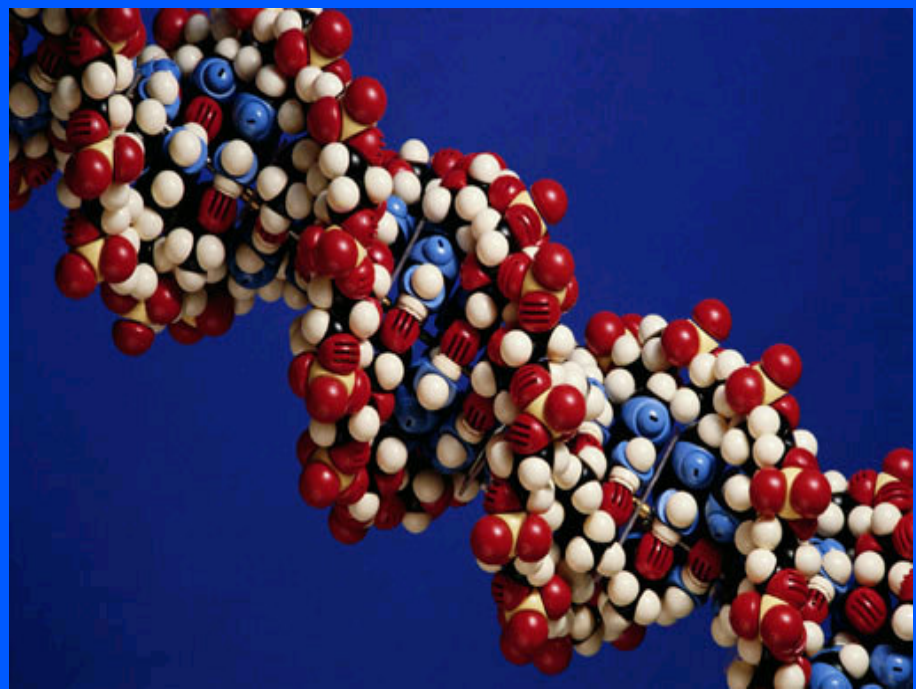
PHILIPS

Molecular Imaging:

- SPECT agents under development
- Imaging challenges

Jody Garrard, CNMT
Gamma Camera Product Manager
Philips Nuclear Medicine
jody.garrard@philips.com



“When you reach turning points in life, it is best to turn!”

Dr. Henry Wagner

“The world of biological sciences and medicine is in the midst of one of the greatest turning points it has ever experienced.”

Dr. Michael Phelps

JNM Feb 2002

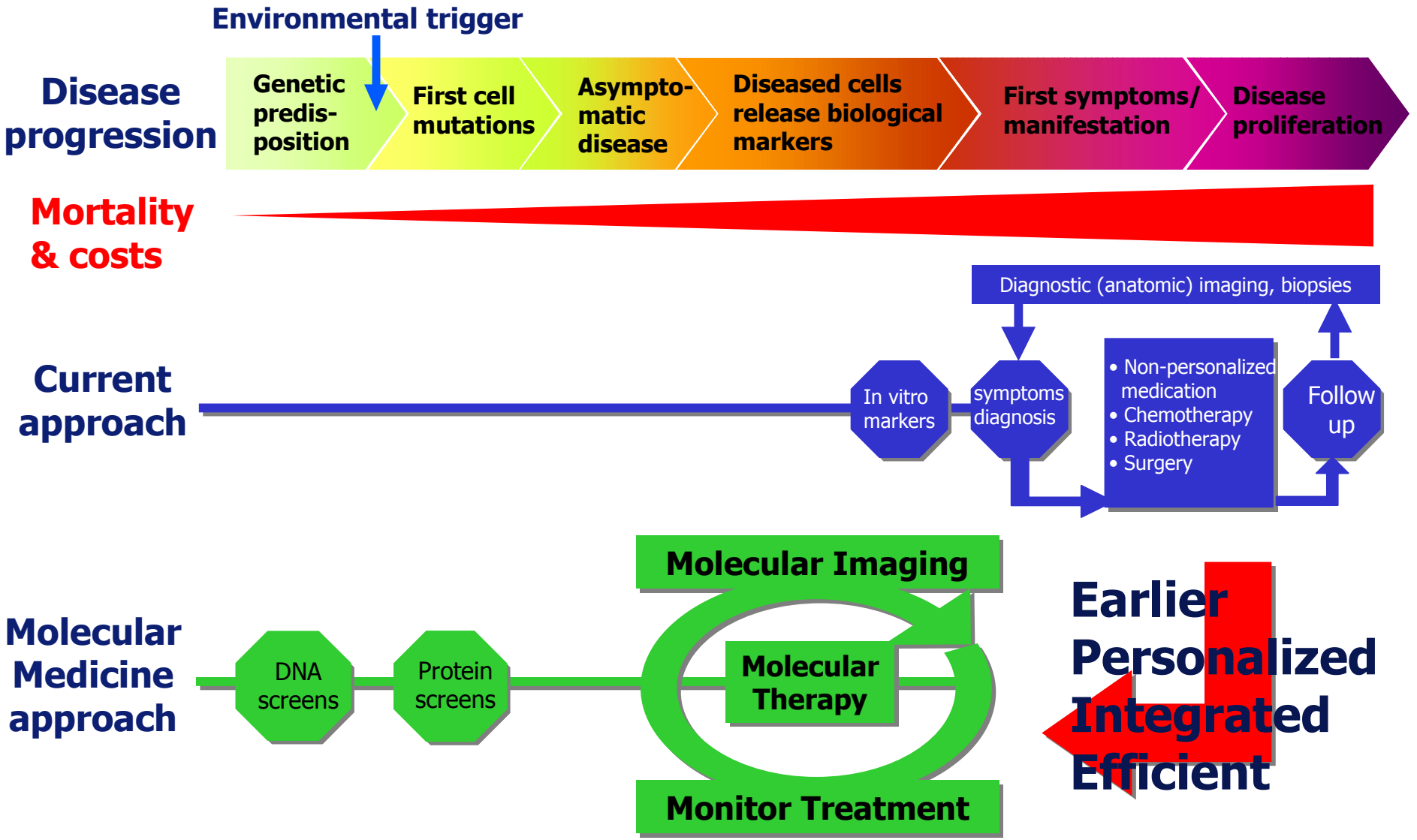
Society of Nuclear Medicine

– *Advancing Molecular Imaging*

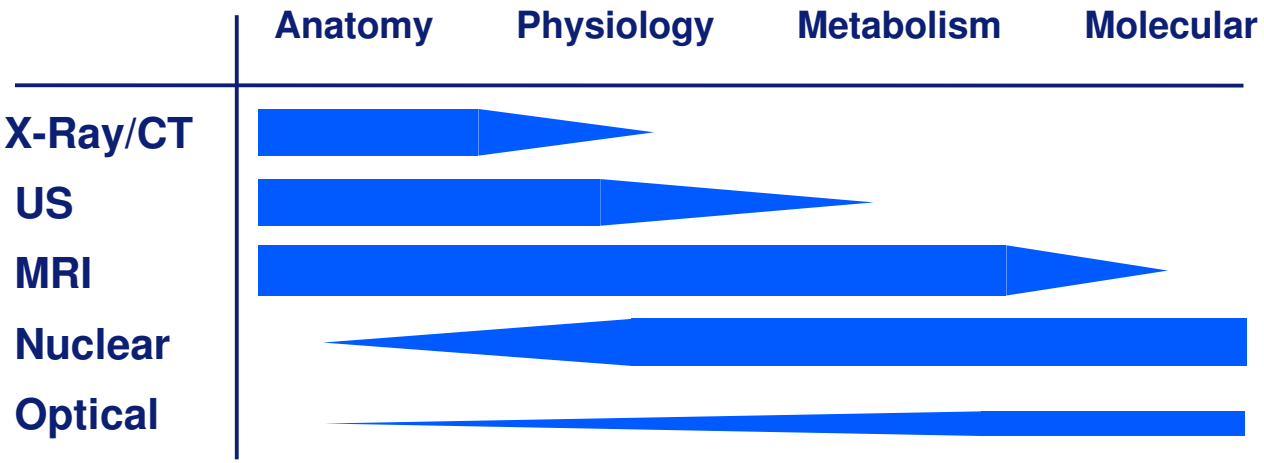
Molecular Imaging: *See & Treat*

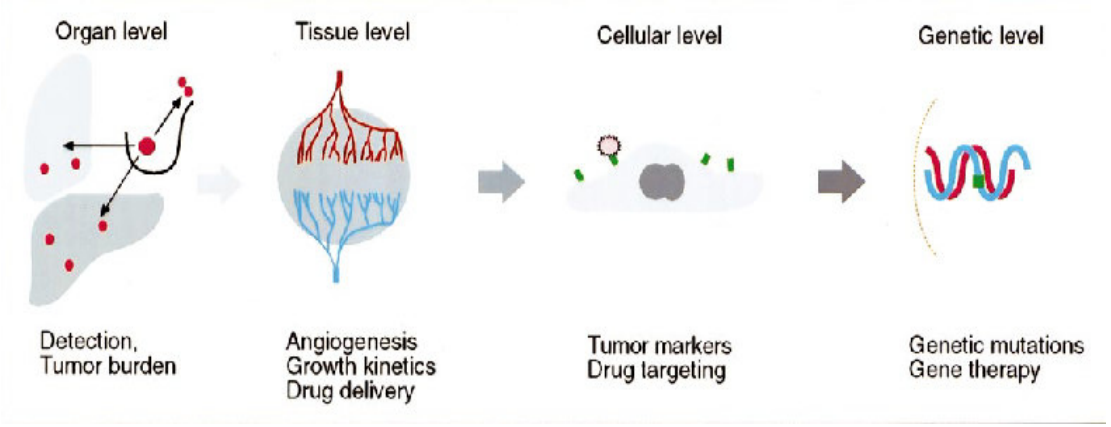
- ***See:*** **Tag gamma-emitter to molecular agent, inject in patient, goes to the target molecule, make *images*.**

- ***Treat:*** **Add beta-emitter to molecular agent, inject, goes to the target molecule and delivers the *therapy*.**


Environmental trigger
Disease progression
Genetic predis-position
First cell mutations
Asympto-matic disease
Diseased cells release biological markers
First symptoms/ manifestation
Disease proliferation
Mortality & costs
Diagnostic (anatomic) imaging, biopsies
Current approach
In vitro markers
symptoms diagnosis
• Non-personalized medication
• Chemotherapy
• Radiotherapy
• Surgery
Follow up
Molecular Medicine approach
DNA screens
Protein screens
Molecular Imaging
Molecular Therapy
Monitor Treatment
Earlier
Personalized
Integrated
Efficient

Role of Imaging Modalities

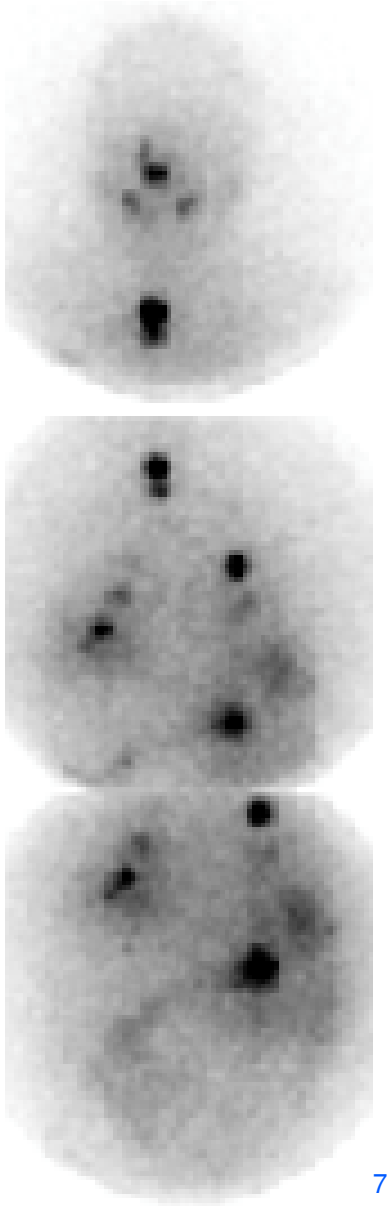




I-131:
Thyroid Cancer

See & Treat

- First atomic cocktail (1946)
  - Iodine goes to thyroid gland
  - Atomic cocktail of I-131
  - Given to Thyroid CA patient
  - Thyroid CA disappeared
- Now common NM procedure



Zevalin: *See & Treat*

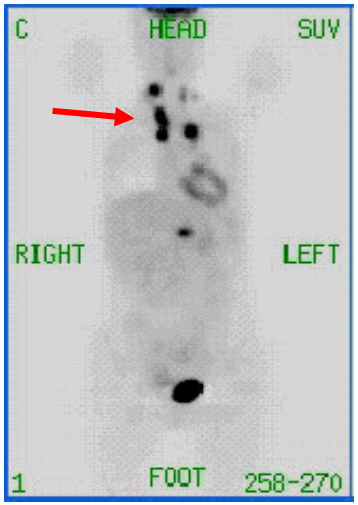
Non-Hodgkin's Lymphoma

Monoclonal antibody, very specific to certain NHL

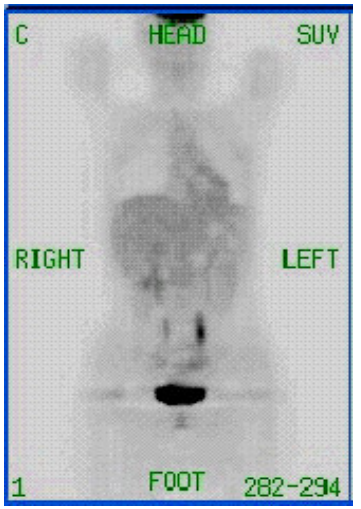
- **FDA Clearance Jan 2002**
- ***See***
  - **In-111 (gamma)**
- ***Treat***
  - **Y-90 (beta)**

ChemoRx	**60% untreatable** **$60K cost**
Zevalin	**80% response in 6 mos** **$25K cost**

PET: Pre-Zevalin



PET: 3 mos Post-Zevalin



Molecular Agents Available Today

- I-131: Thyroid CA
- FDG: Tumors, inflammation, viability, neurology
- NeoTect: Lung, Breast CA
- OncoScint: Colon, Ovarian CA
- ProstaScint: Prostate CA
- OctreoScan: Neuroendocrine tumors
- Zevalin: NHL

Why are so few sites using them?

- Typically tagged with In-111 (not ideal imaging energy)
- Difficult to tag with Tc-99m (ideal for imaging)
- Poor target to background (image quality)
- Very specific
- Not ideal for solid tumors

Next Generation of Molecular Agents

	Available:
• ^{99m}Tc EC Deoxyglucose: Metabolism	18 mo
• ^{99m}Tc Annexin V: Apoptosis	12 mo
• ^{123}I Cardiodine: Ischemia	12 mo
• ^{99m}Tc EC Metronidazole: Hypoxia	24 mo
• ^{99m}Tc EC Endostatin: Anti-angiogenesis	24 mo
• ^{99m}Tc Anti-fibrin nanoparticles: Vulnerable plaque	18 mo

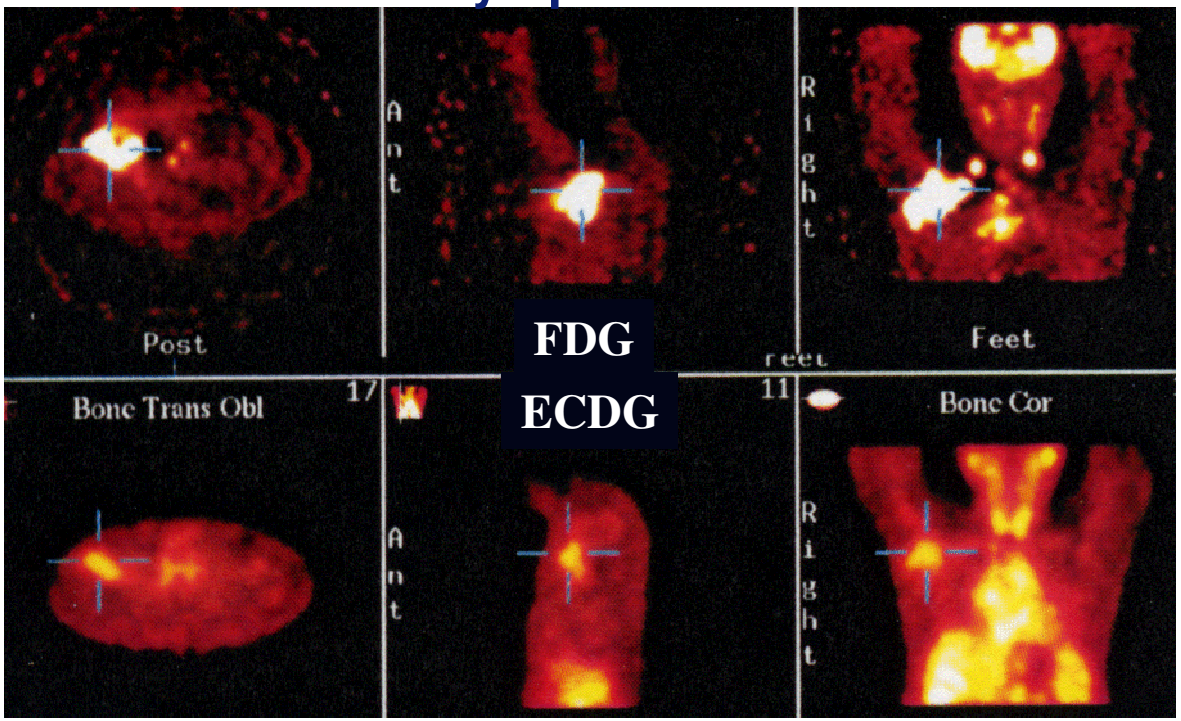
PHILIPS

Cell Point

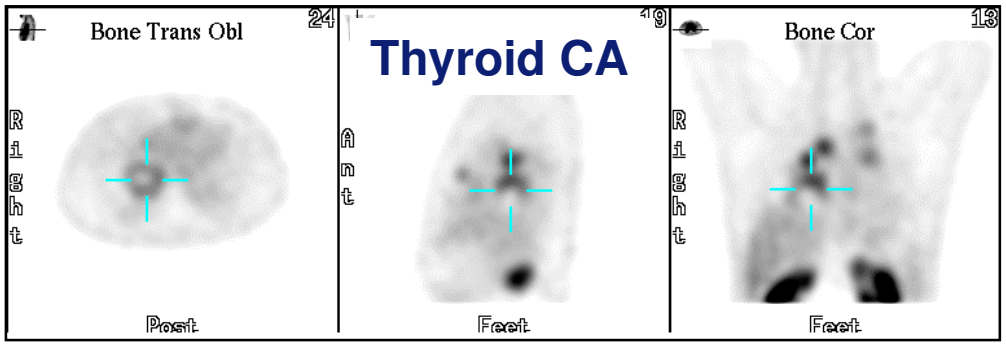
Tc-99m ECDG

Ethylene Dicysteine Deoxy-Glucose

Lymphoma



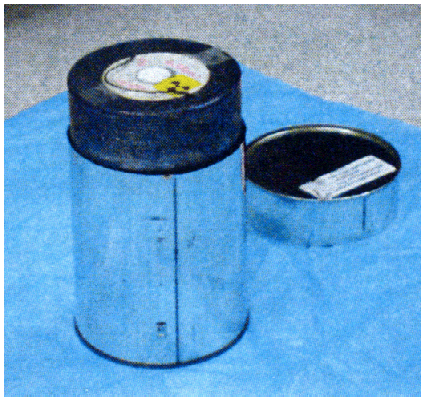
Oncology: Tc-99m ECDG



See & Treat

Re-188 ECDG

- 2.1 MeV β-emission
- 155 keV γ-emission
- 17 hr T ½
- Outpatient Rx
- Low cost



W-188 generator

Theseus

Tc-99m Apomate

Apoptosis

- Programmed cell death
- Normal process of cell turnover
- Characteristic of pathology, cell stress
  - Autoimmune disease
  - Transplant rejection
  - Stroke
  - Acute myocardial infarction
  - Cancer therapy

Oncology

Tc-99m Apomate

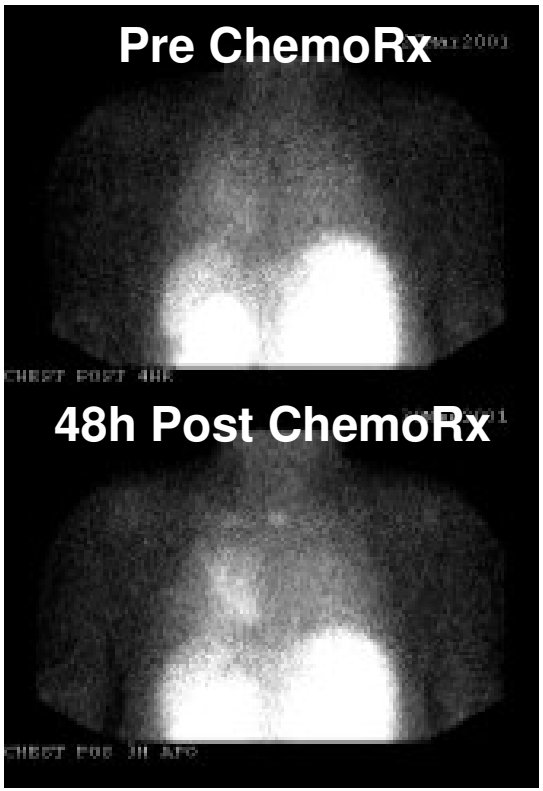
See

- Measure efficacy of Rx
- Results 6 hrs after 1st treatment
- Avoid unsuccessful Rx

Treat

- Add Re-188 guided missile
- Boost effects of initial Rx
- Eliminate debilitating effects of ChemoRx

Lung CA

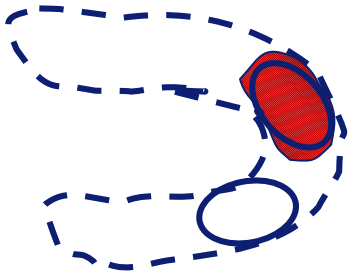


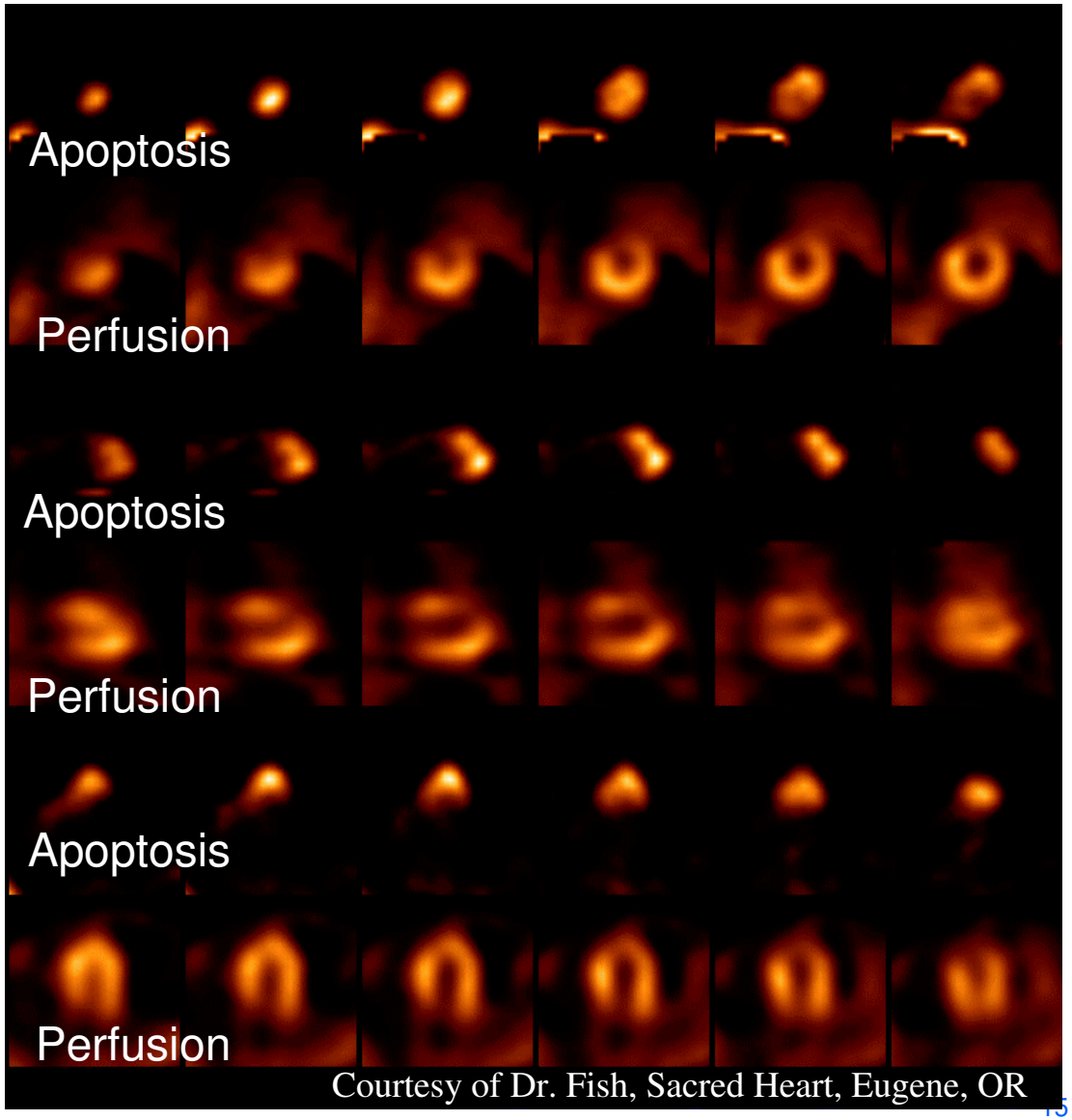
Courtesy Dr. Abdel-Dayem, St. Vincent's, NY

Cardiology: Tc-99m Apomate

Acute MI:

- Apoptosis
- Perfusion
- Function
- Quantification





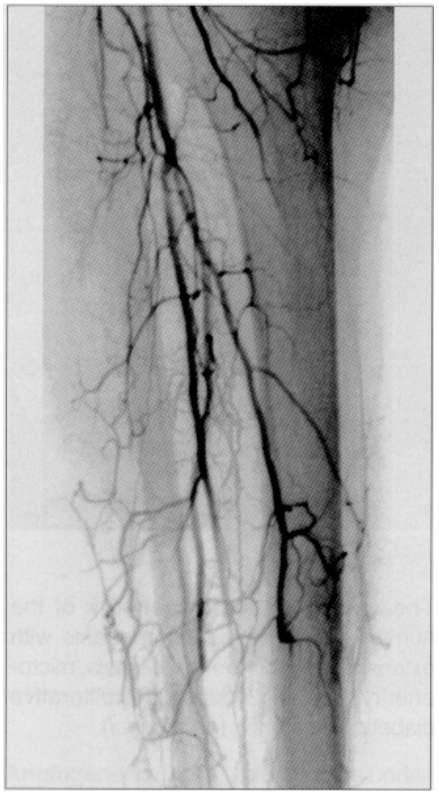
Courtesy of Dr. Fish, Sacred Heart, Eugene, OR

Cardiovascular Disease

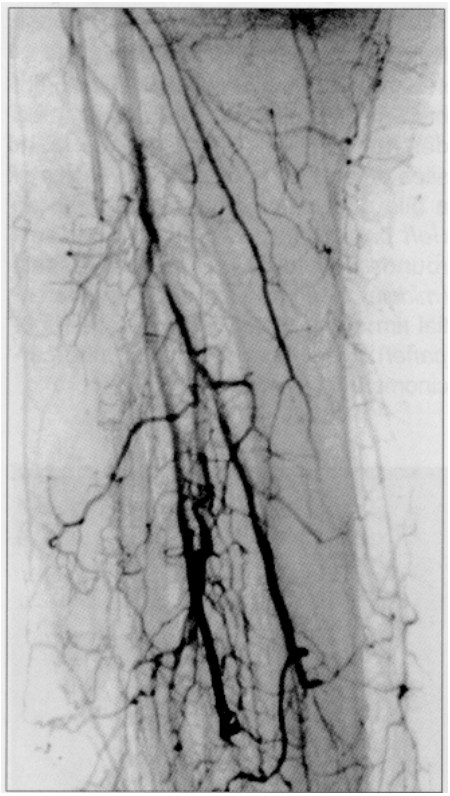
Tc-99m Annexin V VEGF

Angiogenesis

- VEGF: Vaso Endothelial Growth Factor (peptide)
- Approved for use by FDA
- Deliver to area of compromised bloodflow
- New blood vessels develop within weeks



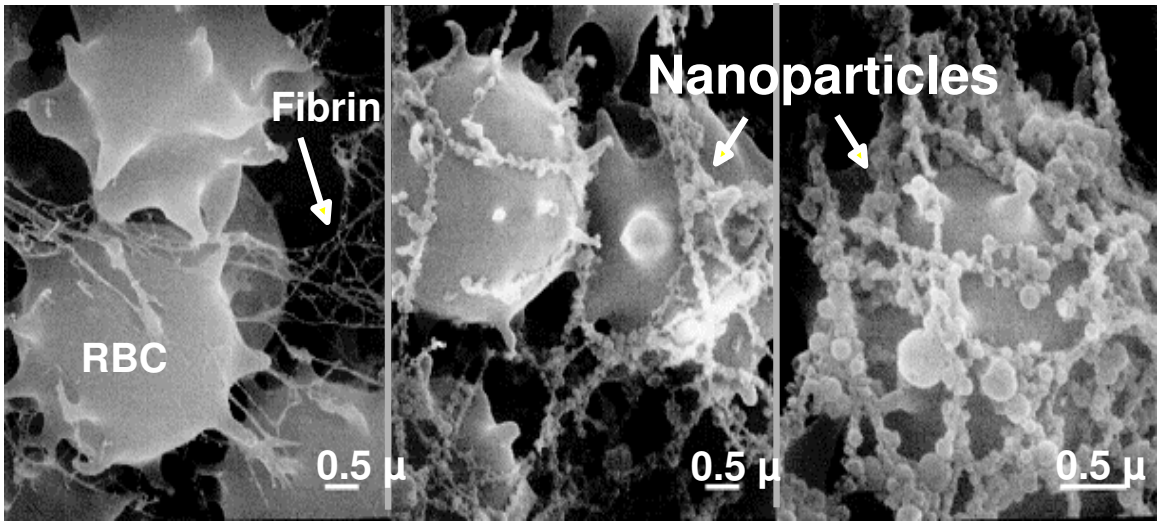
Leg- Before administration



4 Weeks post VEGF

Kereos Tc-99m Anti-fibrin Nanoparticles

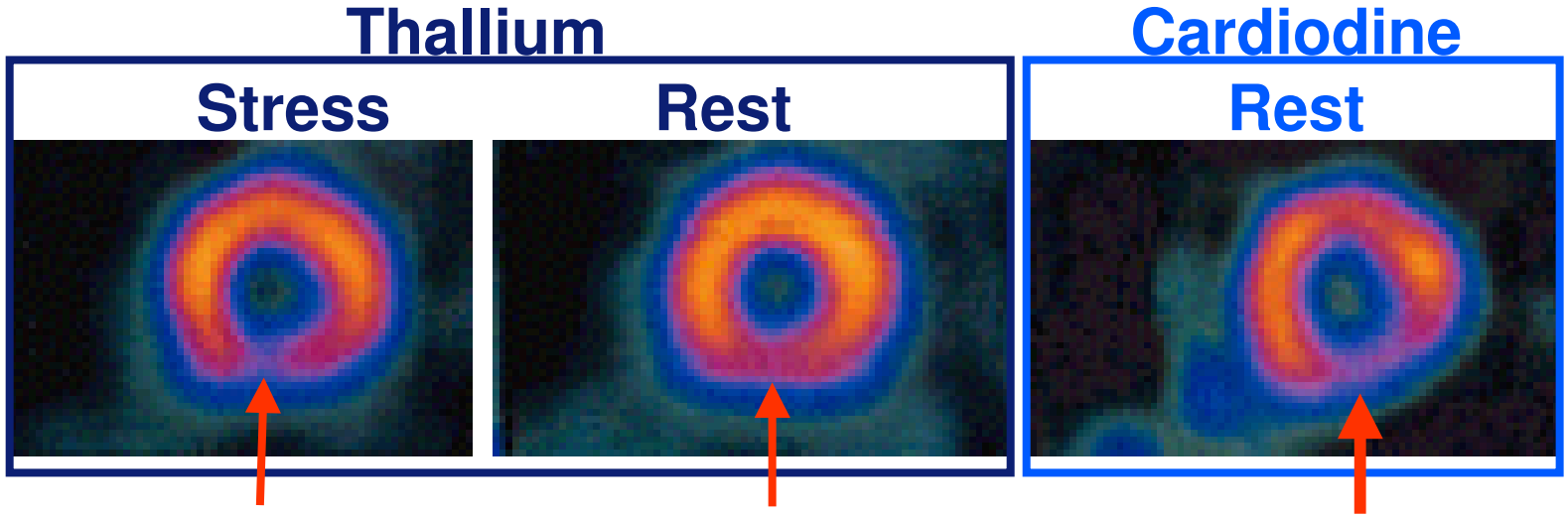
- Image vulnerable plaque
- 10-15 atoms In-111 per nanoparticle
- 500 atoms Tc-99m per nanoparticle
- Excellent signal
- Image very small lesions
- Valuable for emergency providers



Before After

Biostream I-123 Cardiodine

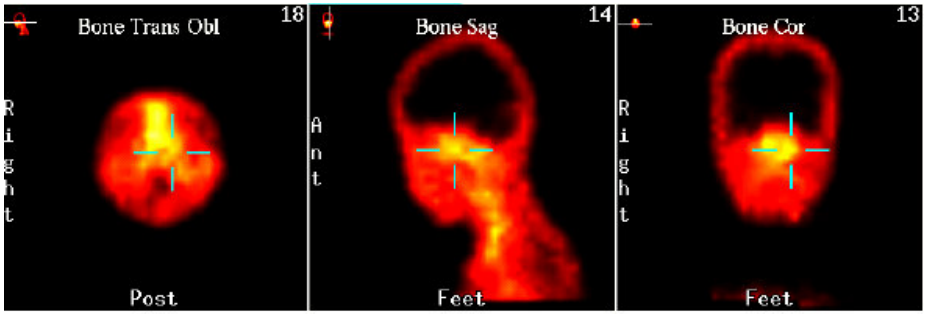
- Ischemic memory up to 1 week post event
- Rest-only imaging
- Image 10 min p.i.



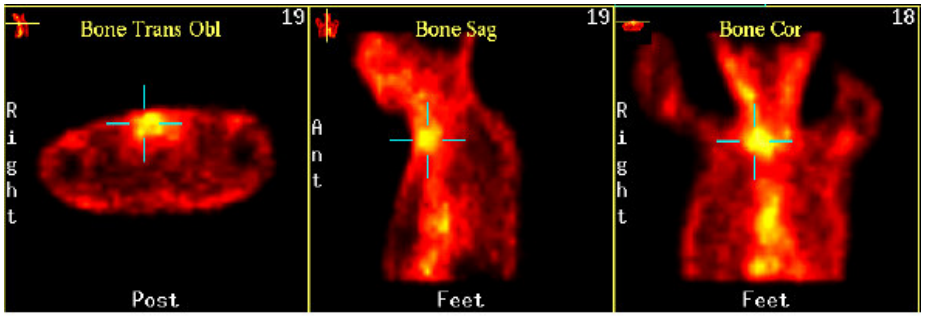
Oncology

Tc-99m Metronidazole

- Accumulates in hypoxic tissue
- Hypoxic CA cells don't respond to therapy
- Screen patients prior to therapy
- Identify patients who need radio-sensitizing drugs prior to Rx



Nasopharyngeal CA

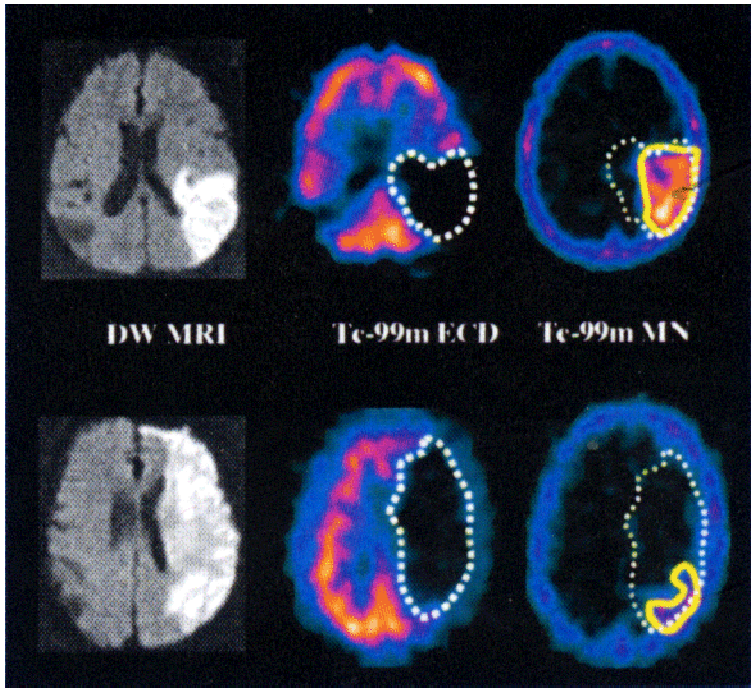


Esophageal CA

Neurology

Tc-99m Metronidazole

- Image with conventional brain perfusion agent to identify *ischemic volume*
- Image with Tc-99m-MN to identify *hypoxic volume*
- *Viability ratio* = IV/HV
- The greater the viability ratio, the better the neurological outcome*



*Stroke; 2003; 34: 982-986

What are some of the imaging challenges of the molecular agents?

Challenge #1:

Gantry aperture

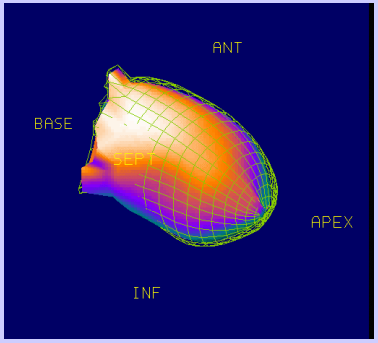
- More opportunities to combine with RTP and positioning devices
- Image in treatment position
- Can all patients fit into the gantry with the positioning device?
- Can you use alternate beds?

Challenge #2:

Combined molecular & conventional imaging

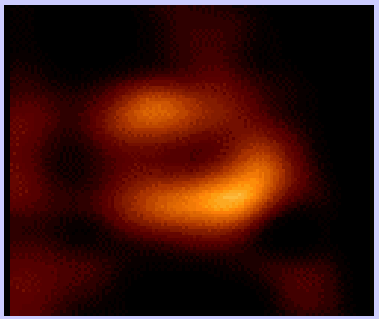
- Accurate quantification vs image quality
- Matrices and zooms may be different
- Gated and ungated may both be desired
- Registration accuracy important

Function
64 x 64



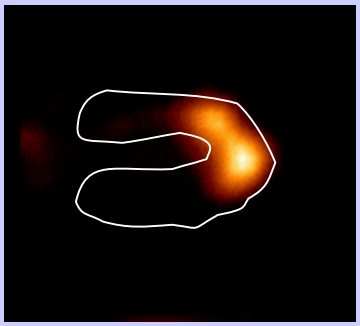
Beat rejection for accurate EF

Perfusion
64 x 64



All data saved for higher image quality

Apoptosis
128 x 128

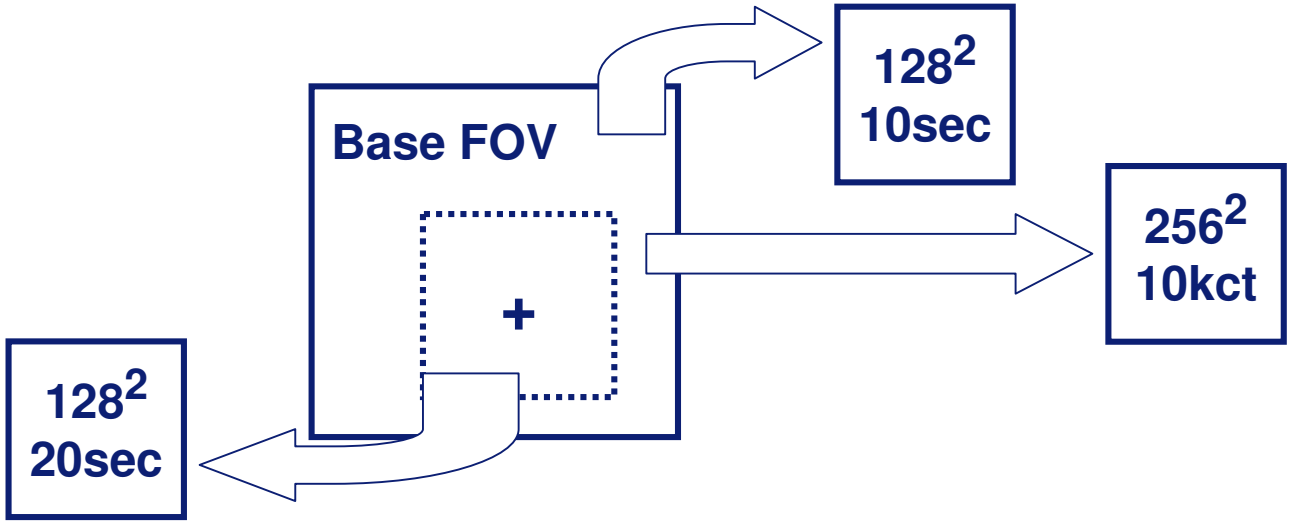


Accurate registration important for quantification

Concurrent Imaging

Views can vary based on

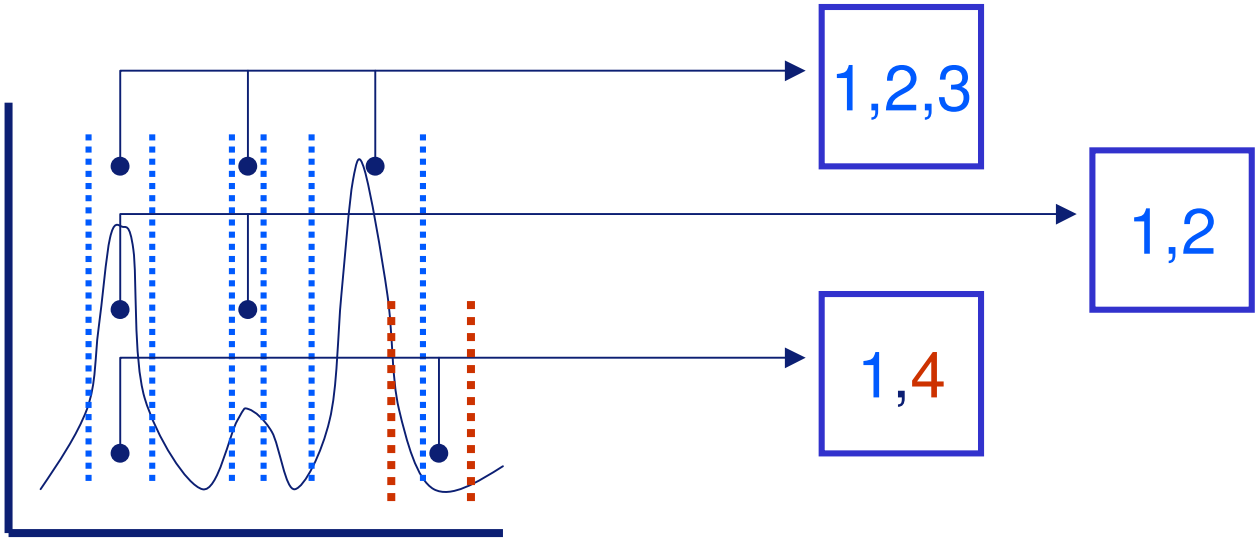
- Imaging Parameters
  - Zoom, mask location, matrix size, detector
  - Stop criteria: counts, time, beats
  - Dynamics can vary number of phases and frames/phase



Concurrent Imaging

Views can vary based on

- Imaging Parameters
- **Energy Windows**
  - **For a given acquisition including all views, up to 16 windows per detector**



Concurrent Imaging

Views can vary based on

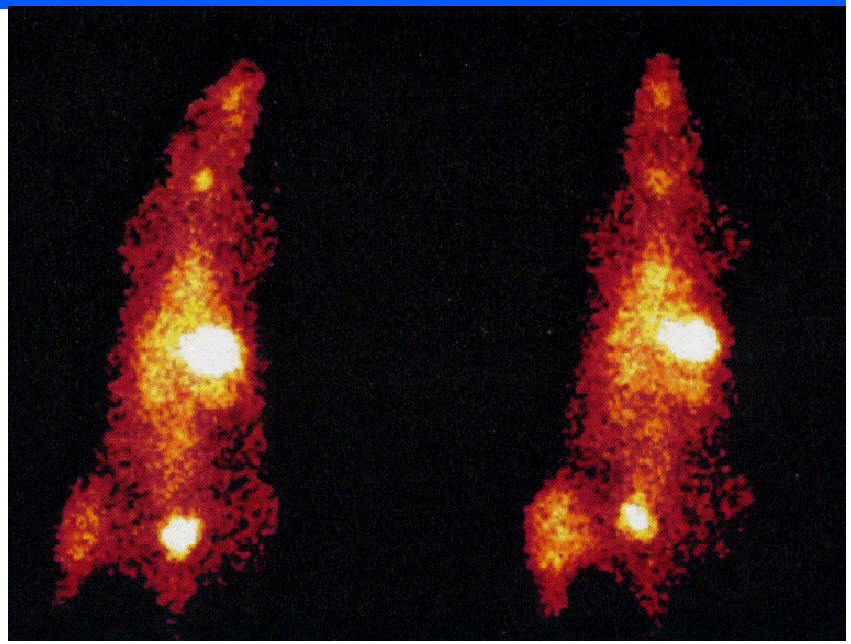
- Imaging Parameters
- Energy Windows
- **Gating**
  - **Gating on/off**
  - **Number of bins, time/bin, arrhythmia rejection**

…or any combination of the above given the gantry/patient positioning constraints

Challenge #3:

Hot spot imaging

- Target specific localization
- Target/background improves over time



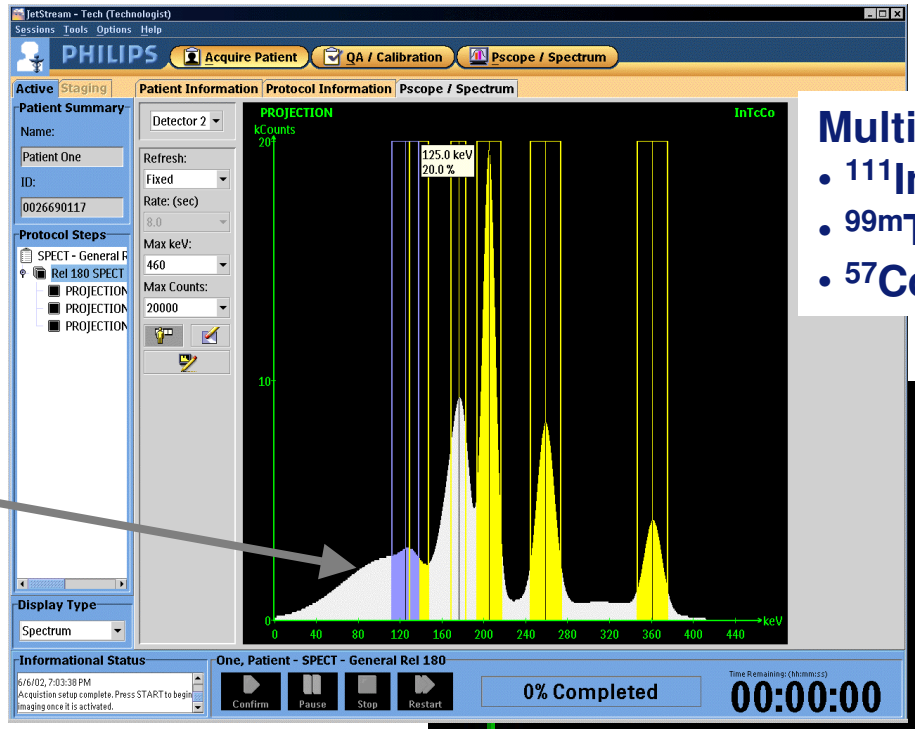
Challenge #4:

Scatter correction

- Important for quantitative accuracy
- Tends to increase noise
- Accurate scatter modeling and noise reduction techniques

Multiple Window Capabilities

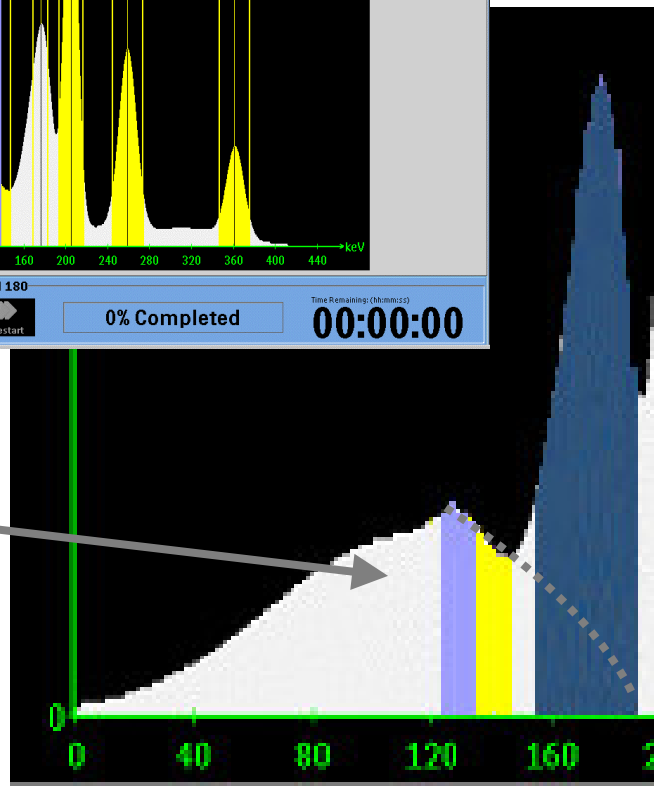
Multiple simultaneous acquisitions:
- **Gated & non-gated**
- **Multiple energies**



Multiple radionuclides
- **^{111}In (177 & 234 keV)**
- **^{99m}Tc (140 keV)**
- **^{57}Co (122 keV)**

Overlapping scatter windows (1 blue / 1 yellow)

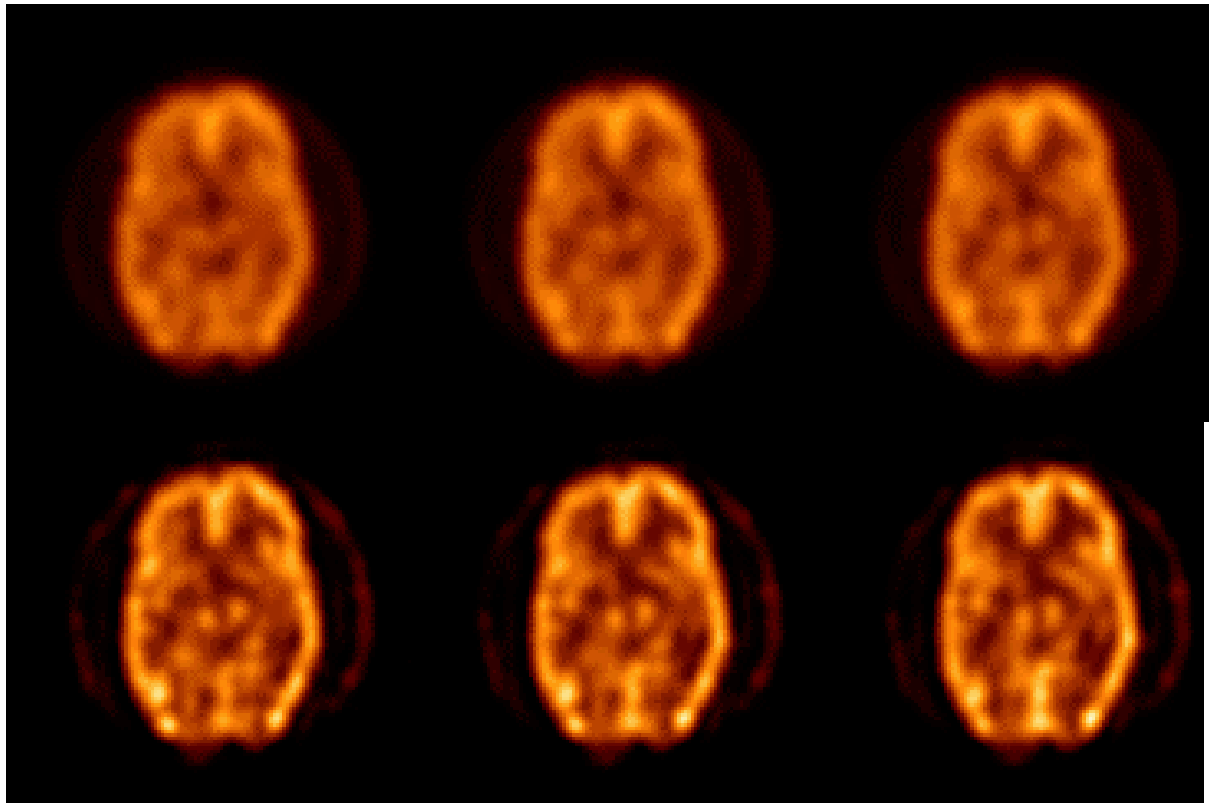
Scatter correction
- **Overlapping windows**
- **Estimate scatter under primary photopeak**



Challenge #5:

Optimized Reconstruction Filters

OSEM at shoulder distance

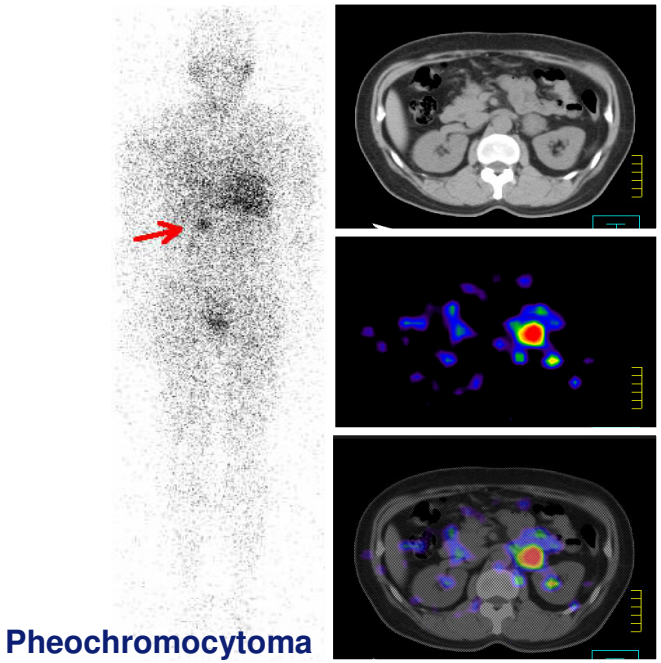


3D OSEM with Resolution Recovery

Challenge #6:

Anatomic localization

- How small of a lesion do you need to see?
- How can you make diagnostic quality CT affordable?
- How accurate is the registration?
- How easy is it to correct/override the registration?

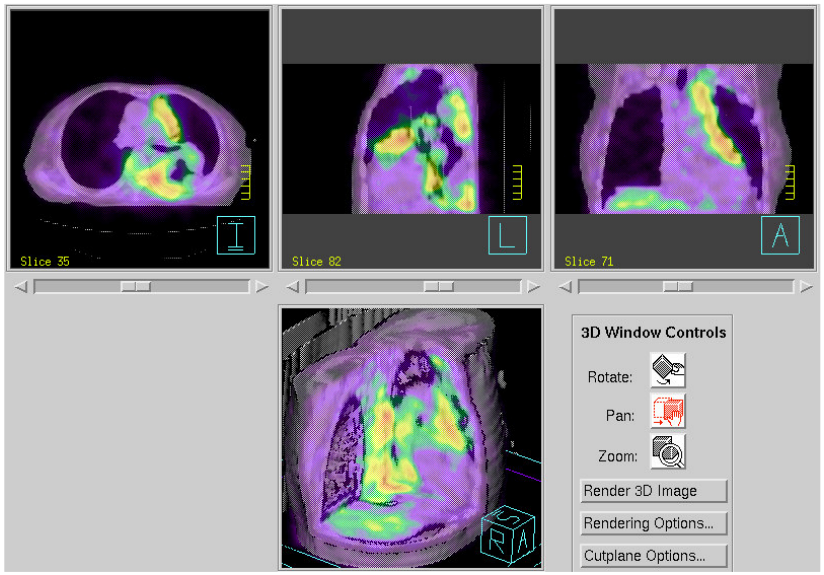


Pheochromocytoma

Challenge #7:

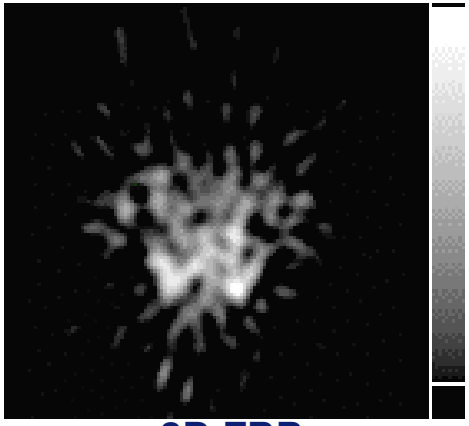
Attenuation correction

- Improve accuracy of quantification
- Agents other than Tc-99m (In-111, I-123, Ga-67)
- Truncation compensation may be needed
- Quality control tools
- Measure of registration accuracy

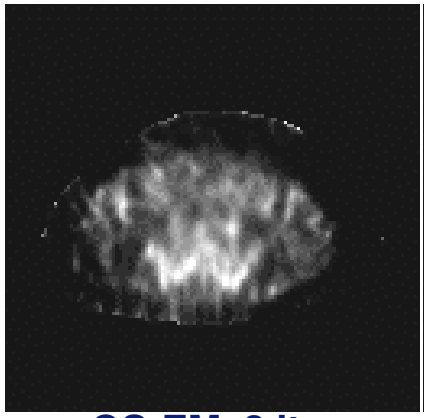


Courtesy of Dr. Kashiwagi, Hyogo College of Medicine, Japan

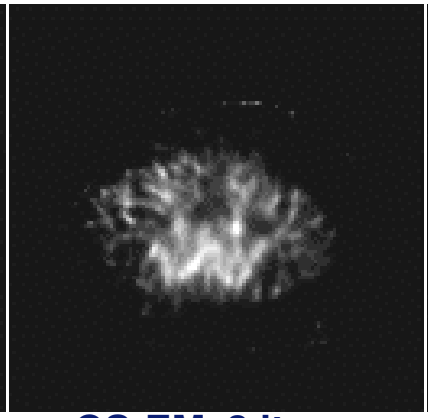
In-111 Prostascint



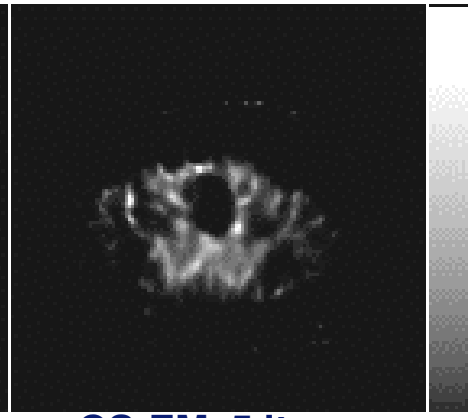
3D FBP
Butterworth, n=8, fc=0.15/p



OS-EM, 2 it.
w/ CDR correction



OS-EM, 3 it.
w/ CDR, attenuation correction

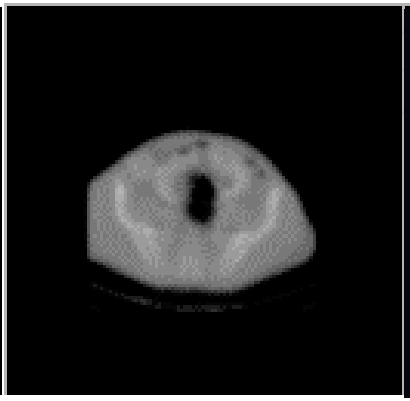


OS-EM, 5 it.
w/ CDR, attenuation & scatter correction

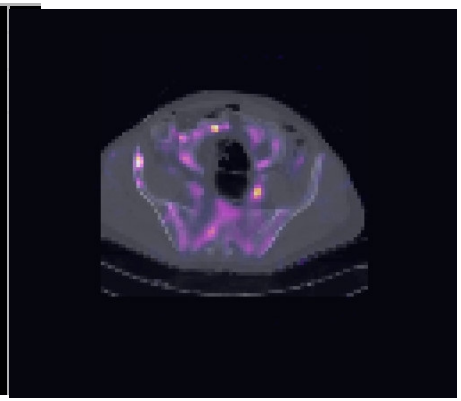
76 yr old white male post prostatectomy in 1998 & recent increased PSA

SPECT images show asymmetric radiotracer focus at the left common iliac suspicious for lymph node involvement

Original CT



Transformed attenuation map



Fused CT & SPECT image

Slice #55 ~12,573 counts/slice

Philips Role in Molecular Imaging

Interpret	**Quantification**	**Prognostic indices** **Fusion/registration**
Process	**Algorithms**	**Scatter correction** **Attenuation correction**
	Reconstruction	**Filter optimization** **Enhanced image quality**
Acquire	**Acquisition**	**Energy windows** **Acquisition protocols**
	Gantry	**Gantry design** **Imaging positions**

Relationships with MI Companies

Benefits from Optimized Imaging

- Improve diagnostic accuracy of lesion detection
- Improve accuracy of diagnosis and prognosis
- Reduce/avoid unnecessary/ inappropriate invasive procedures
- Reduce diagnostic and treatment costs
- Improve confidence of referring physicians and their patients in clinical value of diagnostic procedures

PHILIPS

See & Treat

Because we have reached a turning point, it is best to turn