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Nuclear Medicine Section

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Nuclear Medicine Service

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& 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?

Nuclear Medicine	Radiology
Emission	Transmission
Gamma Rays	X-Rays
Physiology	Anatomy
(Function)	(Structure)

Brief History of Nuclear Medicine

1920s	First human "experiment"
1930s	First serious clinical use
1950s	Scientific developments (AEC)
1960s	New instruments
	Formal clinical training
1970s	"Modern" radiopharmaceuticals
	"Modern" cameras
	American Board of Nuclear Medicine
	(Internal Medicine, Radiology, Pathology)

Developments in Nuclear Medicine

- Instrumentation
- Radiopharmaceuticals
- Clinical Applications

Key Point in Nuclear Medicine

Nuclear Medicine cameras are detectors of radiation (not generators).

What is the Difference Between SPECT and PET?

SPECT (SPET)	PET (DPET)
	Positron
Single	(Dual
Photon	Photon)
Emission	Emission
Computed	(Computed)
Tomography	Tomography

Developments in Nuclear Medicine

- ♦ Instrumentation
- ♦ **Radiopharmaceuticals**
- ♦ Clinical Applications

What is a Radiopharmaceutical?

<u>Isotope</u>………… + ………..….<u>Carrier</u>

Gallium-67…………………………..citrate

Iodine-123…………………………sodium iodide

Iodine-131…………………………sodium iodide

Tc-99m……………………………..pertechnetate

Tc-99m……………………………..diphosphonate

Tc-99m……………………………..DTPA

Tc-99m……………………………..sestamibi

Radiopharmaceuticals

Renal Radiopharmaceuticals

Isotope	Carrier
Cr-51	EDTA
Tc-99m	TcO4
Tc-99m	DTPA
Tc-99m	DMSA
Tc-99m	MAG3
Tc-99m	GHA
I-123	Hippuran
I-131	Hippuran
I-125	iothalamate

Developments in Nuclear Medicine

- Instrumentation
- Radiopharmaceuticals
- Clinical Applications

Procedures in Nuclear Medicine

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

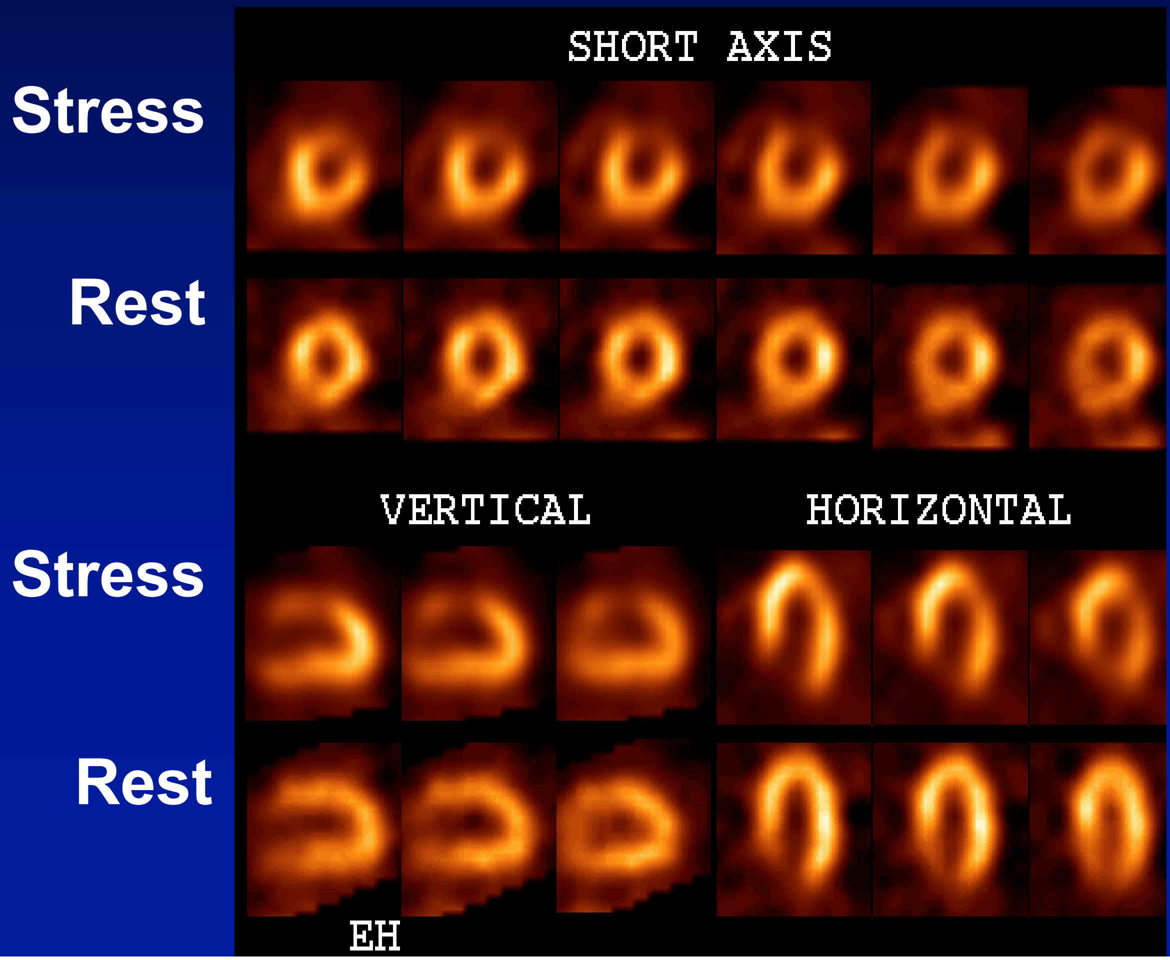
- Myocardial Perfusion Imaging
- Bone Scan
- Lung Scan
- Hepatobiliary Scan
- Renal Scan
- White Blood Cell Scan
- Thyroid Scan/Uptake
- Gastrointestinal Hemorrhage Scan
- PET (FDG) scans

Classification of Radionuclide Cardiac Studies

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

$^{99m}TC/^{201}TL$

- Anterior Wall Ischemia



Diagnosis of Thyroid Disease

Thyroid Uptake Vs. Thyroid Scan

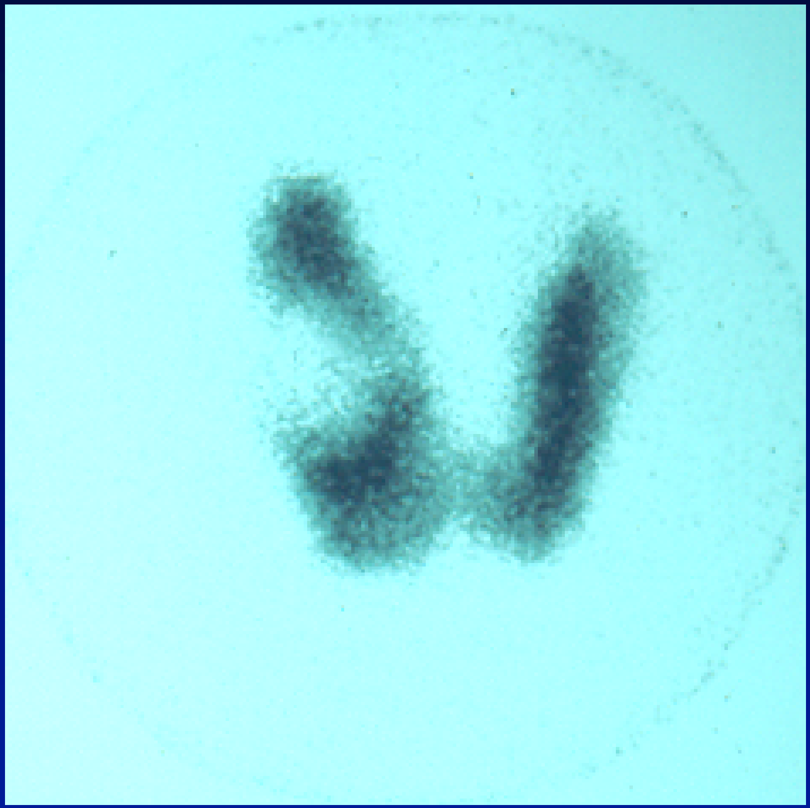
Uptake	=	number
Scan	=	picture

Diagnosis of Thyroid Disease

Thyroid Uptake

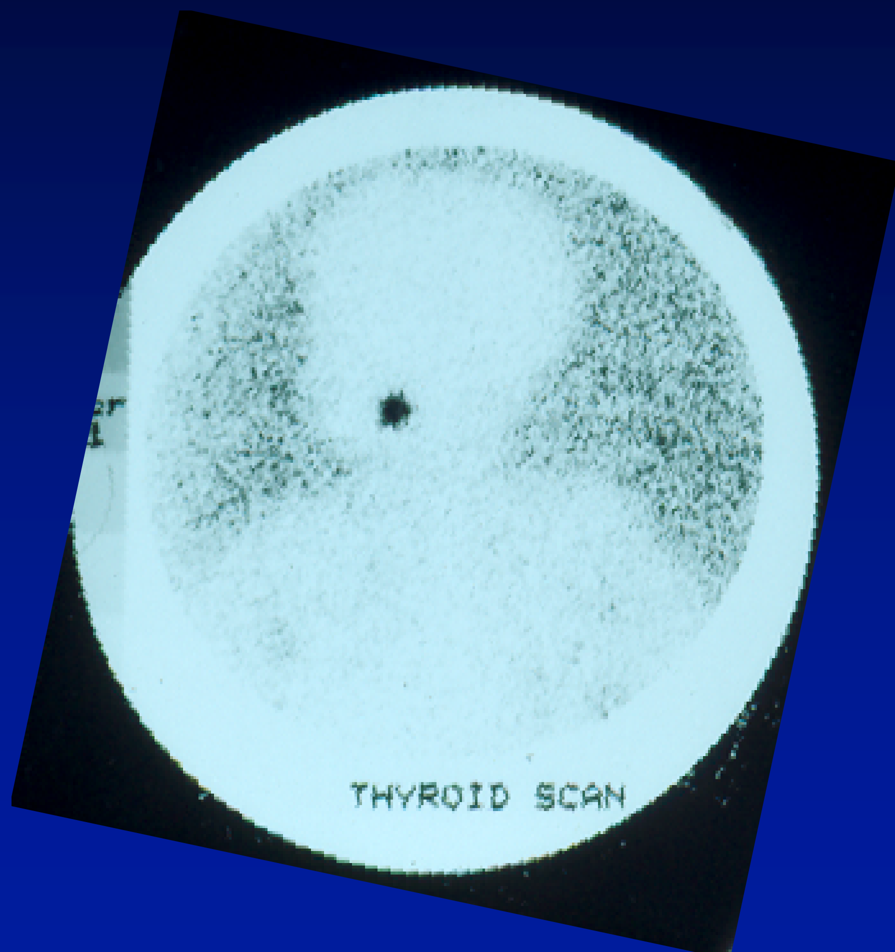
28%

Nuclear Medicine



- Thyroid Scan
- Cold Nodule
- Risk of Cancer

Neonatal Thyroid Scan



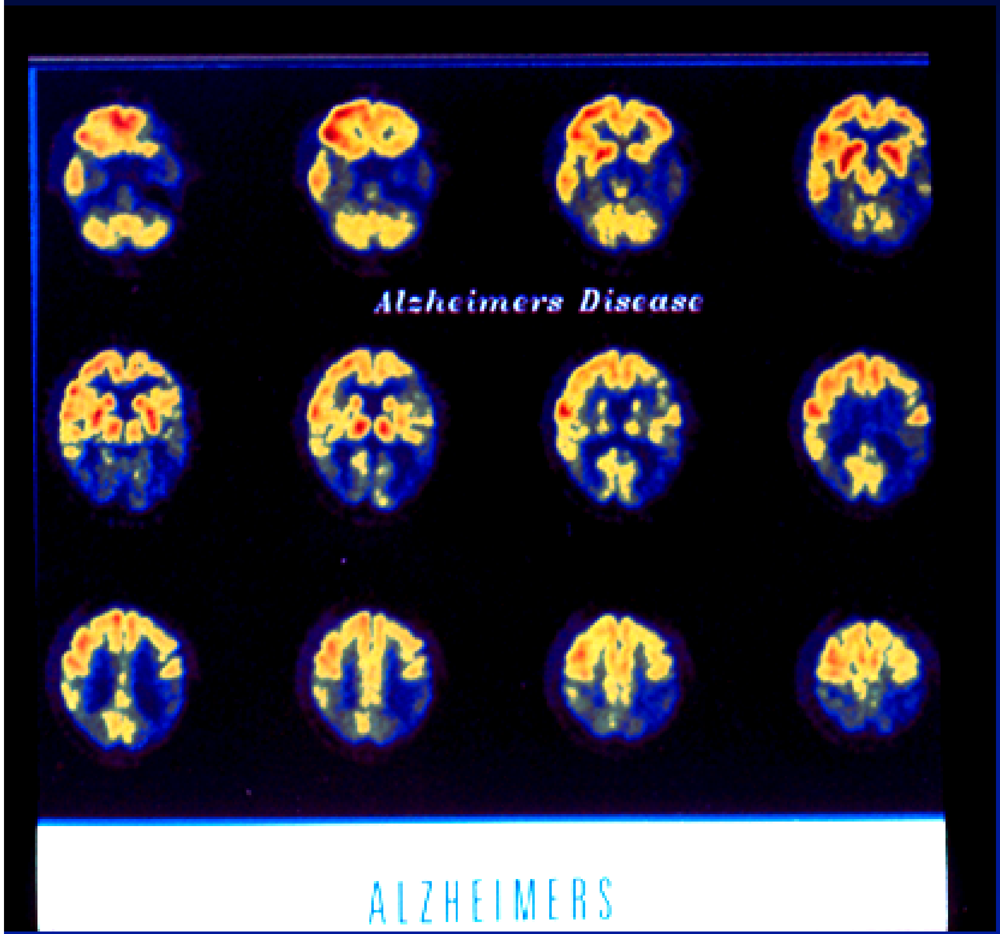
Radioisotopes for Initial Diagnosis of Thyroid Disease

- **Technetium (pertechnetate) is cheaper than I-123 and gives better quality images in less time than I-131. <u>However</u>,**
  - **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.**
- **<u>Therefore</u>, I-123 is the agent of choice for radioisotope diagnosis of thyroid function and thyroid nodules.**

Functional GI Imaging
Drug Stimulation Tests

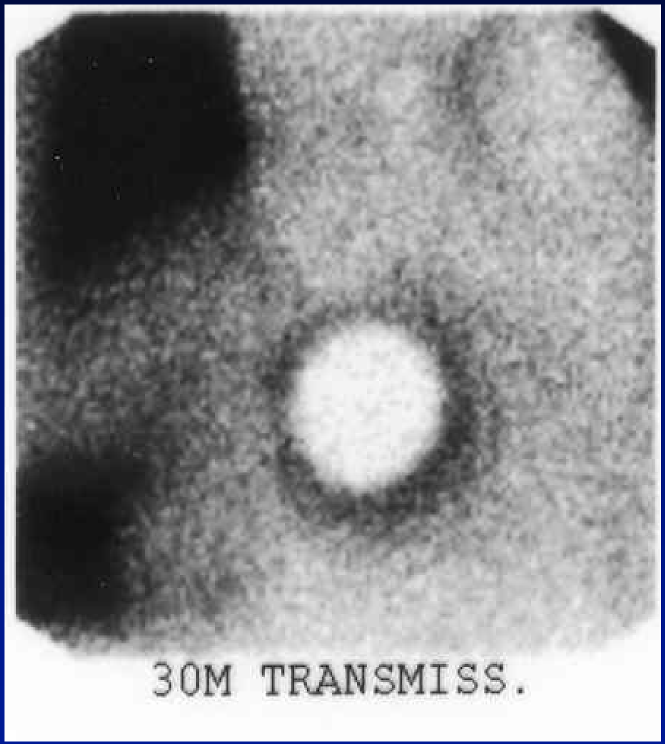
- Hepatobiliary (HIDA)
  - Morphine to shorten study and decrease equivocal states
  - Cholecystokinin (CCK) to evaluate biliary dyskinesia
- Gastric Emptying
  - Erythromycin to evaluate increased motility with drug treatment

Nuclear Medicine

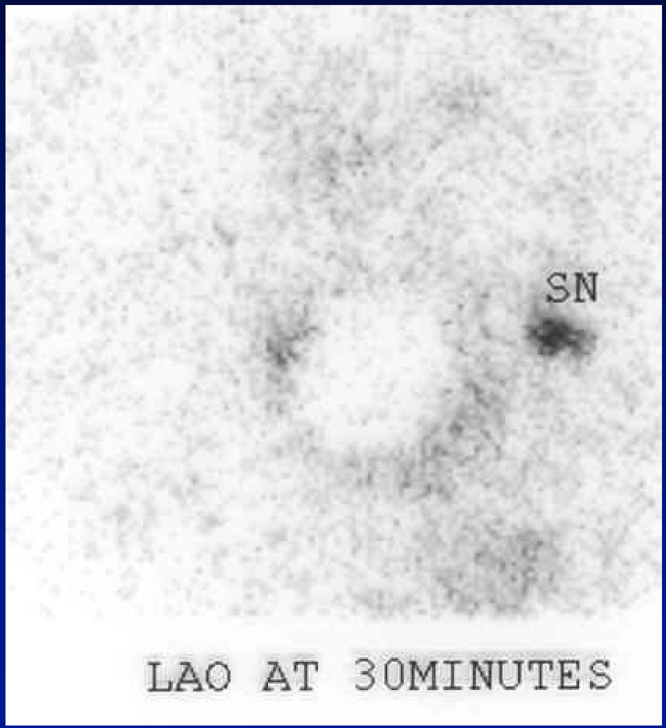


- Alzheimer’s Disease
- (Abnormal glucose uptake)
- F-18 flurodeoxyglucose

Sentinel Node Mapping



Sentinel Node Mapping



U.S. Approved Tumor Imaging Radiopharmaceuticals

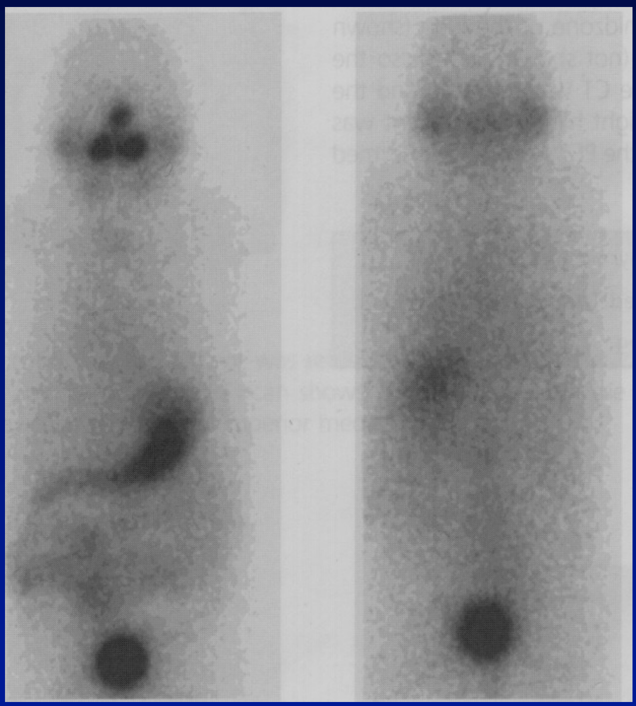
- Ga-67 citrate…………….nonspecific
- Tc-99m MDP, HEDP…….osteoblasts
- I-131 sodium iodide………….thyroid
- In-111 Oncoscint……....colon, ovary
- Tc-99m Miraluma……………...breast
- Tc-99m CEA-Scan……….colorectal
- I-131 MIBG………….neuroendocrine
- In-111 octreotide….. neuroendocrine
- Tc-99m Verluma*…………………lung
-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

<u>Unapproved</u> Tumor Imaging Radiopharmaceuticals

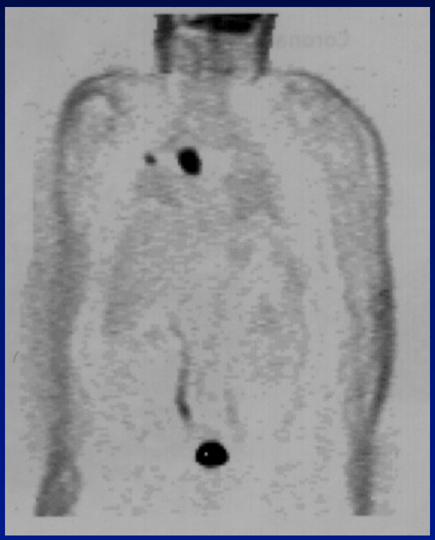
- Tc-99m pertechnetate…….….…thyroid
- I-123 sodium iodide……….….…thyroid
- In-111 Oncoscint*……………...breast
- Tc-99m MIBI…………………..….multiple
- Tc-99m tetrofosmin…………..….multiple
- Tl-201 chloride………………….multiple
- Tc-99m CEA-Scan…………GI, breast
- I-123 MIBG…………...neuroendocrine
- In-111 Zevalin…………………….NHL
- PET agents (not FDG)……….multiple

FDG - PET

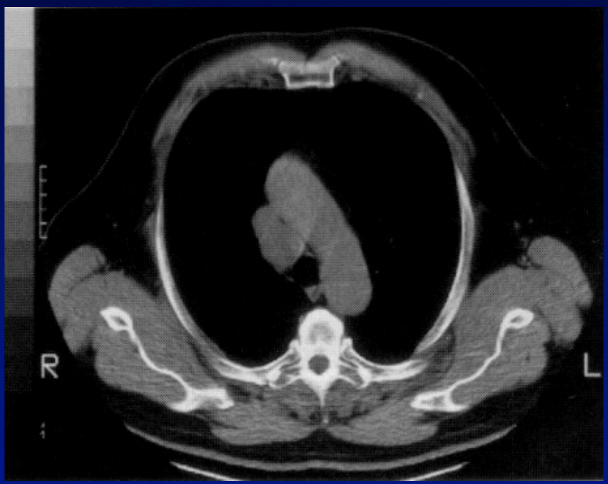
I-131



FDG PET



CT



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

<u>NOT</u>

Children/Young Age

Old Age

Childbearing Potential

Iodine Allergy

Benign Thyroid Disorders Treatable with I-131

♦ **Diffuse hyperthyroidism** ♦ **Graves' Disease**	**treatment of choice**
♦ **Nodular hyperthyroidism** ♦ **Plummer's Disease**	**common treatment**
♦ **Subclinical hyperthyroidism**	**new, but increasing**
♦ **Thyroid-related** ♦ **cardiac dysfunction**	**old, rarely used**

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

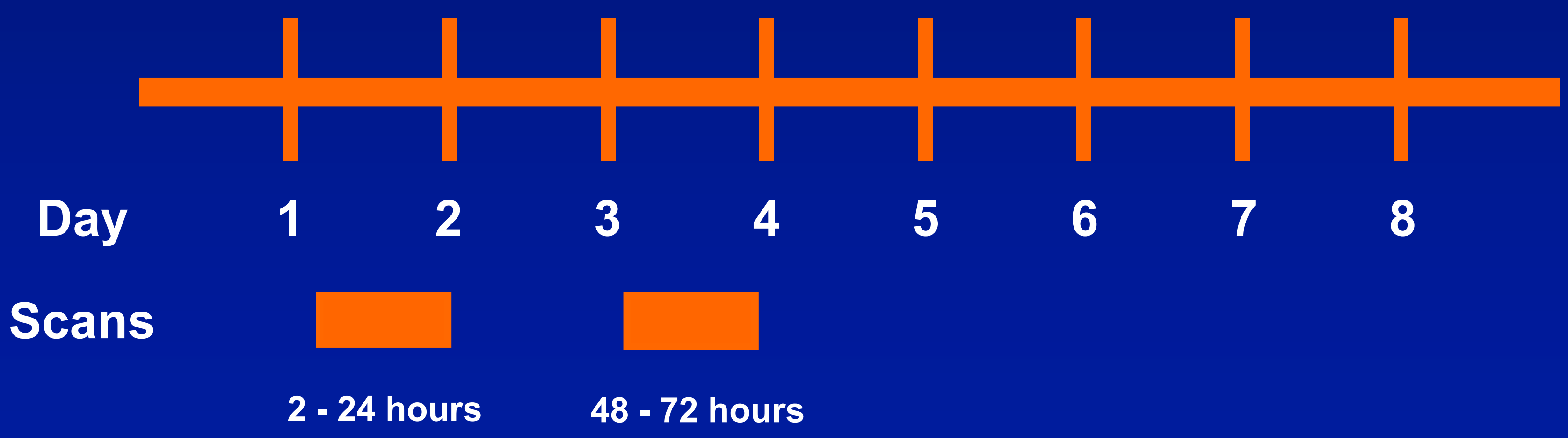
Rituximab (250 mg/m^2)

Followed by
^{111}In Zevalin
5 mCi (1.6 mg)

Therapeutic dose

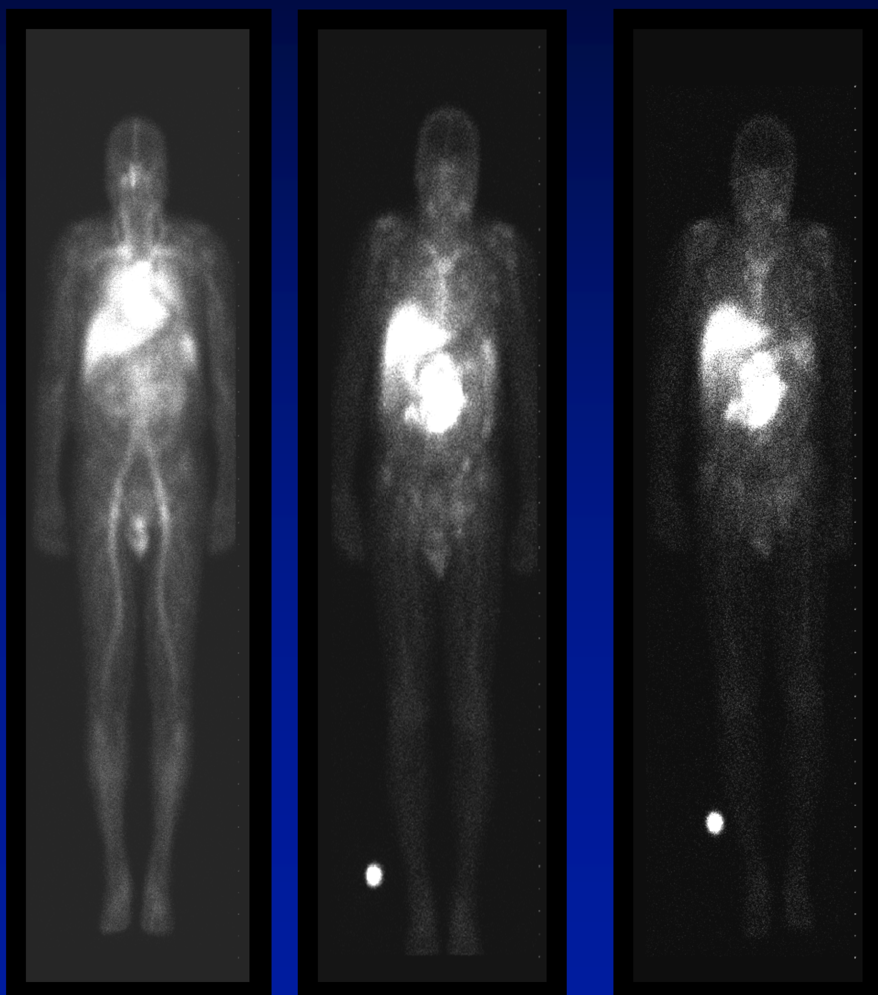
Rituximab (250 mg/m^2)

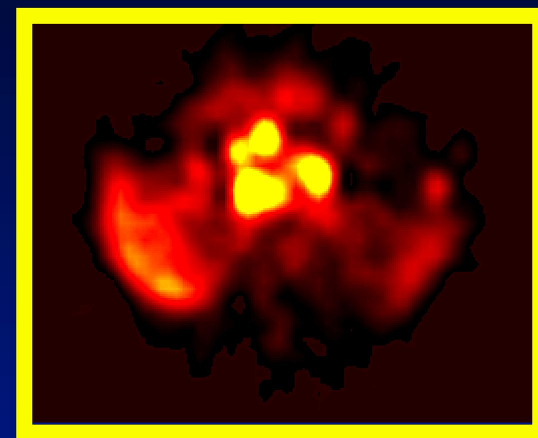
Followed by
^{90}Y Zevalin
(0.4 or 0.3 mCi/kg;
max dose 32 mCi)



^{111}In-Labeled Zevalin Imaging

4 hours 66 hours 139 hours

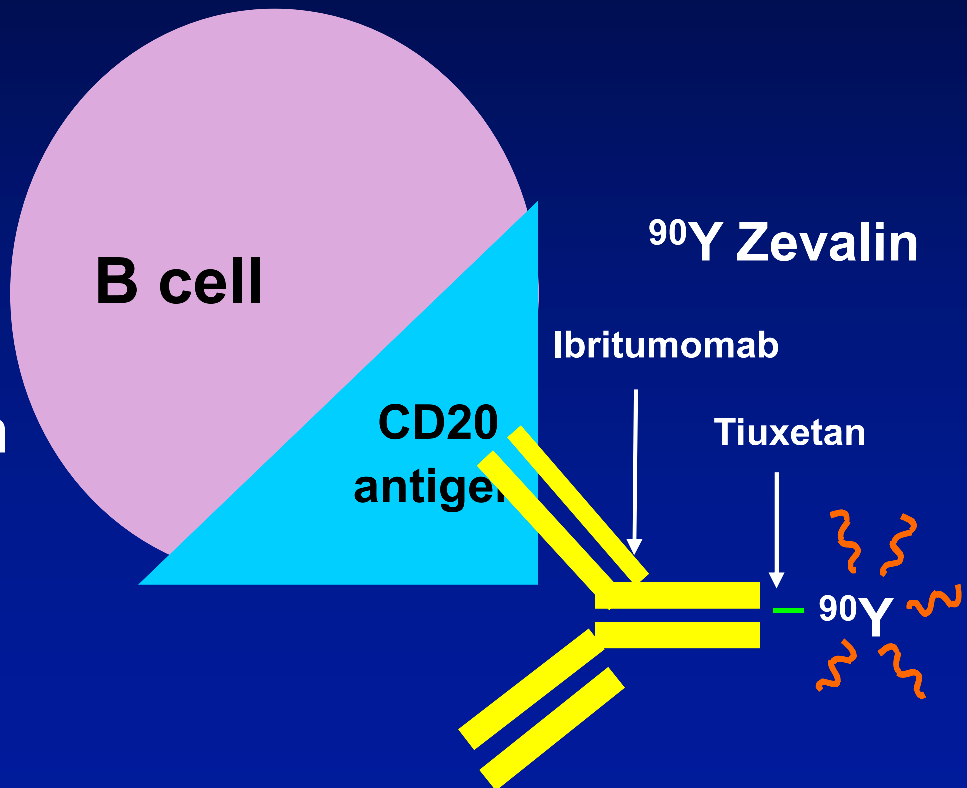




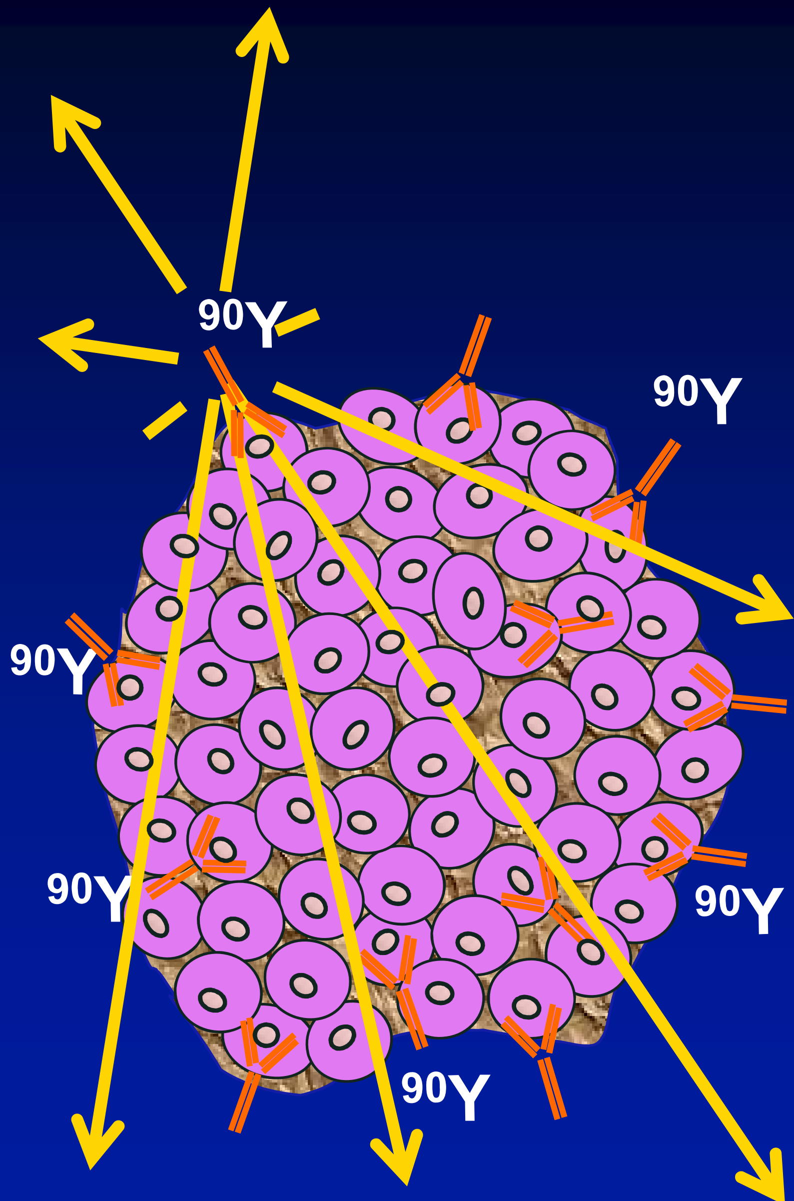
Abdominal SPECT

Abdominal CT

- Zevalin (ibritumomab tiuxetan)
  - Ibritumomab (murine parent of rituximab)
    - Binds CD20
  - Tiuxetan
    - Stable retention of ^{90}Y
- CD20 antigen
  - Expressed only on B-lineage cells
  - Important for cell cycle initiation and differentiation
  - Does not shed or modulate



Choice of Isotope



	Yttrium-[90]
Half-life	64 hours
Energy emitter	Beta (2.3 MeV)
Path length	χ_{90} 5 mm
Administration	Outpatient

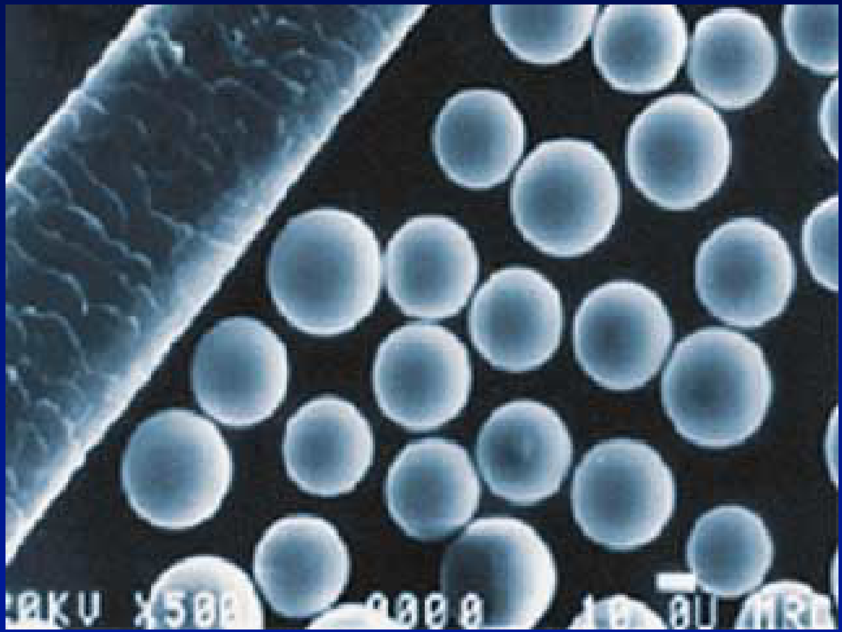
Palliative Treatment of Bone Pain with Radiopharmaceuticals

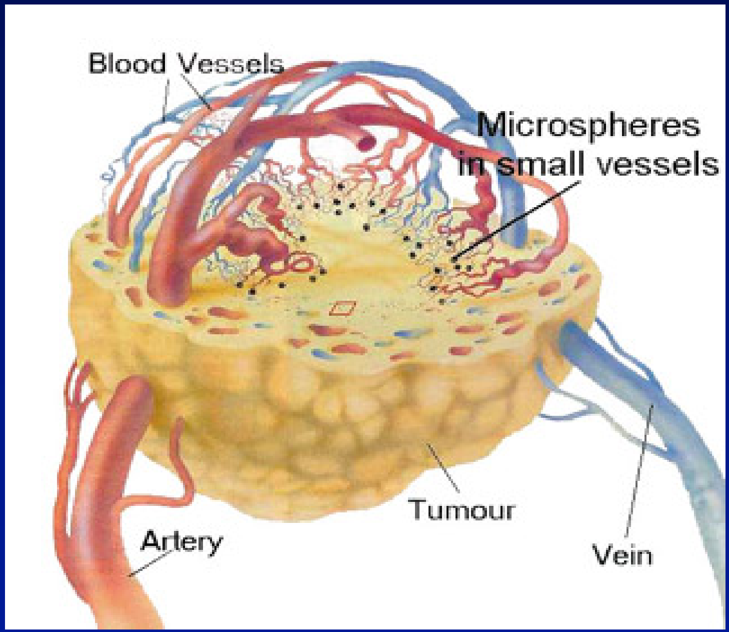
- Available Agents
  - P-32, Sr-89, Sm-153, others coming
- Indications
  - osteoblastic neoplastic disease
    - multifocal lesions
    - pain in areas of prior maximal irradiation
    - pain refractory to prior irradiation

Palliative Treatment of Bone Pain with Radiopharmaceuticals

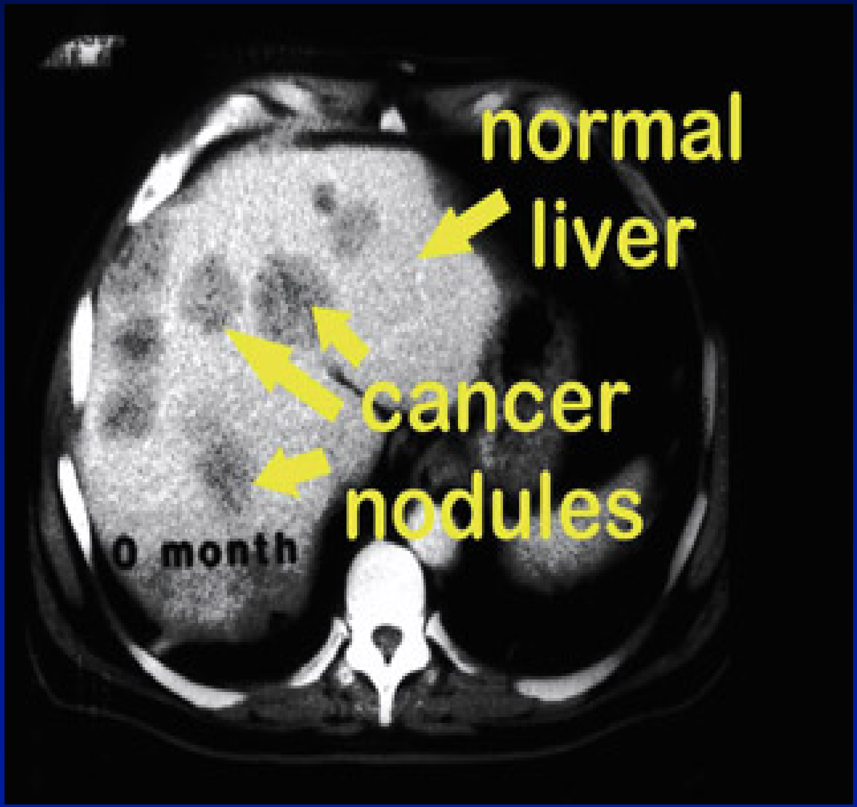
- Results
  - simple outpatient procedure
  - successful in 80+% of patients
    - improved quality of life (less pain, less medication)
  - few serious side effects
    - thrombocytopenia, neutropenia, anemia
  - cost effective in multifocal disease
  - can be repeated without increasing side effects

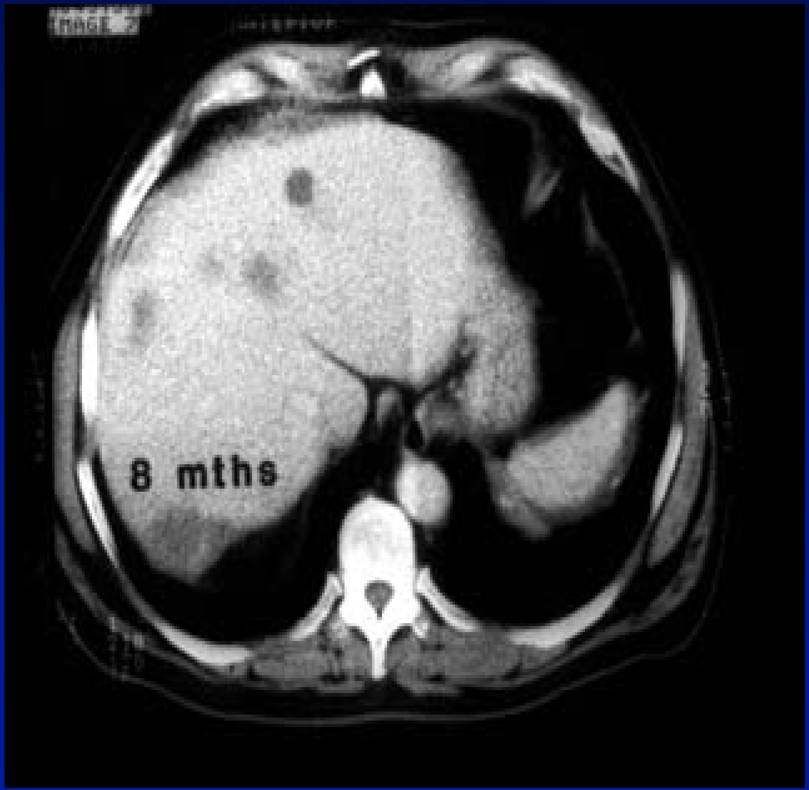
Therapeutic Y-90 Spheres





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 <u>optimal</u> clinical use
- Therapeutic uses are increasing rapidly

Nuclear Medicine Directions

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)

Nuclear Medicine Directions

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

Training & Experience in Nuclear Medicine

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

Nonimaging Procedures in Nuclear Medicine

Measures of Vitamin B12 absorption

Methods: Schilling Test(s)
Glass Test
(why not measure B12 in blood?)

Nonimaging Procedures in Nuclear Medicine

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

Nonimaging Procedures in Nuclear Medicine

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)

Nonimaging Procedures in Nuclear Medicine

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

Myocardial Perfusion Imaging Agents Currently Approved

TL-201 chloride	1974	
Tc-99m isonitrile	1990	(Cardiolite)
Tc-99m teboroxime	1990	(Cardiotec)
Tc-99m tetrofosmin	1996	(Myoview)

Myocardial Perfusion Imaging

- Clinical Indications for Perfusion Imaging
  - Presence of CAD
  - Extent/Severity of CAD
  - Effects of CAD
  - Viability
  - Pre/Post Revascularization
  - Prognosis