

NUCLEAR MEDICINE

Basics, Principles, 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 2×511 keV

EC (K,L,M..): characteristic Xray + gamma

alpha particle (+gamma)

plus neutrons:

beta (from nucleus) + gamma (metastabil)

Production: cyclotron and reactor (artificial 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

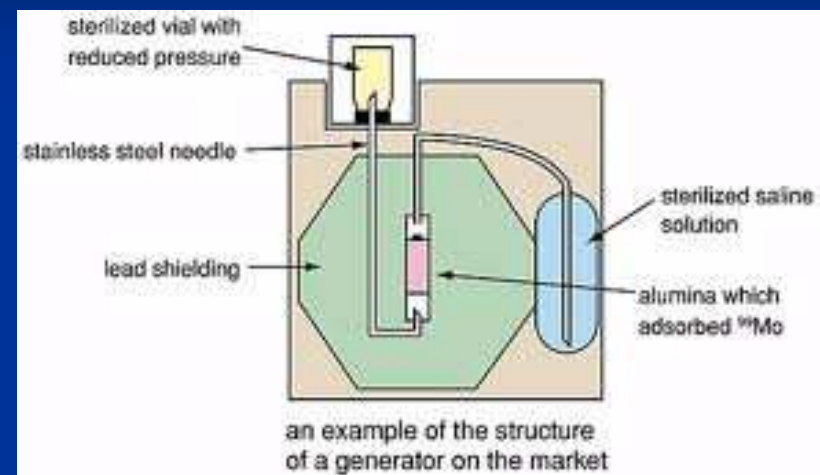
e.g. glucose (FDG: success of PET!)

Too slow biokinetics

e.g. steroid hormon synthesis

Tc-99m GENERATOR

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



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: continuous radiation)

„tailored”, „personalized”

Role of radioisotopes only for detection or for therapy

„**Theranostics**”: the same molecules

radioiods: I- 123 -124 -125 -131

small ligand In-111, Tc-99m, Ga-68,

Y-90, Lu-177, Bi-213,

BIOLOGICAL MECHANISM

Physical

Compartment

Diffusion

Chemical reaction

Phagocytosis

Cells

Excretion

SLN

MUGA blood pool

DTPA, ventilation

MDP, PIB

colloid spleen

leucocyte

HIDA, EC

Active transport

Metabolism-enzymes

Antigen

Receptor

Beta-amyloid

Others

thyroid, adrenergic

FDG, FET, FCH, FLT,..

antibody, fragment, peptid

ligand

florbetapir

hypoxia, angiogenesis, etc.

DETECTION: IMAGING

Gamma camera

scintillation crystal, rectangular detectors

static and dynamic acquisitions

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 acquisition)

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

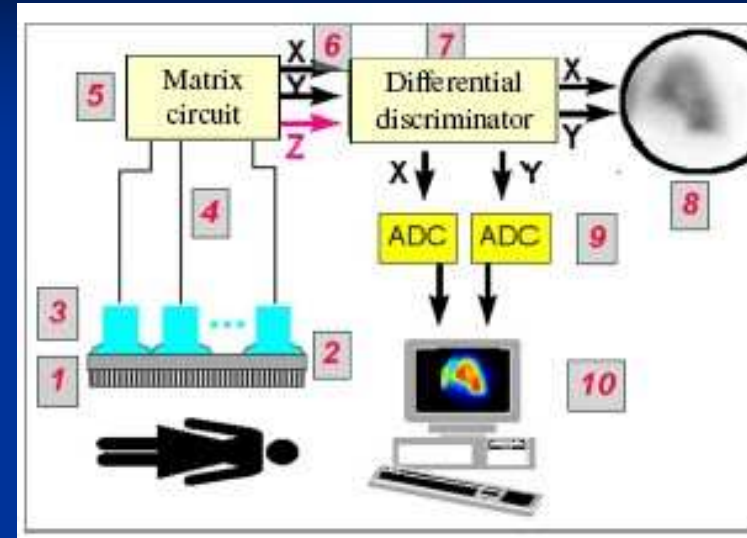
e.g. sentinel lymph node detection

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

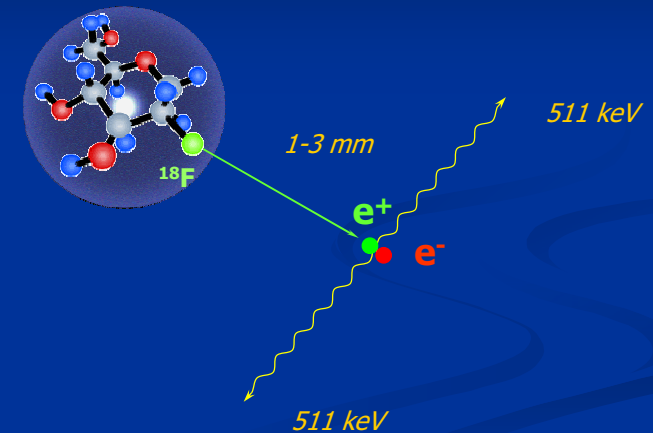
Rotation: steps, continuous
circular, elliptic (close!)
64-128 projections

Reconstruction
filtered backprojection or iterative

Corrections:
attenuation, Compton, detector-response (depth)

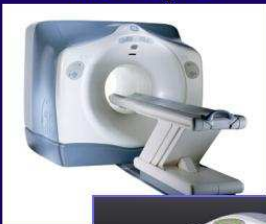
Slices:
transvers (axial), coronal, sagittal
3 D, rotating

POSITRON: ANNIHILATION



PET/CT-s in the early 2000s

GE Medical System
Discovery LS



Siemens/CTI
Biograph / REVEAL HD or RT



GE Medical System
Discovery ST



Philips/ADAC
GEMINI

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/background)
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

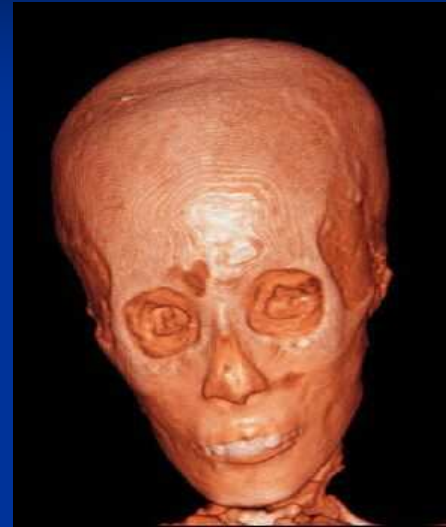
Organs: heart (perfusion, contraction)
lung (perfusion, ventilation)
flow (blood, lymphatic)
kidney (glomerular, tubular, urinary flow)
liver (parenchymal, excretion, biliary flow)
gastrointestinal (motility, excr., absorption)

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

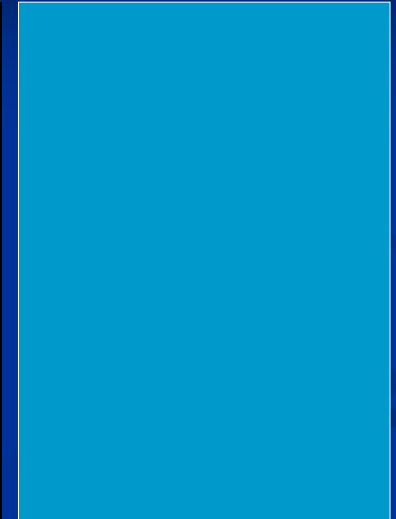
Molecular: biochemical, metabolic processes
e.g. angiogenesis, apoptosis, hypoxia, etc.

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 !

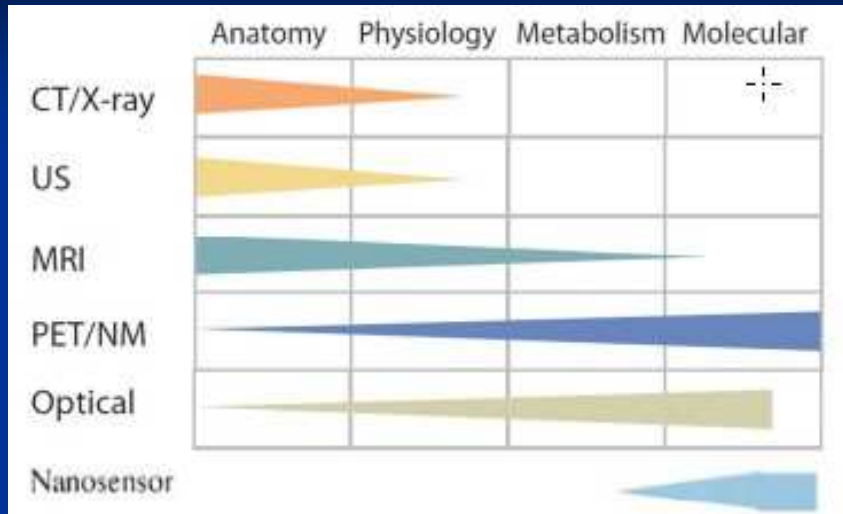
■ MR

■ 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

clinically today: 30-40 substances

MOLECULAR NUCLEAR MEDICINE THE TARGETS!

Enzymes – 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

■ Apoptosis

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-deoxythymidine

etc. !!!!!