Nuclear and Molecular Cardiovascular Imaging

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Disclosure Information

One or more of the following relationships exist related to this presentation: Grant support, consultant, advisory board

- GE Healthcare
- Siemens
- Astellas

Non-FDA approved products will be discussed in this presentation: None
Coronary Artery Physiology

Conductance vessel

Endothelial cell

Resistance vessels

Vascular smooth muscle cell

Shear

Basic Cardiovascular Biology

Flow

% Stenosis

Ischemic Threshold
Imaging of Myocardial Blood Flow Reserve

SPECT Imaging

Short axis

Vertical long axis

Horizontal long axis
Heart with long axis indicated ---  Sum of all the slices viewed at end
Myocardial Segmentation, Nomenclature and Vascular Territories

Characteristics of Thallium-201

- Thallium decays emitting Hg x-rays (69-83 keV)
- It is cyclotron produced with a half-life of 73 hrs.
- It is distributed according to cardiac output, and taken up by all viable cardiac cells. Tl+ ion is of similar size to potassium ion (K+) and behaves biologically somewhat like K+. It enters cells quickly via the Na/K pump, and becomes part of the intracellular K pool.
THALLIUM-201 IMAGING FOR VIABILITY

- Early (2-4 hour) redistribution after stress
- Late (8-72 hour) redistribution after stress
- Rest-redistribution
- Reinjection after stress-redistribution
Abnormal Myocardial Perfusion SPECT

Short axis

Vertical long axis

Horizontal long axis

Stress
Rest
Stress
Rest
Stress
Rest
Thallium Reinjection Imaging

A. Graph showing the activity of $^{201}$TI over time after stress and after redistribution and reinjection.

B. Timeline of thallium injection and imaging procedures:
- Stress injection
- Stress image
- Redistribution image
- Reinjection image

Rest-Redistribution Thallium SPECT

A 70-year old patient new onset congestive heart failure. Coronary angiography was performed and it revealed severe 3-V CAD with an LVEF of 35%. A rest-4 hr redistribution thallium study was performed to assess myocardial viability. Which is the best next management option?...Please select your answer on the next slide.
Characteristics of Tc-99m Perfusion Agents

- Technetium-99m (Tc-99m) is generator produced with a physical half-life of 6 hours and a photon energy of 140 keV.

- A consequence of the higher energy Tc-99m is less attenuation and scatter when compared to thallium-201 resulting in higher resolution images.
Tc-99m Sestamibi and Tetrofosmin

- Both Tc-99m sestamibi and tetrofosmin accumulate in the heart in proportion to regional myocardial blood flow.

- Once the tracers have entered a myocardial cell, they are retained within the mitochondria at least in part due to a large negative transmembrane potential.
Accuracy of Myocardial Perfusion SPECT for CAD Detection

- Sensitivity: 91%
- Specificity: 72%
- Normalcy: 91%

N = 1827

Value of Stress SPECT in the General Population: Prognostic Significance

n=12,360 from 14 different studies; however, it is possible that some patients enrolled in the largest study were also included in earlier, smaller studies.

Prognostic Value of Normal Myocardial Perfusion SPECT Imaging

Cumulative survival

Follow-up (mo)

$^{201}$TI ($N = 3,257$)
$^{99m}$Tc-Tetrofosmin ($N = 4,728$)
$^{99m}$Tc-Sestamibi ($N = 2,423$)

Pharmacologic Stress Imaging

- Approximately 30% of patients are incapable of reaching adequate exercise levels
  - Heart rate at least 85% of maximum predicted for age
  - Increase in systolic blood pressure of 8-10 mm Hg

- Potential limitations of exercise include:
  - Poor physical condition/motivation
  - Aortic Aneurysm
  - Lower-limb amputation
  - Peripheral vascular disease
  - Medications (B-blockers)
  - Arthritis/rheumatism/orthopedic conditions
  - Systemic muscular disease
  - Other conditions which limit physical exertion

Pharmacologic Stress Agents

Coronary Vasodilators

- Dipyridamole Injection USP (Persantine®)
- Adenosine Injection (Adenoscan®)
- Regadenoson Injection (Lexiscan™)

Persantine is a registered trademark of Boehringer Ingelheim International GmbH. Adenoscan is a registered trademark King Pharmaceuticals Research and Development, Inc. Lexiscan is a registered trademark of Astellas US LLC.
Diagnostic Accuracy of Pharmacologic Stress Myocardial Perfusion Imaging

- Exercise: Sensitivity 84%, Specificity 87%, n=3266
- Adenosine: Sensitivity 88%, Specificity 85%, n=763
- Dipyridamole: Sensitivity 87%, Specificity 81%, n=1272

This representative data set was derived from a variety of published sources. It shows the sensitivity and specificity of pharmacologic stress compared to exercise stress.

Tc-99m Perfusion Agents: Gated SPECT

- The high count statistics of Tc-99m based myocardial perfusion tracers makes it possible to acquire ECG gated SPECT images, thereby adding functional information to the conventional perfusion information with a single radiopharmaceutical injection and a single acquisition sequence.

Myocardial Perfusion Gated SPECT Scan

Courtesy of Howard Lewin, MD, of San Vicente Cardiac Imaging Center.
Incremental Value of Gated SPECT to Tc-99m Myocardial Perfusion Imaging

- May enhance diagnostic accuracy
- Allow simultaneous evaluation of myocardial perfusion and left ventricular function
- Provide assessment of regional and global left ventricular dysfunction
- Add incremental prognostic information to myocardial perfusion imaging

Positron Annihilation

conservation of energy and momentum

Before: 2 electrons, each with a rest mass of 511keV

After: 2 photons, each with 511keV and travel in opposite direction.

Decay via positron emission
Positron Emitting Radionuclides*

O-15: 123 seconds
N-13: 10 minutes
C-11: 20 minutes

F-18: 1.83 hours

\(^{18}\text{FDG} - \text{Fluorodeoxyglucose}

*Can only be made in a Cyclotron.
PET

- Easier Chemistry
- Easier Attenuation Correction
- Intrinsic Collimation
CARDIAC PET APPLICATIONS

Myocardial blood flow
- $^{15}$O-water
- $^{82}$Rb
- $^{13}$N-ammonia

Myocardial metabolism
- $^{11}$C-palmitate
- $^{18}$F-deoxyglucose
- $^{11}$C-acetate
Diagnostic Accuracy of $^{82}\text{Rb}$ PET for CAD

64 suspected CAD and 38 control subjects
Coronary angiography within 6 months

- CAD defined as 70% luminal narrowing
- High diagnostic accuracy 87% (CI 79 to 93%)
  - Sensitivity 93% (CI 87 to 99%)
  - Specificity 83% (CI 71 to 91%)
  - Normalcy 100% (CI 91 to 100%)
- Sensitivity for SVD of 92% (CI 74 to 99%)
- Sensitivity for MVD of 95% (CI 74 to 99%)

Relative Tracer Uptake vs Absolute Flow

Schelbert HR. “PET Quantitation of Coronary Artery Disease”
Noninvasive Assessment of Medical Therapy

Baseline

Followup

Schelbert HR et al. in Atlas of Nuclear Cardiology, 4th ed, Springer 2013
Prognostic Value of MFR by Stress Rubidium-82 PET

Figure 2b. Adjusted MACE Free Survival

Figure 3. MACE within subgroups of SSS for different levels of MFR

Functional Correlates to Coronary Anatomy

Courtesy of Dr. Marcelo DiCarli
Adaptation to Reduced Oxygen Delivery Results in the Prevention of Irreversible Tissue Damage

↓ Flow
↓ Oxygen supply
Alteration in fatty acid & glucose metabolism
↓ Programmed Cell Survival
PET Mismatch Pattern

PET Mismatch: Heart Failure Symptoms and Recovery of Function

Ischemic Cardiomyopathy
2-chamber and short-axis views showing enhancement in the septal, lateral and anterior wall in a patient with Sarcoidosis

Cardiac Sarcoidosis
Cardiac Sarcoidosis
FDG PET mismatch pattern in a patient with Sarcoidosis and normal coronary arteries

Falk RH and Dubrey SW, Prog Cardiovasc Dis 2010;52:336-346
3. The following perfusion image was obtained in a 24-year-old with chest pain and palpitations on exertion:
End-Stage HCM