NUCLEAR / MOLECULAR IMAGING (SCINTIGRAPHY)

INTRODUCTION

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Professor of Radiology and Pediatrics

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X-rays (CT), UltraSound, MRI

External Source of Radiation

Nuclear: Planar/SPECT/PET

The Patient becomes the Source of Radiation
NUCLEAR / MOLECULAR IMAGING
(SCINTIGRAPHY)

It is based on Molecular Action

It follows a predefined Task for numerous applications:

- Identify The Target
- Find its Biological Properties
- Select the Carrier (Molecule to reach the Target)
- Radiolabel the Carrier ➔ Radiopharmaceutical
- Inject the patient – Incubate
- Image and Interpret
NUCLEAR IMAGING (SCINTIGRAPHY)

Of particular Importance are:

• The **Biological** Properties of the Radiopharmaceutical

• And the **Chemical** and **Physical** Properties of the Radioisotope
NUCLEAR IMAGING (SCINTIGRAPHY)

The Nuclear Cameras generate Images of the Distribution inside the body of the given Radiopharmaceutical.
In Nuclear Medicine we use

Radiopharmaceuticals

(Organic or Inorganic Molecules labeled with)

Radioactive Atoms
HISTORY OF NUCLEAR MEDICINE

It is related to the
Rational Science and Rational Medicine

When and how the whole thing started?
HISTORY

HIPPOCRATES
Father of Rational Medicine

DEMOCRITOS
Father of the Atomic Theory of the Matter

EPICUROS
Father of Nuclear Science and Nuclear Medicine

The Miracle of the 5th Century BC
HISTORY OF NUCLEAR MEDICINE
HUMAN INTELLIGENCE PROGRESS

1) **SURVIVAL**: Labor, use of Animals (Slaves)
   
   Observation/Machines : **Primitive Science**

2) **WONDER** about the world around/inside us
   
   a) Mysticism: Gods and Super-Powers
      
      **Religions** (Prophets, Saints, Preachers)
   
   b) Rational Thinking: Reason, Dialectics
      
      **Philosophy**-Theories (Philosophers)

3) **EXPERIMENT** /Theories = **Advanced Science**

4) **SEPARATION** of Science from Philosophy

5) Introduction of **COMPUTER** and **GENETICS**
RATIONAL THINKING:

Epilepsy:

“...It is not in my opinion any more divine or more sacred than other diseases, but it has a natural cause......

It is also curable, no less than other diseases.......”

HIPPOCRATES

RELIGIOUS THINKING:

“Epilepsy is the result of effect of the gods or the devils”
Science deals with Known Facts

Philosophy with Speculation
A philosopher Loves *(philos)* the Knowledge *(sophia)*

Originally, in ancient times,

a philosopher was also a scientist

*(Pythagoras: Philosopher and Mathematician)*

Later, after the renaissance

Science was separated from philosophy
PHILOSOPHY

The First Philosophers (+Scientists)

*How does Change occur?*

Change is a rearrangement of atoms that remain themselves unchanged.
The First Philosophers (+Scientists) lived here
DEMOCRITOS

Father of the Atomic Theory of the Matter

“The World Outside and the World Inside Us is made of small invisible, indivisible and indestructible Particles the Atoms”
The Miracle of the 5th Century BC
Art Reflected Nature And Beauty

Aphrodite (Venus) of Milos
Victory of Samothrace
THE CLASSICAL CIVILIZATION WAS TRANSFERRED EAST

THE EMPIRE OF ALEXANDER THE GREAT
CLASSICAL CIVILIZATION WAS ALSO TRANSFERRED WEST

THE ROMAN EMPIRE
PHILOSOPHY AND SCIENCE THRIVED IN THE ROMAN EMPIRE (GRECO-ROMAN CIVILIZATION)

DE RERUM NATURA

by LUCRETIUS CARUS

In this poem he reviews the ancient philosophers of the classical and the roman periods
EPICUROS

A PHILOSOPHER OF THE ROMAN PERIOD

Father of Nuclear Science and Nuclear Medicine

“The Atoms may pass through an Unstable Phase before they are stabilized in their perpetual form”
• The ancient Greek Philosophers introduced the Theory of the Atom and the Theory of the Unstable (=Radioactive) Atom

• In Nuclear Medicine We use radioactive Atoms

Radiopharmaceuticals

Injection of Patients

Decay of Radioactive Atoms
Byzantium imposed Christianity and persecuted Philosophy
The Arabs imposed Muslim Religion
but some of their philosophers preserved the ancient philosophy
AND THE MEDIEVAL TIMES

CHRISTIANS

MUSLIMS
THE RENAISSANCE IN THE 14th CENTURY REVITALIZED

SCIENCE AND PHILOSOPHY

LEONARDO DA VINCI: MONA LISA
## HISTORY

It took more than 2000 years for Science to Recover

<table>
<thead>
<tr>
<th>Modern Atomic Theory</th>
<th>Discovery of Natural and Artificial Radioactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>John Dalton 1880</td>
<td>Henry Becquerel 1896</td>
</tr>
<tr>
<td></td>
<td>Marie Curie 1897</td>
</tr>
</tbody>
</table>
RADIATION FROM RADIUM

The Atom is not indestructible
**HISTORY**

Dmitry Ivanovic Mendeleyev 1896  
The Periodic Table of the Elements

![Periodic Table](image)
Figure 30.1  (a) The nuclear atom.
(b) The "plum pudding" model of the atom (now discredited).
SCIENCE PHILOSOPHY AND ART RETURNED TO CLASSICS

MODERN THEORY ABOUT THE STRUCTURE OF THE ATOM

Les Bourgeois de Calais by Rodin
**HISTORY**

**Theory of Relativity 1905-1916**

Albert Einstein

---

Albert Einstein:

1905  Mass and energy are interchangeable

1907  $E=mc^2$ - Photoelectric Effect

1916  General theory of relativity
MEDICINE LAGGED BEHIND BASIC SCIENCES

The Alarming History of Medicine
Amusing Anecdotes from Hippocrates to Heart Transplants

Richard Gordon
KING CHARLE’S II in his TUBERCULOSIS CLINIC
THE PRACTICE OF SURGERY

Medicine was one of the last sciences to recover and still suffers
FINALLY RENAISSANCE CAME TO MEDICINE

Discovery of X-Rays 1895: Wilhelm Conrad Roentgen
The first use of radioisotopes in humans
The Tracer Principle
Georg de Hevesy 1913

Nobel Price winner 1943
PHYSICS AND INSTRUMENTATION
SPECTRUM OF ELECTROMAGNETIC RADIATION
RADIOACTIVE ATOM DECAY

a) Electromagnetic radiation: Single Photon Imaging / SPECT

b) Particular radiation: Therapy and PET

2 x 511keV photons
<table>
<thead>
<tr>
<th><strong>NUCLEAR MEDICINE IMAGING/THERAPY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SINGLE PHOTON (γ,x)</strong></td>
</tr>
<tr>
<td><strong>PLANAR / TOMOGRAPHY</strong></td>
</tr>
<tr>
<td>(SPECT)</td>
</tr>
<tr>
<td>Single Photon Emitters:</td>
</tr>
<tr>
<td>$^{99m}$Tc, $^{201}$Tl, $^{67}$Ga, $^{131}$, $^{123}$I, $^{111}$In</td>
</tr>
<tr>
<td>Anatomical/Functional Imaging</td>
</tr>
<tr>
<td></td>
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<tr>
<td><strong>POSITRON (e⁺)</strong></td>
</tr>
<tr>
<td><strong>EMISSION TOMOGRAPHY</strong></td>
</tr>
<tr>
<td>(PET)</td>
</tr>
<tr>
<td>Positron Emitters:</td>
</tr>
<tr>
<td>$^{18}$F, $^{15}$O, $^{13}$N, $^{11}$C, $^{82}$Rb, $^{68}$Ga</td>
</tr>
<tr>
<td>Metabolic Molecular Imaging</td>
</tr>
<tr>
<td></td>
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<tr>
<td><strong>THERAPY</strong></td>
</tr>
<tr>
<td>Particle Emitters: $e^-$ electron (beta) and alpha (a)</td>
</tr>
<tr>
<td>$^{32}$P, $^{131}$I, $^{89}$Sr, $^{90}$Y, $^{153}$Sm, $^{166}$Ho</td>
</tr>
<tr>
<td>Therapy of benign and malignant diseases</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>IN VITRO STUDIES</strong></td>
</tr>
<tr>
<td>low energy gamma or electrons ($^{125}$I, $^{3}$H, $^{14}$C)</td>
</tr>
</tbody>
</table>
# Radioisotopes in Nuclear Medicine

## Patient Imaging

<table>
<thead>
<tr>
<th>Planar and SPECT:</th>
<th>SINGLE PHOTON $\gamma$, x RAYS energy $&gt; 80$keV ($^{99m}$Tc-$^{203}$TI etc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET Studies</td>
<td>POSITRONS $e^+$ ($^{18}$FDG etc)</td>
</tr>
</tbody>
</table>

## Patient Therapy

<table>
<thead>
<tr>
<th>Partialicular Radiation</th>
<th>electrons ($^{131}$I) or alpha particles</th>
</tr>
</thead>
</table>

## In Vitro Studies

<table>
<thead>
<tr>
<th>Gamma or Electrons</th>
<th>low energy ($^{125}$I, $^3$H, $^{14}$C)</th>
</tr>
</thead>
</table>
NUCLEAR MEDICINE

RADIOPHARMACEUTICALS

Organic or Inorganic Molecules labeled with Radioactive Isotopes

Radioactive Isotopes can be
Single Photon Emitters: $\gamma$, x rays (Planar and SPECT)
Positron Emitters: $e^+$ or positron (PET studies)
Particle Emitters: $e^-$ electron or beta, and alpha (Therapy)
Low Energy $\gamma$ or $e^-$ Emitters: (in vitro studies)
A. SINGLE PHOTON IMAGING
PLANAR and TOMOGRAPHIC (SPECT)
HISTORY
Development of Rectilinear Scanner 1950
Benedict Cassen

1950 Benedict Cassen invents rectilinear scanner
1954 William Myers operates a rectilinear scanner
HISTORY

Development of Gamma Camera 1957
Hal Anger

1957: Hal Anger invents gamma camera
ANGER GAMMA CAMERA
1) SINGLE PHOTON SCINTIGRAPHY
   (Anger Gamma Camera Principle)

Collimation

(gamma/x-rays)
SPECT JASZCZACK PHANTOM STUDIES

Data Spectrum’s SPECT Phantoms

JASZCZACK PHANTOM

0003 RODS

0004 TRANSVERSE

JASZCZACK PHANTOM

0001 SPHERES
PORTABLE GAMMA CAMERA
TOMOGRAPHY

SINGLE PHOTON ($\gamma, x$)

POSITRON EMISSION TOMOGRAPHY (PET)

SPECTRUM TOMOGRAPHY (SPECT)
THE THREE TOMOGRAPHIC PLANES
SPECT HOFFMAN PHANTOM STUDIES
THE FIRST SPECT CAMERA
SPECT CAMERA THREE DETECTOR
SPECT CAMERA THREE DETECTOR
Functional Nuclear Studies

Sculpture by Colder
Anatomical Studies

Aphrodite of Milos
SPECT/CT

Combines a Dual-headed Gamma Camera for Functional Imaging and a Multislice CT Scanner for anatomical definition.

PHILIPS Precedence

SIEMENS Symbia

Approx. Price Tag: $1M depending on the configuration.
$^{67}$Ga SPECT / CT

SPECT / CT for accurate localization of the abscess
Prostate cancer – Accurate localization of LN metastasis
$^{111}$In Prostascint  SPECT / CT

*Recurrence*
111In Octreotide SPECT/CT

Primary and metastatic Carcinoid tumor
\textbf{Is there a recurrence?}
$^{111}$In Octreotide SPECT/CT

Primary (Pancreas) and Metastatic (Pelvis) Carcinoid
$^{111}$In Octreotide SPECT/CT

Paraganglioma
$^{99m}$Tc-Sestamibi SPCT/CT
Parathyroid Adenoma

Early Study
$^{99m}$Tc-Sestamibi SPCT/CT
Parathyroid Adenoma

Late Study
B. POSITRON EMISSION TOMOGRAPHY (PET)
HISTORY
Development of Cyclotron
Ernest O. Lawrence

Ernest O. Lawrence (1901–1958)
HISTORY
Development of PET Scanner
Ter-Pogossian

Wagner in the Ter-Pogossian scanner at Washington University, 1973
PROPERTIES OF POSITRON EMITTERS

• CHEMICAL
  Can Label Metabolic Molecules (Glucose, AA, etc)

• PHYSICAL
  ✓ Small: Do not alter the Biochemical Properties
     of the Metabolic Molecules (Biochemical Recognition Maintained)
     Therefore allow Molecular Imaging

  ✓ Emit Positrons: Need special Cameras (PET cameras)
     Allow Tomography and Quantitation

  ✓ Have short half lives: Low Radiation Exposure

  ✓ Need Cyclotrons to produce them (or special generators)
Electromagnetic core of the cyclotron for acceleration of charged subatomic particles
Charged particles (p,d) are highly accelerated and hit the target, a stable nucleus; they are incorporated and produce radioisotopes
Radiopharmaceuticals are synthesized in heavily shielded cells, using the newly produced radioactive isotopes.
Small Hospital Cyclotrons are available for clinical production
Once a Positron $e^+$ is out of the decaying nucleus, soon encounters an Electron $e^-$ and they Annihilate producing Two Photons very energetic (511 keV), which run on the same Straight Line but Opposite Direction.
2. POSITRON EMISSION TOMOGRAPHY

a) COINCIDENCE

b) TIME OF FLIGHT

**HOW PET WORKS**

- **DECAY** → **ANNIHILATION**

<table>
<thead>
<tr>
<th>Decay</th>
<th>Annihilation</th>
<th>Petromium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positron travels 1-3 mm (depending on energy) before annihilation.</td>
<td>Annihilation process conserves energy and momentum.</td>
<td>Simultaneous detection of the two 511 keV photons indicates an event along a line between the detectors.</td>
</tr>
<tr>
<td>- Photons are 511 keV</td>
<td>- Photons almost colinear</td>
<td></td>
</tr>
</tbody>
</table>

**COINCIDENCE**

**TIME of FLIGHT** $t_2 - t_1$
POSITRON EMISSION TOMOGRAPHY (PET)
Commonly Used Positron-Emitting Radionuclides

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-Life (min)</th>
<th>Positron Yield</th>
<th>Positron Energy (MeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cyclotron-Produced</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>2.04</td>
<td>99+%</td>
<td>1.72</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>9.96</td>
<td>99+%</td>
<td>1.19</td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>20.4</td>
<td>99+%</td>
<td>0.96</td>
</tr>
<tr>
<td>$^{18}$F</td>
<td>110.0</td>
<td>96.9%</td>
<td>0.64</td>
</tr>
<tr>
<td><strong>Generator-Produced</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{82}$Rb</td>
<td>1.26</td>
<td>96%</td>
<td>3.35</td>
</tr>
<tr>
<td>$^{68}$Ga</td>
<td>68.1</td>
<td>90%</td>
<td>1.90</td>
</tr>
</tbody>
</table>
RADIOPHARMACEUTICALS FOR PET

- $^{11}$C(20min)-Carbon Monoxide: Blood Pool-Volume
- $^{11}$C-Carbon Dioxide: Tissue pH
- $^{11}$C- Dopamine: Neuroreceptors
- $^{11}$C- N-methyl-spiperone: Neuroreceptors
- $^{13}$N(10min)- Ammonia: Perfusion
- $^{13}$N- Amino Acids: Tumors
- $^{15}$O$_2$(2min) - Oxygen: Metabolism/Tumors
- $^{15}$OH$_2$ - Water: Blood Flow
- $^{18}$F(110min)-2 Deoxy-Glucose: Metabolism/Tumors
- $^{18}$F-DOPA: Parkinson/Tumors
- $^{18}$F-Haloperidol: Neuroreceptors
- $^{18}$F- Amino Acids: Tumors
PET CLINICAL APPLICATIONS

- Brain Function and Tumors
- Myocardial Perfusion and Viability
- Oncologic Applications
- Infection / Inflammation etc
PET APPLICATIONS

CLINICAL

\(^{18}\text{F-FDG} (^{18}\text{F-Fluoro-Deoxy-Glucose})\)

\(^{18}\text{F-DOPA} (^{18}\text{F-Di-Oxy-Phenyl-Alanine})\)

\(^{82}\text{Rb} \text{ and } ^{68}\text{Ga} \text{ Generators}\)

UNDER DEVELOPMENT

\(^{18}\text{F-Aminoacids, } ^{11}\text{C-Aminoacids / Nucleotides, } ^{18}\text{F-Receptors}\)

RESEARCH

Blood Flow / Blood Pool / Utilization of \(\text{O}_2\)

Imaging Receptors / Organelles

DNA / RNA / Gene Studies / Treatments

Special Studies of Ischemia, Alzheimer's etc.
WHAT IS FDG-PET AND HOW DOES IT WORK?

- Most **Tumors metabolize glucose** in excess of normal tissues

- **Myocardium** and **Brain Cortex** metabolize excessively glucose

- FDG-PET quantitates **in vivo the glucose metabolic activity** of **tumors** and normal organs (**brain and heart**)
A. Modify the molecule of Glucose to 2-Deoxy-Glucose (DG).

B. Label 2-Deoxy-Glucose with a radioisotope, $^{18}$F, which does not alter its properties for biochemical recognition:

$^{18}$F-2-Deoxy-Glucose = FDG
FDG enters the cells

and it is phosphorylated like Glucose

FDG-6-PO₄ is not metabolized and accumulates, thus allowing imaging
CLINICAL EXPERIENCE with FDG/PET TUMOR IMAGING

APPLICATIONS

• CNS Function and Tumors
• Myocardial Viability
• Tumor Evaluation
• Infection / Inflammation
CLINICAL EXPERIENCE with FDG/PET TUMOR IMAGING

ADVANTAGES

- It provides **Accurate** information about most Tumors
- The information is **Functional** and **Quantitative**
- It is **Easy** to recognize the Tumors on PET studies
- Covers the **Entire Body**
CLINICAL EXPERIENCE with FDG/PET TUMOR IMAGING

DISADVANTAGES

- **Brain, Heart and Liver** accumulate FDG and this limits the sensitivity for low intensity lesions in or around these organs.

- The **Kidneys** recognize the difference between Glucose and FDG and do not reabsorb FDG and create interpretation issues.

- **Muscles and Brown Fat** accumulate FDG as Glucose and this results in bowel, vocal cords, body muscles and fat visualization issues.

- **WBCs (Infections) Muscles etc (Inflammations)** accumulate FDG and this generates problems in differentiating them from tumors, but this may diagnose infection or inflammation if needed.
CLINICAL EXPERIENCE with FDG/PET TUMOR IMAGING

SOLUTIONS

- **Four hours NPO** eliminates visualization of the heart
- **Rest** during incubation (+day before) eliminates the muscles
- **Warm Environment** eliminates visualization of brown fat
  (Propranolol 20-40mg before FDG may also work)

- **Accurate localization** could be achieved using the CT
  a) Correlation with previous CT “side-by-side” visually
  b) Fusion PET+CT with “computer programs”
  c) PET/CT “combined acquisition” Imaging
The EVOLUTION of CLINICAL FDG/PET IMAGING
Cameras and Crystals

Hybrid PET/SPECT NaI
Dedicated PET NaI
New Crystal Technology

Combined PET/CT

ADAC-PHILIPS GSO
GE BGO
SIEMENS/CTI LSO
Design features & benefits

**image fusion**

- side by side display of 2 different studies
- Simultaneous processing of both studies
- automatic overlay and manual alignment
- applicable to brain- and WB studies
- import of other modalities via optional DICOM software

Meningioma after RT? malignant lesion? in visual cortex?

Image courtesy of Prof. Dr. Carreras, Madrid, Spain
EQUIPMENT FOR PET and PET/CT SCINTIGRAPHY

DEDICATED PET CAMERAS

- Ring-Detectors
- NaI/BGO LSO-GSO using coincidence principle
- Provide independent PET images

PET/CT CAMERAS

- Combinations of ring PET detectors and CT X-ray machines
- Provide independent and fused PET/CT images
Patient with a recent left CVA had an FDG-PET
QUANTIFICATION OF PET STUDIES

Accurate Quantification
PRACTICAL QUANTIFICATION of PET

Standardized Uptake Value (SUV)

SUV units indicate uptake = % of injected dose (weight corrected) /gram tissue

Recurrence 9 SUV
Bone Mets 3 SUV
The EVOLUTION of CLINICAL FDG/PET IMAGING

Clinical Utilization

CLINICAL FOCUS OF PET IMAGING CHANGES WITH GROWING VOLUME

Mid-'80s
- Neuro: 10%
- Cardiac: 15%
- Tumors: 75%

Fewer than 10,000 exams per year

2000 - 2002
- Neuro: 10%
- Cardiac: 80%
- Tumors: 10%

More than 250,000 exams per year

2008
- Neuro: 6%
- Cardiac: 6%
- Tumors: 88%

More than 5,000,000 exams per year

Tumors
IN VIVO (NON-IMAGING) STUDIES

1) THYROID UPTAKE
2) VITAMIN B-12 ABSORPTION (SHILLING’S TEST)
3) BLOOD/PLASMA/RBC VOLUMES
4) PLATELET SURVIVAL AND SEQUESTRATION
5) RBC SURVIVAL AND SEQUESTRATION
6) GI TRACT BLOOD OR PROTEIN LOSS
7) HELICOBACTERIUM PYLORI STUDIES
8) FERROKINETICS
9) RENAL CLEARANCES (GFR-ERPF-FF)
NUCLEAR MEDICINE STUDIES

Safe
Easy
Available
Cost effective
NUCLEAR MEDICINE PROCEDURES ARE CLINICALLY USEFUL BECAUSE

• They provide comprehensive information about **structure and function** simultaneously
• They have **high sensitivity or specificity** or both
• Many examine the **whole body** or organ systems
• They are **non-invasive** and well tolerated tests
• Often provide information **no other tests** can
• They are **less expensive** than most test or sequences of tests for similar information (except PET/CT)
Nuclear Imaging involves a very low dose of radiation harmless to infants, children and adults.
QUANTITATIVE SCINTIGRAPHY 1

1. GRAPH GENERATION FROM DYNAMIC STUDIES FOR SEMI-QUANTITATION
   Renography, GI Motility, GE emptying, EF, EF, Flow

2. SEMI-QUANTITATION OF ORGAN UPTAKE FROM STATIC IMAGES
   \(^{67}\text{Ga}\) Pulmonary, Renal, Thyroid Uptake, Lung V/Q,
   \(^{201}\text{TI}\) tumor, etc
QUANTITATIVE SCINTIGRAPHY 2

3 ACCURATE QUANTIFICATION OF ORGAN PERFUSION AND FUNCTION USING BLOOD (URINE) SAMPLING AND IMAGING (PET) WITH SOPHISTICATED ANALYSIS

4 PROBE GENERATED STRIPCHART OR DIRECT COUNTING (old, non-used in most centers)
   (Thyroid uptake, Renography, Xe washout, Flow)
TIME ACTIVITY GRAPHS:
FLOW GRAPHS

RENOGRAMS
FACTORS AFFECTING THE USE OF RADIONUCLIDES IN CHILDREN

- Short half-life isotopes ($^{99m}\text{Tc} - 6\text{ hrs}$)
  - No Particular Radiation
  - High efficiency cameras

The Radiation Exposure from Nuclear Imaging is equivalent and even lower than x-ray studies (cystography)
NUCLEAR MEDICINE STUDIES AT JMH/UM

EQUIPMENT
We have the best SPECT camera (3 detector at JMH)
6 Dual-Head and 4 Single-Head SPECT
3 Planar (1 portable), 1 SPECT/CT (DFB)
1 hybrid PET, 1 dedicated PET (JMH) and 3 PET/CT (UMHC, DFB, BBL)

RADIOPHARMACEUTICALS
We use a Tc generator and Kits
commercially available Planar and SPECT RPs
and $^{18}$FDG, the only commercially available RP for PET

We expect soon a second SPET/CT camera (UMHC)
and a CYCLOTRON for short lived positron emitters (UMHC)
($^{15}$O, 2 min; $^{13}$N, 10 min; $^{11}$C, 20 min)

We pursue
A PET/CT camera for JMH

September 2009
Planar Static and Dynamic Imaging applications

Organ Imaging, Hypertension, Infections, Tumors

Tomography

Single photon (SPECT), Positron (PET)

Non Imaging Studies

Renal Clearance, Blood Volume, Vitamin B12 absorption

Therapy

Benign {Thyrotoxicosis, Arthropathies (Rheumatoid, Hemophiliac)}

Malignant (Thyroid cancer, Lymphomas, Bone Pain from Mets)
THERAPY WITH SYSTEMIC USE OF UNSEALED RADIOPHARMACEUTICALS
Penetration of Particulate and Electromagnetic Radiation

HUMAN TISSUES

- Subcutaneous tissue
- Dermis
- Epidermis

Alpha particles
Beta particles
Gamma rays

Environmental Protection Needed

Adapted from Wootton. Radiation Protection of Patients. 1993.
Radiation Safety Issues (environment)

Alpha and Beta rays are not a problem (attenuated)
Gamma rays are a problem because they emerge and irradiate environment
Therefore pure Beta emitters are preferable ($^{90}$Y)
THERAPY WITH UNSEALED RADIOPHARMACEUTICALS

A) BENIGN DISEASES

Thyrotoxicosis

- Graves Disease  (10-30 mCi $^{131}$INa po)
- Toxic Adenoma  (30-150 mCi $^{131}$INa po)
- Toxic Multinodular Goiter  (20-150 mCi $^{131}$INa po)
- Non Toxic Multinodular Goiter  (100-300 mCi $^{131}$INa po)

Synovectomy (Hemophiliac or Rheumatoid Arthritis)

  (5-10 mCi $^{32}$P Chromic Phosphate (Colloid) intraarticulary)
GRAVES DISEASE

At treatment (15 mCi $^{131}$Na po)  
4 months later
TOXIC ADENOMA
PRE AND POST THERAPY WITH $^{131}$I

At treatment (29.2 mCi $^{131}$INa po)  8 months later
Nuclear Synovectomy

INDICATIONS
Hemophiliac joints
Rheumatoid arthritis

METHOD
Arthrocentesis
Test with $^{99m}$Tc--SC
Instillation of 05-15 mCi of $^{32}$P-colloid

RESULTS
Improvement in motion
Relief of pain
Prevent hemorrhage
THERAPY WITH UNSEALED RADIOPHARMACEUTICALS

B) MALIGNANT DISEASES

Treatment of **Thyroid Cancer** (150 - 300 mCi $^{131}$INa orally)

[Ablation of the Thyroid gland or Remnants (150 mCi $^{131}$INa orally)]

Treatment of **Bone Pain from Metastasis**

(4 mCi $^{89}$Sr iv or 1.2 mCi/kg $^{153}$Sm EDTMP iv)

**Bone Marrow Ablation** Holmium-166-DOTMP iv

(or $^{90}$YMoAb or $^{131}$IMoAb)

Treatment **Non-Hodgkin’s Lymphoma** ($^{131}$IMoAb or $^{90}$YMoAb)

Treatment of **Pheochromocytomas Paragangliomas and Neuroblastomas**

($^{131}$I-MIBG)
THERAPY OF TUMORS with UNSEALED or SYSTEMIC RADIOPHARMACEUTICALS

A) INDICATION

Biopsy proven diagnosis

B) PREREQUISITES

Proof that the tumor accumulates sufficient percentage of the dose of the radiopharmaceutical (dosimetry)

Dose not to exceed safety limits for normal tissues (dosimetry)

Patient’s clinical condition and laboratory values permit
TREATMENT of METASTATIC THYROID CANCER

Dosimetry

4th day during dosimetry
With 2 mCi of $^{131}$INa po

lungs

standard

Treatment

7 days post treatment with
302 mCi of $^{131}$INa po

15 yo boy with thyroid carcinoma after thyroidectomy + ablation, rising TGB
THERAPY OF INTRACTABLE BONE PAIN DUE TO BLASTIC METASTATIC DISEASE

- **Phosphorous-32** (Bone marrow suppression)
  \( (T-1/2 = 14 \text{ days}) \) 60-90\% efficacy
- **Strontium-89** (Mild transient BM suppression)
  \( (T-1/2 = 8 \text{ days}) \) *(Metastron)*
  Effective in 80\% prostate, 81\% breast metastasis
- **Complexes** (Mild transient BM suppression)
  Samarium-153-EDTMP \( (T-1/2 = 47 \text{ hr}) \) *(Quadramet)*
  Yttrium-90-DTPA-Ab \( (T-1/2 = 64 \text{ hr}) \)
TREATMENT OF INTRACTABLE BONE PAIN FROM METASTATIC CANCERS

Deteriorating metastatic disease with intractable bone pain proof that the tumor accumulates the radiopharmaceutical
RADIOIMMUNOTHERAPY IN NON-HODGKIN’S LYMPHOMA
External Beam Radiation vs Radioimmunotherapy for Indolent NHL

External beam radiation

Radioimmunotherapy
Rituximab: First Monoclonal Antibody Approved for the Treatment of NHL

FDA-approved indication: relapsed or refractory low-grade or follicular, CD20+, B-cell non-Hodgkin’s lymphoma
90Y Zevalin/ 131I Bexxar Produce a Crossfire Effect

Naked antibody  Radiolabeled antibody

Rituxin  90Y Zevalin/ 131I Bexxar
Radioimmunotherapy

Yttrium 90 ibritumomab tiuxetan (Zevalin®)
  – Anti-CD20
  – Approved for commercial use in the United States, February 2002

Yttrium 90 epratuzumab
  – Anti-CD22
  – Investigational

Iodine 131 tositumomab (Bexar®)
  – Anti-CD20
  – Approved for commercial use in the United States, June 2003
## Radionuclides Commonly Used in RIT

<table>
<thead>
<tr>
<th>Physical half-life</th>
<th>Decay type</th>
<th>Particle energy (MeV)</th>
<th>Gamma energy (MeV)</th>
<th>Particle path length (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{90}$Y</td>
<td>$\beta$</td>
<td>2.3</td>
<td>None</td>
<td>5.3</td>
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<tr>
<td>$^{131}$I</td>
<td>$\beta, \gamma$</td>
<td>0.6</td>
<td>0.364</td>
<td>0.8</td>
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</tbody>
</table>
**90Y Ibritumomab Tiuxetan**

**Ibritumomab**
- Murine monoclonal antibody that binds to the CD20 antigen

**Tiuxetan (chelator)**
- Conjugated to antibody, forms strong urea-type bond with radioisotope

**Isotope: 90Y (pure β emitter)**
**131I Tositumomab**

- Murine IgG2 alpha monoclonal antibody that binds to the CD20 antigen

Tyrosine residue bond conjugates antibody with radionuclide

Radionuclide—**131I** (β and γ emitter)
Zevalin Integrated Safety (N = 349): Median Blood Counts After Treatment

- Hemoglobin (g/dL)
  - Hb = 10

- ANC (10^3/µL)
  - ANC = 1000

- Platelets (10^3/µL)
  - Plts = 50,000

<table>
<thead>
<tr>
<th>Study week</th>
<th>ANC (10^3/µL)</th>
<th>Hemoglobin (g/dL)</th>
<th>Platelets (10^3/µL)</th>
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<tr>
<td>0</td>
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<td>12</td>
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<tr>
<td>2</td>
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</tr>
<tr>
<td>4</td>
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<td>6</td>
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<td>12</td>
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</tr>
<tr>
<td>8</td>
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</tr>
<tr>
<td>14</td>
<td>1000</td>
<td>12</td>
<td>50,000</td>
</tr>
</tbody>
</table>
REQUIREMENTS FOR LICENSING TO ADMINISTER UNSEALED RADIOPHARMACEUTICALS TO PATIENTS (DIAGNOSIS-THERAPY)

200 hours of Basic Training

Physics-Radiopharmacy-Instrumentation

Radiobiology-Radiation Protection

Mathematics-Statistics-Computers

4-12 months Clinical Experience
BOARDS IN NUCLEAR MEDICINE

1) AMERICAN BOARD OF NUCLEAR MEDICINE (3-years)
   1 year “preparatory” training
   (Rad/Path/Med/Surgery/Pedi, etc)
   3 years training in all aspects of Nucl Med (incl. >8 mos CT)

2) RADIOLOGY WITH BOARDS IN NM (new 5-year program)
   1 year “preparatory” training
   4 Years Radiology (including 8 months Nuclear Medicine)
   1 Year straight Nuclear Medicine training