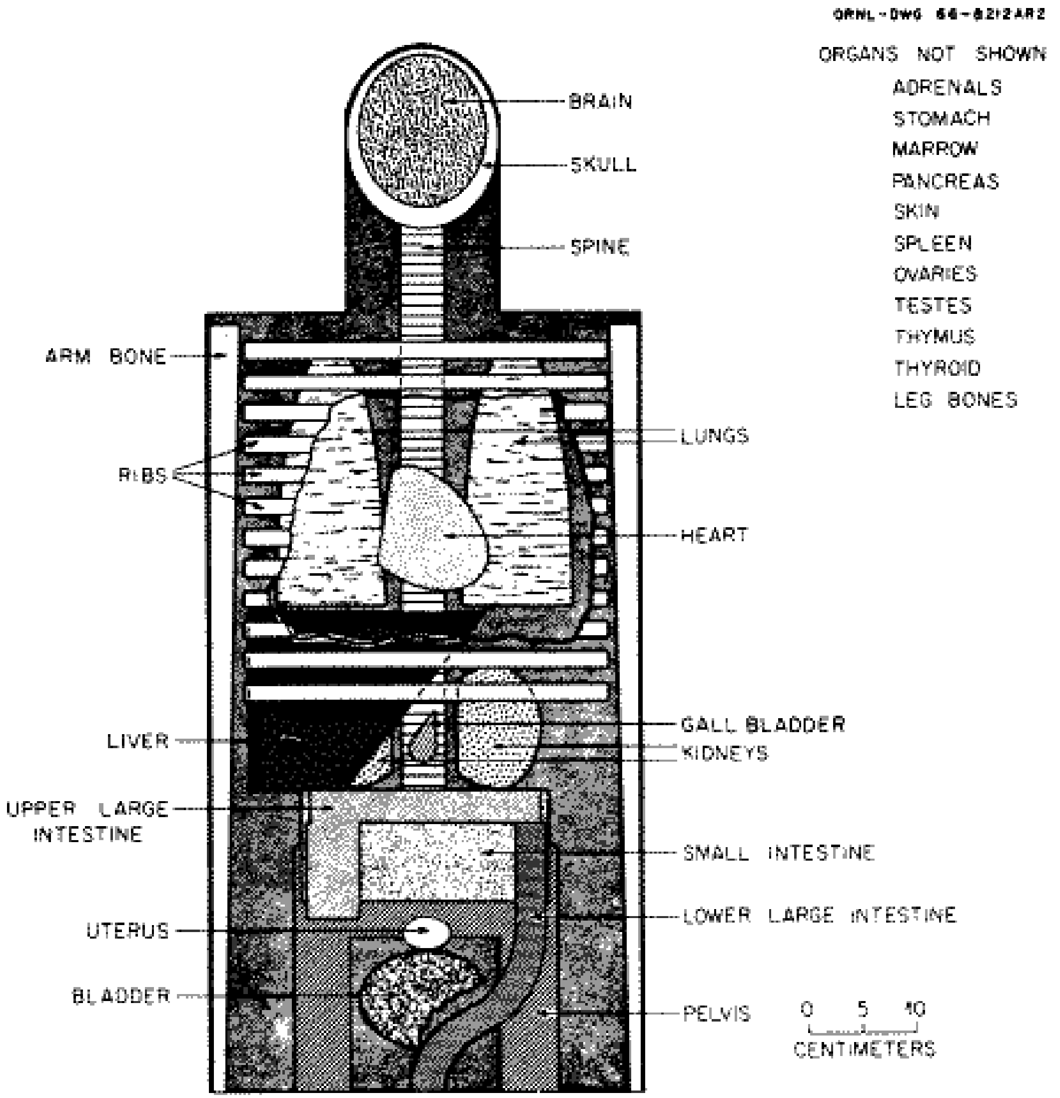
Three Steps to Calculate Absorbed Doses

I. Quantitative Imaging (multiple time-points)

II. Integration of the Time-Activity Curve

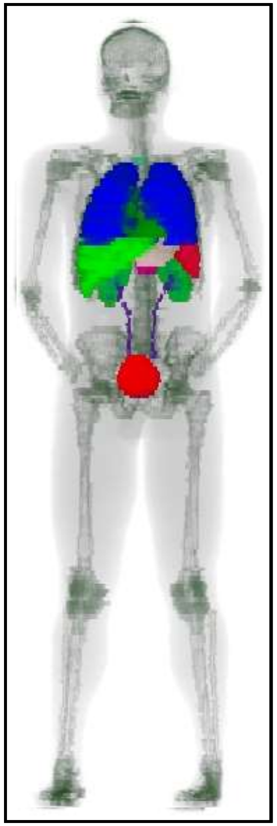
III. Determination of the S-Values

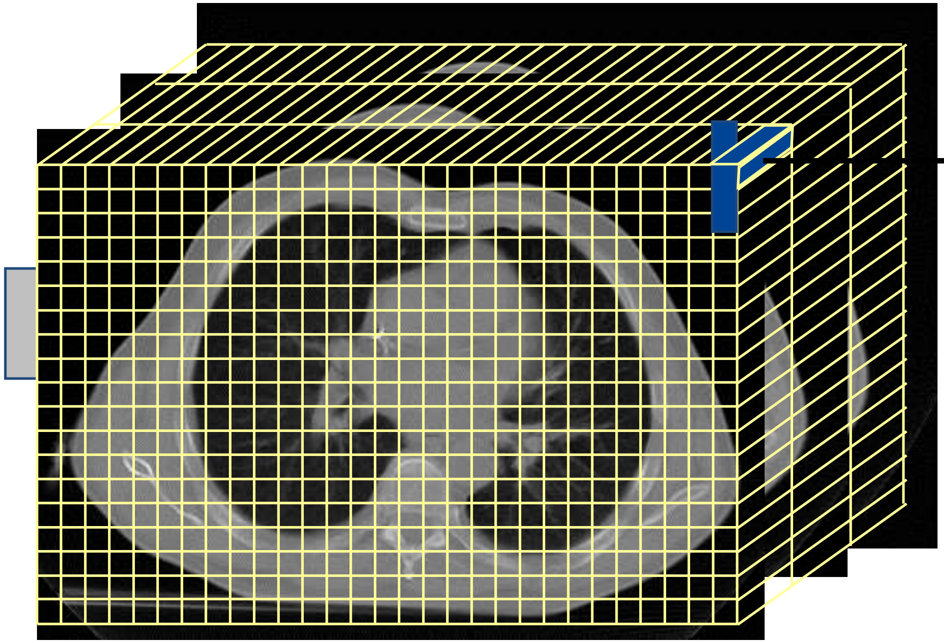
Anthropomorphic phantoms

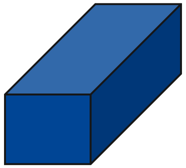


Human anatomy representation:
- simplified organ shapes
- realistic density

Patient specific dosimetry





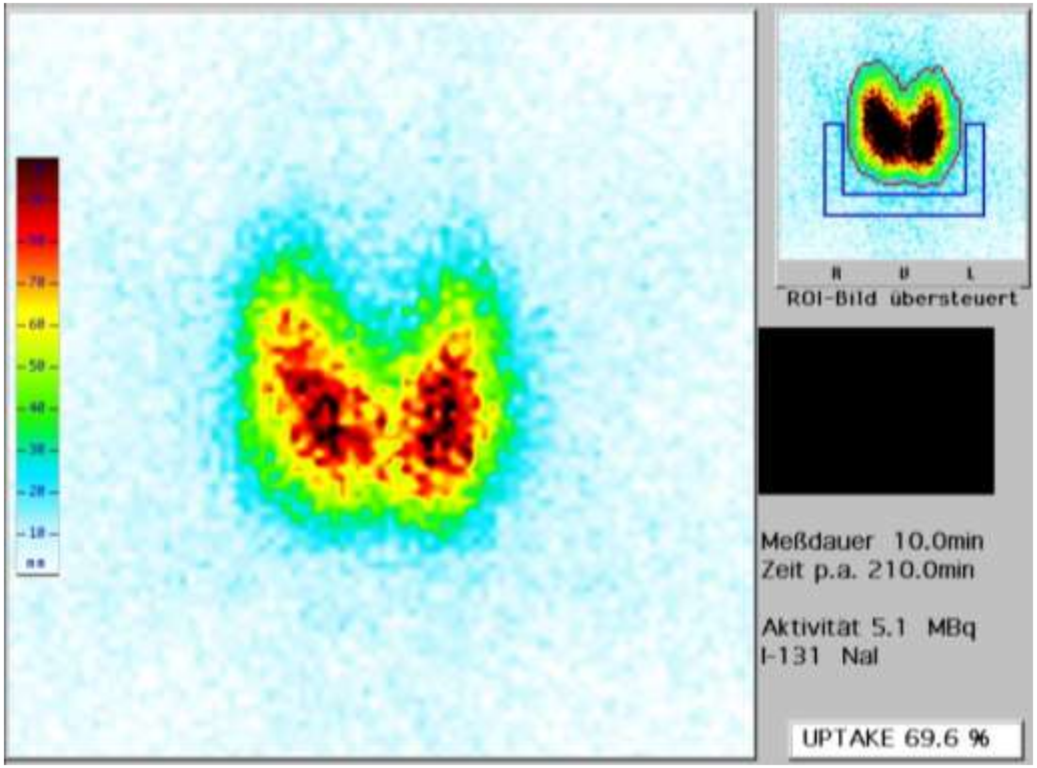


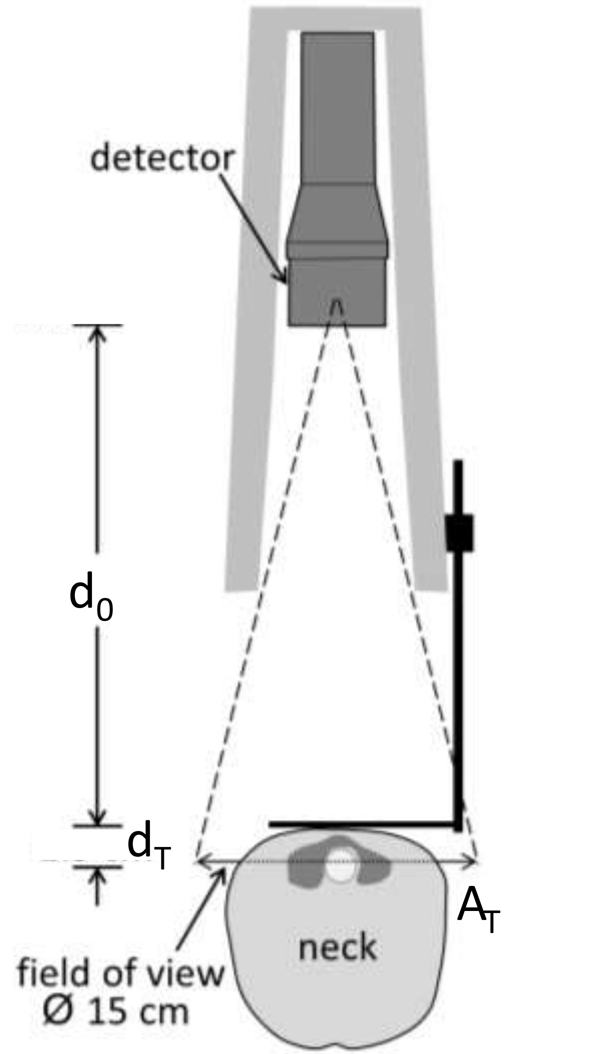
voxel

Specific S values

Contents

The Treatment of Benign Thyroid Diseases with I-131





Dosing: Either fixed activities (< 1 GBq) or dosing based on pre-therapeutic dosimetry

The Treatment of Benign Thyroid Diseases

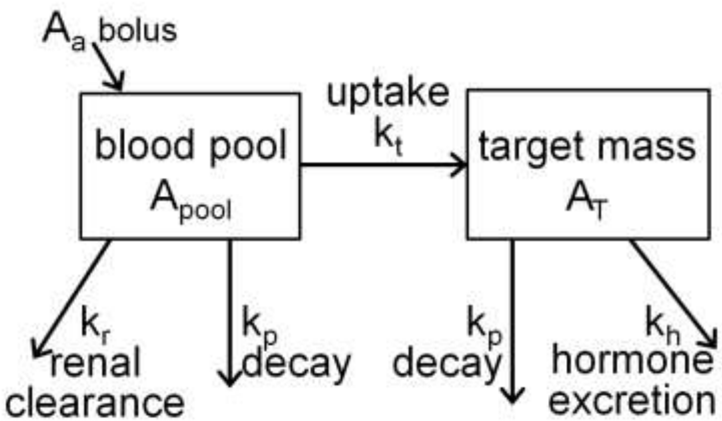
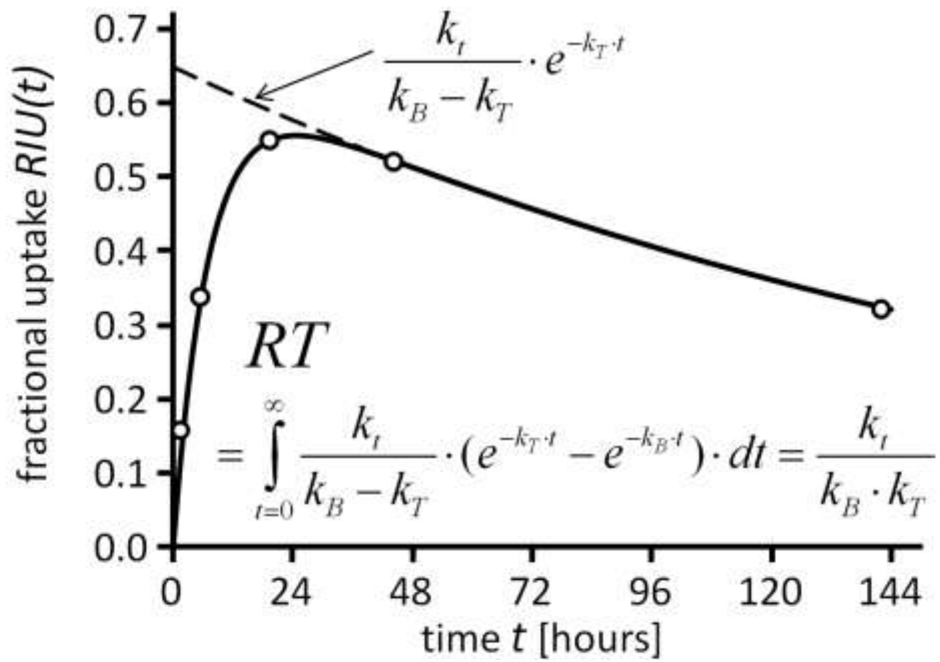


Fig. S3 *Model of the* ^{131}I *kinetics in benign thyroid disease with 2 compartments, blood pool and target mass.* A_x *denote activities,* k_x *transfer rates.*



Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-013-2387-x

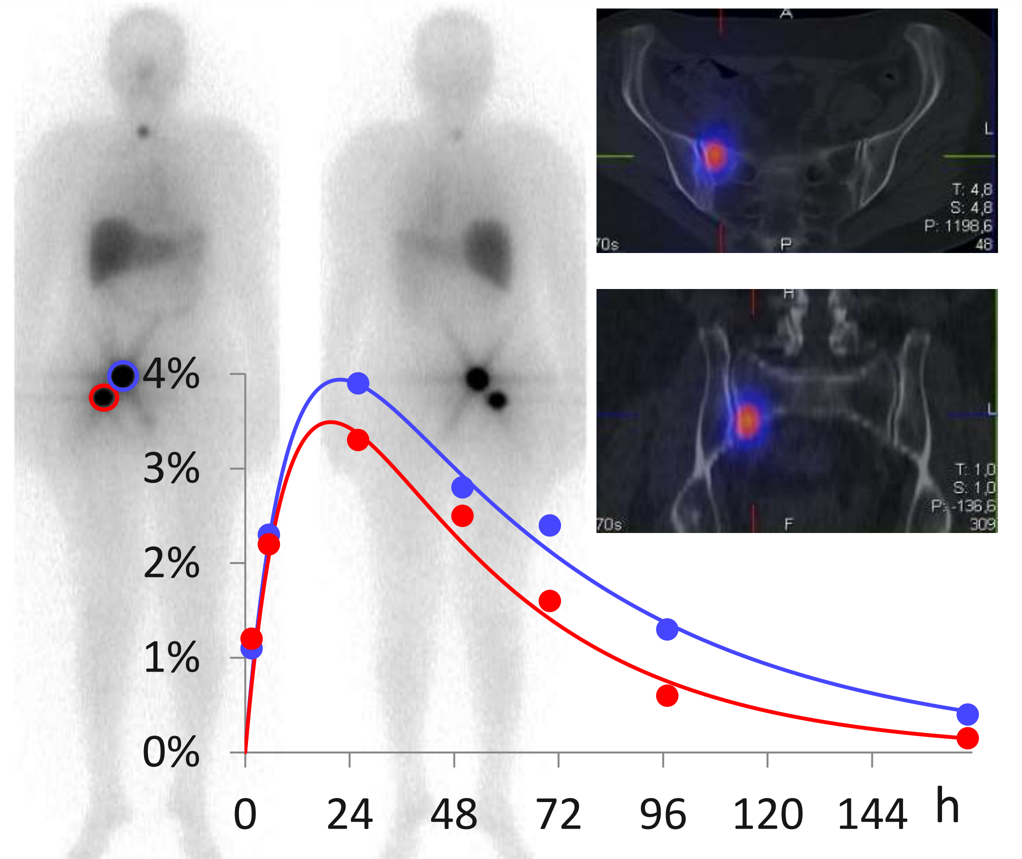
GUIDELINES

EANM Dosimetry Committee Series on Standard Operational Procedures for Pre-Therapeutic Dosimetry II. Dosimetry prior to radioiodine therapy of benign thyroid diseases

Heribert Hänscheid · Cristina Canzi · Wolfgang Eschner · Glenn Flux · Markus Luster · Lidia Strigari · Michael Lassmann

Radioiodine Therapy of Thyroid Cancer with I-131

$$D(r_T) = \sum_S \left(\int A(r_S, t)\,dt \cdot S(r_T \leftarrow r_S) \right)$$

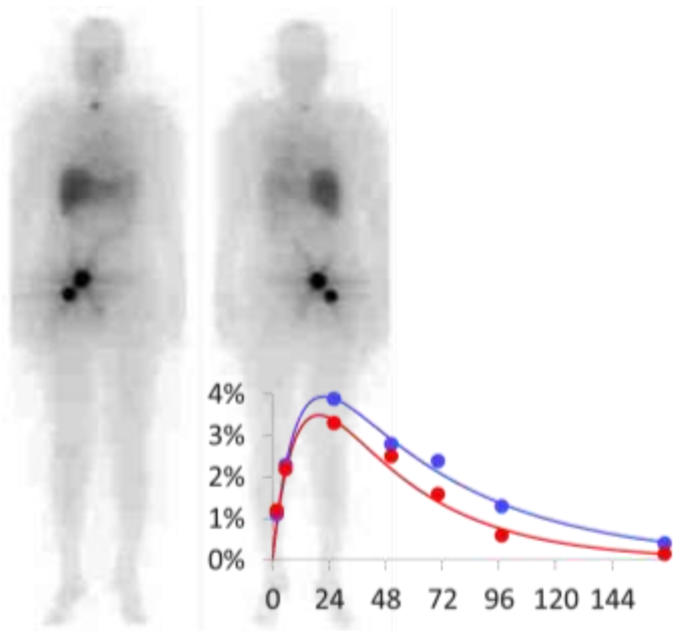


Title:
Z Med Phys
December 2011

Dosing: Either fixed activities (> 1 GBq) or dosing based on pre-therapeutic dosimetry

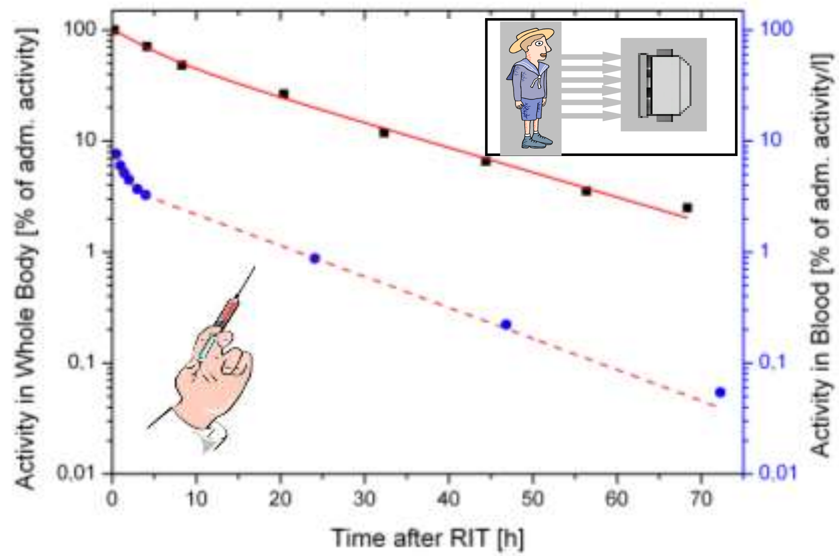
The Role of Dosimetry in the Treatment of Thyroid Cancer

Lesion Dosimetry



Dose to the Lesion in Gy/GBq

Blood (Bone Marrow) Dosimetry



Critical Blood Activity (max 2 Gy)

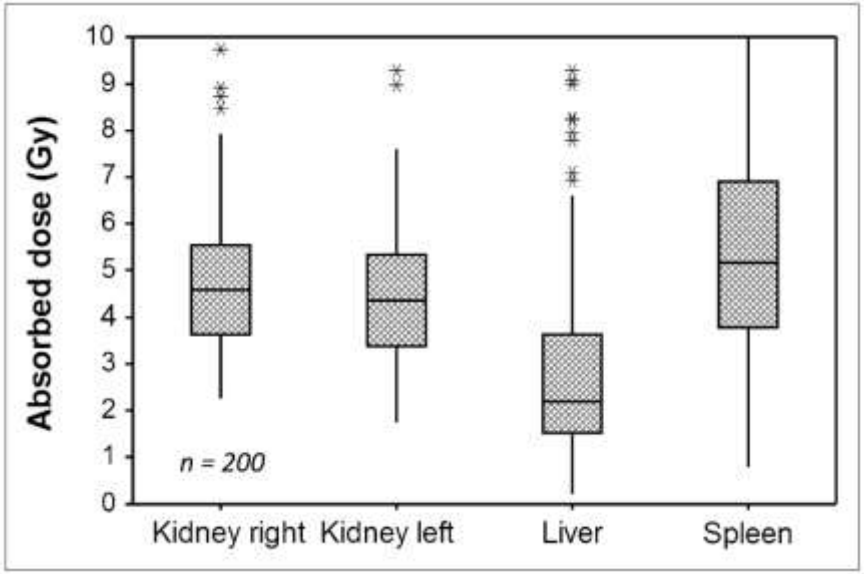
Eur J Nucl Med Mol Imaging (2008) 35:1405–1412
DOI 10.1007/s00259-008-0761-x

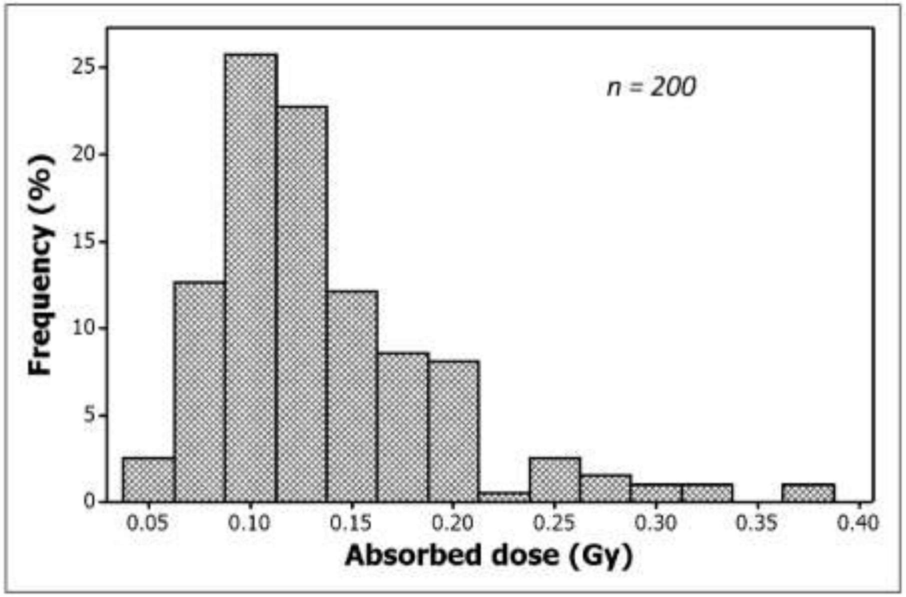
GUIDELINES

EANM Dosimetry Committee series on standard operational procedures for pre-therapeutic dosimetry
I: blood and bone marrow dosimetry in differentiated thyroid cancer therapy

Michael Lassmann · Heribert Hänscheid ·
Carlo Chiesa · Cecilia Hindorf · Glenn Flux ·

The Treatment of Neuroendocrine Tumors





Dosing: 4 or more cycles of 7.4 GBq Lu-177

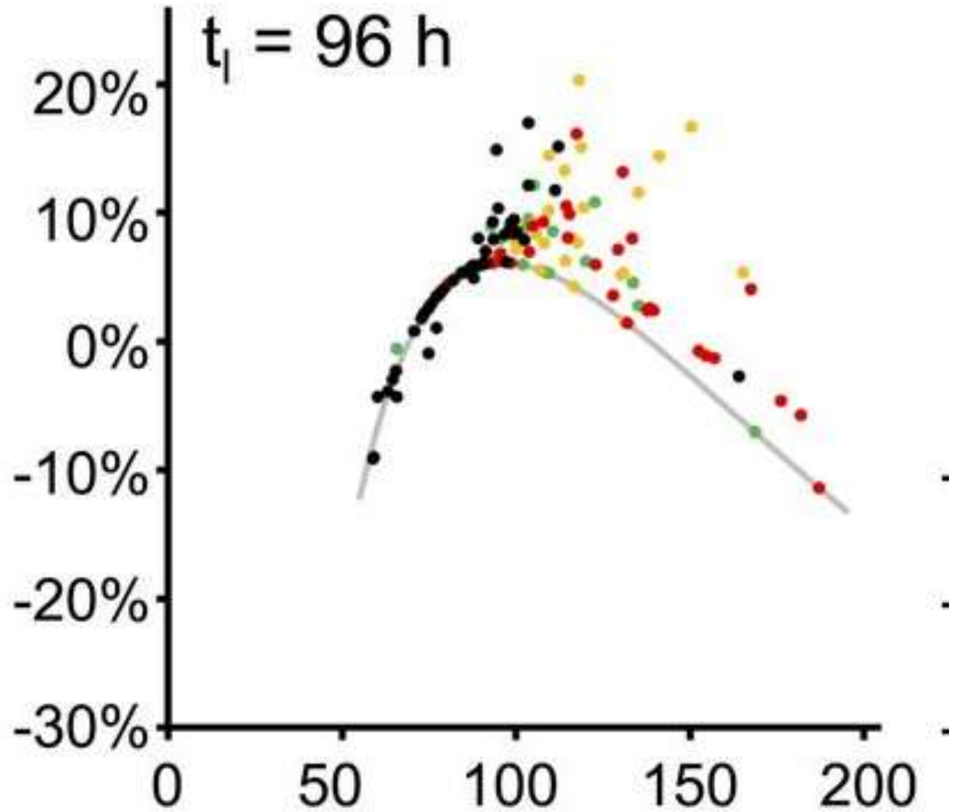
J Nucl Med 2013; 54:1–9

Individualized Dosimetry of Kidney and Bone Marrow in Patients Undergoing ^{177}Lu-DOTA-Octreotate Treatment

Mattias Sandström[1,2], Ulrike Garske-Román[2,3], Dan Granberg[3], Silvia Johansson[2], Charles Widström[1], Barbro Eriksson[3], Anders Sundin[2,4], Hans Lundqvist[5], and Mark Lubberink[2]

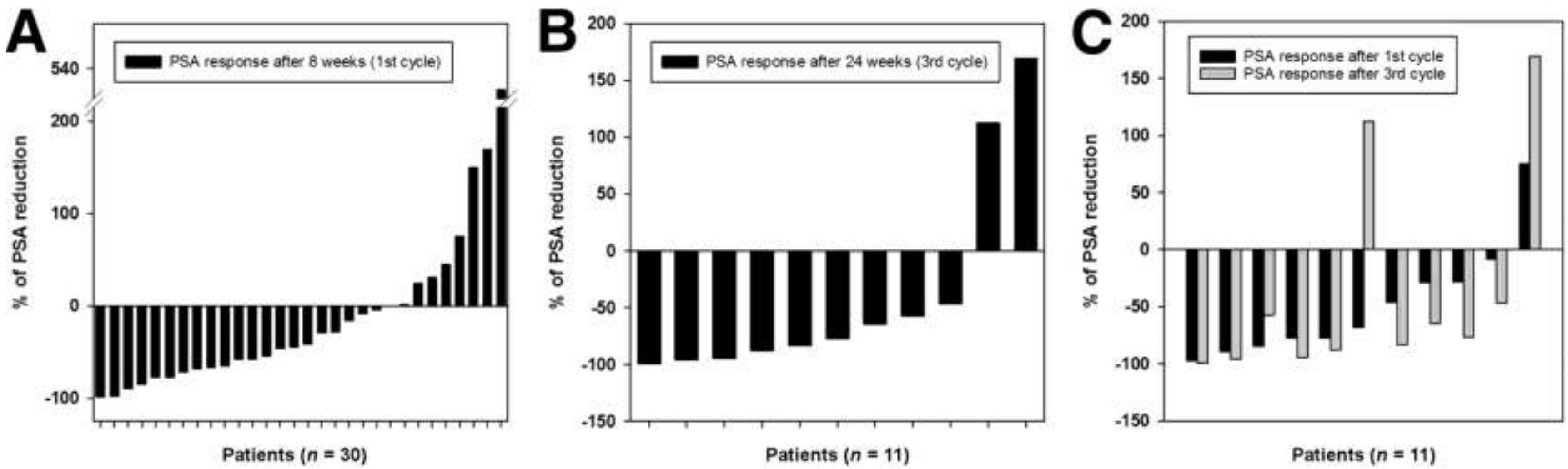
The Treatment of Neuroendocrine Tumors

Dose Mapping After Endoradiotherapy with ^{177}Lu-DOTATATE/DOTATOC by a Single Measurement After 4 Days



Percentage deviation of approximation from actual time integral for single measurements after t = 96h

The Treatment of Prostate Cancer with Lu-177-PSMA



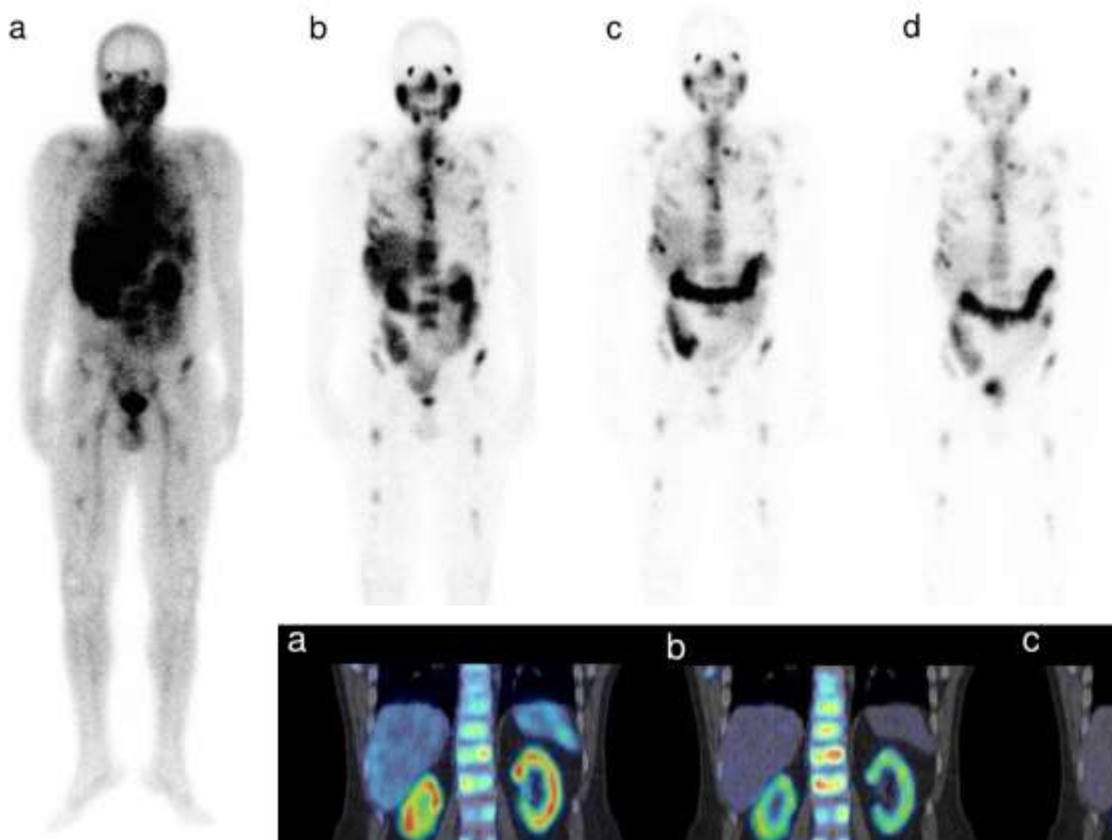
Waterfall graph presenting PSA response after 1 cycle of ^{177}Lu-PSMA-617 therapy.

Clemens Kratochwil et al. J Nucl Med 2016;57:1170-1176

JNM The Journal of NUCLEAR MEDICINE

Dosing: 4 or more cycles of 5 - 7.4 GBq Lu-177

The Treatment of Prostate Cancer with Lu-177-PSMA

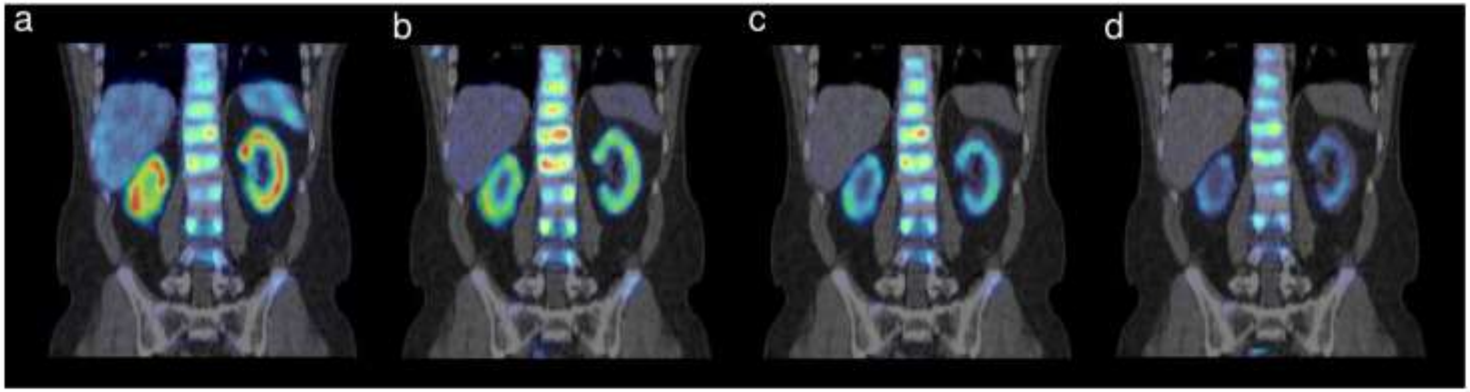


Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-015-3174-7

ORIGINAL ARTICLE

Dosimetry for ^{177}Lu-DKFZ-PSMA-617: a new radiopharmaceutical for the treatment of metastatic prostate cancer

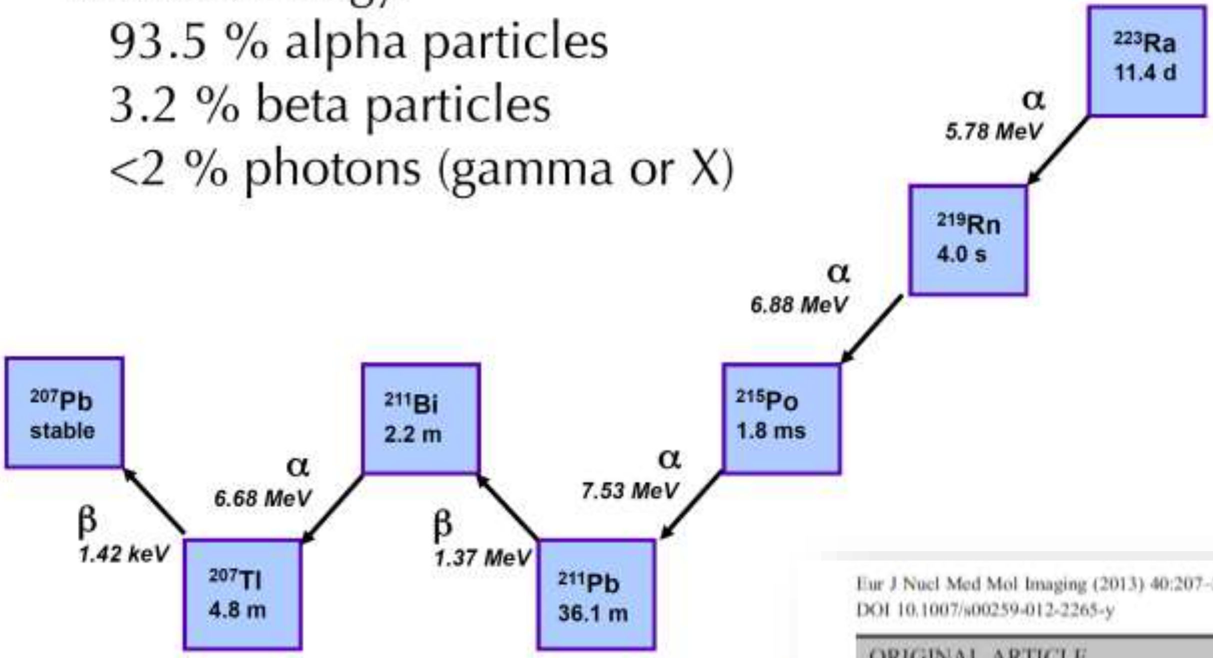
Andreas Delker[1] · Wolfgang Peter Fendler[1] · Clemens Kratochwil[2] · Anika Brunegraf[1] · Astrid Gosewisch[1] · Franz Josef Gildehaus[1] · Stefan Tritschler[3] · Christian Georg Stief[3] · Klaus Kopka[4] · Uwe Haberkorn[2] · Peter Bartenstein[1] · Guido Böning[1]



The Treatment of Prostate Cancer with Ra-223

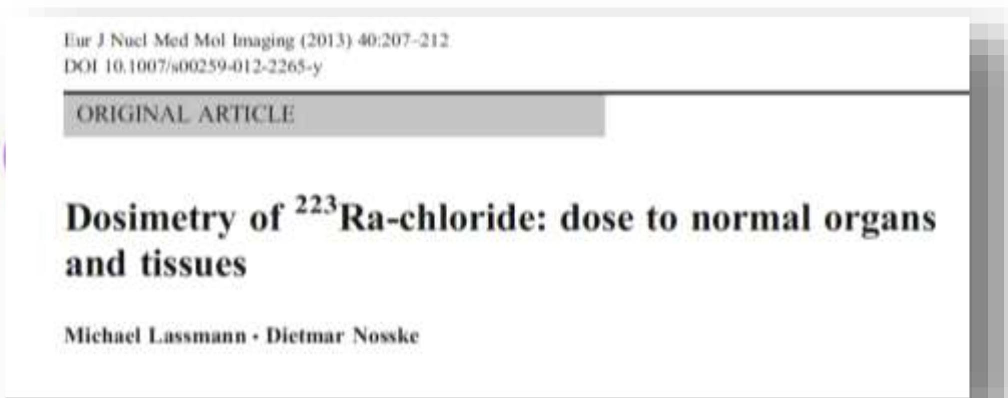
Ra-223: Energies released per decay

Emitted energy:
- 93.5 % alpha particles
- 3.2 % beta particles
- <2 % photons (gamma or X)



Range of alpha particles < 100μm

- Activity to administer: 55 kBq/kg, 6 cycles
- 11.4 days half-life
- 20 MeV of energy per starting atom and the first two daughters
- 28 MeV through complete decay of the progeny

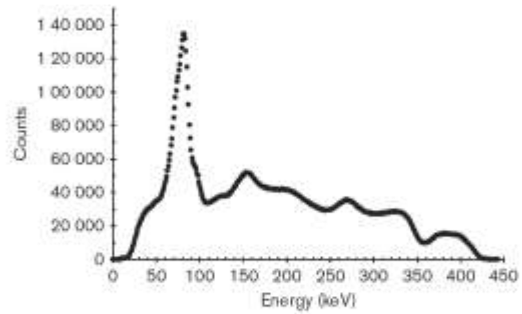

Eur J Nucl Med Mol Imaging (2013) 40:207–212
DOI 10.1007/s00259-012-2265-y

ORIGINAL ARTICLE

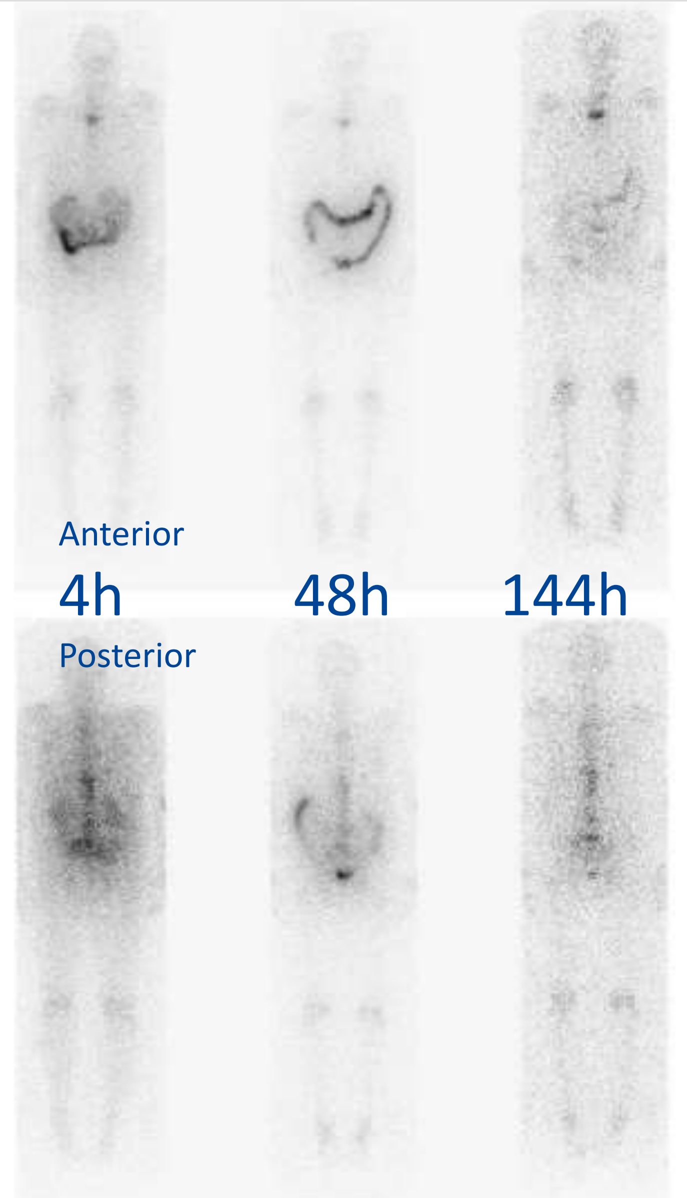
Dosimetry of ^{223}Ra-chloride: dose to normal organs and tissues

Michael Lassmann · Dietmar Nosske

The Treatment of Prostate Cancer with Ra-223



- Patients with painful osseous metastases and reduced quality of life
- Increased uptake in places of augmented bone metabolism
- Sparing of sound bone tissue



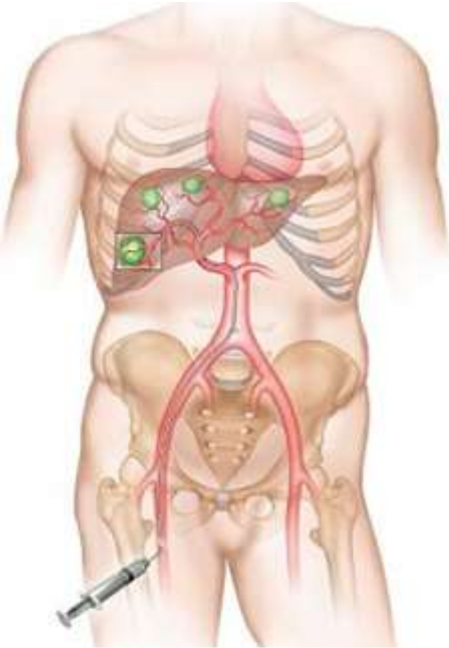
Original article

Nuclear Medicine Communications

Quantitative imaging of ^{223}Ra-chloride (Alpharadin) for targeted alpha-emitting radionuclide therapy of bone metastases

Cecilia Hindorf[a,d], Sarah Chittenden[a], Anne-Kirsti Aksnes[c], Chris Parker[b] and Glenn D. Flux[a]

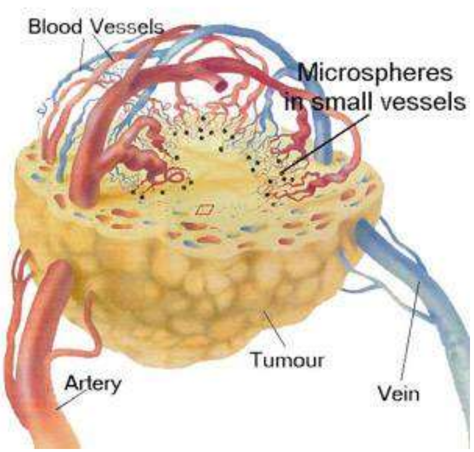
Selective Internal Radiotherapy with Y-90

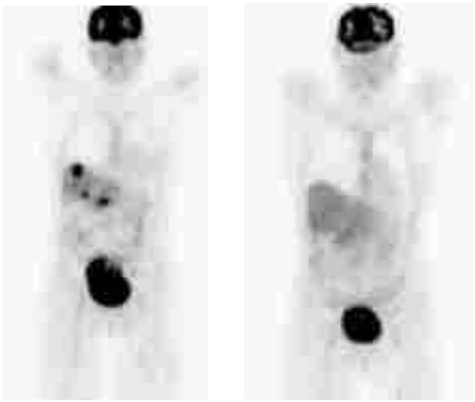


Activity: 2-4 GBq (Y-90), dosing based either on dosimetry or BSA or vendor-specific calculations

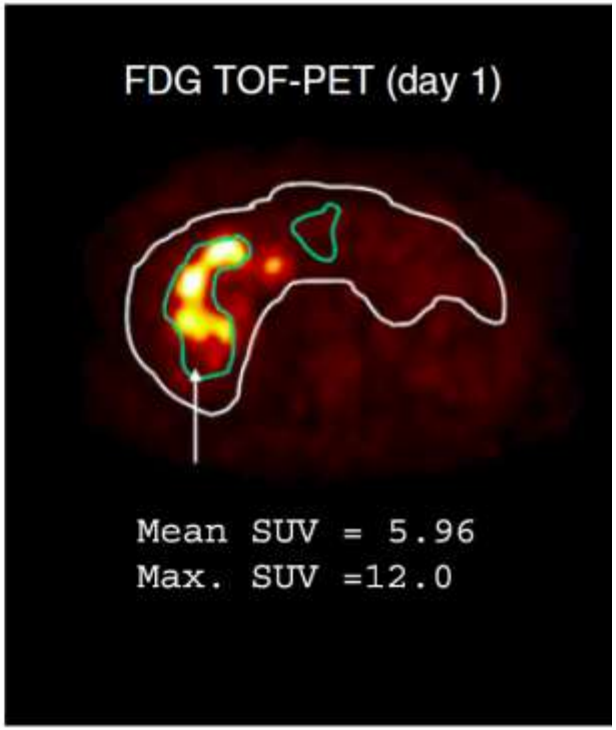
Transarterial embolization of radioactive labeled microspheres

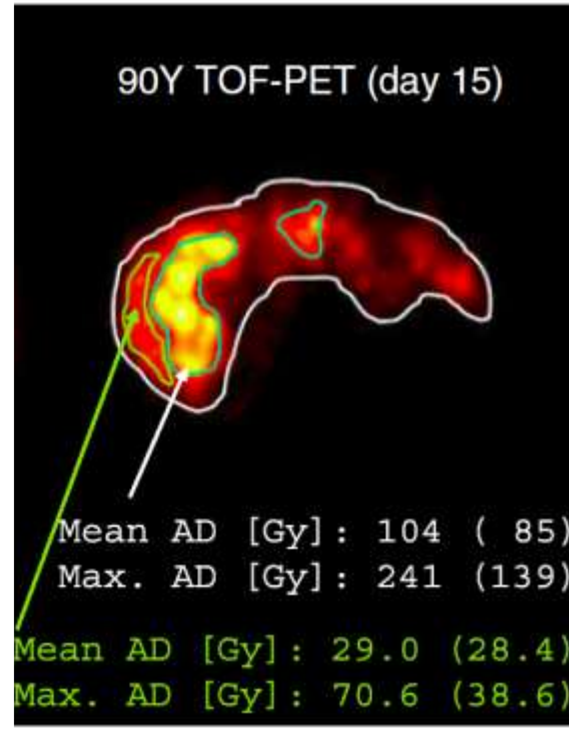
Highly selective tumor uptake by intra-arterial administration of the particles through the a. hepatica





Selective Internal Radiotherapy with Y-90





Eur J Nucl Med Mol Imaging (2010) 37:1654–1662
DOI 10.1007/s00259-010-1470-9

ORIGINAL ARTICLE

Feasibility of ^{90}Y TOF PET-based dosimetry in liver metastasis therapy using SIR-Spheres

Renaud Lhommel · Larry van Elmbt · Pierre Goffette · Marc Van den Eynde · François Jamar · Stanislas Pauwels · Stephan Walrand

Contents

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- Basic Principles of Dosimetry
- Major Clinical Applications
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  - Treatment of Neuroendocrine Tumors and Prostate Cancer
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  - Locoregional Treatment of Liver metastases
- Dosimetry Practice in Europe
- Conclusion and Outlook

Internal Dosimetry Task Force Report on:

Treatment Planning For Molecular Radiotherapy: Potential And Prospects

European Association of Nuclear Medicine

Analysis of Potential and Prospects for Treatment Planning in Preparation of the Implementation of the European Council Directive 2013/59

Available at: https://www.eanm.org/publications/idtf-report/

Therapy Modalities

Dosimetry or Not?

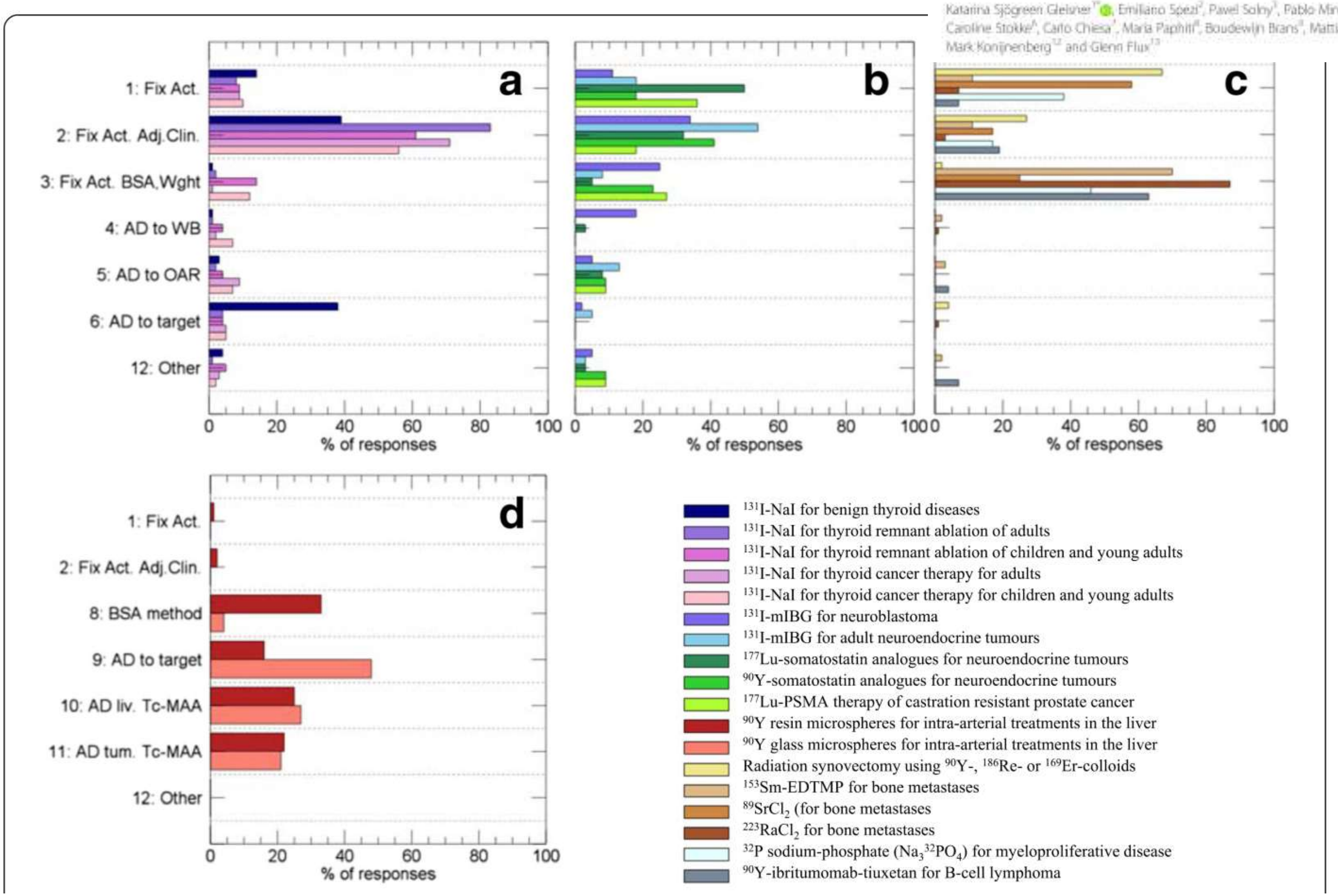
Sjögreen Gleisner et al. EJNMMI Physics (2017) 4:28
DOI 10.1186/s40658-017-0193-4

EJNMMI Physics

ORIGINAL RESEARCH Open Access

Variations in the practice of molecular radiotherapy and implementation of dosimetry: results from a European survey

Katarina Sjögreen Gleisner[1*], Emiliano Spezi[2], Pavel Solny[3], Pablo Minguez Gabina[4], Francesco Cicone[5], Caroline Stokke[6], Carlo Chiesa[7], Maria Paphiti[8], Boudewijn Brans[9], Mattias Sandström[10], Jill Tipping[11], Mark Konijnenberg[12] and Glenn Flux[13]



Dosimetry Practice in Europe

Sjögreen Gleisner et al. EJNMMI Physics (2017) 4:28
DOI 10.1186/s40658-017-0193-4

EJNMMI Physics

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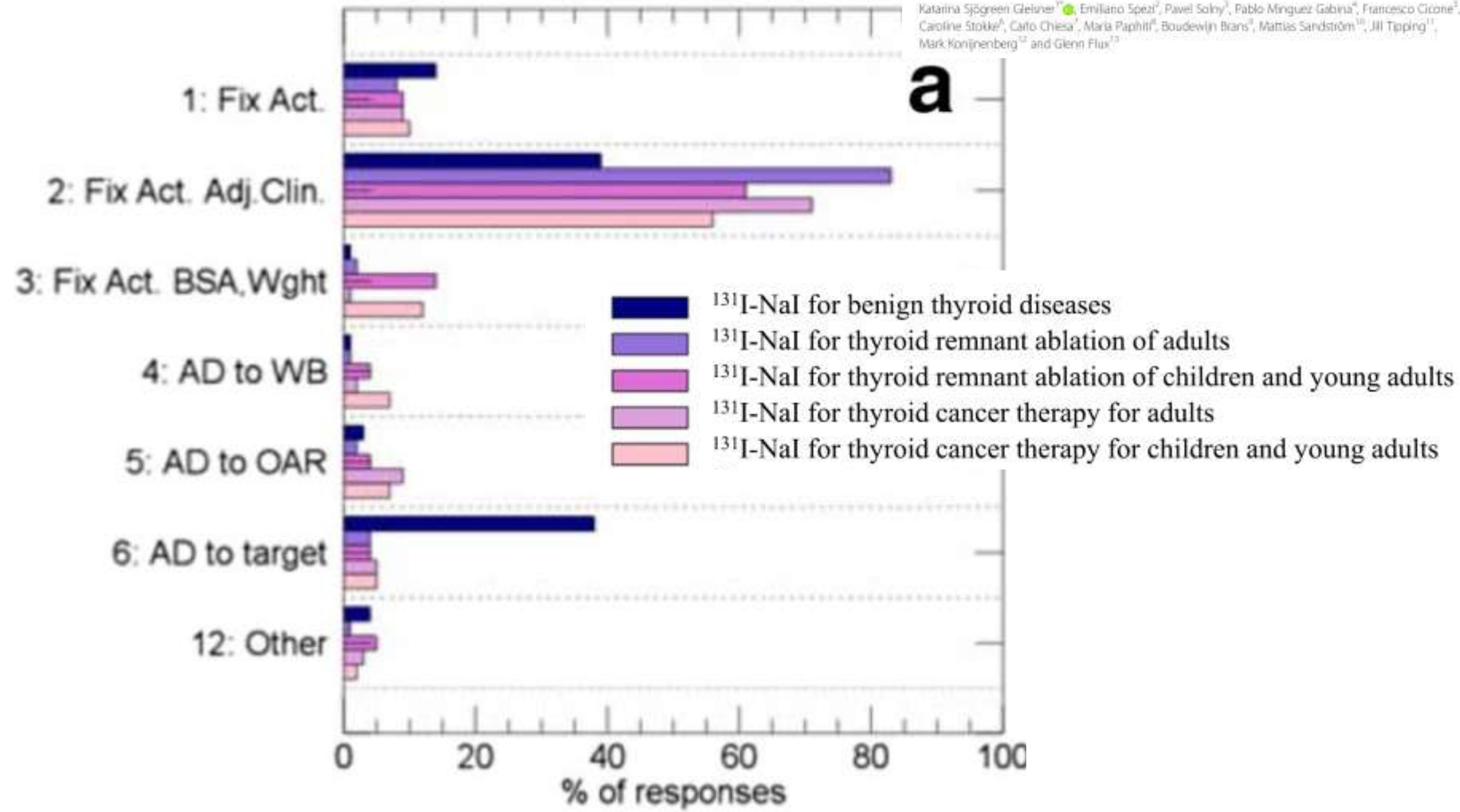

Conclusions and Outlook

- General MIRD equation: $$\overline{D}_k = \sum_h \tilde{A}_h \cdot S_{(k \leftarrow h)}$$

- How dosimetry is performed depends on the
  - Clinical Application
  - Local Practice
  - Availability of Resources
  - Legal Requirements

- Dosimetry has been successfully applied in a several clinical applications, however there is further need for standardization

Conclusions and Outlook

MEDIRAD

Implications of Medical Low Dose Radiation Exposure

WP 2, Task 2.3:
Dose evaluation and optimisation of multimodality imaging

WP 3:
Impact of low dose radiation exposure from I-131 radioiodine (NaI) ablation of thyroid cancer

Start date: 01-June-2017
Duration: 48 Months

MRT DOSIMETRY

Metrology for clinical implementation of dosimetry in molecular radiotherapy

WP No	Work Package Title
WP1	Activity standards for quantitative imaging
WP2	Image-based quantification of 3D activity distributions
WP3	Computer modelling of time-variable activity distributions in multimodal imaging
WP4	Accuracy and traceability of dose calculations

Start date: 01-June-2016
Duration: 36 Months

Thank you!

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