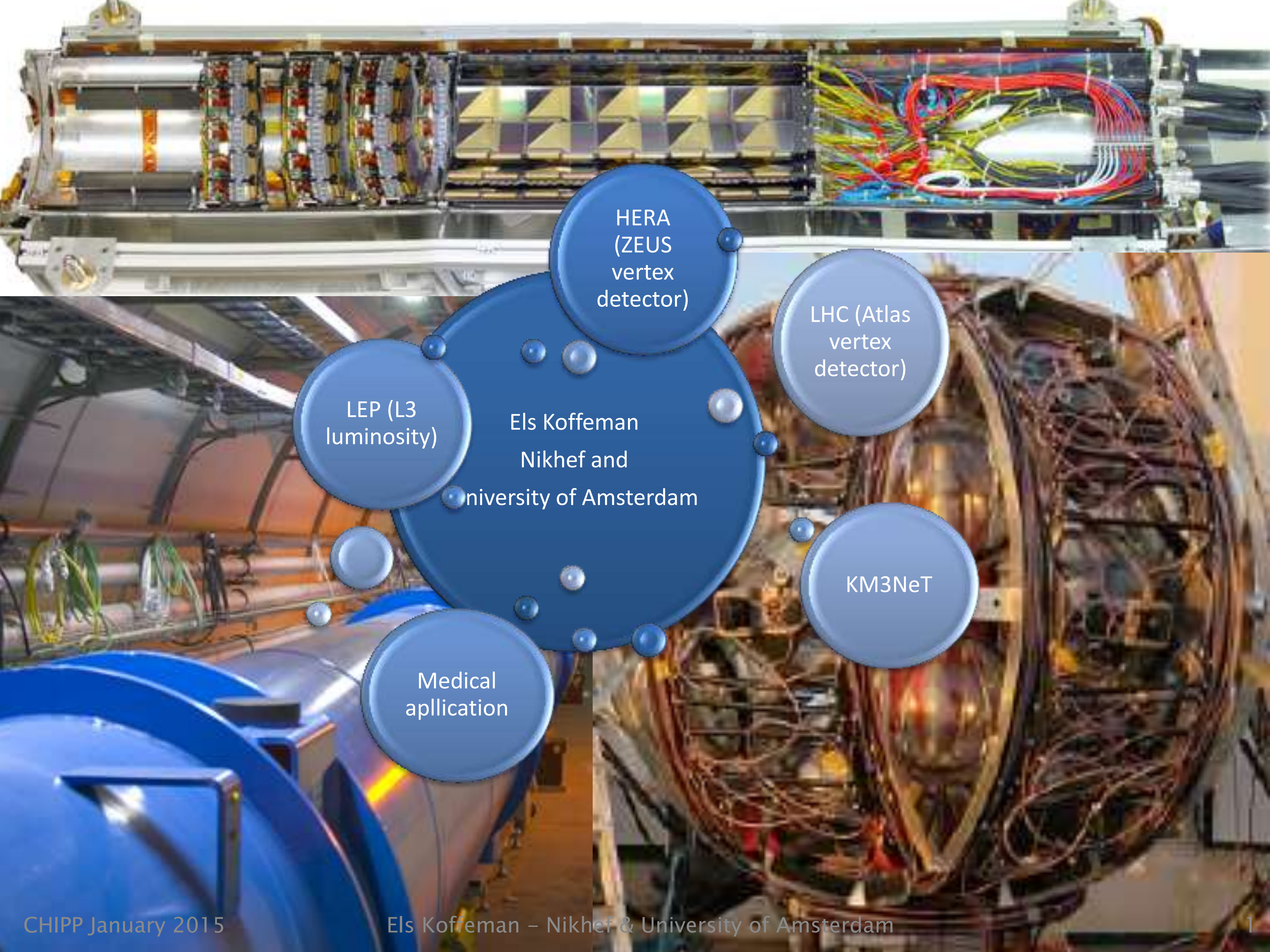
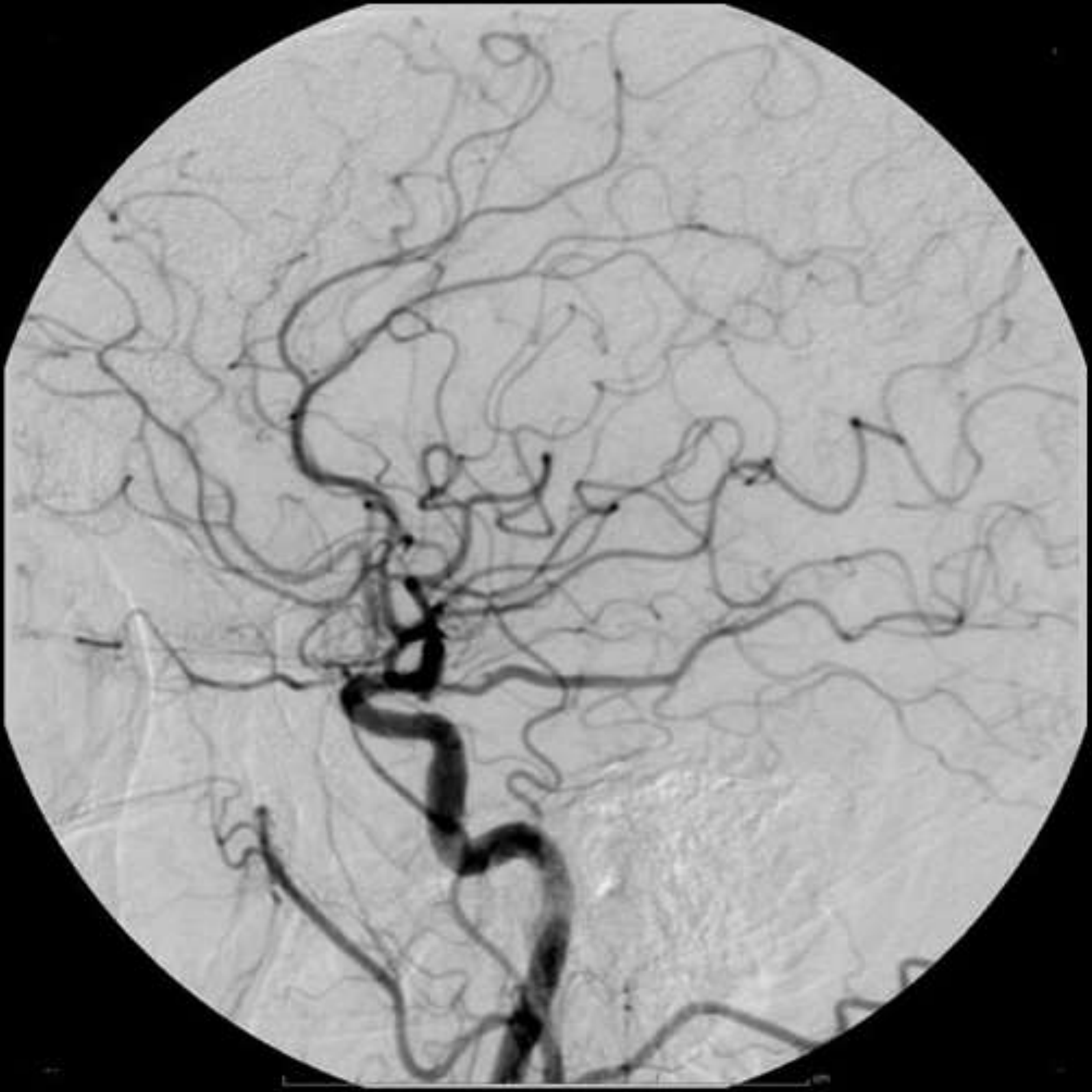

HERA (ZEUS vertex detector)
LHC (Atlas vertex detector)
LEP (L3 luminosity)
Els Koffeman
Nikhef and
niversity of Amsterdam
KM3NeT
Medical apllication

I: Observables
II: Particle Interactions
III: Tracking
IV: Medical applications

Els Koffeman
koffeman@nikhef.nl



Nuclear imaging

- External source:
  - X-ray images (with/without contrast fluid)
  - CT: Computed Tomography scan
- Radiopharmaceutical emitters in the body:
  - SPECT (Single Photon Emission Computed Tomography)
  - PET (Positron Emission Tomography)
- NMRI (not treated today)
  - nuclear magnetic resonance image

IONISING RADIATION

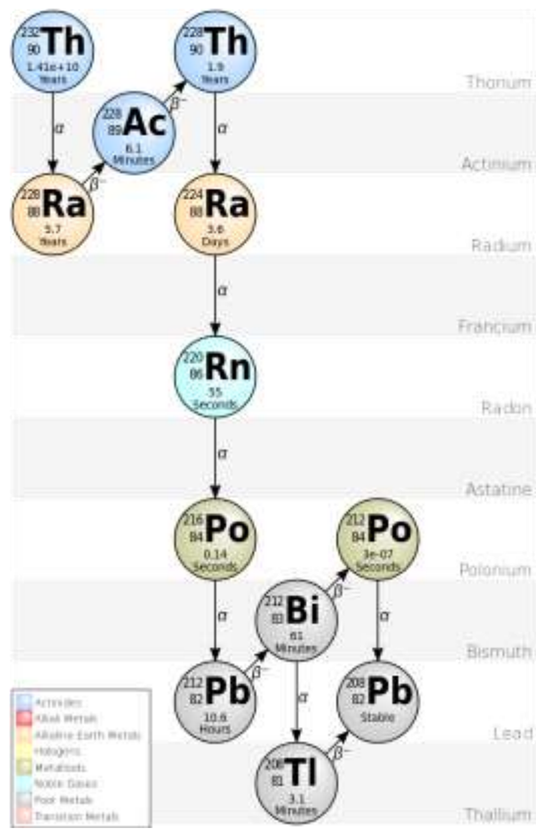
- Charged particles and photons (X-rays and gamma rays)

- INTRINSIC risks
  - exposure of healthy tissue
    - in patient
    - staff
- SAFETY
    - production radioactive waste
    - accidents during production
    - accidents during treatment

Natural sources

$$\frac{dN}{dt} = -\lambda N$$

- Atmospheric muons (and neutrino's)
- In food/body isotopes like
  - ^{40}K and ^{14}C
- Rock can contain Thorium generating Radon (which is a gas and can be inhaled



Photon attenuation

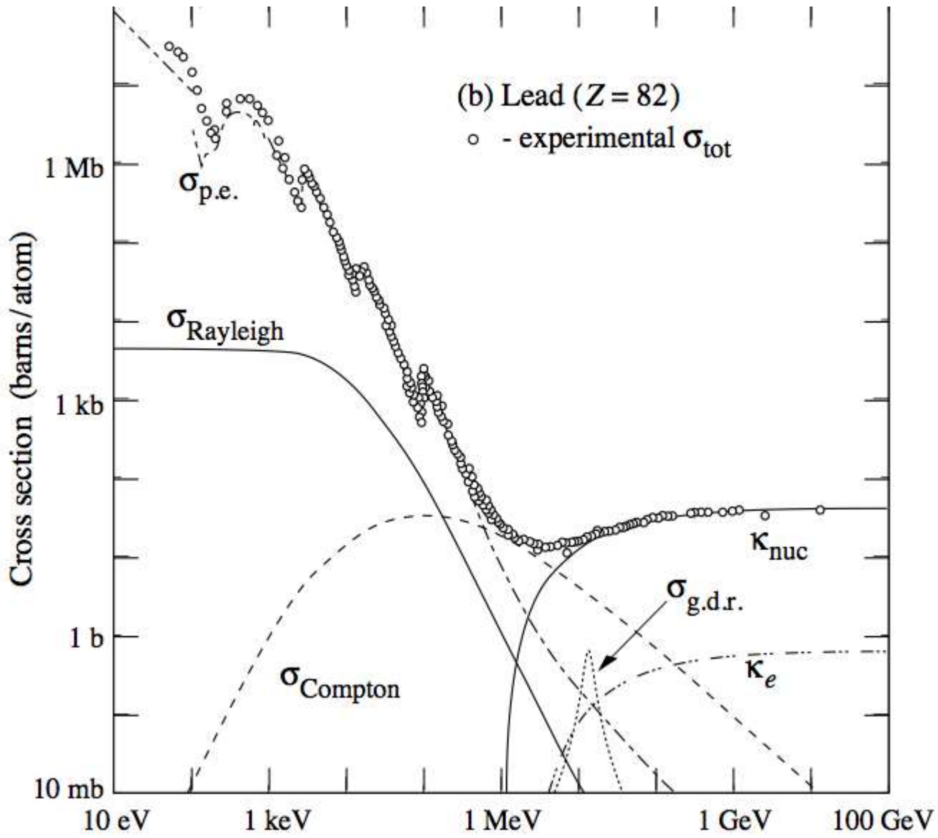
$$\frac{dI}{dx} = -\mu I$$

- Photo electric effect (cross section like Z^4/E^3)
- Pair creation
- Compton scattering

$$I(t) = I_0 e^{(-\mu x)}$$

$$\mu = \mu_{foto} + \mu_{compton} + \mu_{pair}$$

$$\frac{\mu}{\rho} = \sum_i w_i \left(\frac{\mu_i}{\rho_i} \right)$$



Example

- Diagnostic image of two (healthy) lungs
  - typical dose 0.1 mSv

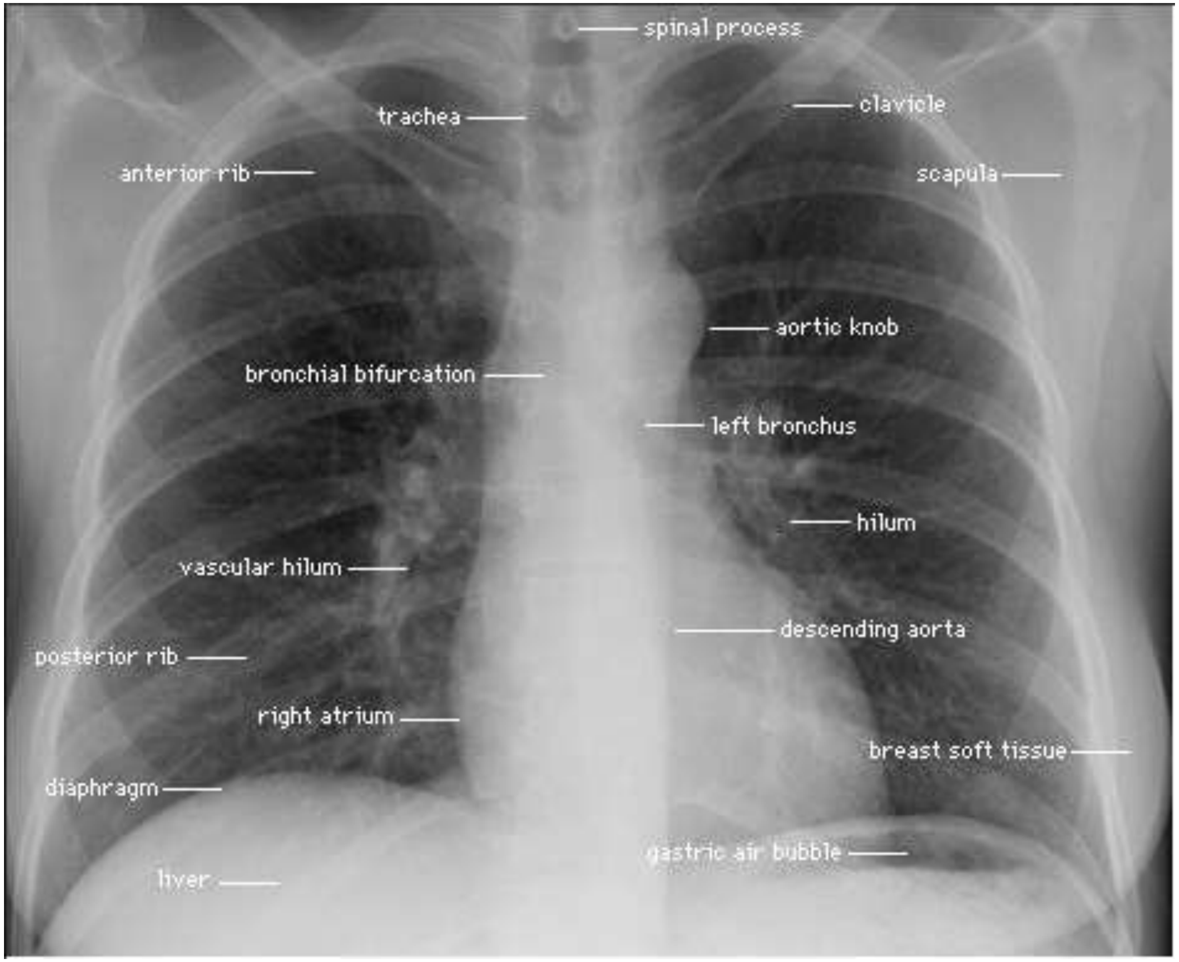
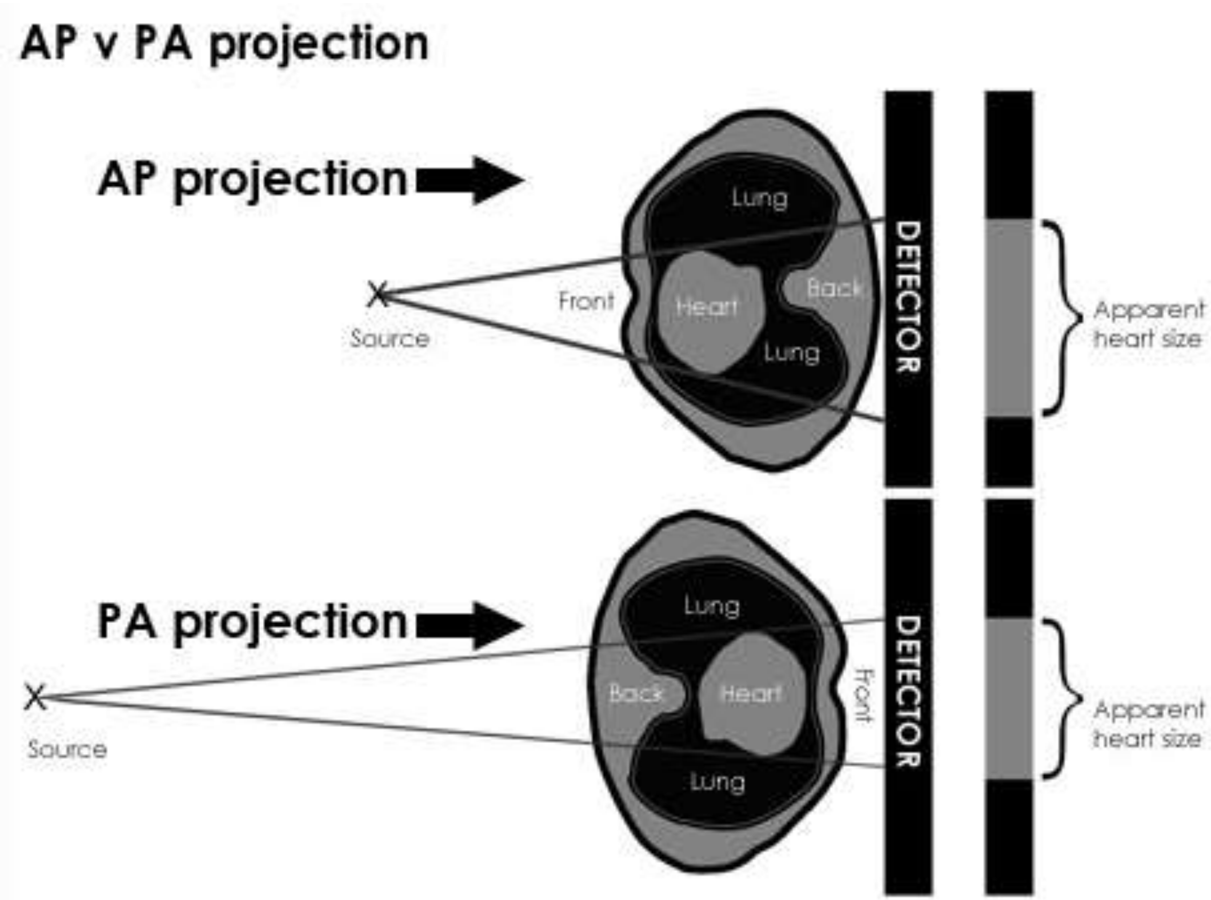


Image quality

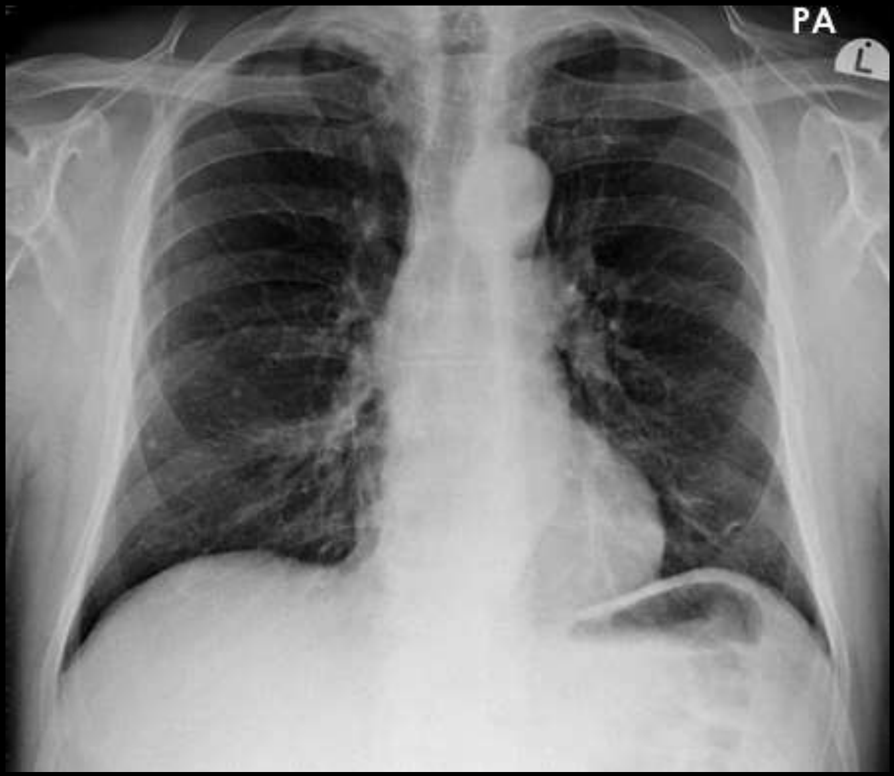
- Resolution in energy, position and time (correlated!)
  - statistical fluctuations in signal
  - noise
  - shadowing
  - beam hardening
  - scattering of (signal) photons
  - granularity of recording device
- Sensitivity
  - interactions depending on electron density
  - chemical/biological intake of tracers

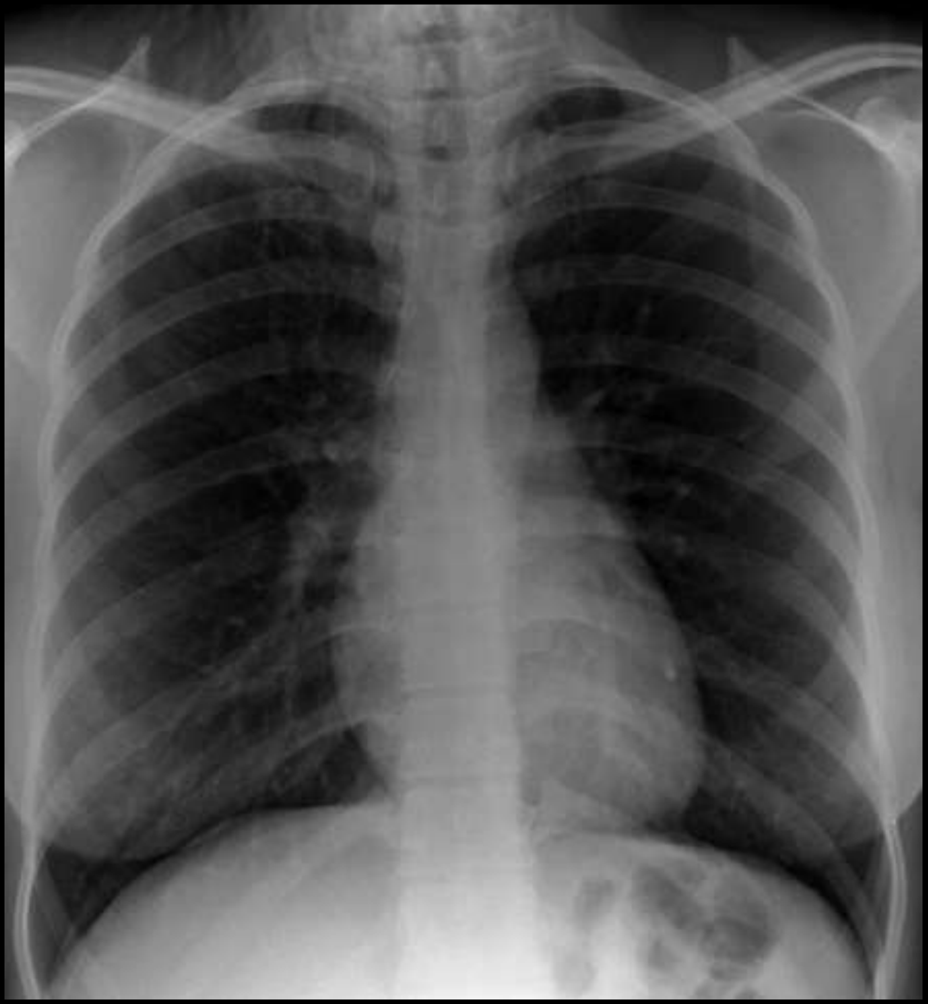
Chest Xray example



http://www.radiologymasterclass.co.uk/tutorials/chest/chest_quality/chest_xray_quality_projection.html

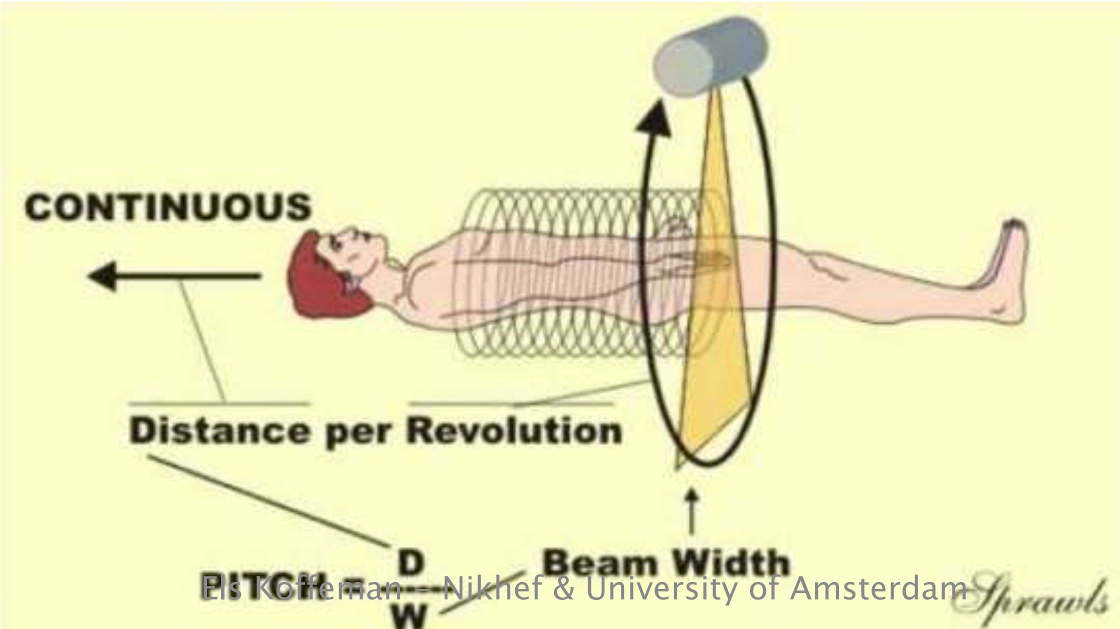
Artefacts….





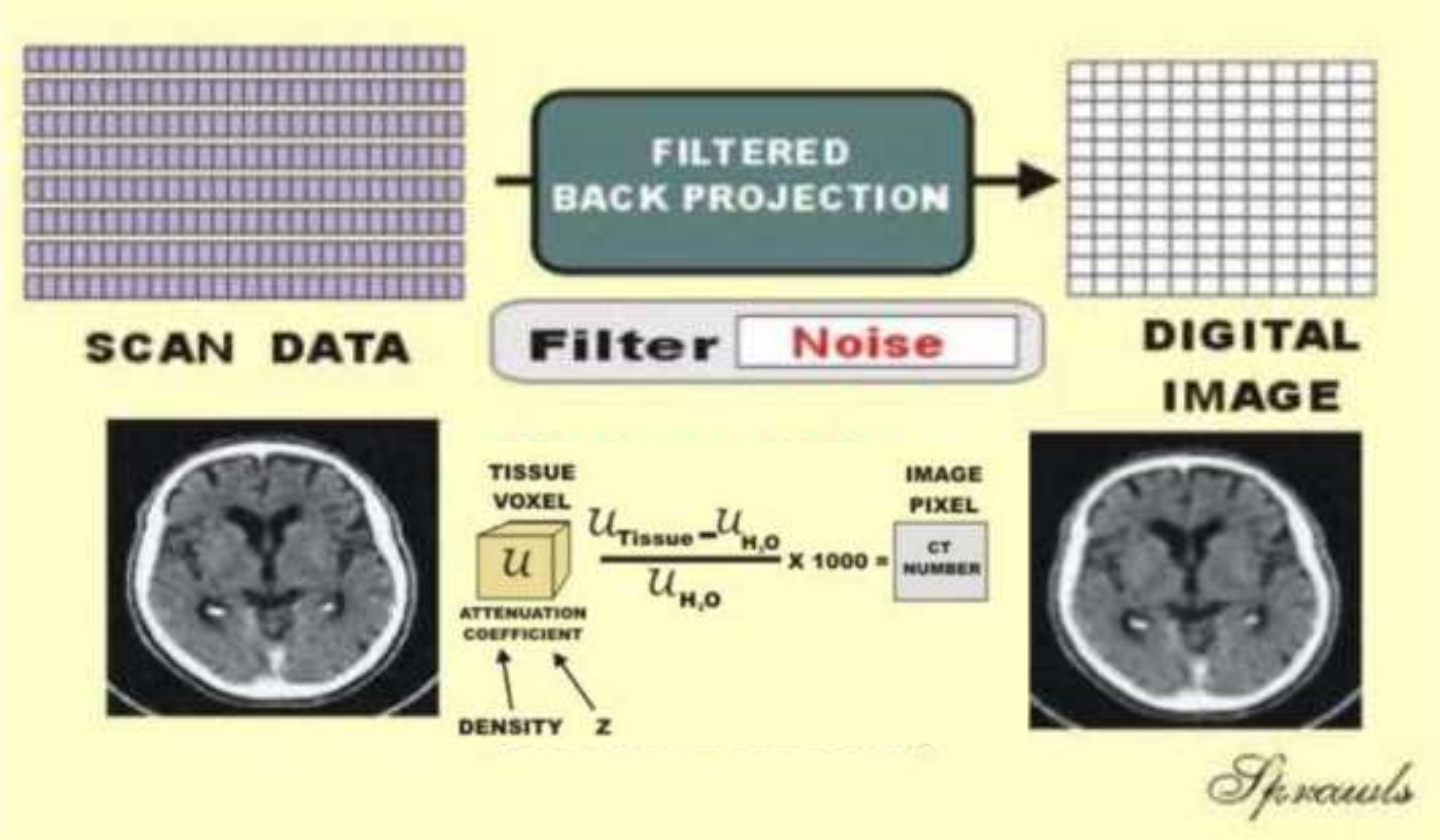
CT scan

- CAT = computed axial tomography
  - source and detector rotate around the patient to make between 10 and 100 projection of the object
  - after the introduction scan took hours and the reconstruction days
- Radiation dose is fairly high



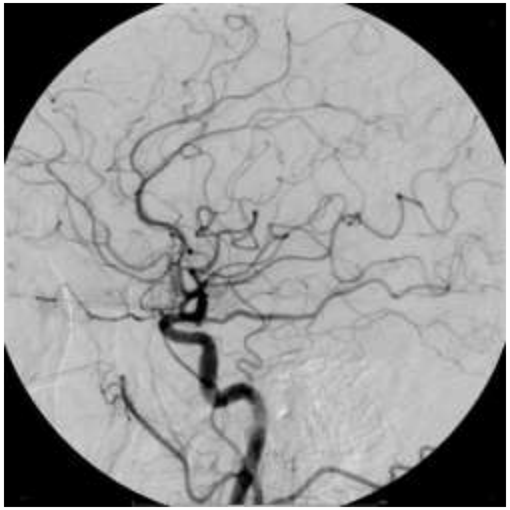
CT scan : image reconstruction

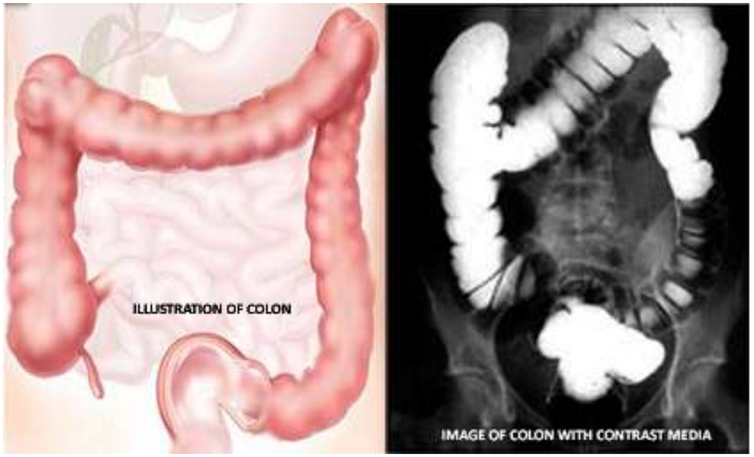
- array met N(positie) => matrix van het object



Pharmaceutica: contrast

- contrast fluids
  - Iodine
  - Barium
  - Air
- Chemical properties not relevant but physical properties
  - soluble
  - degradable
  - permeable





Radioactive tracers

	18- F Na F	Tc-99m MDP
Chemical structure	Sodium salt of 18-F fluorine	Polyphosphonates labeled with Tc-99m
Radioisotopic characteristics	Positron emitter, Half Life – 110 mins	Gamma emitter Half Life – 6 hours
Availability	Cyclotron 18O (p,n) 18F	99Mo-99Tc Generator
Imaging System	PET scanner PET/CT scanner	Gamma Camera SPECT/CT cameras
Dose	6-10 mCi	20-25 mCi
Imaging window	< one hour postinj.	3 hours postinj.
Uptake characteristics	Two fold higher than polyphosphonates	
Blood Clearance Post-administration	Faster clearance than MDP	
Protein Binding	Nil, Faster excretion	Yes, slower excretion
Target to Bkg. ratio	Superior	Good

http://humanhealth.iaea.org

Radiopharmaceutica

- Isotope decays and body expells radioactive tracer

$$Q = \frac{-dN}{dt} = \lambda N$$

$$N(t) = N_0 \exp(-\lambda t)$$

$$\tau_{1/2} = \frac{\ln 2}{\lambda}$$

$$\text{biological halftime} \; : \; \frac{1}{\tau_{\text{eff}}} = \frac{1}{\tau_{1/2}} + \frac{1}{\tau_{bio}}$$

Radiopharmaceutica

- Nuclear reaction
  - Neutron induced (reactor)
  - Proton induced (accelerator)
- Example of a generator “milking” Technetium

$$^{235}_{92}U + ^{1}_{0}n \rightarrow ^{236}_{92}U \rightarrow ^{99}_{42}M + ^{133}_{50}Sn + 4\,^{1}_{0}n$$

$$^{99}_{42}\mathrm{Mo} \xrightarrow{\tau=66h} \mathrm{b} + ^{99}_{43}\mathrm{Tc} \xrightarrow{\tau=6h} ^{99}_{43}\mathrm{Tc} + \gamma$$

Radiopharmaceutica

- Isotopes decay and body expells tracers

$$Q = \frac{-dN}{dt} = \lambda N$$

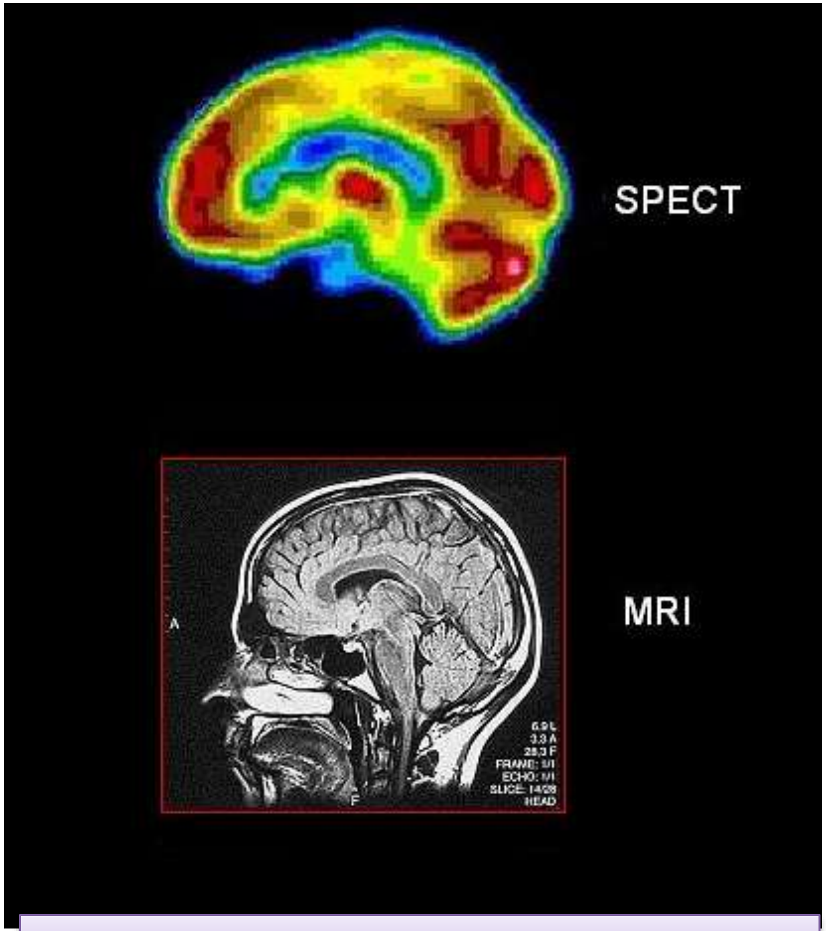
$$N(t) = N_0 \exp(-\lambda t)$$

$$\tau_{1/2} = \frac{\ln 2}{\lambda}$$

$$\text{biological halftime} \;:\; \frac{1}{\tau_{\text{eff}}} = \frac{1}{\tau_{1/2}} + \frac{1}{\tau_{bio}}$$

SPECT (single photon emission)

- Radioactive tracer (Technetium)
  - isolated single photons emitted from the body (140 keV)
  - wide range of sources (tune activity and decay time)
  - Position resolution is rather limited



http://www.brain-spect.com/SPECTscans/NormalSag.htm

PET principle

- positron emissie tomography
- e^+e^- => 2 photons
  - conservation of Energy and momentum does not allow single photon emission

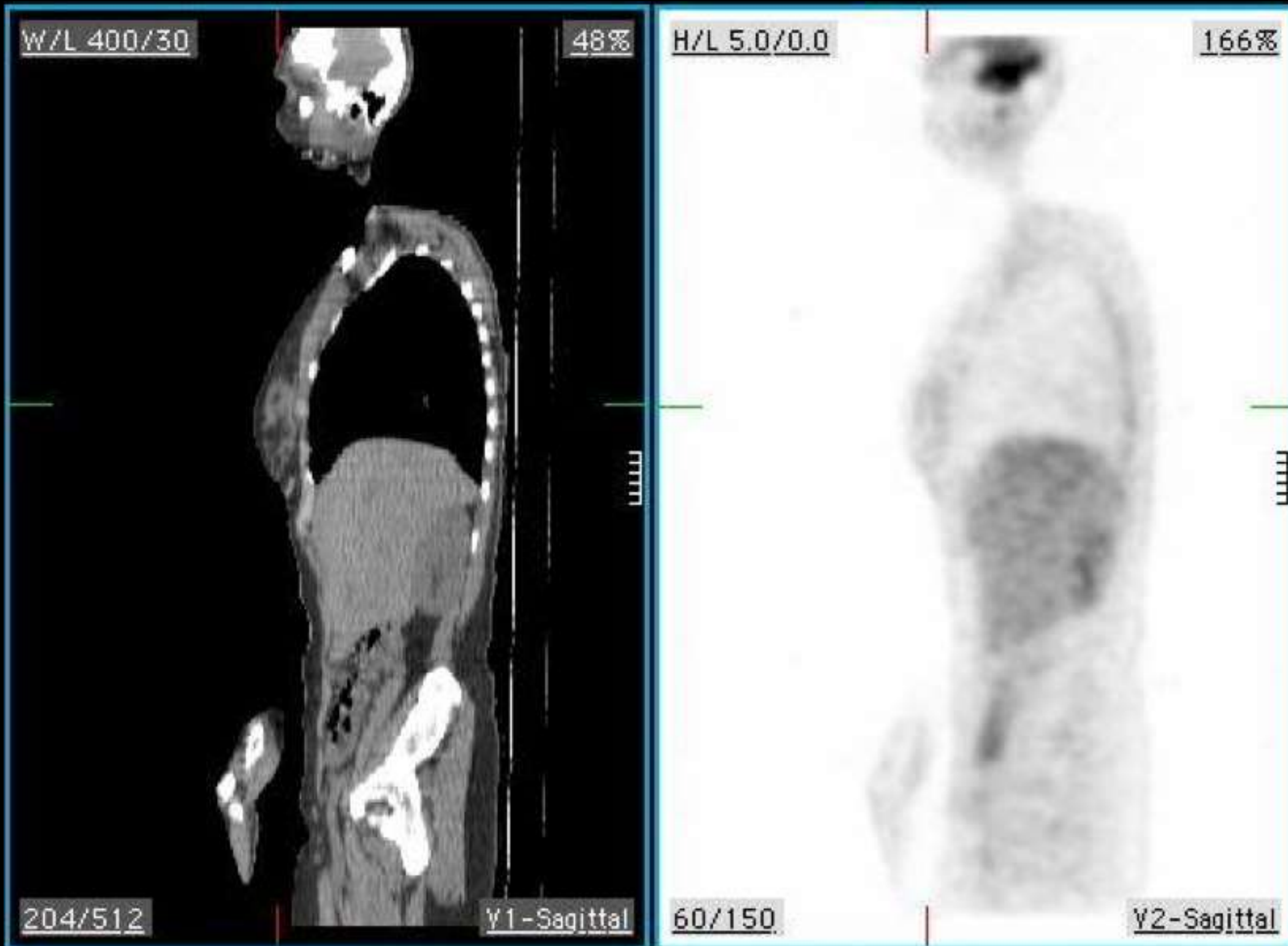
- most e^+ emitters have short live time: need cyclotron nearby

$$p^+ \rightarrow n + e^+ + \nu_e$$

PET (positron emission)

- PET
  - β+ emitter leads to annihilation and simultaneous emission of two photons
  - better position resolution and noise reduction(wrt SPECT)
  - state of the art is the use of timing information to add depth resolution
  - combination with CT to correct for attenuation

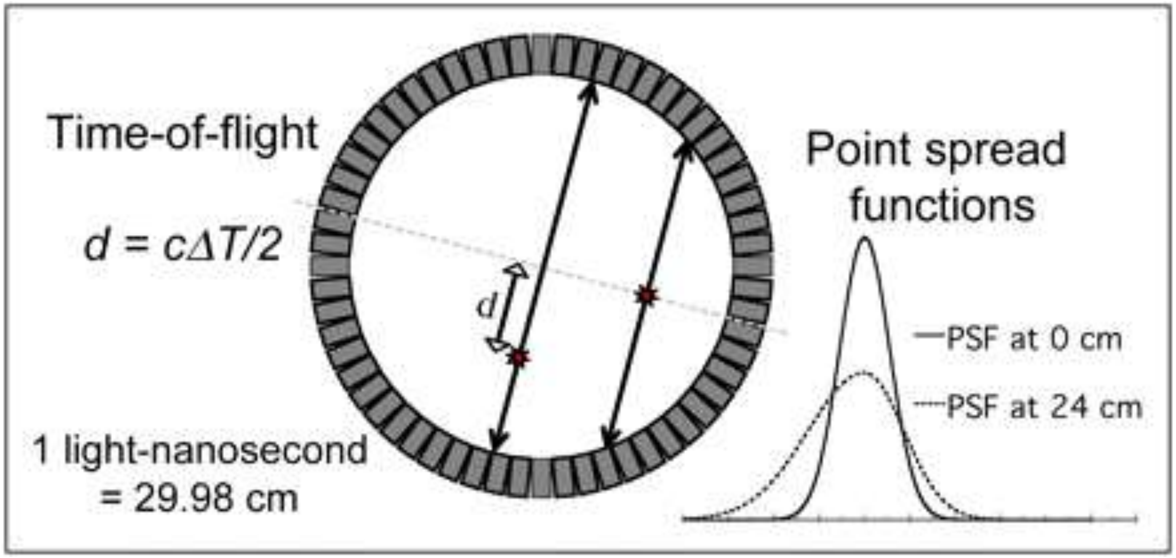
http://nucleus.iaea.org/HHW/NuclearMedicine/PET_CT_Gallery/Non_FDG_Imaging/01_SKELETAL_IMAGING/flouride_PET.pdf



http://nucleus.iaea.org/HHW/NuclearMedicine/PET_CT_Gallery/FDG_Biodistribution/2._Normal_Variants/1._Breast.pdf

PET advantages

- mix your isotope with a sugar/protein
- Cannot measure the ‘direction’ of a photon
  - Record time to suppress the background
  - Peter Dendooven KVI kart – Groningen

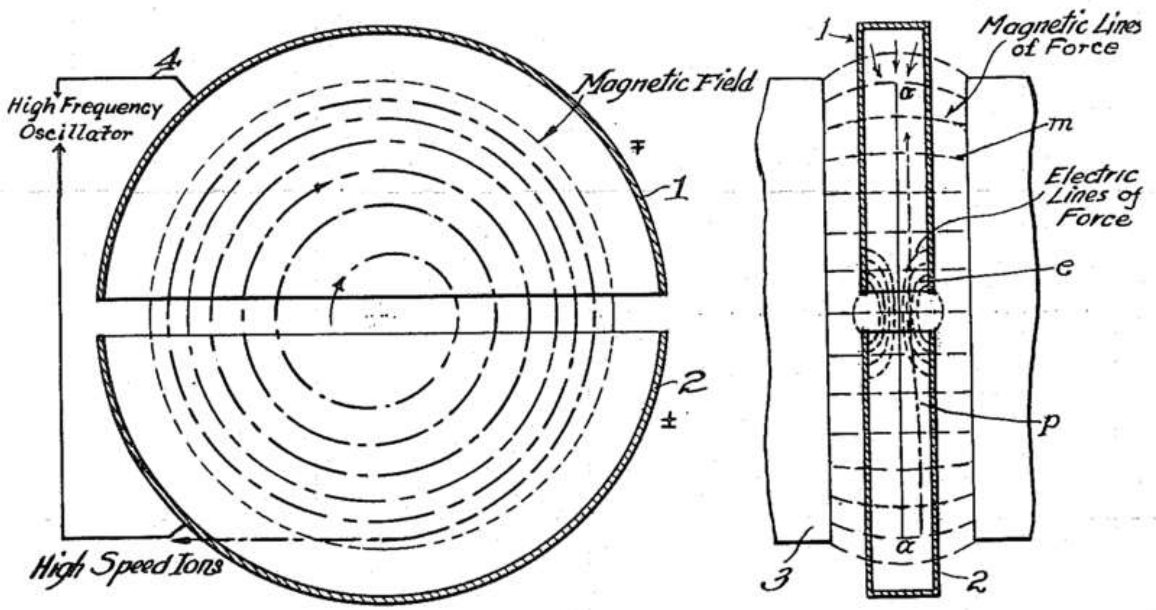


Radiotherapy

1946: *Radiological use of fast protons, Robert R. Wilson, Radiology 47(1946)487-491*

Dosage due to 140 MEV Protons in tissue

Cyclotron dates back to 1936



drawing made in 1936!

The Nobel Prize in Physics 1939 was awarded to Ernest Lawrence *"for the invention and development of the cyclotron and for results obtained with it, especially with regard to artificial radioactive elements".*

Dutch government

Regeling Protonentherapie

Nieuwsbericht | 31-07-2013

…is a new form of treatment

Protonentherapie is een nieuwe vorm van radiotherapie d behandeling van specifieke vormen van kanker. In Nederland bestaan nu nog geen faciliteiten om protonentherapie aan te bieden. De nieuwe Regeling protonentherapie maakt de verlening van maximaal vier vergunningen mogelijk, op grond van de Wet op bijzondere medische verrichtingen, voor protonentherapie met een behandelcapaciteit van in totaal 2200 patiënten.

Er is ruimte voor één aanbieder in het noorden van Nederland, twee in de Randstad en één in het zuiden. De vergunningprocedure staat alleen open voor Universitair Medische Centra (UMC's) of instellingen die een samenwerkingsverband hebben met een UMC. Vergunningen kunnen tot 30 augustus worden aangevraagd waarna deze getoetst zullen worden. Alleen indien aan alle voorwaarden wordt voldaan zal de vergunning verleend worden.

De Regeling protonentherapie met de daarbij horende vergunningvoorwaarden is te vinden in de Staatscourant: https://www.officielebekendmakingen.nl/stcrt-2013-22203.html

Radiotherapy in Netherlands

- used for cancer treatment
- Teletherapy
  - external sources
- Brachytherapie
  - internal source, less accurate mostly pain relief.
- 50.000 patients per year
  - 50% is treated to be cured

Recap: dosimetry

- Acticivity
  - expressed in nr. of decays per second or Becquerel (Bq)
  - fluence is per area dN/dA
  - flux is per time: dN/dt

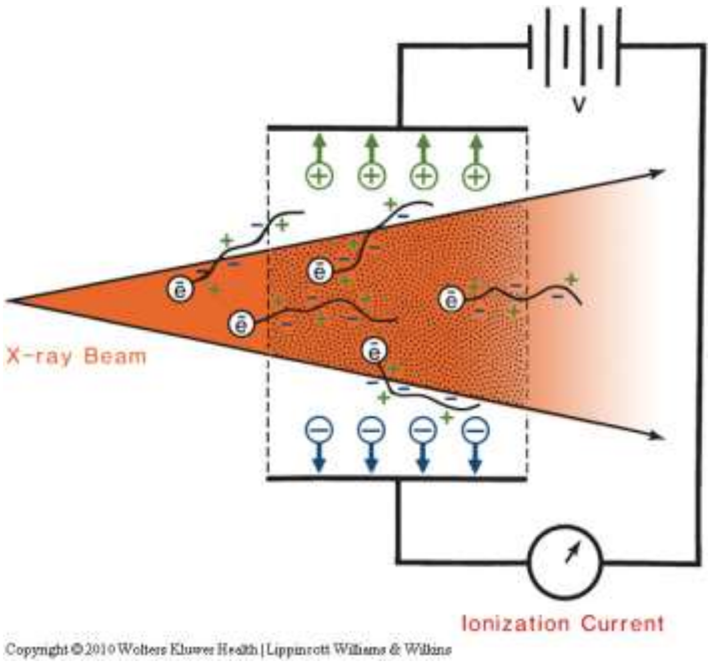
- Dose
  - energy deposit Gray (J/kg)
  - kerma Gray
  - Dose Gray
  - Equivalent (radiation) dose Sievert (Sv)
  - Effective (tissue) dose Sievert (Sv)

Tissue sensitivity

Tissue	ω_{tissue}
Gonaden /Glands	0,20
Rood beenmerg/ red bone marrow	0,12
Dikke darm / colon	0,12****
Longen / Lung	0,12
Maag / Stomach	0,12
Blaas /Blatter	0,05
Borstweefsel / Breast	0,05
Lever /Liver	0,05
Slokdarm /Esophagus	0,05
Schildklier /Thyroid	0,05
Huid /skin	0,01
Botoppervlak / Bone surface	0,01
Overige / Other	0,05** ***

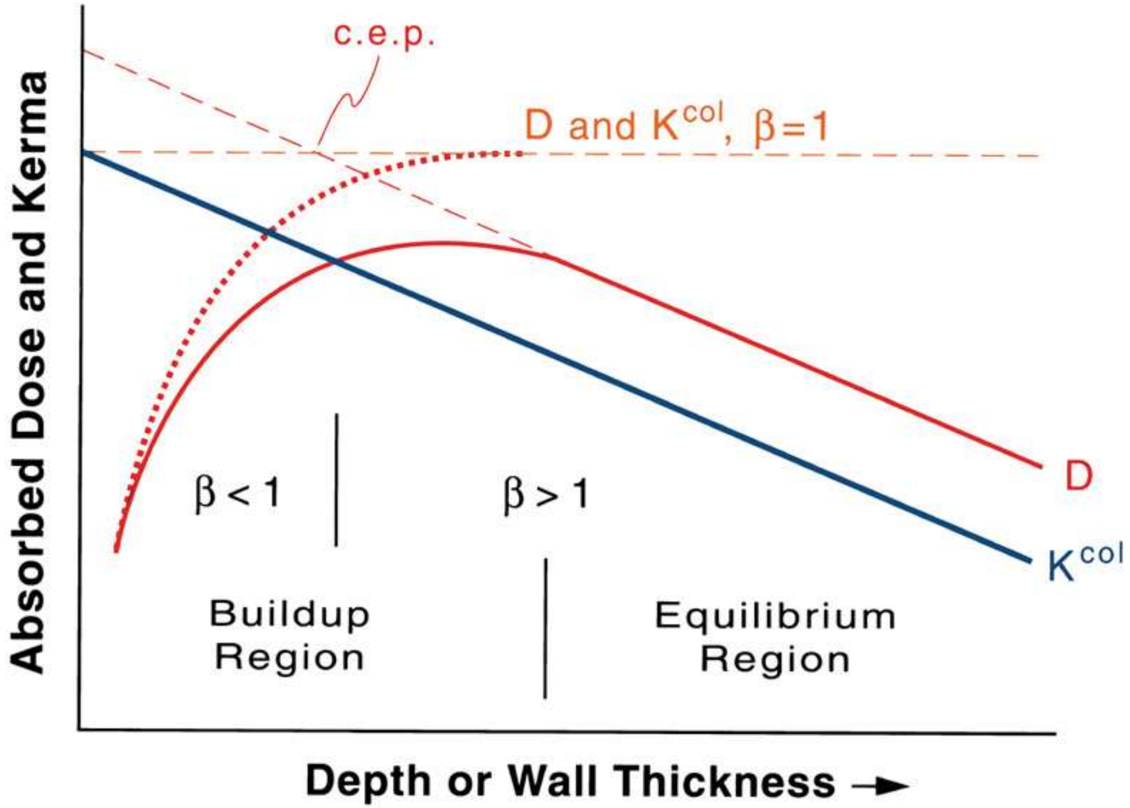
Exposure = X

- $E = dQ/dm$ (C/kg)
- Defined when balance has been achieved



Dose

- energy *deposit*
- E = dE/dm in J/kg or Gray (Gy)



Whole body radiation

- Acute damage when over threshold:
  - radiation disease (skin burn, hair loss, muceous damage)
  - NOT relevant at small dose, lethal at high dose
  - 3 Gy (LD50/60)
- Stochastic effects
  - no threshold
  - each interaction may cause mutation
  - MOST available data on small dose are NOT used: all patient data is discarded!

Biological effects

- LET = Linear energy transfer (keV/μm)
  - Optimum at 100 keV/μm
  - If LET is higher the result is overkill and reduction of the damage per Gray
- Physics of LET
  - exact ionisation mechanism
  - charged particles: Bethe Bloch (large fluctuations)
  - photons: photoelectric effect (compton in general does not contribute to deposited dose)
  - 1/(distance per energy)

Biological scales

remember that a photon with wavelength of 1 nm corresponds to an energy of about 1 keV

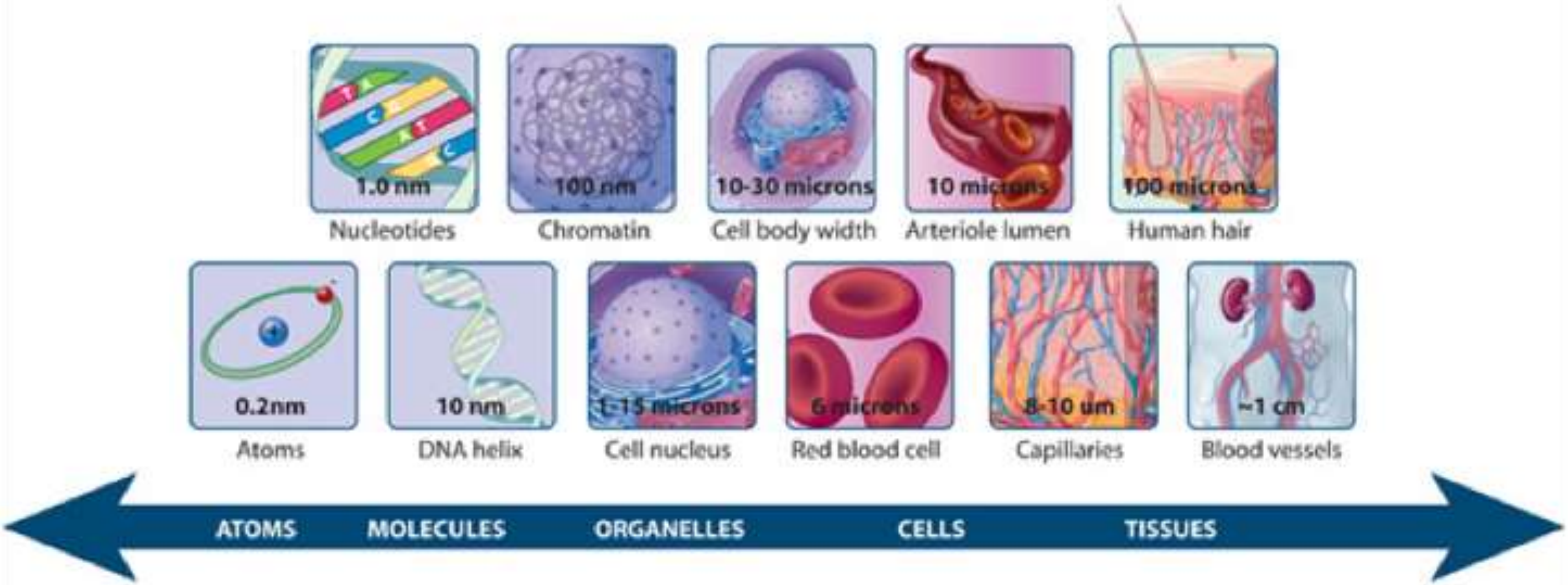


Figure 3: The relative scale of biological molecules and structures

Cells can vary between 1 micrometer (µm) and hundreds of micrometers in diameter. Within a cell, a DNA double helix is approximately 10 nanometers (nm) wide, whereas the cellular organelle called a nucleus that encloses this DNA can be approximately 1000 times bigger (about 10 µm). See how cells compare along a relative scale axis with other molecules, tissues, and biological structures (blue arrow at bottom). Note that a micrometer (µm) is also known as a micron.

Cel Damage

- Mechanism
  - DNA damage
  - oxygen radicals
- Programmed cel death (apoptosis)
  - Natural mechanism against DNA damage
- Radiation hardness depends on
  - cycle of cel
  - reproduction rate
  - oxygen supply
  - Specificity

Radiotherapy with photons

- Linac with electrons accelerated (up to 20 MeV)
- convert electrons to photons (20 MV)
- Treatment plan
  - design shape and different angles to get high dose in target and low dose around it
  - MC simulation using input from CT or MRI

Activities that give you a 'one in a million' probability to die

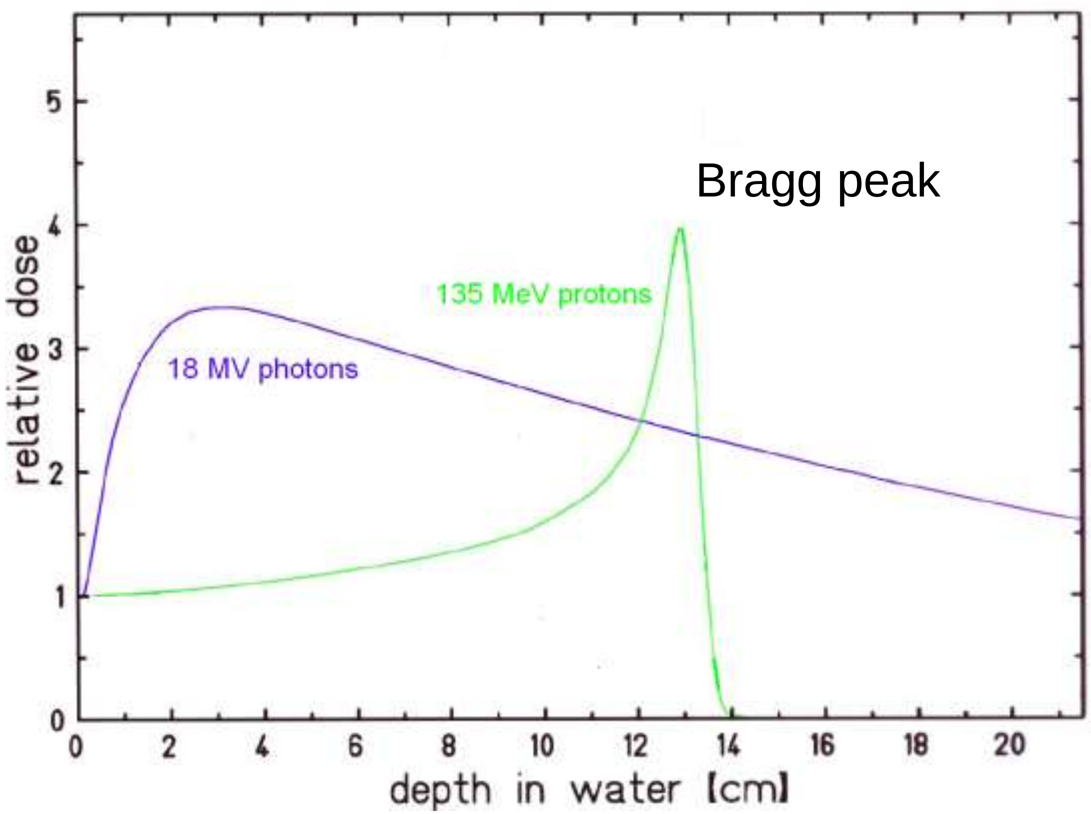
Smoking 1.4 cigarettes (lung cancer)
Radiation dose of 10 mrem (cancer)
Eating 40 tablespoons of peanut butter (liver cancer)
Eating 100 charcoal broiled steaks (cancer)
Spending 2 days in New York City (air pollution)
Driving 40 miles in a car (accident)
Flying 2,500 miles in a jet (accident)
Canoeing for 6 minutes (accident)

Cel damage

- Kill tumour with 20 – 80 Gy in total
  - (upto 10^{11} particles in a cubic centimeter, roughly one per cubic micron)
- Radiation hardness depends
  - oxygen supply (tumour cell profits from low oxygen)
  - phase of the cell
  - proliferation (bone marrow sensitive)
  - specificity (nerve cells insensitive)
- Tissue repair in hours (re-population)
  - in between fraction healthy tissue recovers
  - tumour tissue to some extent

Average dose

- reminder: curve only holds for photon beam: *<u>the 'range' of a single photon is unpredictable</u>*



courtesy GSI biophysics

LET

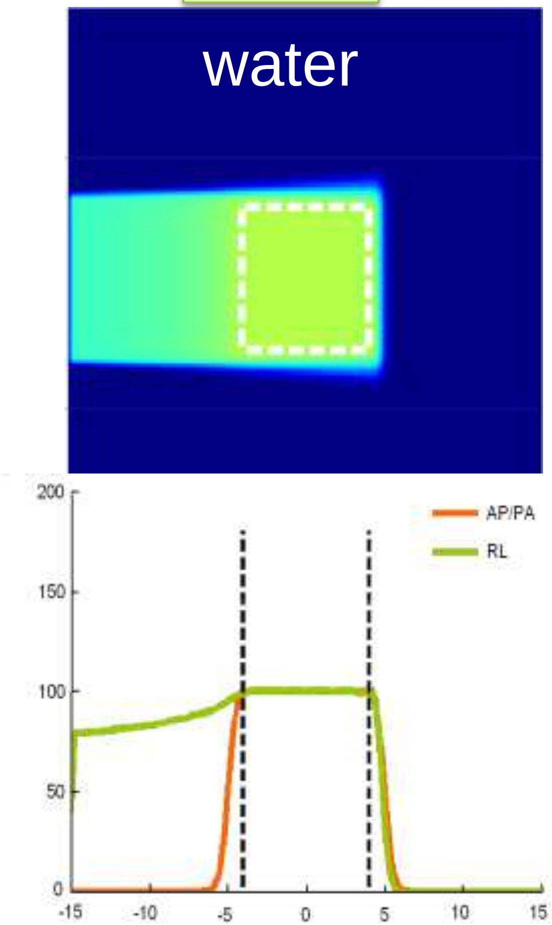
- Energy transfer per unit of length
  - looks like stopping power but this is ill defined for photons

type	dE/dL
heavy ion	~1000
alpha	200
protons	1-50
gamma	1

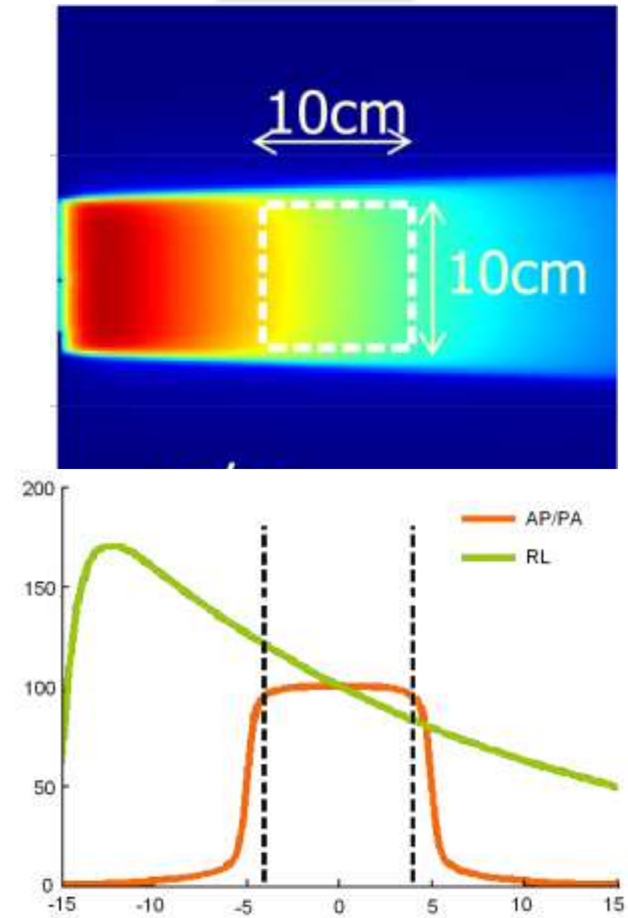
Dose comparison

courtesy R. Slopsema, FPTI

proton



photon



Charged particle therapy

- major advantage is less side effects
  - less dose in healthy tissue
  - reduce dose in vital organ close to tumour
- practical issue
  - patient position (day-to-day variations)
  - patient movement (breathing, swallowing)
- physics issue
  - stopping power derived from MRI or CT
- medical issue
  - Irradiation of the tissue closely surrounding a tumour may be beneficial

Keep track of tumour

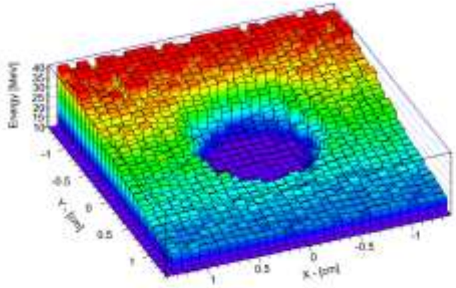
bron S. Mori en G.T.Y Chen, MGH

start of treatment

after five weeks

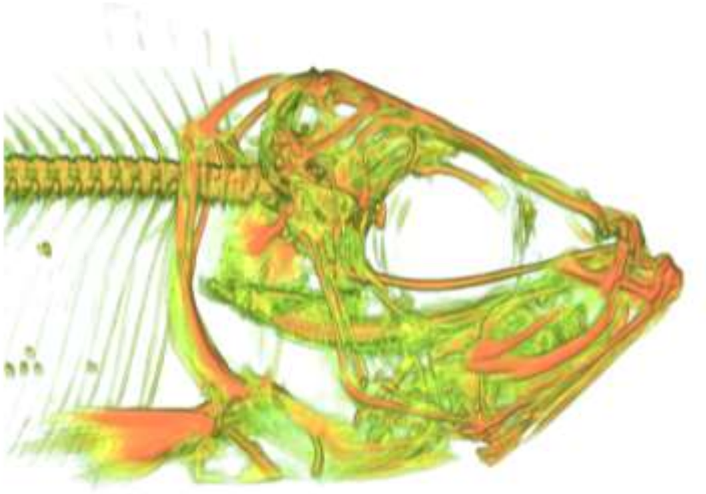
Nikhef R&D

- Develop better imaging to make sure the dose delivery is reliable and accurate



proton radiagraphy

colour CT scan



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