Warren H. Moore, M.D.

Nuclear Medicine Section
Nuclear Medicine Residency Program
Baylor College of Medicine

Nuclear Medicine Service
St. Luke’s Episcopal Hospital
& Texas Heart Institute
Texas Children’s Hospital

Diplomate
American Board of Nuclear Medicine
American Board of Internal Medicine
What is Nuclear Medicine?

Nuclear Medicine is a medical specialty that uses the nuclear properties of radioactive and stable nuclides (i) to make diagnostic evaluations of the anatomic and physiologic conditions of the body and (ii) to provide therapy with non-sealed sources of radioactivity.
Nuclear Medicine Applications

- Best physiologic assessment of targeted organ(s) and/or cell type(s)
- Higher sensitivity than other modalities
- Lower specificity than other modalities for particular diagnosis
- Rare side effects from diagnostic testing
- Optimal information requires proper preparation for some studies
What is Nuclear Medicine?

What is the difference between Nuclear Medicine and traditional Radiology?

<table>
<thead>
<tr>
<th><strong>Nuclear Medicine</strong></th>
<th><strong>Radiology</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Emission</td>
<td>Transmission</td>
</tr>
<tr>
<td>Gamma Rays</td>
<td>X-Rays</td>
</tr>
<tr>
<td>Physiology (Function)</td>
<td>Anatomy (Structure)</td>
</tr>
<tr>
<td>Decade</td>
<td>Event</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>1920s</td>
<td>First human “experiment”</td>
</tr>
<tr>
<td>1930s</td>
<td>First serious clinical use</td>
</tr>
<tr>
<td>1950s</td>
<td>Scientific developments (AEC)</td>
</tr>
<tr>
<td>1960s</td>
<td>New instruments</td>
</tr>
<tr>
<td></td>
<td>Formal clinical training</td>
</tr>
<tr>
<td>1970s</td>
<td>“Modern” radiopharmaceuticals</td>
</tr>
<tr>
<td></td>
<td>“Modern” cameras</td>
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<tr>
<td></td>
<td>American Board of Nuclear Medicine</td>
</tr>
<tr>
<td></td>
<td>(Internal Medicine, Radiology, Pathology)</td>
</tr>
</tbody>
</table>
Developments in Nuclear Medicine

- Instrumentation
- Radiopharmaceuticals
- Clinical Applications
Nuclear Medicine cameras are detectors of radiation (not generators).
<table>
<thead>
<tr>
<th>SPECT (SPET)</th>
<th>PET (DPET)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S</strong>ingle</td>
<td><strong>P</strong>ositron</td>
</tr>
<tr>
<td><strong>P</strong>hoton</td>
<td>(Dual <strong>P</strong>hoton)</td>
</tr>
<tr>
<td><strong>E</strong>mission</td>
<td><strong>E</strong>mission</td>
</tr>
<tr>
<td><strong>C</strong>omputed</td>
<td>(Computed) <strong>T</strong>omography</td>
</tr>
<tr>
<td><strong>T</strong>omography</td>
<td><strong>T</strong>omography</td>
</tr>
</tbody>
</table>
Developments in Nuclear Medicine

- Instrumentation
- Radiopharmaceuticals
- Clinical Applications
## What is a Radiopharmaceutical?

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Carrier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallium-67</td>
<td>citrate</td>
</tr>
<tr>
<td>Iodine-123</td>
<td>sodium iodide</td>
</tr>
<tr>
<td>Iodine-131</td>
<td>sodium iodide</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>pertechnetate</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>diphosphonate</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>DTPA</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>sestamibi</td>
</tr>
</tbody>
</table>
# Radiopharmaceuticals

## Renal Radiopharmaceuticals

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Carrier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr-51</td>
<td>EDTA</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>TcO4</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>DTPA</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>DMSA</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>MAG3</td>
</tr>
<tr>
<td>Tc-99m</td>
<td>GHA</td>
</tr>
<tr>
<td>I-123</td>
<td>Hippuran</td>
</tr>
<tr>
<td>I-131</td>
<td>Hippuran</td>
</tr>
<tr>
<td>I-125</td>
<td>iothalamate</td>
</tr>
</tbody>
</table>
Developments in Nuclear Medicine

- Instrumentation
- Radiopharmaceuticals
- Clinical Applications
ALARA in Daily Practice: What is reasonable?
Why give higher than the minimal dosages?

Higher dosage = shorter imaging time
(but same images may be possible with lower dose if greater imaging time is accepted)

Shorter imaging time = more patients/day/camera
More patients = lower expenses (amortization)
also

Shorter time = better patient comfort
Better comfort = less motion
Less motion = better quality images = better medical decision making
Procedures in Nuclear Medicine

Classifications

Group I: nonimaging tests of in vivo function

Group II-III: diagnostic imaging procedures

Group IV+: therapy procedures
Nonimaging Procedures in Nuclear Medicine

“Common” Group I Tests

- thyroid iodine uptake by probe technique
- GFR by blood and/or urine sample technique
- Schilling tests
- plasma/RBC volume

* = CLIA (Clinical Laboratory Improvement Act)
Common Nuclear Medicine Imaging Procedures

- Myocardial Perfusion Imaging
- Bone Scan
- Lung Scan
- Hepatobiliary Scan
- Renal Scan
- White Blood Cell Scan
- Thyroid Scan/Uptake
- Gastrointestinal Hemorrhage Scan
- PET (FDG) scans
Classification of Radionuclide Cardiac Studies

- Perfusion Imaging ("Cold Spot")
- Infarct Imaging ("Hot Spot")
- Ventricular Function
- Metabolic Activity
- Miscellaneous Imaging
- Radioassay
Anterior Wall Ischemia

99mTc/201TL
# Diagnosis of Thyroid Disease

<table>
<thead>
<tr>
<th>Thyroid Uptake</th>
<th>Vs. Thyroid Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uptake = number</td>
<td>Scan = picture</td>
</tr>
</tbody>
</table>
Diagnosis of Thyroid Disease

Thyroid Uptake

28%
Nuclear Medicine

- Thyroid Scan
- Cold Nodule
- Risk of Cancer
Neonatal Thyroid Scan
Radioisotopes for Initial Diagnosis of Thyroid Disease

- Technetium (pertechnetate) is cheaper than I-123 and gives better quality images in less time than I-131. However,
  - Technetium is not organified and is not optimal for uptake measurements, and
  - 5% of cold nodules on iodine scanning are not seen on pertechnetate scans.
- Therefore, I-123 is the agent of choice for radioisotope diagnosis of thyroid function and thyroid nodules.
Hepatobiliary (HIDA)
- Morphine to shorten study and decrease equivocal states
- Cholecystokinin (CCK) to evaluate biliary dyskinesia

Gastric Emptying
- Erythromycin to evaluate increased motility with drug treatment
Nuclear Medicine

- Alzheimer’s Disease
- (Abnormal glucose uptake)
- F-18 flurodeoxyglucose
Sentinel Node Mapping
Sentinel Node Mapping

LAO AT 30MINUTES
U.S. Approved Tumor Imaging Radiopharmaceuticals

- Ga-67 citrate...............nonspecific
- Tc-99m MDP, HEDP........osteoblasts
- I-131 sodium iodide.........thyroid
- In-111 Oncoscint..........colon, ovary
- Tc-99m Miraluma..............breast
- Tc-99m CEA-Scan...........colorectal
- I-131 MIBG............neuroendocrine
- In-111 octreotide..... neuroendocrine
- Tc-99m Verluma*...............lung
- Tc-99m Prostascint........prostate
- In-111 Zevalin................NHL
- F-18 FDG.....................multiple
Unapproved Tumor Imaging Radiopharmaceuticals

- Tc-99m pertechnetate ............. thyroid
- I-123 sodium iodide ............ thyroid
- In-111 Oncoscint* ............... breast
- Tc-99m MIBI ...................... multiple
- Tc-99m tetrofosmin ............. multiple
- TI-201 chloride .................. multiple
- Tc-99m CEA-Scan ................ GI, breast
- I-123 MIBG .................... neuroendocrine
- In-111 Zevalin ................. NHL
- PET agents (not FDG) .......... multiple
Patient with thyroidectomy and I-131 therapy for papillary carcinoma presented with rising thyroglobulin levels (170 ng/ml). Diagnostic I-131 WB scan was negative. FDG PET showed abnormal foci in the right hilum and in the right lung. CT showed a single soft tissue mass at the right hilum.
Nonsealed Radiopharmaceuticals Approved for Therapy

- I-131 sodium iodide
  - benign and malignant thyroid disorders
- P-32 phosphate and colloid
  - hematologic disorders
- Sr-89 and Sm-153
  - osteoblastic bony metastases
- Y-90 Zevalin
  - NHL
- Y-90 microspheres*
  - Hepatic neoplasm
Thyroid Cancers Amenable to Iodine Therapy

- Papillary Adenocarcinoma
- Follicular Adenocarcinoma
- (Papillary-Follicular Adenocarcinoma)

I-131 is commonly accepted as a routine part of the treatment and the follow-up of these tumors.
Contraindications to Radioiodine Therapy

Pregnancy

**NOT**

Children/Young Age
Old Age
Childbearing Potential
Iodine Allergy
<table>
<thead>
<tr>
<th>Benign Thyroid Disorders</th>
<th>Treatable with I-131</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse hyperthyroidism</td>
<td>treatment of choice</td>
</tr>
<tr>
<td>Graves’ Disease</td>
<td></td>
</tr>
<tr>
<td>Nodular hyperthyroidism</td>
<td>common treatment</td>
</tr>
<tr>
<td>Plummer’s Disease</td>
<td></td>
</tr>
<tr>
<td>Subclinical hyperthyroidism</td>
<td>new, but increasing</td>
</tr>
<tr>
<td>Thyroid-related</td>
<td>old, rarely used</td>
</tr>
<tr>
<td>cardiac dysfunction</td>
<td></td>
</tr>
</tbody>
</table>
Treatment of B-cell NHL with Anti-CD-20 Monoclonal Antibody

- I-131 tositumomab (Bexxar)
- Y-90 ibritumomab tiuxetan (Zevalin)

- Role of formal dosimetry
- Effect on patient
- Effect on patient outcomes
Zevalin Regimen

**Imaging dose**
- Rituximab (250 mg/m²)
- Followed by $^{111}$In Zevalin 5 mCi (1.6 mg)

**Therapeutic dose**
- Rituximab (250 mg/m²)
- Followed by $^{90}$Y Zevalin (0.4 or 0.3 mCi/kg; max dose 32 mCi)

**Day**
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8

**Scans**
- 2 - 24 hours
- 48 - 72 hours
$^{111}$In-Labeled Zevalin Imaging

4 hours  66 hours  139 hours

Abdominal CT  Abdominal SPECT
Zevalin (ibritumomab tiuxetan)

- Ibritumomab (murine parent of rituximab)
  - Binds CD20

- Tiuxetan
  - Stable retention of $^{90}\text{Y}$

CD20 antigen

- Expressed only on B-lineage cells
- Important for cell cycle initiation and differentiation
- Does not shed or modulate
### Choice of Isotope

<table>
<thead>
<tr>
<th></th>
<th>Yttrium-[90]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Half-life</strong></td>
<td>64 hours</td>
</tr>
<tr>
<td><strong>Energy emitter</strong></td>
<td>Beta (2.3 MeV)</td>
</tr>
<tr>
<td><strong>Path length</strong></td>
<td>$\chi_{90} 5$ mm</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Outpatient</td>
</tr>
</tbody>
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**Yttrium-[90]**
- Half-life: 64 hours
- Beta energy emitter: 2.3 MeV
- Path length: $\chi_{90} 5$ mm
- Administration: Outpatient
Palliative Treatment of Bone Pain with Radiopharmaceuticals

♦ Available Agents
  ♦ P-32, Sr-89, Sm-153, others coming

♦ Indications
  ♦ osteoblastic neoplastic disease
    • multifocal lesions
    • pain in areas of prior maximal irradiation
    • pain refractory to prior irradiation
Palliative Treatment of Bone Pain with Radiopharmaceuticals

- **Results**
  - simple outpatient procedure
  - successful in 80+% of patients
    - improved quality of life (less pain, less medication)
  - few serious side effects
    - thrombocytopenia, neutropenia, anemia
  - cost effective in multifocal disease
  - can be repeated without increasing side effects
Therapeutic Y-90 Spheres
Therapeutic Y-90 Spheres
Treatment of Malignancies with Radiopharmaceuticals

- Leukemia………………..P-32
- Thyroid Cancer…………I-131 sodium iodide
- Lymphoma……………..Y-90 or I-131 anti CD-20
- Solid tumors……………Y-90 microspheres etc
- Pheochromocytoma…..I-131 MIBG
- Neuroendocrine.........In-111 somatostatin

- drugs, antibodies, peptides, other biologicals, particles, ?devices
Nuclear Medicine Directions

- Test options are increasing
- Test complexity is increasing
- There will be great financial pressure for nontraditional users ("turf wars")

- Diagnostic drug interventions and oncology will be the main development focus for the next 10 years
- PET imaging alone and even more in association with CT will be standard care for many more tumors
- Image fusion will be critical to optimal clinical use
- Therapeutic uses are increasing rapidly
Regulatory Issues for NM:

- General feeling of overregulation
- Costs (in hospital personnel) of regulation is not commensurate with the risks
- Official training and experience criteria are unclear and variable across the country
- Training and experience criteria are extremely variable from one hospital/clinic to another
- Decisions are being made by commercial entities rather than by scientific groups (financial and political)
- New applications occur faster than regulations can adapt (lymphoscintigraphy, I-123 MIBG, pediatric applications)
Concerns for the future of NM:

- High costs of drug development are not compensated by payers (e.g. Zevalin)
- Costs of operation of NM laboratories (drugs, supplies, technologists salaries) are increasing while general income is declining
- Shortage of well-trained personnel (technologists, physicians, and scientists-graying of the profession)
- Turf wars between specialty groups
  (unequal training and experience are not appropriately reflected in the marketplace and credentialing committees)
Training & Experience in Nuclear Medicine

ABR Certification
Included automatic NRC approval for Groups I-III

ABNM Certification
Included automatic NRC approval for Groups I-IV

Now accepts a non-ABMS board (CBNC) for automatic approval.

? Future of didactic training (80-120-200 hours)
Training & Experience
NRC Regulations vs. State Trends

Length of training
(700 hours vs. “1200” hours, 3 months vs. 6 months)

Scope of training (selective licensure)

New modalities/applications
(PET, PET/CT, RIT)

Site of training
ACGME institutions vs. any approved user
Why is 10 cases of handling 10 mCi of I-131 required to treat hyperthyroidism with less than 30 mCi, but only 3 cases of handling 29 mCi of I-131 required to give 350 mCi to treat thyroid cancer?
Developments in Nuclear Medicine

♦ Instrumentation
♦ Radiopharmaceuticals
♦ Clinical Applications
Measures of Vitamin B12 absorption

Methods: Schilling Test(s)
    Glass Test
(why not measure B12 in blood?)
GFR measurement/estimation/prediction

Radioisotope clearance methods

A. Cr-51 EDTA (not available in U.S.)
B. Tc-99m DTPA
   - venous injection
   - 2-6 blood samples (usually 3-4)
   - 2-8 hours (usually 4)
C. I-125 iothalamate (Glofil)
   - venous or subcutaneous injection
   - blood and/or urine samples
   - 3-24 hours depending on GFR
Nonimaging Procedures in Nuclear Medicine

“CLIA”
Clinical Laboratory Improvement Act of 1988
CLIA (CMS) certification is required for federal reimbursement for:
performing any test in which you:
Analyze (by any method)
Any tissue or body component
Removed from the body
For clinical diagnostic purposes
(research use is excluded)
If any sample is centrifuged, you must perform and document:

Annual mechanical certification of the speed at which the centrifuge spins

And have a written policy stating how fast it should spin, how it is tested, who tests it, what to do if it doesn’t pass, etc., etc.
### Myocardial Perfusion Imaging Agents
Currently Approved

<table>
<thead>
<tr>
<th>Agent</th>
<th>Year</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>TL-201 chloride</td>
<td>1974</td>
<td></td>
</tr>
<tr>
<td>Tc-99m isonitrile</td>
<td>1990</td>
<td>(Cardiolite)</td>
</tr>
<tr>
<td>Tc-99m teboroxime</td>
<td>1990</td>
<td>(Cardiotec)</td>
</tr>
<tr>
<td>Tc-99m tetrofosmin</td>
<td>1996</td>
<td>(Myoview)</td>
</tr>
</tbody>
</table>
Clinical Indications for Perfusion Imaging

- Presence of CAD
- Extent/Severity of CAD
- Effects of CAD
- Viability
- Pre/Post Revascularization
- Prognosis