RADIOISOTOPES
in
MEDICINE:
Requirements - Production - Application
and future prospectives

2
Imaging with Radiotracers

Gerd-Jürgen BEYER
Prof. Dr. rer. nat. habil. (i.R.)
Geneva, Switzerland

THIRD INTERNATIONAL SUMMER STUDENT SCHOOL
NUCLEAR PHYSICS METHODS AND ACCELERATORS
IN BIOLOGY AND MEDICINE
Dubna, July 01-11, 2005
G.V. Hevesy: The Absorption and Translocation of Lead (ThB) by Plants \( [\text{ThB} = ^{212}\text{Pb}] \)
Biochem. J. 17, 439 (1923)

Measurements of the tracer’s radioactivity provided thousand fold increases in sensitivity and accuracy over existing chemical assays. The foundation and basic rationale of much of Hevesy’s work visualized that a radioactive atom might be used as a “representative” tracer of stable atoms of the same element whenever and wherever it accompanied them in biological systems.

1943 Nobel Prize Chemistry

G.V. HEVESY the father of Nuclear Medicine
NUCLEAR MEDICINE = in vivo APPLICATION of RADIOTRACERS

1923 First tracer study with $^{210}$Pb/$^{210}$Bi, G.Hevesy
1925 $^{214}$Bi arm-to-arm circulation time, H.Blumgart
1935 $^{32}$P renewal of mineral constituents of bone, O.Chieivitz & G.Hevesy
1937 dynamics of sodium transport in vivo, J.G.Hamilton
1937 $^{128}$I, thyroid physiology, R.Hertzs, A.Roberts, R.Evans
1938 $^{131}$I discovered by G.T.Seeborg, 1939 first diagnostic use J.G.Hamilton et al.
1947 $^{131}$I –Fluorescine, 1950 $^{131}$I –HSA, 1955 $^{131}$I-rose bengale & hippurane, …
1957 $^{99}$Mo-$^{99m}$Tc generator (1960 first sale), $^{133}$Xe for lung ventilation
1969 $^{67}$Ga accumulation in cancer, C.L.Edwards
1970 Instant KIT’s for $^{99m}$Tc
1973 $^{201}$Tl, $^{123}$I, $^{111}$In, many other isotopes and tracer compounds
1978 first $^{18}$FDG PET scan

11 million individuals receive every year a radiotracer for diagnosis
ISOTOPES IN MEDICINE

**DIAGNOSIS**

- **in vitro**
  - $^{14}$C
  - $^{3}$H
  - $^{125}$I
  - others

- **in vivo**
  - $^{99}$Mo-$^{99m}$Tc
  - $^{201}$Tl
  - $^{123}$I
  - $^{111}$In
  - $^{67}$Ga
  - $^{81}$Rb-$^{81m}$Kr
  - others
  - $^{32}$P and others

**THERAPY**

- **internal**
  - $^{131}$I, $^{90}$Y
  - $^{153}$Sm, $^{186}$Re
  - $^{188}$W-$^{188}$Re
  - $^{166}$Ho, $^{177}$Lu, others
  - $^{149}$Tb
  - $^{125}$I

- **external**
  - sealed sources
    - $^{192}$Ir, $^{182}$Ta, $^{137}$Cs
    - many others
  - needles for brachytherapy:
    - $^{103}$Pd, $^{125}$I
    - many others
  - stants
    - $^{32}$P and others
  - seeds
    - $^{90}$Sr or $^{90}$Y, others
  - applicators
    - $^{137}$Cs, others

**sources**

- sealed sources
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- seeds
  - $^{90}$Sr or $^{90}$Y, others
- applicators
  - $^{137}$Cs, others

- **tele radio**
  - $^{60}$Co
  - gamma knife
  - $^{137}$Cs
  - blood cell irradiation

G.J.BEYER, HUG Geneva, 2002
### ISOTOPES in MEDICINE

<table>
<thead>
<tr>
<th>Application</th>
<th>Requirement</th>
<th>Isotope</th>
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<tr>
<td>DIAGNOSIS</td>
<td></td>
<td></td>
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<tr>
<td>in vitro</td>
<td></td>
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<tr>
<td>DIAGNOSIS</td>
<td><strong>T$_{1/2}$ = long biogenic behavior</strong></td>
<td><strong>$^3$H, $^{14}$C, $^{125}$I</strong></td>
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<tr>
<td>In vivo</td>
<td></td>
<td></td>
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<tr>
<td>SPECT</td>
<td>single photons</td>
<td>99m$^{99mTc}$, $^{123}$I, $^{111}$In, $^{201}$Tl, $^{11}$C, $^{13}$N, $^{15}$O, $^{18}$F</td>
</tr>
<tr>
<td>DIAGNOSIS</td>
<td>no particles</td>
<td></td>
</tr>
<tr>
<td>in vivo</td>
<td>biogenic behavior</td>
<td></td>
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<tr>
<td>PET</td>
<td><strong>T$_{1/2}$ = moderate</strong></td>
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<td>DIAGNOSIS</td>
<td>$\beta^+$-decay mode</td>
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<td></td>
<td><strong>T$_{1/2}$ = short</strong></td>
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Diagnostic in vitro RIA

Rosalyn S.YALLOW
Nobel Prize 1977

S.A.BERSON

Introduced the radioimmunoassay (RIA)
assay for insulin based on the principle of competitive binding by antibody of natural and radioactive labeled hormone)
## ISOTOPES in MEDICINE

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J.G. Hamilton, M.H. Soley:

“Studies of iodine metabolism by thyroid in situ”

1940, Am. J. Physiol. 131, 135

Photo published 1942

Kidney Isotope Nephrogram
GAMMA CAMERA
H.O. ANGER
1958

Planar scintigram

Scan Thyroid normal

Pre-amplifier
PM-tube
Pb-shielding
NaI-Detector
Collimator
Object

signals
x⁺, x⁻, y⁺, y⁻
electronics
Pb shielding
PM tubes
light guide
window
NaI-Detector
collimator

B. CASSEN
SCANNER

H.O. ANGER

NaI-Detector
Collimator
Object

Planar scintigram

Scan Thyroid normal

Pre-amplifier
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Collimator
Object

B. CASSEN
SCANNER
SPECT

Single Photon Emission Computed Tomography

1984 $^{99m}$Tc DMPE
## Nuclear Medicine Instrumentation

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<th>Point sensitive</th>
<th>DETECTOR’s are</th>
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<td>dynamic</td>
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- **67GaCIT**
- **99mTc DMPE**

![Images of nuclear medicine equipment and data](image)
Modern SPET Cameras
(GE Medical Systems)
NUCLEAR MEDICINE 2005

**DIAGNOSIS**

**SPECT** (SINGLE PHOTON EMISSION TOMOGRAPHY)
- increase of diagnostic value
- new radiopharmaceuticals
- dedicated instrumentation & quantification

**PET AS RESEARCH TOOL**
- Molecular in vivo biochemistry
- Gene expression
- Clinical research

**PET AS CLINICAL TOOL**
- Oncology
- Reimbursement of FDG-studies
- Neurology
- Cardiology

**Multi-modality Imaging**
- combined SPECT-PET (image of the year at the 46.SNM)
- Function and morphology

**THERAPIE**

**NEW APPROACHES IN RADIONUCLIDE THERAPY**
- bio-selective antibodies
  (mab = monoclonal antibodies)
- bio-specific peptides
  (Octreotides, others)
- gene therapy
- free chelators like EDTMP
- Lyposomes
- Nanoparticles

**NEW RADIONUCLIDES**
- for THERAPY
  - $\beta$ - emitters
  - $\alpha$-emitters

**$\alpha$-THERAPY & AUGER THERAPY**

**PET FOR IN VIVO DOSIMETRY**
- metallic positron emitters
- labelled drugs
- dose localization

G.BEYER (HUG, Geneva, 2005)
141 keV photons - the strength of $^{99m}$Tc
$^{99m}$TcO$_4^-$

0.9% NaCl solution

KIT's

many different $^{99m}$Tc-tracer

for imaging of many different organ and tissue functions
<table>
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<th>Tc-HMPAO</th>
<th>Tc-MIBI</th>
<th>Tc-O12</th>
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<tr>
<td>Tc-NOEt</td>
<td>Tc-P53</td>
<td>Tc-BATO</td>
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**99mTc Perfusion Tracers**
Ventilation study
LUNG Function
Perfusion Study

HEART
Perfusion

99mTc TRACER Examples

BONE
metabolic activity
NUCLEAR MEDICINE 2005

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  - *(PET – CT)*

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**NEW RADIONUCLIDES for THERAPY**
- β - emitters
- α - emitters

**α-THERAPY & AUGER THERAPY**

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**G.BEYER (HUG, Geneva, 2005)**
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PET = Positron Emission Tomography

0.51 MeV
FDG-PET  Dementia - Alzheimer’s
FDG-PET  Melanoma therapy control

before

after
CANCER

About 1,000,000 new cancer cases per year in EU
58% local disease, 42% generalized

45% cured (5 year survival)

22% surgery alone
12% radiation therapy
6% combination surgery + radiation
5% chemo-therapy

just beginning of systemic radionuclide therapy

HOW: expose cancer cells or cancer tissue with sufficient radiation doses?
3D whole-body PET

ECAT HR+
25 year-old male with Melanoma,
71 kg, 178 cm, 625 MBq FDG, 45 min p.i.

ECAT ACCEL
50 year-old male with colon CA
91 kg, 183 cm, 720 MBq FDG, 162 min p.i.

Emission scan time: 54 min
Transmission scan time: 18 min

Emission scan time: 27 min
Transmission scan time: 18 min

Data courtesy of
Kettering Memorial Hospital, Kettering, USA

Data courtesy of
NC PET Imaging Center, Sacramento, USA
The FIRST FDG SYNTHEZIZER

J. Fowler, BNI
SYNTHESIS OF \([^{18}\text{F}]\text{FDG}\)

- Preparation
- “NAKED” FLUORIDE
- PRECURSOR
- Nucleophilic substitution
- INTERMEDIATE
- De-protection
- Cleaning
- PRODUCT
$^{18}$F]FDG MODULES

- Nuclear Interface
- Coincidence Technology
- FDG microlab (GE)
- JALTECH (EBCO)
- IBA
- CPCU (CTI)
- Sumitomo
- Robot (SCX-
Clinical PET/CT protocols

The biograph

Thomas Beyer, PhD
Fused Image Tomography

Radiology

PET/CT scanner

Nuclear Medicine

Biopsy

Fused image viewer

IMRT

Pre

Post

Diagnosis and Staging

Therapy response

Surgery

Oncology
«Image of the Year » 1999, 46.SNM Los Angeles

CT: 160 mAs; 130 KV_p; pitch 1.6; 5 mm slices

PET: 7 mCi FDG; 2 x 15 min; 3.4 mm slices

University of Pittsburgh Medical Center
Dual-modality PET/CT Prototype

SMART Tomograph (1998)

>300 patients scanned
>70 IV contrast exams


Dual-modality imaging range
biograph

- Height: 158 cm
- Width: 228 cm
- CT PET: 90 cm
- 188 cm
- 145 cm

Dual-modality imaging range
CT - PET or PET - CT?

CT anatomy PET function fused image
CT anatomy PET function fused image

The future of cancer diagnostics – today state of the art
Multi-modality installation