# NUCLEAR MEDICINE
## Basics, Pricnciples, Clinical role

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# DEFINITION OF NUCLEAR MEDICINE

Medical applications of unsealed radioisotopes for
- Diagnosis – Therapy - Research

Unsealed: into the living organism
- iv., sc., per os, inhalation, etc.

Participation in organ-tissue-molecular functions!
(Not the brachytherapy, and in vitro diagnostics)

Independent medical specialty (5 yr specialization)
Diagnosis + Therapy of diseases (not only imaging!)

# HEVESY GYÖRGY
## Georg von Hevesy

Isotopes:
- same chemical (and biochemical) characteristics, no biological differences

First use in biological systems (1924)
Tracer principle: to follow functions
- small amount, same biochem.
- radioactive labelled

„Father of nuclear medicine"
Nobel prize in chemistry 1943

# RADIOISOTOPES IN MEDICINE

Isotope: same number of protons
- chemically the same element! (e.g. C-11, O-15)
- Proton : neutron. Optimal relation. Stability? !
- Unstable nucleus: changes. Radiations.

Types of isotopes (and radiations)
- plus protons:
  - positron emission (+beta)
    - meets electron: annihilation 2x 511 keV
  - EC (K,L,M..): characteristic Xray + gamma
  - alpha particle (+gamma)
- plus neutrons:
  - beta (from nucleus) + gamma (metastabil)

Production: cyclotron and reactor (arteficial isotopes)

## IMPORTANT RADIONUCLIDES

**Diagnostic**: electromagnetic radiation (photons)

+ neutron:

Tc-99m, I-131, Xe-133: gamma (metastable)

+ proton:

- Ga-67, In-111, I-123, Tl-201: Xray +gamma
- C-11, N-13, O-15, F-18, Ga-68: annihilation

**Therapeutic**: particle (absorption in tissue: dose)

+ neutron: beta: Y-90, I-131, Sm-153, Re-186…

+ proton: alpha - At-211, Bi-212, Ra-223

## ADVANTAGES OF Tc-99m

(m=metastable)

in 80 % of SPECT examinations

**Physical (for detection)**

140 keV: ideal for gamma camera (70-400 keV)
monoenergetic: ideal for imaging

**Biologic: low radiation dose**

"pure" gamma (from Mo-99), T1/2: 6 h, optimal

High amount of activity, No. of photons (Poisson)

**Practical**

from generator (Mo-99) elution, phys. saline (!)

stable complexes with many molecules

## SPECT: when NOT Tc-99m ?

Impossible to label

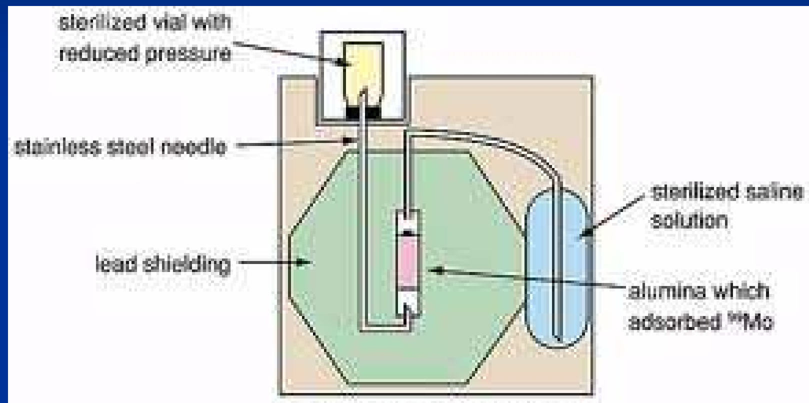
e.g. glucose (FDG: success of PET!)

Too slow biokinetics

e.g. steroid hormon synthesis

## Tc-99m GENERATOR

Mo-99, Aluminoxid, elution phys.saline, T1/2: 2.75 d




an example of the structure of a generator on the market

# RADIOPHARMACEUTICALS

Organ- tissue- molecular-
function-specific labelled molecules
(isotope: e.g. I-131, Sr 89, Rb-82, Ra-223)
Diagnosis:
Functions: organ, tissue, molecular (quantitative)
Tissue characterization – identification
Therapy:
targeted, molecular (selective) radiotherapy
(high dose: continous radiation)
„tailored", „personalized"
Role of radioisotopes only for detection or for therapy
**„Theranostics":** the same molecules
radioiods: I- 123 -124 -125 -131
sms ligandum In-111, Tc-99m, Ga-68, Y-90, Lu-177, Bi-213,

# BIOLOGICAL MECHANISM

| | |
|---|---|
| Physical | SLN |
| Compartment | MUGA blood pool |
| Diffusion | DTPA, ventilation |
| Chemical reaction | MDP, PIB |
| Phagocytosis | colloid spleen |
| Cells | leucocyte |
| Excretion | HIDA, EC |
| *Active transport* | *thyroid, adrenerg* |
| *Metabolism-nzymes* | *FDG, FET, FCH, FLT,..* |
| *Antigen* | *antibody, fragment, peptid* |
| *Receptor* | *ligand* |
| *Beta-amyloid* | *florbetapir* |
| *Others* | *hypoxia, angiogenesis, etc.* |

# DETECTION: IMAGING

**Gamma camera**
scintillation crystal, rectangular detectors
static and dynamic aquisitions
spot, whole-body
planar or SPECT (emission CT: projections)
ECG-gated
dedicated for organs
semiconductors, multipinhole, small animal
**Positron camera:** PET („double-photon ECT")
BGO, GSO, LYSO,… crystals
ring detectors (small block detectors)
16-21 cm axial FOV
coincidence detection (3D data aquisition)

# DETECTION: NON-IMAGING

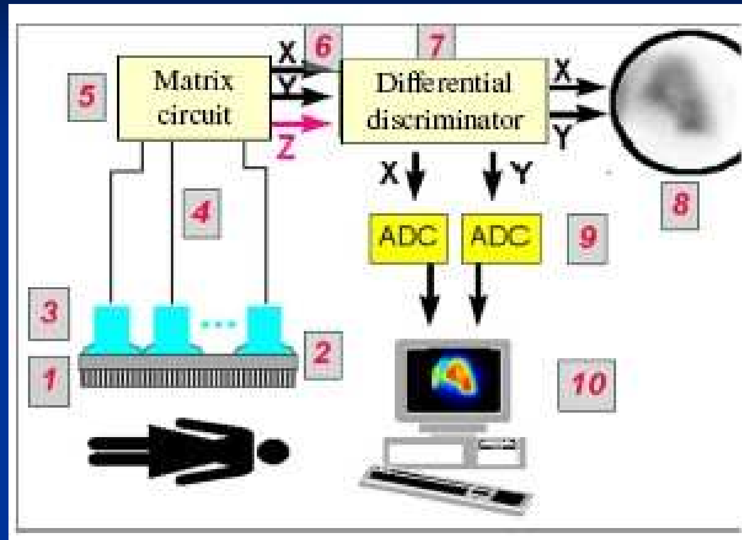
Ex vivo measurements
of biological samples
e.g. clearance (blood), Schilling test (urine)

Small dedicated instruments
Dynamic function studies (e.g. kidney, heart)
Thyroid uptake test
radioiodide therapy, activity calculation
Intraoperative gamma-probes for localization
e.g. sentinel lymph node detection

# INTRAOPERATIVE PROBES

- Geometric resolution
- Sensitivity
- Energy resolution
- Technetium-99m !!!
  (I-125, I-131, In-111, F-18, Ga-68)
- Even small cameras (Sentinella)

# GAMMA CAMERA (Anger type)




Varga J.

# SCINTIGRAPHY

In vivo imaging of distribution of activity (radiopharmaceuticals = functions)

planar or SPECT
static or dynamic
gated or ungated

whole body
pinhole collimators
dedicated (heart, breast)

# GAMMA CAMERA: SPECT

# SPECT

Rotation: steps, continous

circular, elliptic (close!)

64-128 projections

Reconstruction

filtered backprojection or iterative

Corrections:

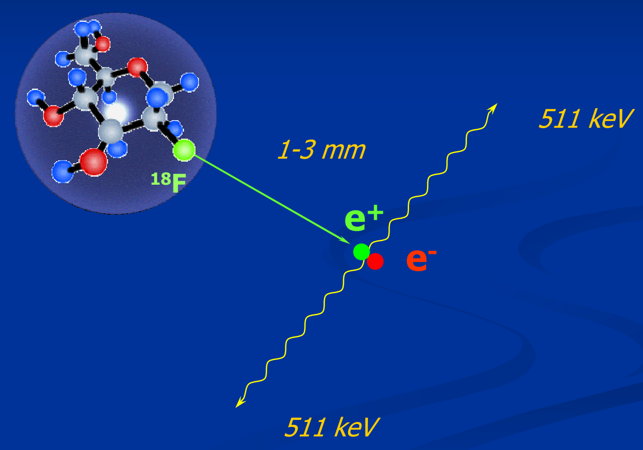
attenuation, Compton, detector-response (depth)

Slices:

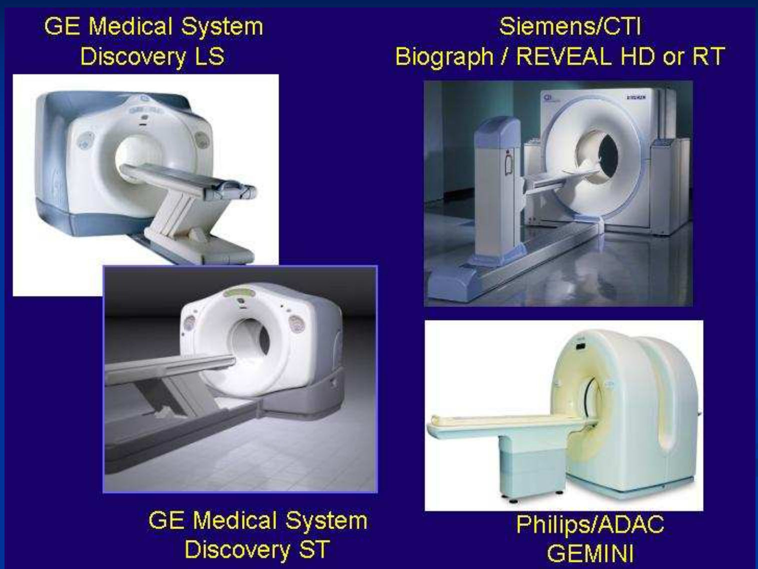
transvers (axial), coronal, sagittal

3 D, rotating

# POSITRON: ANNIHILATION




# PET/CT-s in the early 2000s




# PET vs. SPECT
# double-photon single-photon

1. More sensitive (no collimator!)
2. Spatial resolution is better (anatomic details)

SPECT: 10 mm, PET: 3 - 4 mm

(small animal: 1 mm)

3. Quantitative

absolute (e.g. mL/min/g, mol/min/g)

**4. Biomolecules !!!**

C-11, N-13, O-15, F-18, (but Ga-68)

(glucose, tyrosine, thymidine, H2O, etc…..)

**SLICE OF LIFE**

# HYBRID SYSTEMS

Function + morphology

on the same gantry: „simultaneous" (image fusion?)

Improvement of diagnostic capabilities

**1 +1 = 3 !**

PET/CT (only)

SPECT/CT („good" SPECT= SPECT/CT)

role of CT: localization + attenuation correction

„low dose" ! (non-diagnostic CT)

PET/MR

no radiation (paediatry, brain, oncology, …?)

# SPECT/CTs of Today

Siemens Symbia

Philips Precedence

GE Discovery NM/CT 670

Mediso AnyScan SC

# HYBRID IMAGING II. PET/MR

Detector technology!

- Siemens, Philips, GE, (Mediso)
- Soft-tissue contrast excellent
- No radiation dose!
- Attenuation correction ?
- Duration of the study ?
- Clinical indications ?
- Research !
- Cost-effectiveness ???

# CLINICAL INDICATIONS? Two expensive instruments!

- Pediatric patients
- Follow-up
- Brain, breast, pelvic, cardiac,?
- Functional MR techniques ?

different sequences, STIR, DWI, ADC,..

arterial spin labeling

proton spectroscopy

diffusion-tensor imaging

??

## ADVANTAGES IN DIAGNOSIS

TISSUE CHARACTERIZATION. IDENTIFICATION.
- What is seen on the CT/MR?

FUNCTIONS!
- Organ-Tissue-Cell-Molecular
- Quantitative e.g. renal: split,MTT, clearance
  - thyroid uptake, I-131
  - heart perfusion score
  - PET: SUV, or mol/min/g

NON-INVASIVE
- i.v. injection and (small) radiation dose
- No toxic effects! Allergic reactions very rare.
- Nano-, picomolar amount

## DISADVANTAGES I.

1. Geometric resolution is limited
   - contrast (target/backgoround)
     - stars (size?? light!!)
   - only the function!
   - technical resolution
     - SPECT 10 mm, PET 4 mm
   - biologic resolution
     - hot thyroid nodule vs large liver met.
2. Anatomy, localization
   - SPECT/CT, PET/CT, PET/MR, SPECT/MR?

## DISADVANTAGES II.

3. Radiation dose

| | |
|---|---|
| Gamma | 1- 7 mSv |
| Annihilation | 5-10 mSv |
| EC, conversion e. | 15 mSv |

Principles of radioprotection
- Indication!
- Non-ionizing
- ALARA !
  - only reference levels

Instrumentation (hardware, software)

Gravidity, lactation, small children. RISK-BENEFIT!

## ROLE OF NM IMAGING

**Functional imaging**
- organ- cell- biochemical functions
- tissue characterization
- molecular imaging (at molecular level)

**Radiology: morphological**
- co-operation
  - PET/CT, SPECT/CT
  - in education (multimodality)
  - diagnostic algorithms

## FUNCTIONS

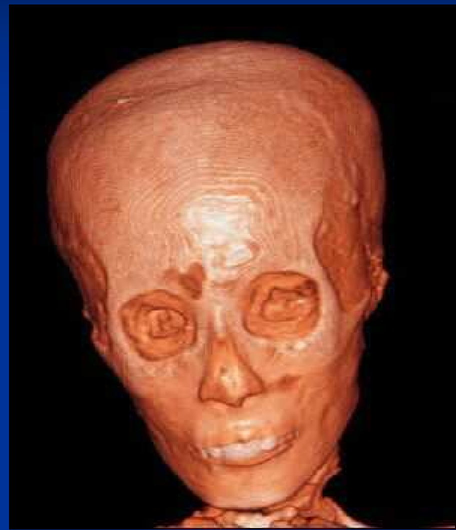
**Organs**: heart (perfusion, contraction)
lung (perfusion, ventilation)
flow (blood, lymphatic)
kidney (glomerular, tubular, urinary flow)
liver (parenchymal, excretion, biliary flow)
gastrointestinal (motility, excr., absorption)

**Cellular**: tissue characterization
e.g. antigens, receptors, enzyme expressions

**Molecular**: biochemical, metabolic processes
e.g. angiogenesis, apoptosis, hypoxia, etc.

**Genetic**: DNS („nuclear"), mRNS (oligonucleotids)

## 3D - CT NM examination



## IMPORTANCE OF MOLECULAR IMAGING

Disease: functional changes

Function before morphology

Early diagnosis

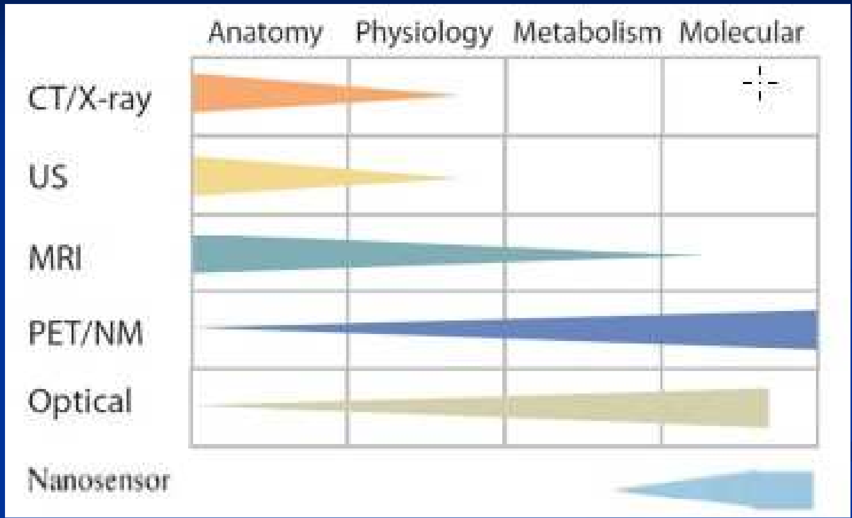
Targeted diagnosis

Targeted therapy

## MOLECULAR IMAGING METHODS

- Nuclear medicine !
- MR
- Optical
- CT
- UH

# MEDICAL IMAGING METHODS




Society of Nuclear Medicine

# MOLECULAR IMAGING

Functions at molecular and at cell levels

„commodore" in molecular imaging: PET

Reasons:

pico-nano-femto-molar amount

hundreds of biomolecules can be labelled

clinicly today: 30-40 substances

# MOLECULAR NUCLEAR MEDICINE THE TARGETS!

Enzyms – substrates
FDG, FLT, FET, FEC, FDOPA
Receptors – ligands
D2, SMS
Antigens – antibodies (fragments)
PSA, CEA, TAG72, CD20
Transport proteins – substrates
NIS
Deposits – bindings molecules
beta-amyloid

# PERSPECTIVES OF NM

- Apotosis — Annexin V, ML
- Angiogenesis — VEGF, integrin antibodies
- Hypoxia — misonidazol, FMISO
- MDR — sestamibi
- ….
- Oncogens — F-18 oligonukleotides
- Genexpressions — Gen therapy (reporter gen) HSV-Tk co-expression with F-18-deoxytimidine

etc. !!!!!