
The clinical diagnostic possibilities in recent years:

Patient history!!!
Physical exam. (Palp., auscultation etc).!!! No idea???

Sampels (Chem. Lab)
Functional map’s (Nuklear medicine: molecular map)
Biochemical, microbiological data
Kamera, SPECT, PET Rtg, UH CT, MR
„Multimodality” methods
SPECT-CT PET-CT PET-MR?

Targets and tools of medical imaging

The beginnings of NUCLEAR MEDICINE: a Nobel priced idea

1924: Principle of radiotracer applications:
Changing an atom in a molecule for its radioisotope will not change its chemical and biological behaviour significantly.

Consequence: the movement, distribution, concentration of the molecule can be measured with radiation detectors.

Selecting the radionuclide for imaging

For external detection: electromagnetic radiation can be used!
The main 2 groups of isotopes in nucl. Med.:

Gamma emitters
- gamma energy: 80-400 keV
  - if lower: attenuated inside the patient
  - if higher: low detection sensitivity

Positron emitters
- annihilation radiation: 2·511 keV

First inventions: spontaneous radioactivity …

ANTOINE HENRI BECQUEREL
1852-1908
1903 Nobel Laureate in Physics

“in recognition of the extraordinary services he has rendered by his discovery of spontaneous radioactivity”

MARIE CURIE
1867-1934
PIERRE CURIE 1859-1906
1903 Nobel Laureates in Physics

“in recognition of the extraordinary services they have rendered by their joint researches on the radiation phenomena discovered by Professor Henri Becquerel”

The main groups of isotopes in nuclear medicine:

- Gamma emitters
- Positron emitters

Source: “What is Nuclear Medicine?” (SNM)

Medical imaging, Historical paralells:

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Internal med.</th>
<th>Oncology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatomy</td>
<td>Physiology</td>
<td>Metabolism Molecular</td>
</tr>
<tr>
<td>CT/X-ray</td>
<td>US</td>
<td>MRI</td>
</tr>
<tr>
<td>PET/NM</td>
<td>Optical</td>
<td>Nanocentor</td>
</tr>
</tbody>
</table>

Source: http://www.nmc.dote.hu/nmt_eng/oktatas_e.htm

- Link to English reference manual:
- Lectures in English:
  http://www.nmc.dote.hu/nmtk/index.html
- In Hungarian:
  http://www.nmc.dote.hu/nmtk/index.html
- Book: A Nukleáris Medicina Tankönyve
  (Szerk. Szilvási I.; B+V Kiadó, 2002, 2010)

Univ. of Debrecen
Department of Nuclear Medicine
2010 02
Most common radionuclides in Nuclear Medicine

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Energy (keV)</th>
<th>Half time</th>
<th>Used for:</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tc-99m</td>
<td>141</td>
<td>6.03 h</td>
<td>many</td>
<td>generator</td>
</tr>
<tr>
<td>TI-201</td>
<td>68-80</td>
<td>73.1 h</td>
<td>myocardium</td>
<td>cyclotron</td>
</tr>
<tr>
<td>I-131</td>
<td>364</td>
<td>8 days</td>
<td>thyroid</td>
<td>+therapy</td>
</tr>
<tr>
<td>I-123</td>
<td>159</td>
<td>13 h</td>
<td>proteins...</td>
<td>cyclotron</td>
</tr>
<tr>
<td>I-125</td>
<td>27-35</td>
<td>60 days</td>
<td>in vitro!</td>
<td></td>
</tr>
<tr>
<td>F-18</td>
<td>Beta+</td>
<td>110 min</td>
<td>PET!</td>
<td></td>
</tr>
</tbody>
</table>

Effective doses (mSv)

Medical & biological applications of radionuclides: the main fields of Nuclear Medicine

Diagnostics
- "In vivo" imaging
- "In vivo" non-imaging
- "In vitro"

Research applications: (nuclear medicine)
- Application of diagnostic methods for research
- "Molecular imaging"
- Combination of analytical laboratory methods with radiotrace technique

Therapy

Why Nucl. Med. is "open" discipline?

Example: Imaging brain receptors:
PET ligands for imaging various receptor systems – MR structur is same!

PET-CT

Planar SPECT CT RIA Fluoro High dose
I. In vivo
Pain killing Synoviol thesis
II. In vitro
Cell labelling Immuno Zevalin
III. Therapy

Fields of Nuclear Medicine: 1A. "In vivo" imaging

1957: Anger camera

Principle:
many photomultiplier tubes "see" the same large scintillation crystal; an electronic circuit decodes the coordinates of each event ("Anger resistant matrix")

Hal Anger (Berkeley) with his positron camera
Developer of the scintillation camera
Planar Gamma cameras (1970-80)

Selecting the „ideal“ human radionuclide:

- Should allow imaging with gamma camera:
  - gamma emitter
  - energy from 80 to 400 keV
    (lower: absorbed in the patient
    higher: bad detector sensitivity)
- Half time: ~ hours
  (shorter: difficulties with production
  longer: high patient dose)
- Should be linked to a suitable compound.

Emission imaging: Study types

Static:
  - imaging an equilibrium distribution
Dynamic:
  - series of images following the accumulation / metabolic pathways / secretion of a radiopharmaceutical
Whole body:
  - static images connected
Tomographic:
  - single photon emission computed tomography (SPECT)
  - positron emission tomography (PET)

Examples of in vivo „single photon isotope“ studies:

Malignant thyroid tumour

decreased activity with pertechnetate

Increased MIBI accumulation

Examples of in vivo „single photon isotope“ static studies

Case of Parathyroid adenoma

99mTc-Pertechnetate

99mTc-MIBI

(More „cell specific“ maps)

Examples of in vivo „single photon isotope“ static studies

Nodular lesions of the liver in cirrhosis

99mTc- 67Cu

Examples of in vivo „single photon isotope“ static studies

Breast scintigraphy: 99mTc-MIBI („mitochondrial map“)

Examples of in vivo „single photon isotope“ static studies

Case of Pulmonary embolisation (Two lung functions re imaged.)

PERF: perfusion images with [Tc-99m] macroaggregated albumin
INH: after inhalation of [Tc-99m] DTPA aerosol
Examples of in vivo „single photon isotope” static studies

Case of lung abscess: $^{67}$Ga-citrate

Examples of in vivo „single photon isotope” static studies

Static kidney: by Tc-99m DMSA (organ specific)

Examples of in vivo „single photon isotope” static studies

Example: Crohn disease in active stage by in vitro labelled leucocytes

Results of normal dynamic kidney study

Examples of in vivo „single photon isotope” Dynamic studies

Monitor bile excretion process - from a single view - at various times

Tomographic reconstruction

1. Projections

2. Filtered backprojection

SPECT

Advantages vs. CT:
- functional imaging
- a wide range imaged
- reslicing is possible

Drawbacks:
- poor resolution
- attenuation
- scatter
Planar Gamma cameras and SPECTs

Examples of in vivo „single photon isotope” static studies

Examples of in vivo „single photon isotope” static studies: SPECT

Examples of in vivo „single photon isotope” static studies: Brain perfusion SPECT (Tc-99m HM-PAO)

Examples of in vivo „single photon isotope” static studies: SPECT

Case: Lung tumor with 111In-Somatostatine-receptor scintigraphy

Reversible defects by cardio C SPECT: short axis slices

Cardio SPECT-Reversible defect: bull’s eye maps

Dual isotope study: Transaxial slice

Case of Carcinoid tu. (Two cell functions framed in same time!)
1. "In vivo" imaging
B. With positron emitters (Brief history)

**Principle:** Two 511 keV photons resulting from annihilation fly in opposite directions. Their coincident detection determines the line of annihilation.

- Michel M. Ter-Pogossian, Mallinckrodt Institute
- Michael E. Phelps, UCLA

Stanley Livingston and Ernest Lawrence with their 8 MeV cyclotron (1935)

**Possibilities to Produce artificial radioactive materials**
- In nuclear reactors (high neutron flux)
- Using accelerators (circular: cyclotron) expensive!

PET - advantages

- **Coincidence detection at 180°:**
  - higher sensitivity
  - better signal/noise ratio
- **Easier attenuation correction**
  (sum of the two paths inside = body thickness)
- **More physiologic radiopharmaceuticals**
  (C-11, N-13, O-15, F-18)

3 dimensional cine display of PET study made by FDG on dedicated PET camera (1996)

Functional vs. structural imaging:
**Case:** Low-grade recidivate glioma (FDG) PET+MRI fusion made by software

Role of PET in oncology: Tumor staging
Based on conventional methods: Stage I

FDG-PET shows stage III S

Previous and recent PET, PET-CT tools

Negatív iontöltés
Ciklotron (PET TRACE) árnyékolás nélkül
Targetkamrák
Gyorsító mágnes
Ionbevezetés helye

PET Center, Debrecen
Recent trends in multimodality in vivo imaging:

2007: start of Gemini TOF 64 slice PET-CT in Debrecen: Step forward in oncology and cardiology

PET tracers: FDG, 11C-metionin

18F-FDG TF PET-CT in mal. tumor diagnostics:
remnant of colon cancer

• Rectum tu. Lokális recidíva?

Dr. Fekésházy A. képanyaga

18F-FDG TF PET-CT in mal. tumor follow up

Tumor localization for targeted radiation therapy by PET-CT

• Newly diagnosed NSCLC
• PET/CT: used to guide radiation treatment volume
• Discrepancy between PET and CT volumes related to respiratory excursion

SPECT-CT Example: right suprarenal adenoma
Radiopharm.: 131I-Nor-cholesterol

More special softwares for 3D volume-rendered fusion images

Protocols in the CardIQ Fusion software (a–d). The main protocols include tools for image coregistration, epicardial contour detection, coronary artery segmentation.

Fields of Nuclear Medicine: 2 In vitro concentration measurements

1960: Yalow and Berson developed a radioassay for measuring insulin concentration from plasma samples (saturation analysis)

RIA: radioimmunoassay (competitive protein binding; the ligand is labeled)
IRMA: immunoradiometric assay („sandwich” assay)

ROSALYN YALOW (1921—)
1977 Nobel Laureate in Medicine
„for the development of radioimmunoassays of peptide hormones”
**Radionuclide therapy**

The administration of open radionuclides for therapeutical purposes. The radiopharmaceuticals get right to the cells to be destroyed, and act there locally.

Generally beta- (rarely alpha-) radiating nuclides are used, as beta radiation reaches only a small neighborhood of its source.

Most common aims of radionuclide therapy:

- **Intracavitary therapy** *(uterus, abdomin cav., Intraarticular)*
- **Radioimmunotherapy** *
- **Palliative therapy of bone metastases** *
- **Radioiodine therapy of hyperthyreosis** *
- **Radioiodine therapy of thyroid carcinoma metastases** *

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**Fields of Nuclear Medicine:**

3. **Therapy** with unsealed radioactive preparations

**Principle:**

Beta-emitting radiopharmaceuticals go directly to the cells or tissue to be destroyed or deactivated

Very specific radiopharmaceuticals are needed

**Unsealed preparation:**

One that mixes in the patients’ body on a molecular level (e.g. after intravenous injection)

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**Examples of Intracavitary therapy**

The injection of radionuclides right into some cavity (not through the bloodstream or lymphatic drains)

- **Synovium**
  - Indication: Chronic synovitis
  - Mechanism: Irradiating the cells of the synovial membrane decreases fluid production.
  - The choice from beta-emitting radionuclides depends on the size of the synovial cavity.

- **Pleura**
  - Indication: Palliative therapy in order to reduce fluid collection caused by tumors (cancer of the breast and lung, lymphoma) or inflammation.

- **Peritoneum**
  - Indication: Palliative therapy in order to reduce ascites caused by tumors. *(Mesothelioma, ovarian adenocarcinoma)*
  - *(Also: radioimmunotherapy)*

- **Intrathecal therapy**
  - Indication: Leukemia with thecal involvement
  - Mechanism: Fagocytosis of the arachnoid membrane cells.

- **Cysts**

Colloidal radiopharmaceuticals are administered, labeled by: Rhenium-188, Erbium-169, Yttrium-90, Phosphor-32, Gold-198