Dose issues in Nuclear Medicine & Hybrid imaging

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Overview

Introduction to radioactivity and radiation

Does quantities

Introduction to radiation protection

Dose in Nuclear medicine

Introduction
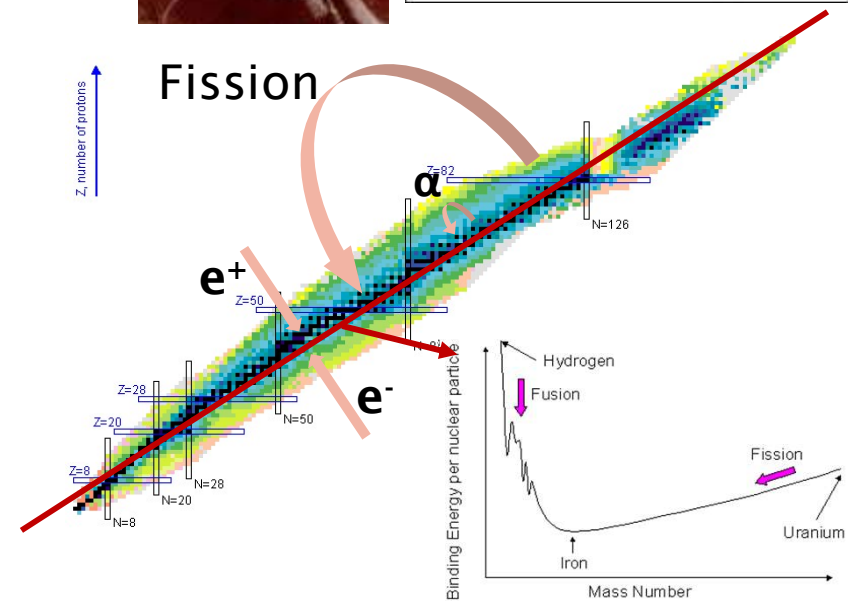

IF you google radioactivity...

Radioactivity

Radioactivity =

Spontaneous emission of radiation resulting from changes in the nuclei
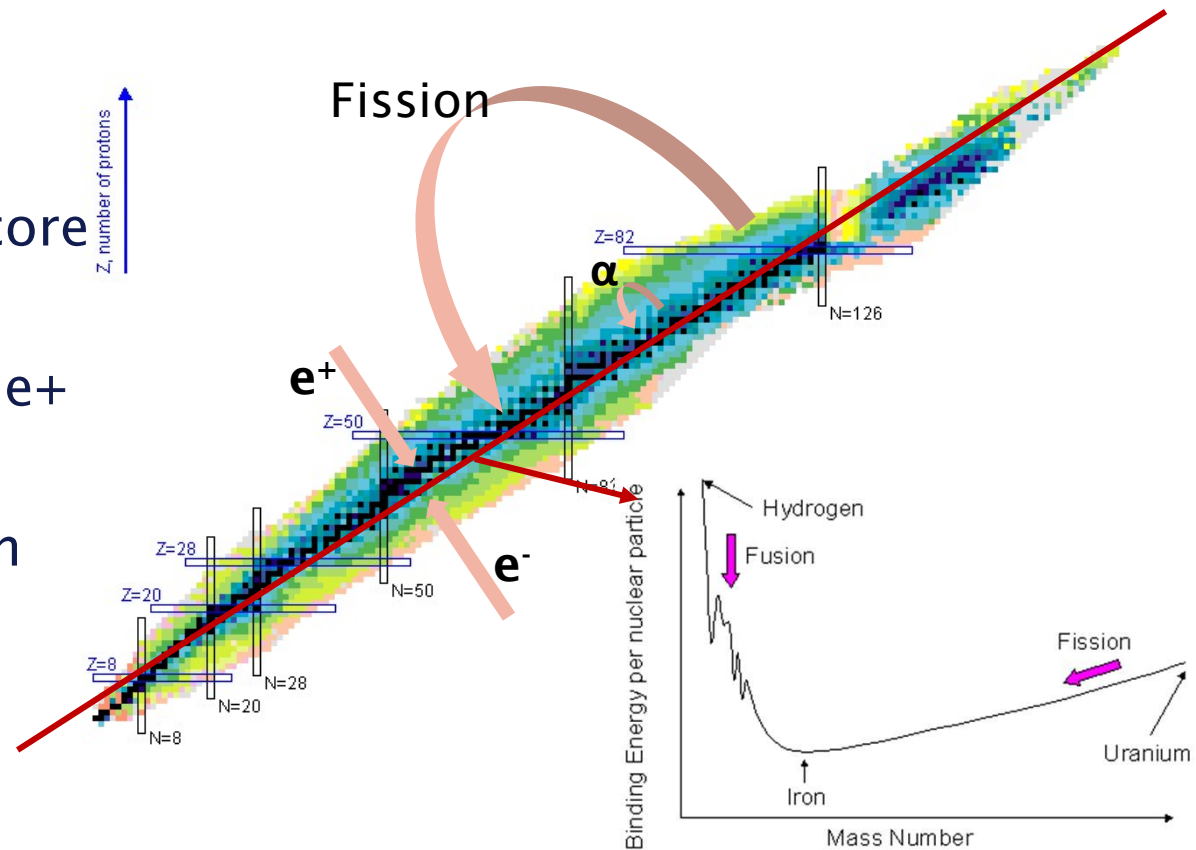
Transition to an energetically favourable state

Discovered by Henry Becquerel in 1896

Radioactivity

Different decays:

➤ Alpha decay =
emission of an ^{4}He core

➤ Beta decay =
emission of an e- or e+

➤ Gamma decay =
emission of a photon
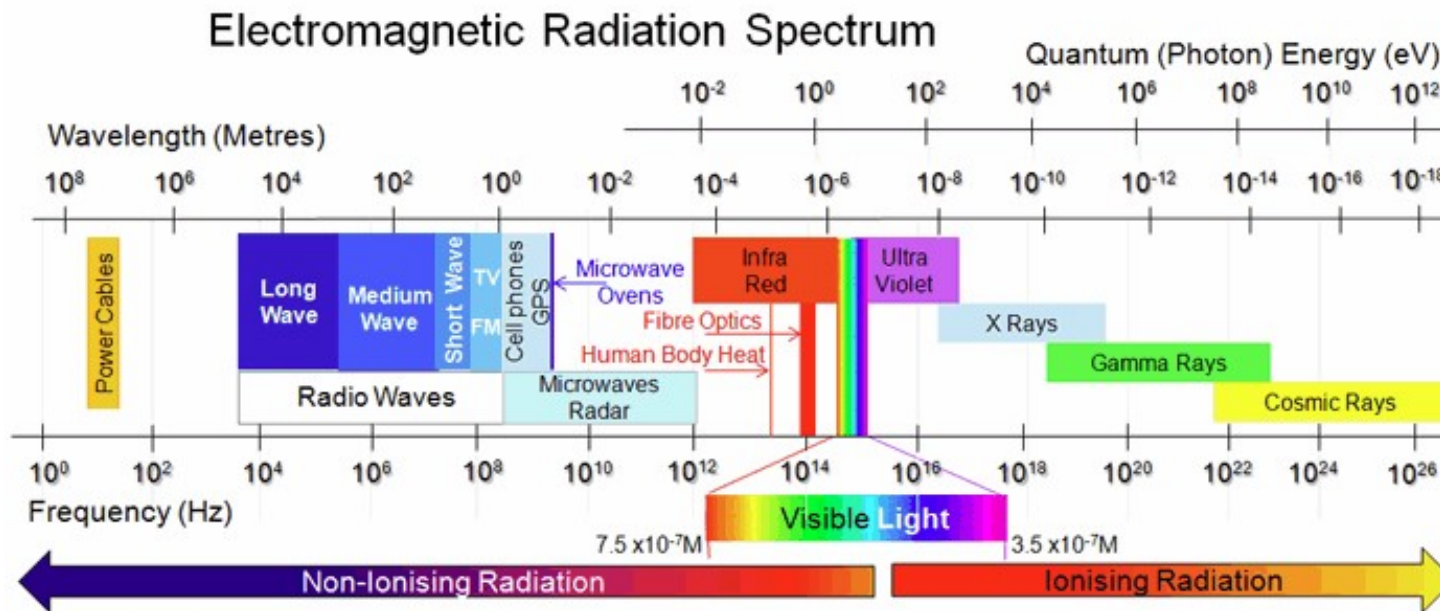
➤ Fission =
splitting of a nuclei

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Ionizing radiation

Radiation which is able to cause ionizations in mater:
One common definition > 10 eV (ICRU Report 85)

Can be particle radiation or photon radiation

Types of radiation
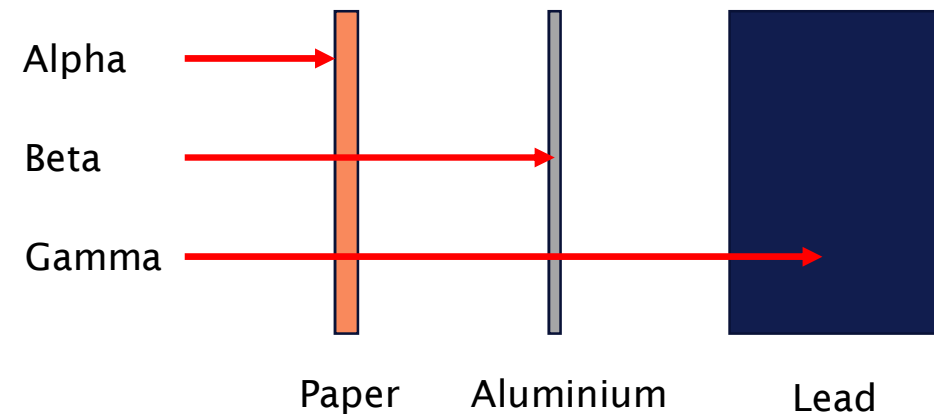
Ionizing radiation (in medicine) can originate from radioactive decays or can be produced artificially (e.g. X-ray)

Particle radiation:
- ➤ electrons / positrons
- ➤ α-particles

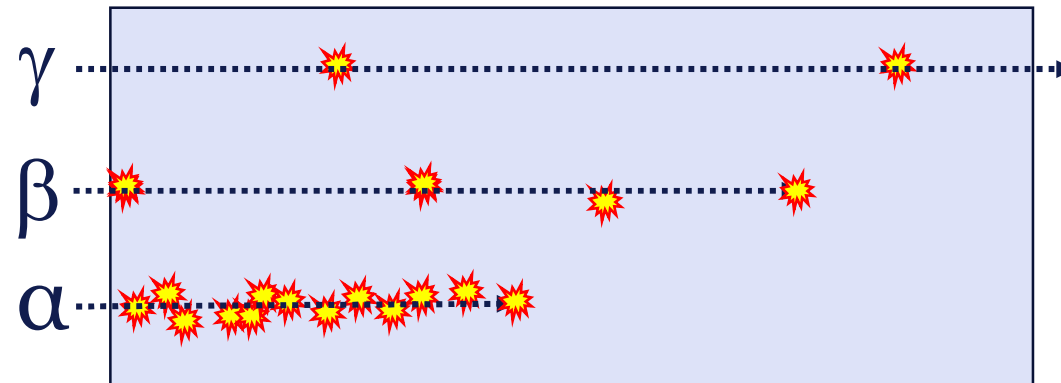EM radiation
- ➤ Photons

Alpha

Beta

Gamma

Paper   Aluminium   Lead

Linear Energy Transfer (LET)

The LET describes how much energy an ionizing particle transfers to the traversed material per unit distance.

α - particles: high LET (therapy)
β - particles: medium LET (therapy)
γ - radiation: low LET (diagnosis)

Dose Quantities

Physical quantity

- Energy Dose

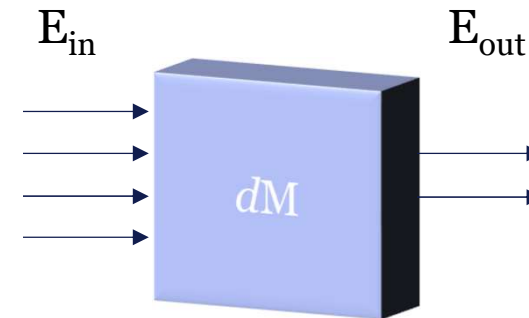Radiation protection quantity

- Equivalent dose

- Effective dose

Img: Bundesamt für Strahlenschutz, GER

Dose is a scalar value -> one value for each point in space

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Energy dose (D)

Locally absorbed energy per unit mass

$$D = \frac{dE}{dM}$$

E_{in} E_{out}

dM

D is given in units of Gray = Joule per kilogram

$$1\,Gy = 1\,\frac{J}{kg}$$

Corresponds to a increase
of T of 0.00024°

Energy dose = deposited energy per unit of mass

Equivalence dose (H)

incorporates the biological efficiency of the radiation type. It is given in units of Sievert.

$$H = Q * D$$

$$1 \, Sv = 1 \frac{J}{kg}$$

Q is the "quality factor" and dependent on the LET of the radiation. In practice Q is substituted with w_r which is an approximation of Q.

Type of radiation	w_r
X-ray, gamma, e-,e+	1
Protons	5
Alpha	20

Energy dose multiplied by a radiation specific factor accounting for differences in biological effectiveness

Effective dose (E)

describes the risk related to radiation exposure for the whole body. E is, like H, given in Sievert.

$$E = \sum_T w_T * H_T \qquad\qquad 1\,Sv = 1\,\frac{J}{kg}$$

w_T is a factor describing the relative sensitivity to radiation for each organ in the human body. Thus, an E of 1 Sv is describes the hazard related to irradiation the whole body with 1Gy of photon radiation.

A measure of the risk related to the radiation exposure

Effective dose (E)

A simple example:

Just the lung and skin was irradiated each with 1 Gy of photons $(\boldsymbol{H} = \boldsymbol{D})$

$$E = \sum_{T} w_T * H_T =$$

$$\underbrace{0.12 * 1}_{\text{Lung}} + \underbrace{0.01 * 1}_{\text{Skin}} = 0.13 \text{ Sv}$$

This corresponds to the same risk as a irradiation of the whole body with 0.13 Sv

Organs	Tissue weighting factors		
	ICRP26 1977	ICRP60 1990[19]	ICRP103 2007[1]
Gonads	0.25	0.20	0.08
Red Bone Marrow	0.12	0.12	0.12
Colon	-	0.12	0.12
Lung	0.12	0.12	0.12
Stomach	-	0.12	0.12
Breasts	0.15	0.05	0.12
Bladder	-	0.05	0.04
Liver	-	0.05	0.04
Oesophagus	-	0.05	0.04
Thyroid	0.03	0.05	0.04
Skin	-	0.01	0.01
Bone surface	0.03	0.01	0.01
Salivary glands	-	-	0.01
Brain	-	-	0.01
Remainder of body	0.30	0.05	0.12
Total	1.00	1.00	1.00

Why radiation protection

Prevent occurrence of serious radiation-induced conditions in exposed persons. These include acute and chronic deterministic effects

Reduce stochastic effects in exposed persons to a degree that is acceptable in relation to the benefits to the individual and society from the activities that generate such exposure
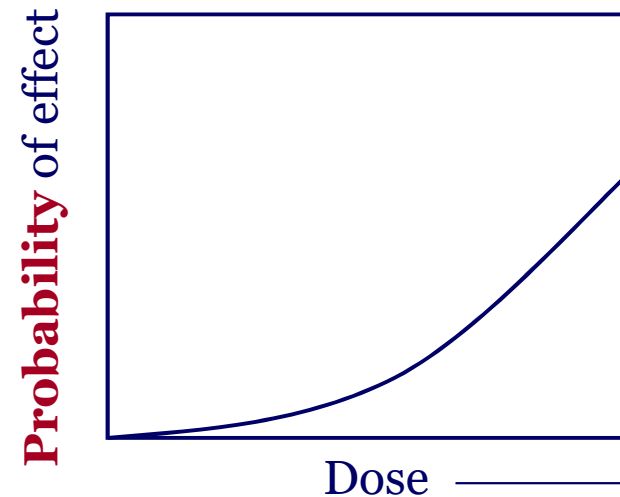
After NCRP Report 116, 1993

Deterministic & stochastic effects
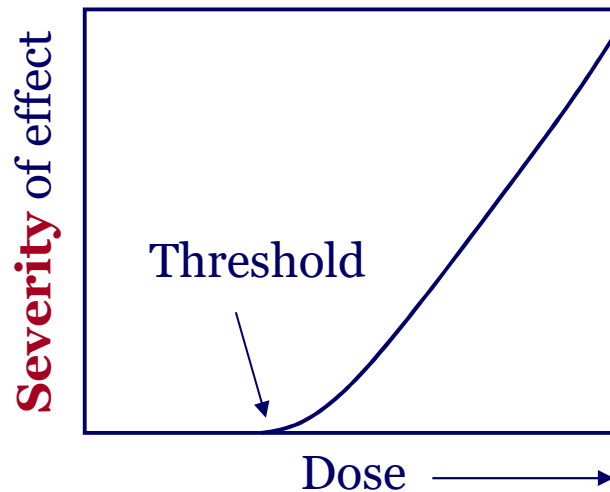
Damage depends on absorbed dose
Threshold exists

Example: cataract, erythema, infertility

Severity is independent of absorbed dose Probability of occurrence depends on absorbed dose

Example: radiation induced cancer, genetic effects

Example deterministic Effect

Local iradiation during multiple angiography procedures accumulated to ~ 20 Gy

www.auntminnie.com

6-8 Weeks

Erythema

16-21 Weeks

Depigmented skin with central necrosis

18-21 Months

Deep necrosis with atrophic borders

Stochastic effects

Risk assessment based on the atomic bomb survivors of WW2
1 Sv ~ 5% increase in risk of dying from cancer

>1Gy

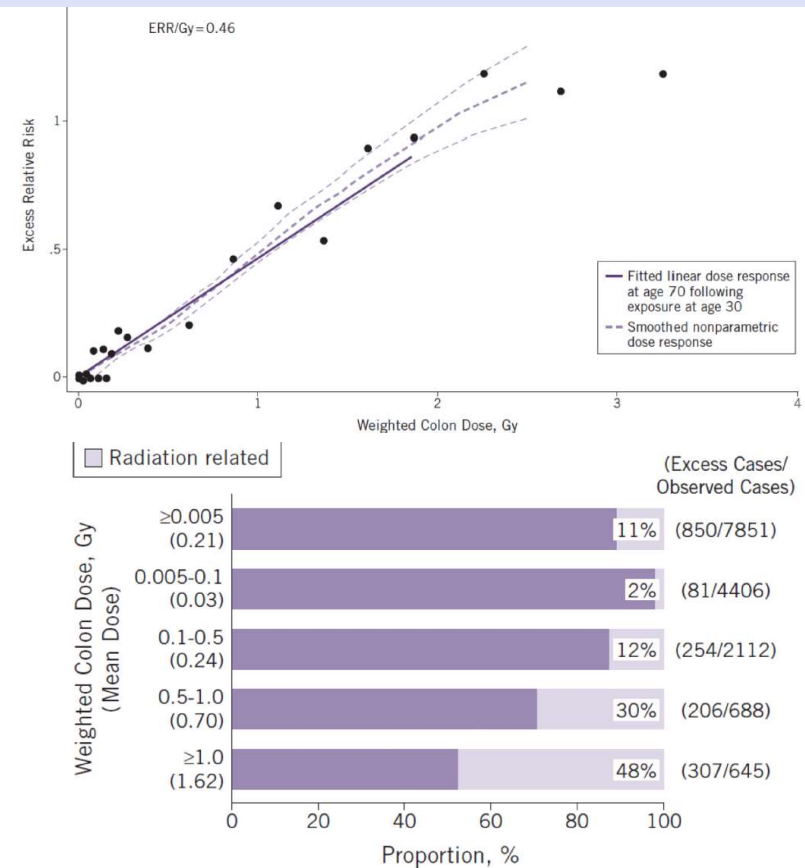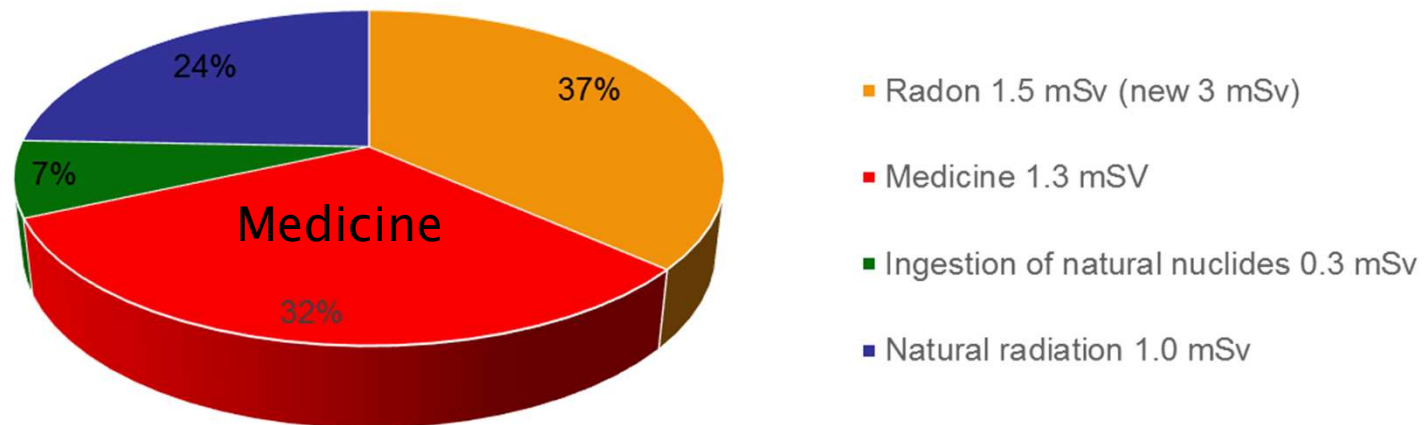~500 mGy

< 5mGy

Douple et al. Disaster Med Public Health Prep. 2011

ERR/Gy=0.46

Excess Relative Risk

Weighted Colon Dose, Gy

— Fitted linear dose response
  at age 70 following
  exposure at age 30
-- Smoothed nonparametric
  dose response

☐ Radiation related

(Excess Cases/ Observed Cases)

Weighted Colon Dose, Gy (Mean Dose)	Proportion, %	(Excess Cases/ Observed Cases)
≥0.005 (0.21)	11%	(850/7851)
0.005-0.1 (0.03)	2%	(81/4406)
0.1-0.5 (0.24)	12%	(254/2112)
0.5-1.0 (0.70)	30%	(206/688)
≥1.0 (1.62)	48%	(307/645)
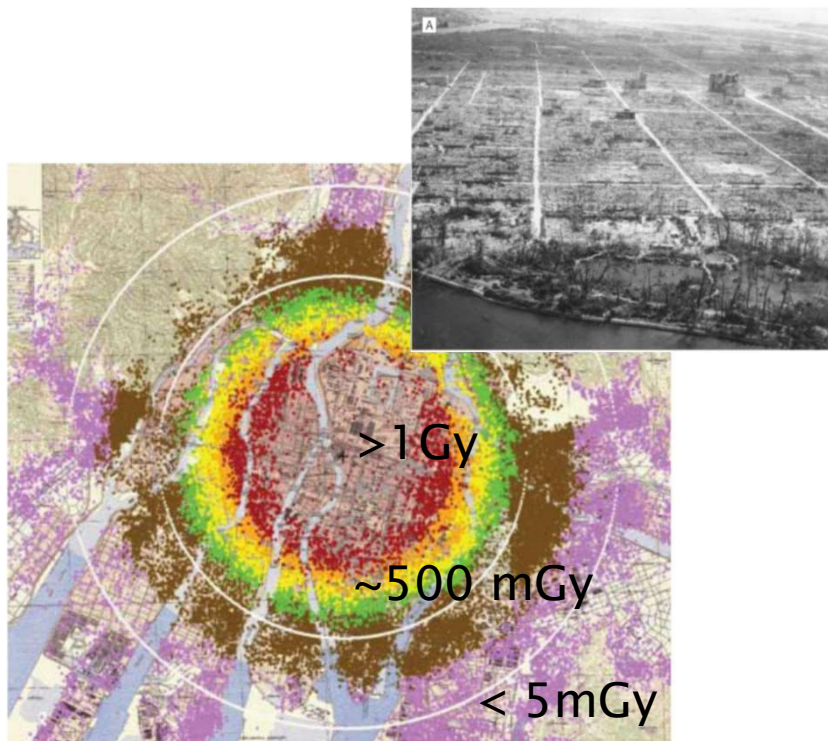
Fig. 6. Estimated proportion (attributable fraction) of radiation-related solid-cancer incidence by radiation dose (1958–1998)

Annual per capita exposure in AUT

Effective dose [Sv]: 1 Sv ~ 5% increase of cancer risk

Example: Annual radiation exposure per capita in Austria

- Radon 1.5 mSv (new 3 mSv)
- Medicine 1.3 mSV
- Ingestion of natural nuclides 0.3 mSv
- Natural radiation 1.0 mSv

source: www.ages.at

Calculating Dose

Energy dose can be calculate if you know:

➢ Radiation type

➢ Radiation intensity

➢ Material composition

Equivalent dose further requires:

➢ Biological effectivnes of the radiation

Dose calculation can be done using Monte Carlo simulations

Dose in Nuclear Medicine

Dose estimation for therapy

➢ Dose needed to treat the patient

➢ Dose limits for organs at risk

Dose in diagnostic imaging

➢ Risk associated with dose needs to be reasonable

Therapy: Deterministic effects!

Diagnostic: Stochastic effects!

The MIRD formalism

MIRD = Medical Internal Radiation Dose formalism

Based on:

➢ There is a source of radiation

➢ There is a target of radiation

➢ The target receives dose from the source
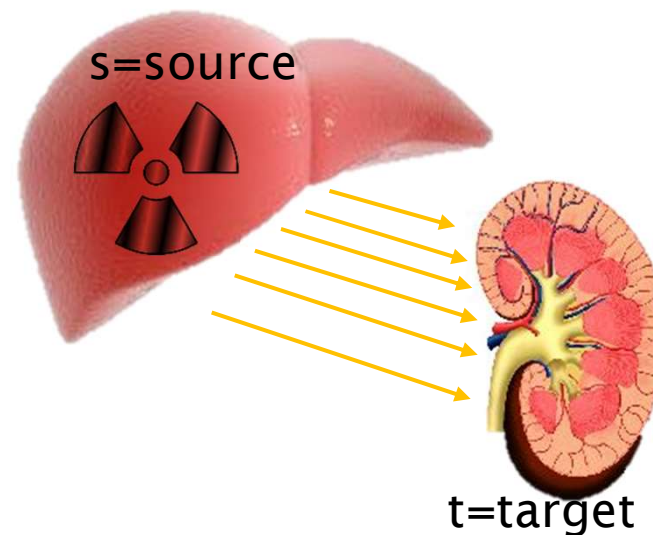
s=source

t=target

The MIRD formalism

Mathematically this can be expressed as

Dose =

Number of decays **x** mean energy arriving at the target from the source for one decay

$$D = \tilde{A} * S$$

Integral of the activity concentration in the source organ (dynamic or multiple measurments)

Describing the geometry and relative location of the target to the source and the type of radiation

The MIRD formalism

A_S = cumulated activity for all organs

$S_{t,s}$ values for all source – target combinations

$$D_t = \sum_s \tilde{A}_s * S_{t,s} \implies H_t = w_r * D_t \implies E = \sum_t w_t \, Ht$$
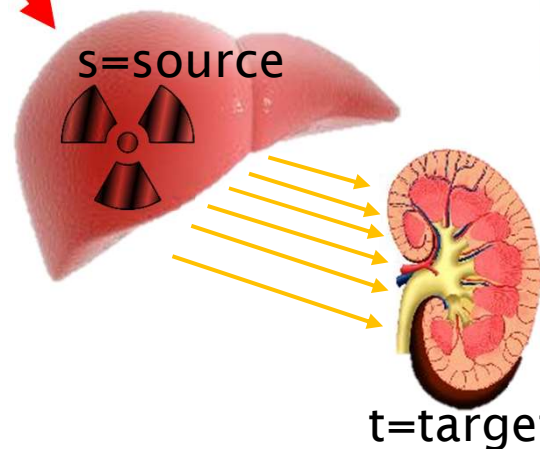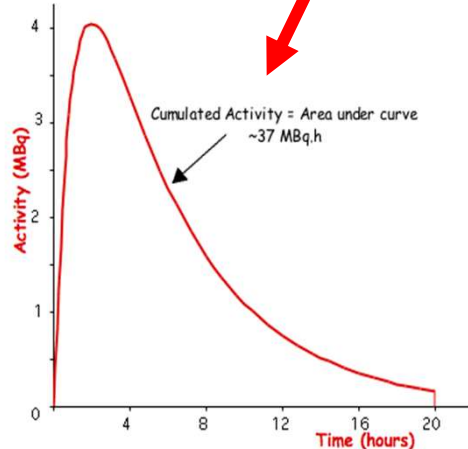
= 1

for radiation types in diagnostic

Cumulated Activity = Area under curve ~37 MBq.h

Activity (MBq)

Time (hours)

s=source

t=target

Dose to a organ = sum of dose from all sources

Practical issues

➢ Definition of the organ size and weight

➢ Estimation of the time activity product

➢ S values are not patient specific

➢ Dose is assumed to be uniform in each organ, no local effects are taken into account

Dose calculation in radionuclide therapy is not exact

Dose in diagnostic Nuclear Medicine

Dose calculation can be done with Monte Carlo simulations

➢ Information on the type of radiation

➢ Information on the patient anatomy

➢ Information on the tracer kinetic

!!! Can not be performed in clinical routine !!!

In diagnostic we know:

Radio pharmaceutical + injected activity

Cumulated Activity = Area under curl
~37 MBq.h

Dose in diagnostic Nuclear Medicine
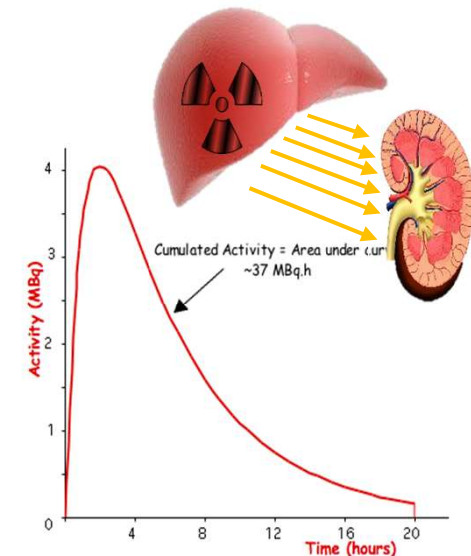
Dose estimation for diagnostics is based on:

- Tracer kinetic is assumed from published kinetic data

- Patient anatomy is estimated from simplified models
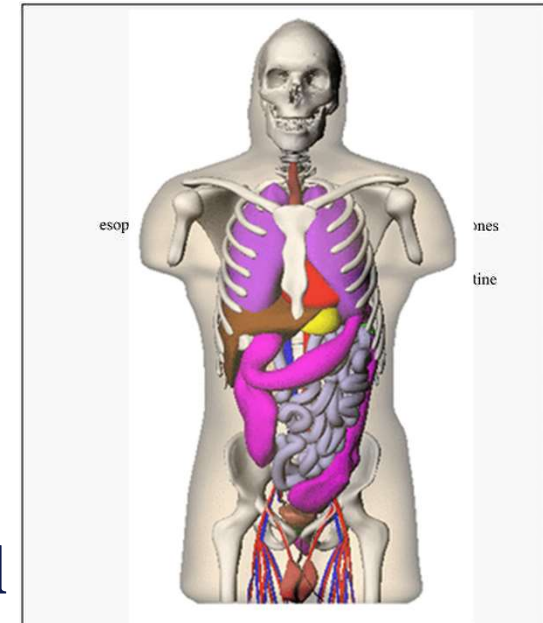
Conversion factors for radio pharmaceutical

image: http://www.doseinfo-radar.com/

$$E = k * A_{injected}$$

Dose in Computed Tomography

Dose calculation can be done with MC Simulations

➢ Information on the radiation field (System)

➢ Information on the patient anatomy

!!! Can not be performed in clinical routine !!!
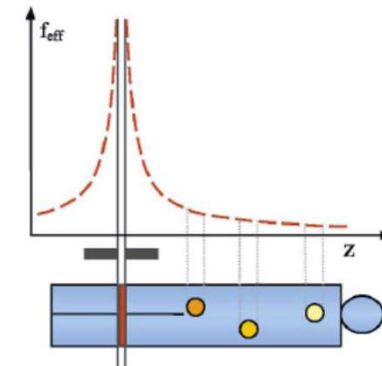
Image: Hanno Krieger, Vieweg+Teubner 2009

What can be done:

Scanner output can be described by CTDI

➢ integrated dose over a slice (includes "tails")

➢ Standardized way of quantifying scanner output

Image: Hanno Krieger, Vieweg+Teubner 2009

Dose in Computed Tomography
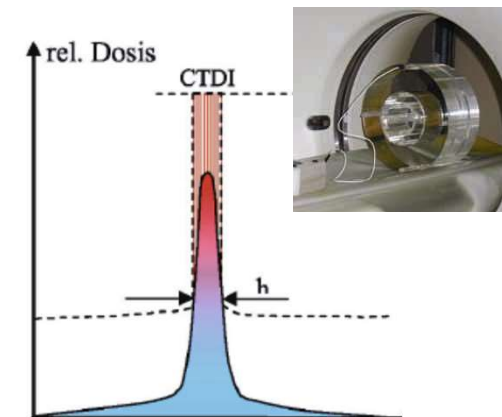
Dose estimation in practice:

- Factors for standardized CT systems

- Slice dependent conversion factor $f(z)$ from Monte Carlo simulations of "standard" patient

Image: Hanno Krieger, Vieweg+Teubner 2009

$$E = \frac{1}{p} * CTDI * \sum_{-z}^{z} f(z)$$

An easy approach is a mean conversion factor for a scan region (frequently found in literature)

$$E = DLP * fmean$$

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Dose in Hybrid Imaging

$$E_{total} = E_{NUC} + E_{CT}$$
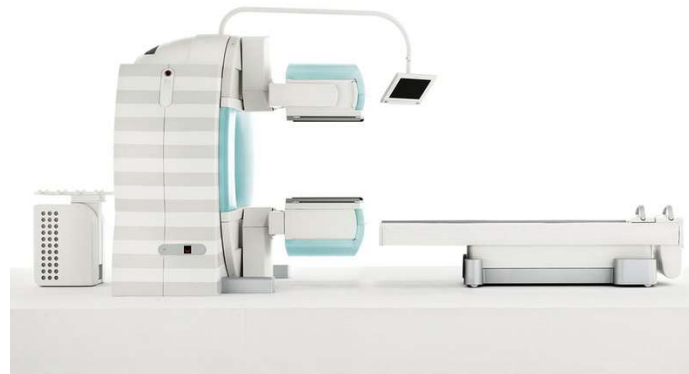
Dose values in SPECT/CT routine

Dose from Tracers
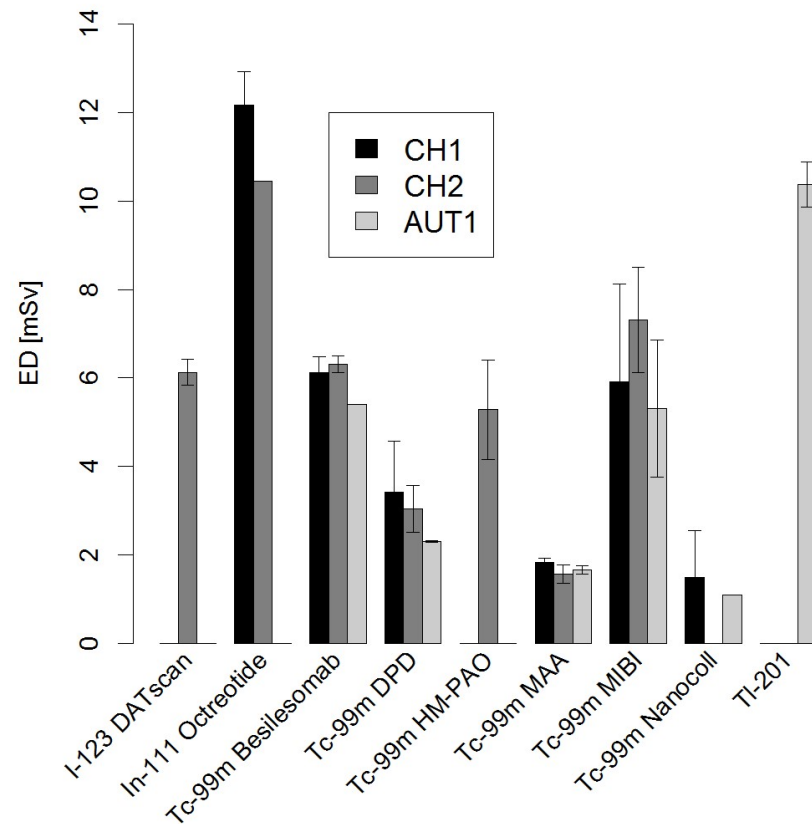
Average: 5.7 mSv

Dose from CT
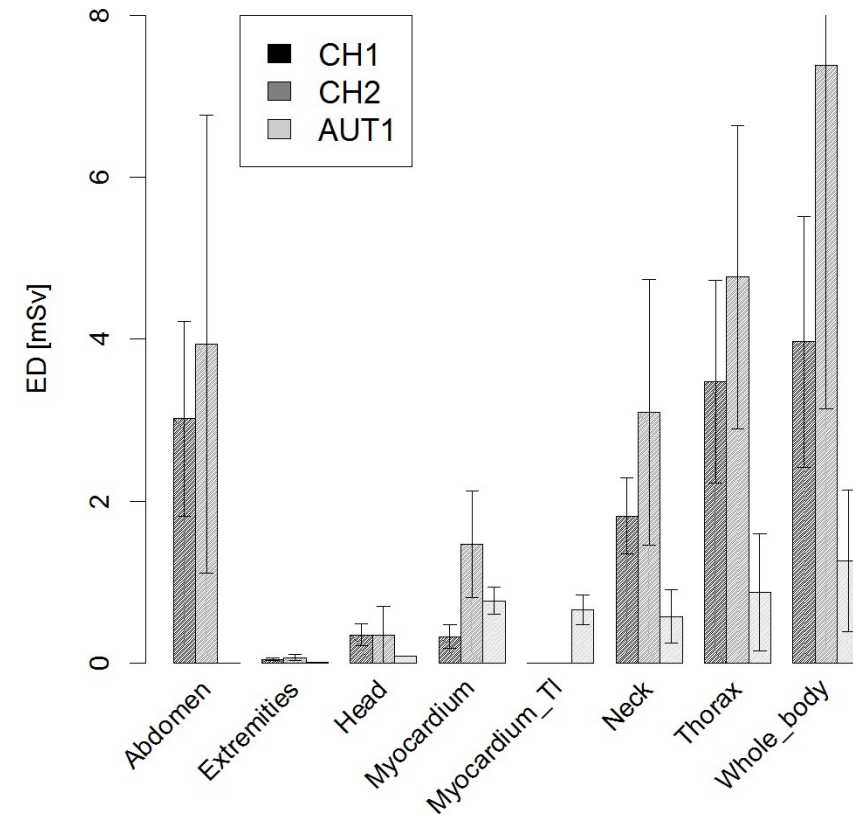
Average: 1.8 mSv

Patient exposure in PET/CT
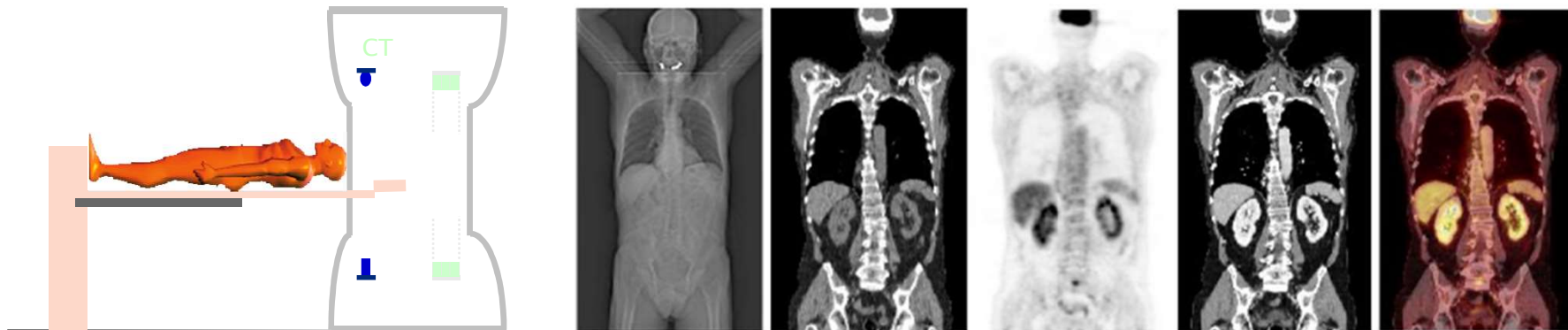
Radiation Exposure of Patients Undergoing Whole-Body Dual-Modality ^{18}F-FDG PET/CT Examinations

Gunnar Brix, PhD[1]; Ursula Lechel, MS[1]; Gerhard Glatting, PhD[2]; Sibylle I. Ziegler, PhD[3]; Wolfgang Münzing, PhD[4]; Stefan P. Müller, MD[5]; and Thomas Beyer, PhD[5]

Brix et al
J Nucl Med 2005
46:608-13

4 German hospitals /w PET/CT installed in 2001-2003
Clinically relevant TLD measurements on anthropomorphic torso phantom

Effective patient dose for WB-FDG-PET/CT: ~ 25 mSv

Comparing SPECT and PET

Bailey D et al, EJNMMI, 2007

Table 1 Effective dose (ED) estimates for a number of procedures in CT and nuclear medicine

Procedure	ED (mSv)	Comment
Ventilation lung scan with [99mTc]DTPA	0.3	Assumes normal clearance from lung [18]
CT head 30 mA on PQ5000	0.36	From reference [19]
		Average routine adult dose: 2.0–2.8 mGy for 336 mAs [16]
Typical dose from Hawkeye CT	0.5	2.5-mA tube current
CT chest 30 mA (50 mA) on PQ5000	1.1	From reference [19]
	(1.8)	Average routine adult dose: 5.5–7.8 mGy for 168 mAs [16]
CT abdomen or pelvis 30 mA (50 mA) on PQ5000	1.2	From reference [19]
	(2.0)	Average routine adult dose: 11.5–13.3 mGy for 180 mAs [16]
V/Q lung scan	2.5–3.0	40 MBq Technegas (no clearance), 200 MBq MAA [18]
[99mTc]MAG3 for renal localisation (300 MBq)	3.7	Assumes normal renal function [18]
[123I]MIBG (4 MBq·kg⁻¹)	5.8	Assumed 80-kg person [18]
[99mTc]MDP bone scan (800 MBq)	4.6	Assumes normal renal clearance [20]
[18F]FDG PET scan (370 MBq)	7.0	Without CT [20]
[99mTc]SestaMIBI (1,100 MBq)	9.0	[18]
[18F]FDG PET/CT scan (370 MBq and 110 kVp/70 mA)	13–15	[19, 20]
201Tl brain SPECT (120 MBq)	26.4	[18]
67Ga (400 MBq)	48.0	[18]

The average adult doses for CT in the 'Comment' column are taken from a recent national survey [16]

Patient dose is usually lower in SPECT than PET

Limitations for Effective Dose

Calculations are not subject specific – just general estimations

COMMENTARY

Application of the Effective Dose Equivalent to Nuclear Medicine Patients

John W. Poston for the MIRD Committee

Department of Nuclear Engineering, College of Engineering, Texas A&M University, College Station, Texas

JNM 1993

icine) and volunteers entering investigational protocols, *it is inappropriate to use the effective dose equivalent for individual patients undergoing nuclear medicine procedures*. Age, sex and dose rate are exceedingly important

Risk is related to age

Nuclide	Radio-labeled compound	Function	Dose coefficent Γ_E (μSv/MBq)
^{11}C	L-Methionine	Amino acid transport and protein synthesis	7.4
	Acetate	Myocardial oxidative metabolism	3.5
^{13}N	Ammonia	Myocardial blood flow	2.0
^{15}O	Water	Regional blood flow	0.93
^{18}F	2-Fluoro-2-deoxy-D-glucose (FDG)	Glucose transport and phosphorylation	19.0
	L-Dopa	Presynaptic dopaminergic function	25.0
	Fluoride	Bone metabolism	24.0
^{82}Rb	Rubidium chloride	Myocardial blood flow	3.4

G Brix et al. EJNMMI 36, 2009
Huang et al. Radiology 251, 2009

370MBq FDG

FDG-PET/CT
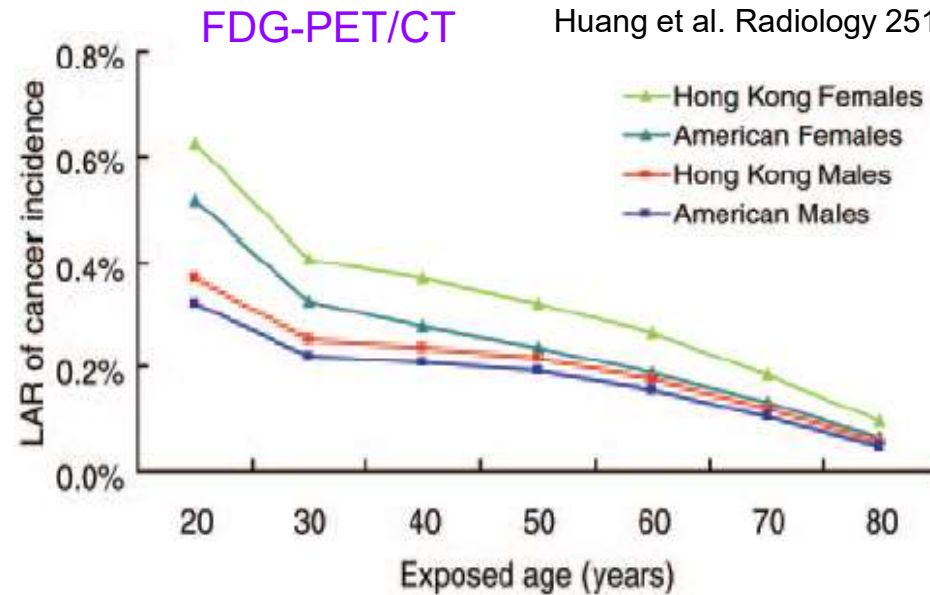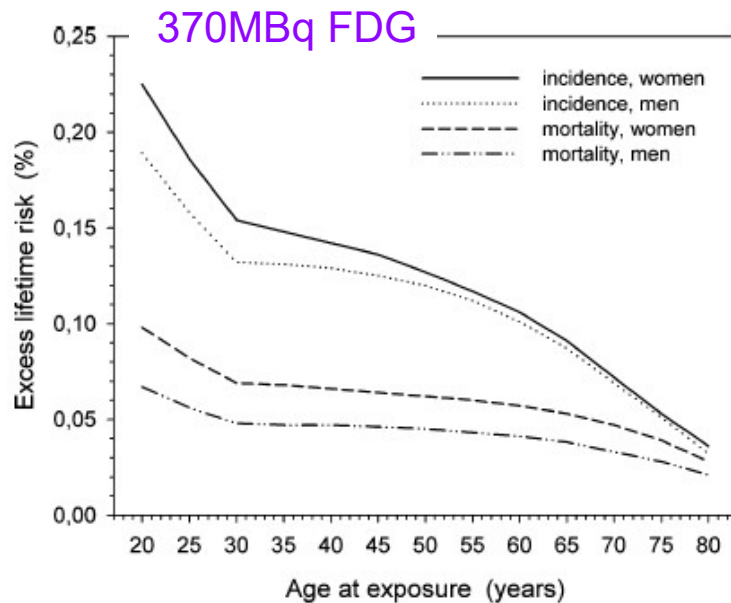
Risk assessment for small doses
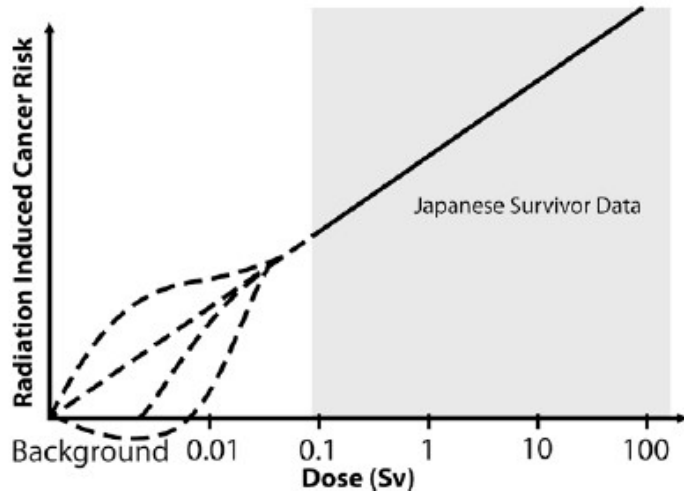
Figure 4: Graph shows models for extrapolating radiation-induced cancer risk to low doses (dashed line and curves). Linear no-threshold (LNT) model = dashed straight line.

WR Hendee and MK O'Connor. Radiology, 2012

Figure 5: Graph shows number of solid cancers as a function of absorbed dose. □ = people who were not in the cities at the time of the bombing. (Data are from table 4 of reference 14.)

- Impossible to predict cancer incidence/death in a population of individuals exposed to doses < 100mSv.

- Children are recognized as part. susceptible to radiation injury, and care should always be exercised to keep dose as low as possible

Risk assessment for small doses

Long-term Radiation-Related Health Effects
in a Unique Human Population:
Lessons Learned from the Atomic Bomb Survivors
of Hiroshima and Nagasaki

Evan B. Douple, PhD; Kiyohiko Mabuchi, MD, DrPH; Harry M. Cullings, PhD;
Dale L. Preston, PhD; Kazunori Kodama, MD, PhD; Yukiko Shimizu, PhD;
Saeko Fujiwara, MD; Roy E. Shore, PhD, DrPH

Douple et al. Disaster Med Public Health Prep. 2011

Radiation Dose-Related Increase Is Well Described by a Linear Dose-Response Relation—The linear response is illustrated in Figure 5 and is found for a number of specific cancer types. A linear-quadratic trend or a dose-threshold model does not fit the data any better than does a linear model. That linear response is largely driven by data in the dose range of 0.2 to 2 Gy, but about 75% of the survivors in the cohort were exposed at doses between 0.005 and 0.2 Gy, which is the range of doses of primary interest for low-dose risk estimation.

It is unclear what happens after exposure to small doses

Nuclear Medicine Patients

Indications for PET/CT

Oncology 86%

Cardiology 2%

Neurology 11%

Other 1%
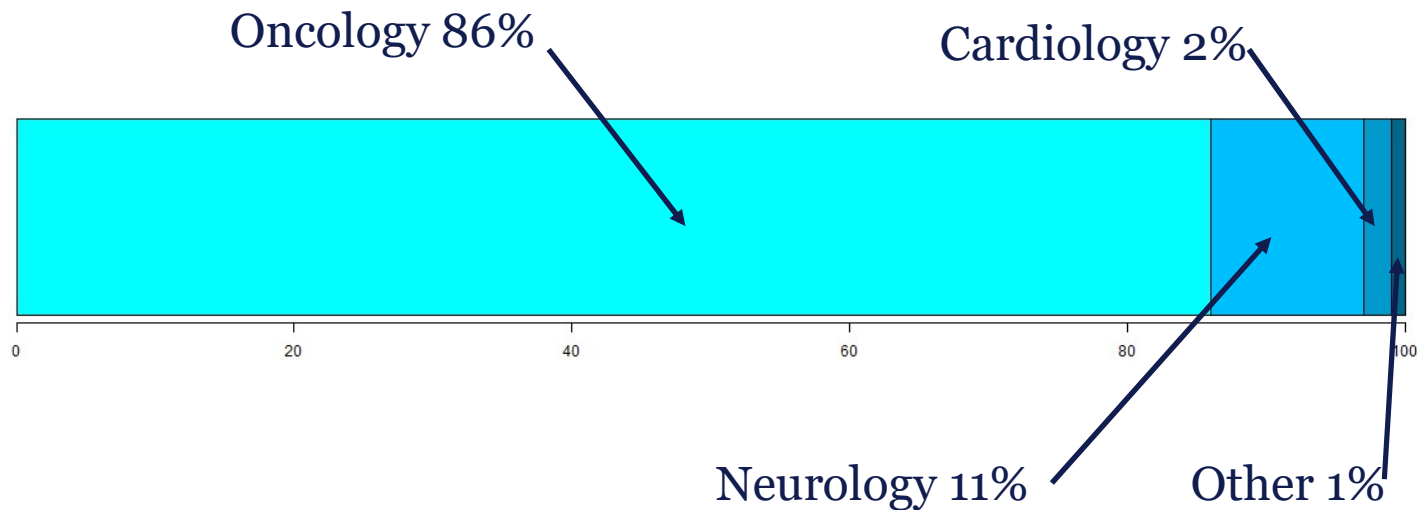
Average patient age ~60 a

Most patients have an extremely low probability to live to see a radiation induced late term effect (e.g. cancer)

Staff exposure

Chest dose [mSv] to staff per 1'000 patients and 370 MBq FDG per patient
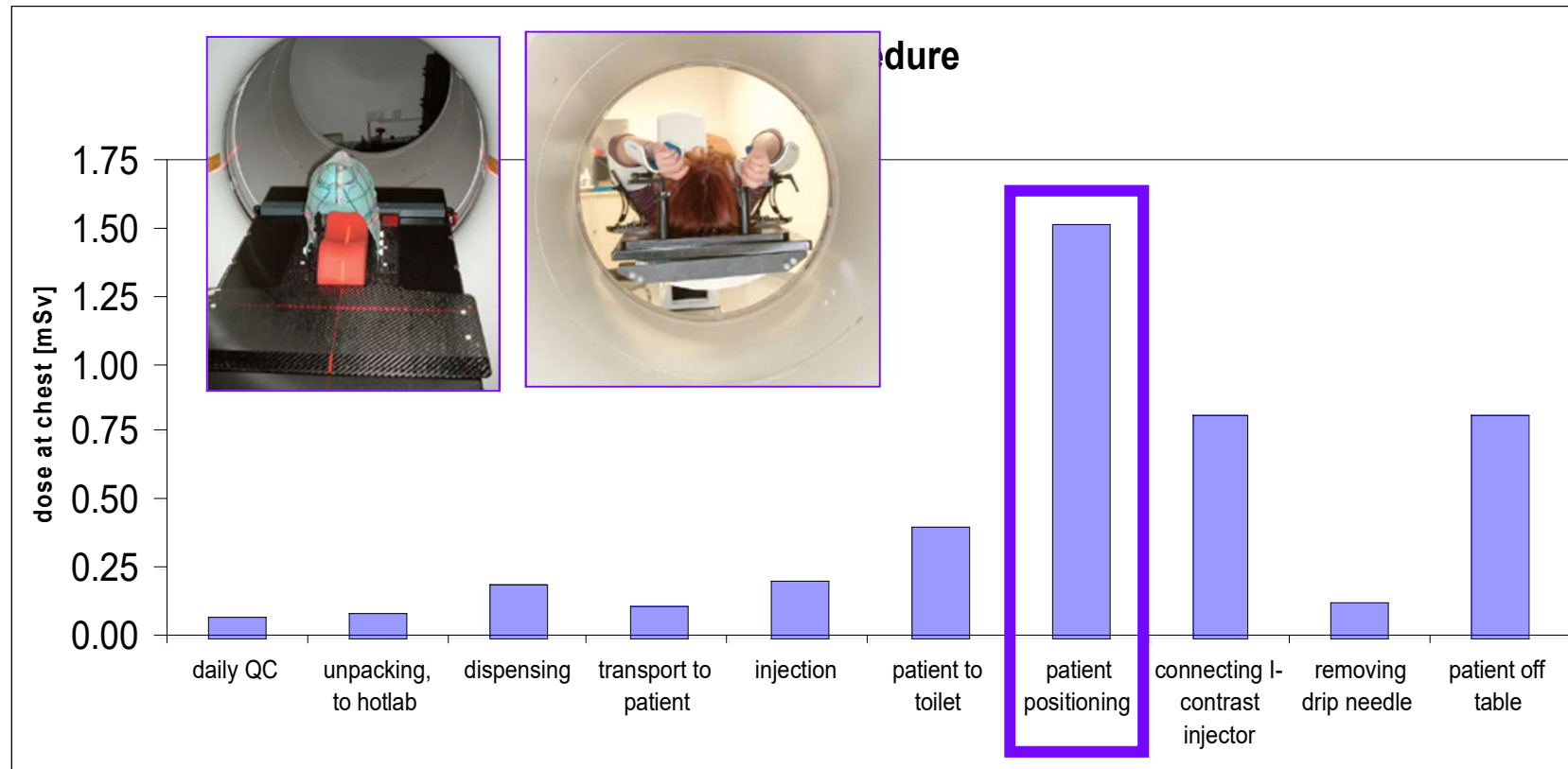
Pakbiers et al, EANM Conference records, abstract #471, 2005

Careful patient positioning vs. Staff exposure

Summary

➢ Ionizing radiation can cause severe health damage

➢ There are different ways to describe "dose"

➢ Radiation effects need to be separated in deterministic and stochastic effects

➢ Dose calculation are important in therapy approaches

➢ Dose calculations for diagnostic are a rough estimation of the general risk for the population and have no value for an individual patient. However, they can be used for protocol optimizations

ivo.rausch@meduniwien.ac.at

Interaction with biological tissue

Direct interactions
Direct damage of the DNA, organells...

Indirect interactions
Formation on reactive molecules in the water content of the cell
Reactive molecules cause damage by chemical reactions

Direct photon-DNA interaction

Indirect interaction

H_2O_2

e_{aq} ← H_2O
+
O_2

$O \cdot$
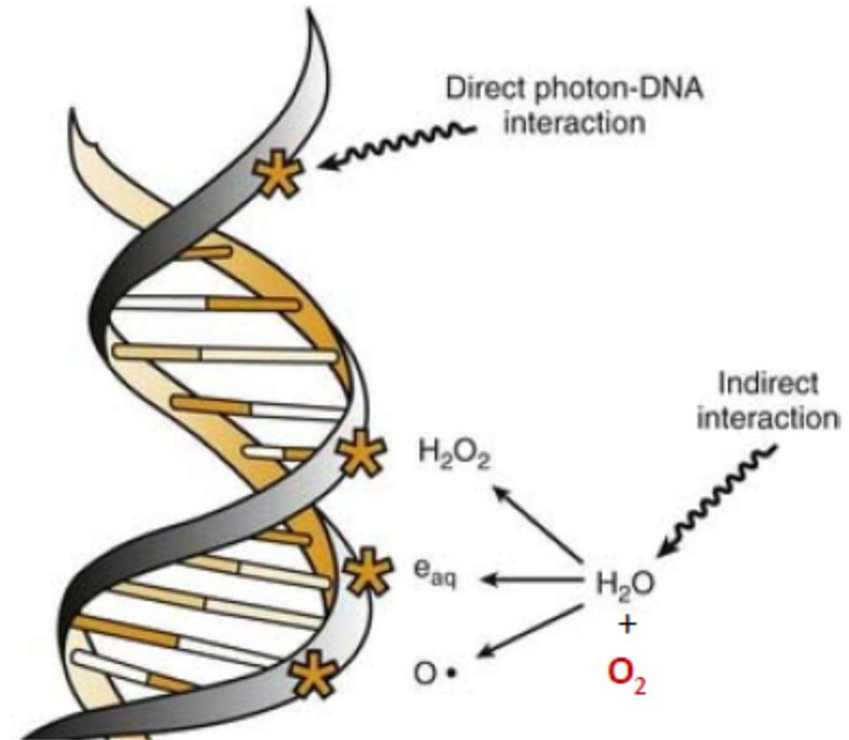
Interlude: Quality factor
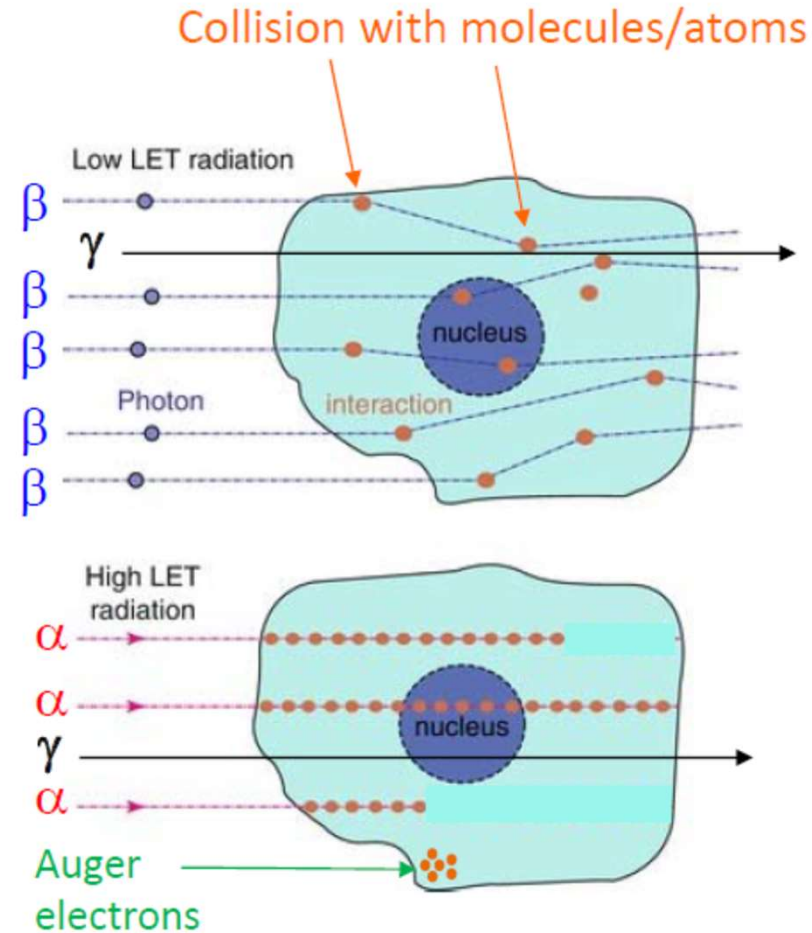
Principle of Nuclear Medicine

Labeled biomolecule = Tracer

^{18}F
Radioactive isotope

Tracer administration to patient

Emission tomography

Tracer distribution showing areas of enhanced metabolism

Introduction
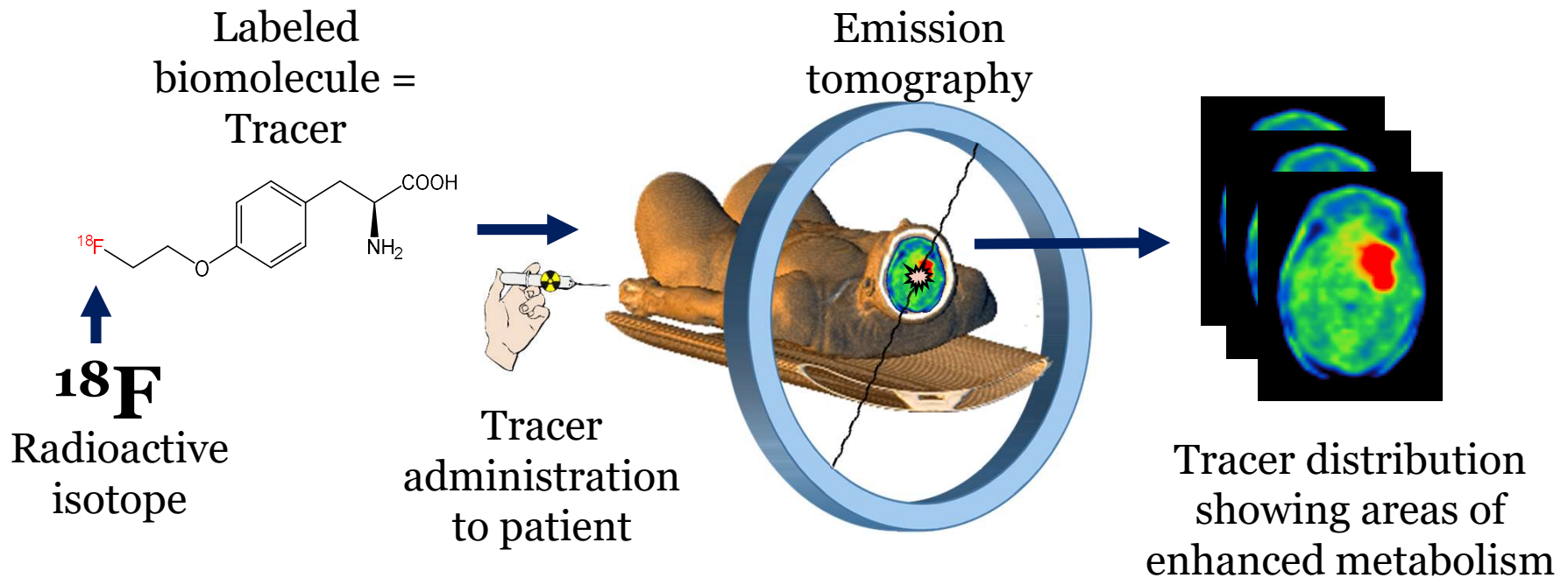
17.1.2014 EN Official Journal of the European Union L 13/1

COUNCIL DIRECTIVE 2013/59/EURATOM

of 5 December 2013

laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation, and repealing Directives 89/618/Euratom, 90/641/Euratom, 96/29/Euratom, 97/43/Euratom and 2003/122/Euratom

THE COUNCIL OF THE EUROPEAN UNION,

Article 58

Procedures

Member States shall ensure that:

(a) written protocols for every type of standard medical radiological procedure are established for each equipment for relevant categories of patients;

(b) information relating to patient exposure forms part of the report of the medical radiological procedure;

(c) referral guidelines for medical imaging, taking into account the radiation doses, are available to the referrers;

(d) in medical radiological practices, a medical physics expert is appropriately involved, the level of involvement being commensurate with the radiological risk posed by the practice. In particular:

Introduction

Calculating Dose: Practical Issues

Radiation type
➢ Known from x-ray output or used isotope

Radiation intensity
➢ Known in x-ray, estimated for internalized isotopes
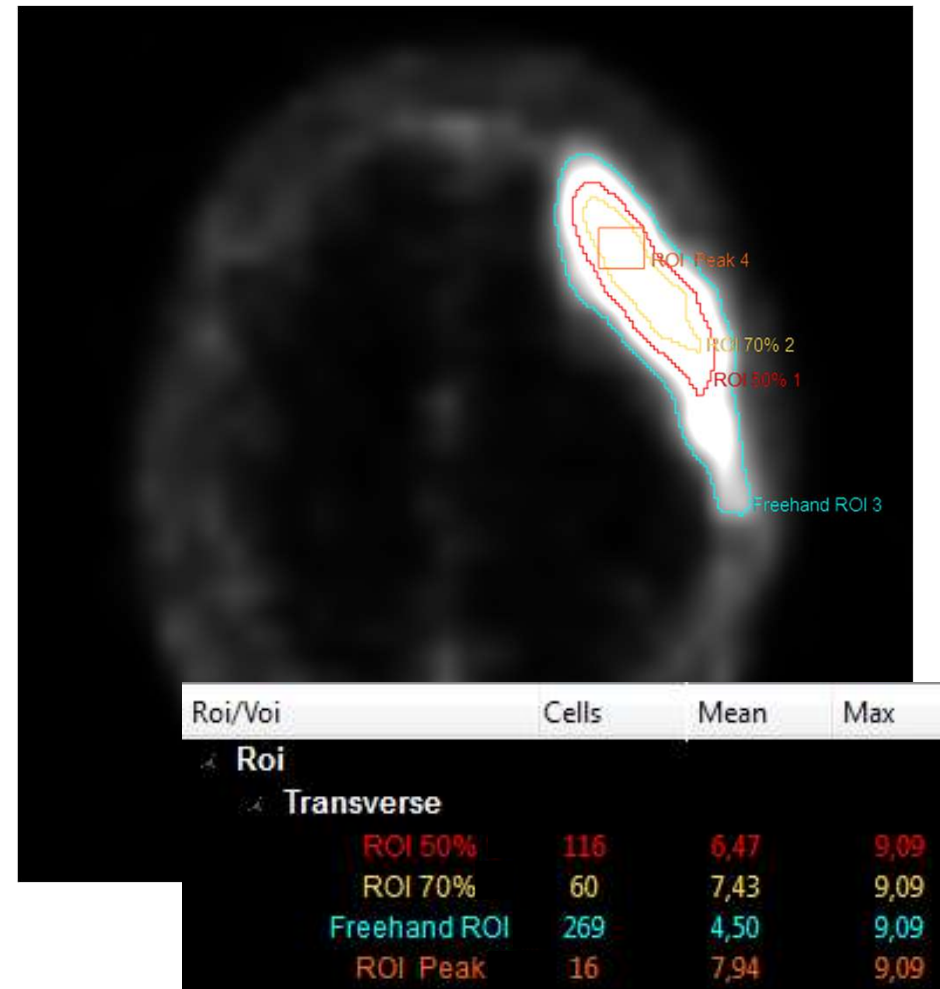➢ Changes in media (e.g. Absorbtion of radiation)

Material composition

Biological effectivnes of the radiation

Dose calculation can be done using Monte Carlo simulations
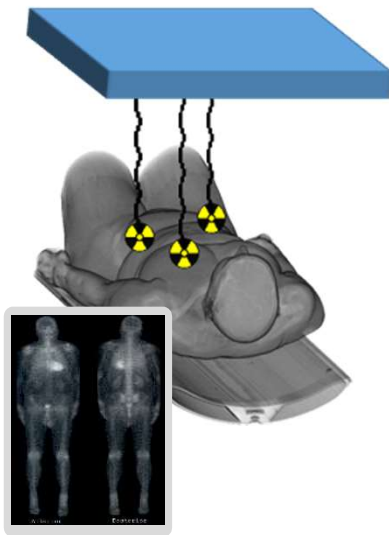
Example: Region of Interest

Different SUV measures

- MAXIMUM Pixel value

- MEAN value of a ROI

  ➢ Hand drawn ROIs

  ➢ Fixed size ROIs
     (e.g. "SUV Peak")
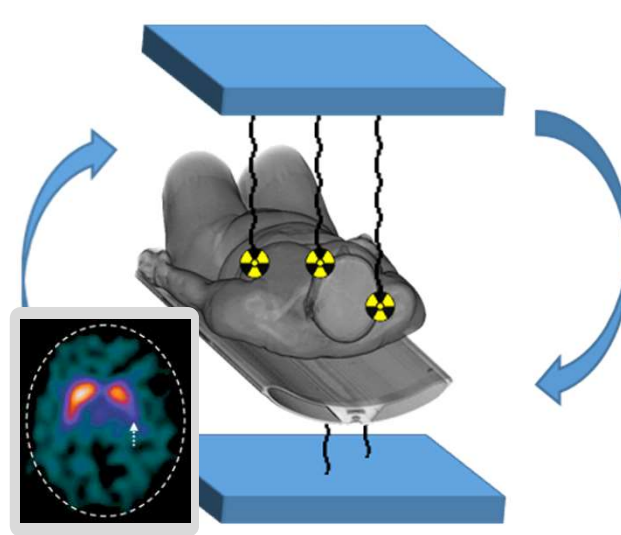
  ➢ Threshold based ROIs

  ➢ Advanced algorithms…

Roi/Voi	Cells	Mean	Max
Roi			
Transverse			
ROI 50%	116	6,47	9,09
ROI 70%	60	7,43	9,09
Freehand ROI	269	4,50	9,09
ROI Peak	16	7,94	9,09

Nuclear Medicine instrumentation
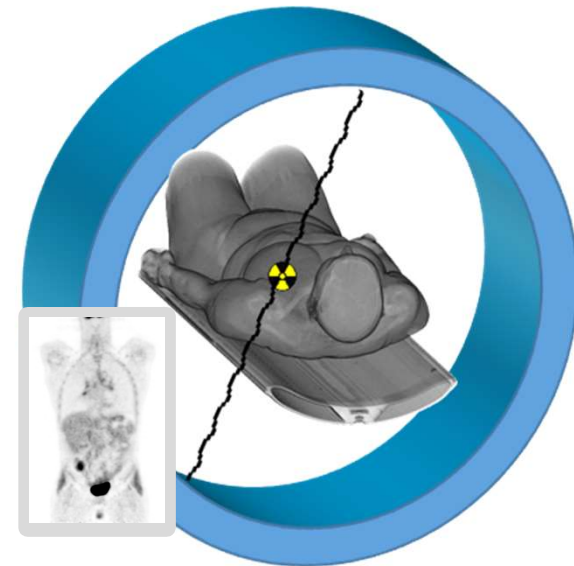

Gamma camera

SPECT

PET

Quantitative when combined with proper corrections (e.g. attenuation and scatter)

Calculating Dose: Practical Issues

Radiation type

➢ Known from x-ray output or used isotope

Radiation intensity

➢ Known in x-ray, estimated for internalized isotopes
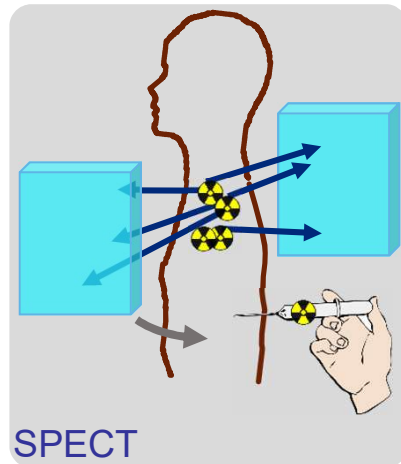
➢ Changes in media (e.g. Absorbtion of radiation)

Material composition

Biological effectivnes of the radiation

Dose calculation can be done using Monte Carlo simulations

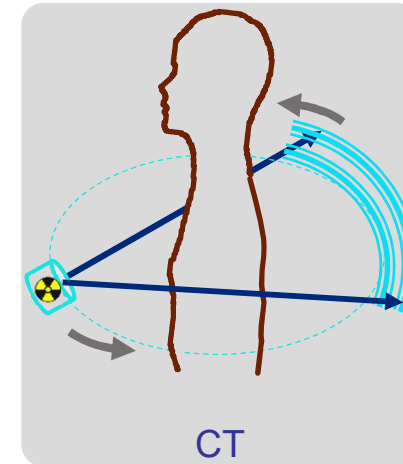# Hybrid Imaging

SPECT

SPECT

+

CT

CT

=

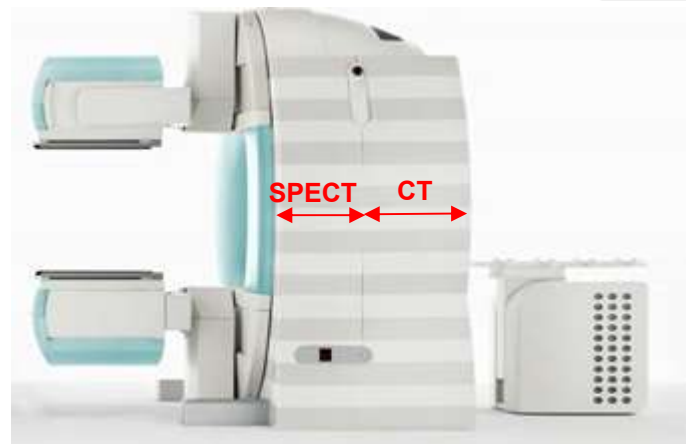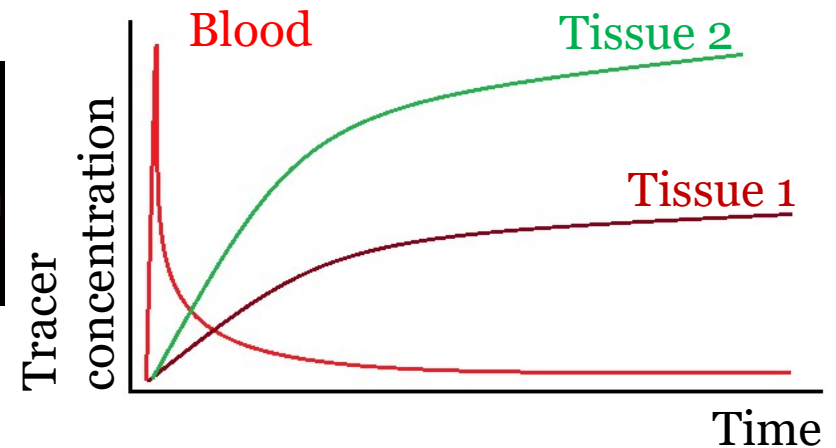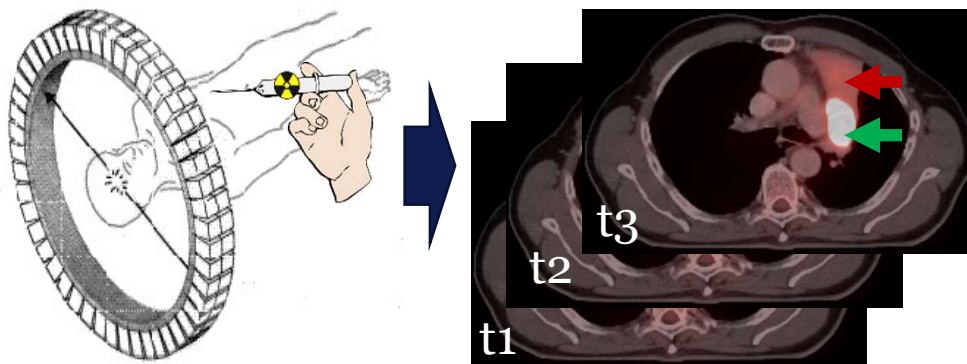SPECT   CT

Example: SPECT/CT

Functional information (SPECT - PET) + anatomical information (CT - MR)
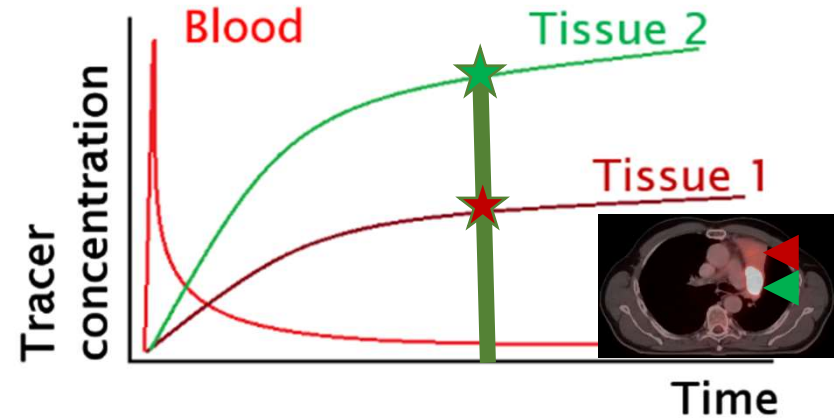
Quantification of metabolic activity

Clinically relevant is the assessment of metabolic activity.

➢ Requires dynamic measurements and kinetic modeling

Standardized Uptake Value

Tissue uptake after a certain uptake period normalized to an estimate of available tracer

$$SUV = \frac{Act_{VOL}\left[\frac{kBq}{ml}\right]}{\frac{Act_{administrated}[MBq]}{BW[kg]}}$$

Normalize to

Body weight

Lean Body mass

SUV: an easy solution to a complicated problem

Summary

➢ Quantitative values from nuclear medicine can substantially vary between different scanners and examinations

➢ Quantitative imaging requires standardized procedures

➢ Harmonization between systems is feasible and an a prerequisite for comparability of inter system results

If you know what you are doing nuclear medicine data is quantitative
else
it is just images !