**SECTION 1**

**Cardiac**

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### Introduction

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### Function and Coronary Artery Disease

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Nuclear Cardiac Imaging
Nuclear cardiology encompasses studies that diagnose and risk stratify coronary artery disease, myocardial infarction and hibernation, left ventricular function, and detection of right-to-left shunt.

Myocardial perfusion imaging evaluates myocardial perfusion at rest and stress, diagnosing regional or global ischemia and myocardial infarction. In 1 meta-analysis of ~39,000 patients, patients with normal or low-risk patterns (e.g., mild reversible perfusion abnormalities in 1 vascular territory) on myocardial perfusion imaging had a 0.6% rate of cardiac death or myocardial infarction per year. In patients with moderate or severe reversible perfusion defects, the cardiac event rate was 6% per year, a much higher rate compared with low-risk or normal scans.

Myocardial perfusion imaging provides risk stratification in symptomatic and asymptomatic patients. Patients at high risk for coronary artery disease include those with diabetes mellitus, hyperlipidemia, hypertension, and a family history of coronary artery disease. If patients with risk factors are asymptomatic, myocardial perfusion imaging provides additional clinical information predicting cardiac events. For example, in asymptomatic diabetic patients with moderate or large perfusion defects, the event rate is 2.4% per year compared with a 0.4% per year event rate in patients with mildly abnormal or normal perfusion scans.

Evidence of severe disease on myocardial perfusion imaging correlates with an annual death rate of 2.9% to 4.2%. Evidence of high-risk disease includes 2-vessel reversible perfusion defects, transient ischemic dilatation (signifying global subendocardial ischemia), and lung uptake on Tl-201 studies.

Stress protocols with myocardial perfusion imaging are tailored to the clinical situation. Exercise stress protocol utilizing the modified Bruce protocol is used when possible. Note that with myocardial perfusion imaging, exercise stress tests are less valuable in patients with left bundle branch block, as this can cause a false-positive reversible perfusion defect in the septum. Pharmacologic stress protocols can be utilized in those patients unable to exercise. Vasodilator stress agents such as adenosine, regadenoson, and dipyridamole are most commonly used, followed by dobutamine if vasodilator stress is contraindicated.

Assessment of myocardial viability can be performed using TI-201 and F-18 FDG PET/CT. In patients found to have underperfused yet viable or hibernating myocardium, regional wall motion is expected to improve after revascularization. One meta-analysis of ~3,000 patients with viable segments showed a 79% reduction in annual mortality after revascularization.

Nuclear cardiac imaging also has a role in risk stratification and management of patients with heart failure. Left ventricular function can be assessed using gated acquisitions of left ventricular function on myocardial perfusion imaging or with Tc-99m-labeled red blood cells (also called MUGA). Left ventricular ejection fractions using MUGA have been shown to have less inter- and intraobserver variability than other modalities, making it especially useful in serial determinations in patients undergoing chemotherapy.

Finally, when anatomic evaluation fails to diagnose a suspected right-to-left cardiac shunt, an indirect method of diagnosis can be obtained using nuclear medicine. If extrapolunmonary localization of the pulmonary perfusion tracer Tc-99m MAA occurs, a right-to-left cardiac shunt is diagnosed.

Imaging Protocols
Myocardial Ischemia and Infarction
Cardiac radiotracers are taken up by the myocardium in proportion to cardiac blood flow. Images are obtained at rest and stress, then compared. Perfusion defects at stress that are not present at rest constitute inducible ischemia. Fixed perfusion defects at stress and rest signify myocardial infarction &/or myocardial hibernation.

Imaging protocols include single- and dual-isotope studies with Tc-99m-based perfusion agents &/or TI-201 or PET/CT perfusion studies using Rb-82. Imaging with single-photon radiopharmaceuticals and gamma cameras is much more available clinically and less expensive than PET/CT myocardial perfusion imaging. In general, imaging with TI-201 is used less commonly due to poorer imaging characteristics and dosimetry considerations as compared to Tc-99m-based radiopharmaceuticals.

Myocardial Viability
Myocardial viability can be assessed though TI-201 rest-redistribution studies and F-18 FDG PET/CT. TI-201 employs traditional gamma camera technology, 1 dose of radiopharmaceutical, and requires limited patient preparation. F-18 FDG PET/CT imaging of anaerobic glycolysis in hibernating, nonperfused myocardium is common, but requires recent myocardial infarction and endogenous insulin response or exogenous insulin administration prior to F-18 FDG administration and PET/CT imaging. In addition, the F-18 FDG PET/CT data must be compared with a resting nuclear myocardial perfusion study, either a Tc-99m-based perfusion agent or TI-201.

LV Function
Left ventricular function can be assessed with left ventriculography using Tc-99m-labeled red blood cells (traditionally called a MUGA scan) or gated myocardial perfusion scintigraphy, usually performed to diagnose cardiac ischemia. End-diastolic and end-systolic counts or volumes are utilized to calculate the left ventricular ejection fraction. Visual analysis of both types of studies allows for visual and quantitative analysis of regional and global left ventricular wall motion.

Right-to-Left Cardiac Shunt
To diagnose a suspected right-to-left cardiac shunt, a Tc-99m MAA pulmonary perfusion study is performed, with anterior and posterior images over the head, chest, and abdomen. In cases of right-to-left shunt, Tc-99m MAA will be present in the brain, lungs, and kidneys.

Practice Guidelines
The American Society of Nuclear Cardiology publishes clinical guidelines and quality standards for appropriate use, imaging, and reporting of nuclear cardiology studies. Content can be found online at www.asnc.org.

Selected References
Approach to Cardiac Imaging

(Left) This myocardial perfusion scan shows short-axis images of the left ventricle at stress (top) and rest (bottom). Note decreased activity in the membranous septum, a normal finding.

(Right) This graphic shows a short-axis bull’s-eye of the left ventricle depicting the 17 segments and the associated vascular supply. These segments are used when reporting nuclear cardiology studies.

(Left) Left anterior oblique raw image from a myocardial perfusion scan shows a photopenic defect around the heart, corresponding to a pericardial effusion. (Right) Short-axis myocardial perfusion scan at stress (top) and rest (bottom) shows the "hurricane" sign, an artifact caused by patient motion during the rest image acquisition.

(Left) Anterior and posterior Tc-99m MAA shunt study shows brain and kidney uptake, signifying a right-to-left cardiac shunt. (Right) Vertical long-axis F-18 FDG PET cardiac viability study shows uptake in a segment of hibernating myocardium on perfusion imaging. Revascularization of this region should improve myocardial contractility.
Left Ventricular Function

KEY FACTS

IMAGING
- Multiple-gated cardiac blood pool acquisition (MUGA)
  - Low inter- and intraobserver variability (< 5%)
  - High reproducibility
- Radiopharmaceutical
  - 15-25 mCi (555-925 MBq) Tc-99m pertechnetate autologous labeled red blood cells (RBCs) IV
  - In vitro RBC labeling: Highest binding of radionuclide (~ 98%)
  - In vivo RBC labeling: > 80% binding
  - ROIs drawn around left ventricle
    - End systole, end diastole, and background
  - Heart must be in regular rhythm for optimal imaging
  - If background drawn over spleen or aorta, ejection fraction (EF) spuriously high
  - If background drawn over stomach or outside body, EF spuriously low
- High unbound Tc-99m pertechnetate with recent transfusion, renal failure, heparin therapy, some chemotherapy, other medications

DIAGNOSTIC CHECKLIST
- Evaluate raw images (cine) for study quality
  - Counts, labeling, gating, views
- Compare qualitative estimation of left ventricular ejection fraction with quantitative calculation
- Comparison with previous studies important: Regions of interest should be similar
- Evaluate
  - Pericardial silhouette
  - Chamber sizes
  - Hypo/akinesis
  - Filling defects
  - Aneurysm
  - Ejection fraction
**Left Ventricular Function**

**IMAGING**

**Imaging Recommendations**

- **Best imaging tool**
  - Multiple-gated cardiac blood pool acquisition (MUGA)
  - Tc-99m labeled autologous red blood cells (RBCs)
    - Images obtained over heart
    - Analysis of counts at end diastole and end systole → left ventricular (LV) ejection fraction (EF)
  - Low inter- and intraobserver variability (< 5%)
  - High reproducibility
  - Excellent correlation with cardiac catheterization ventriculography ($r = 0.94$)

- **Protocol advice**
  - Patient prep: None
  - Radiopharmaceutical: 15-25 mCi (555-925 MBq) Tc-99m pertechnetate autologous labeled RBCs IV
    - In vitro RBC labeling
      - Highest binding of radionuclide (~ 98%)
      - Safety issues with reinjection of blood products
      - Contraindicated if heparin allergy
    - In vivo RBC labeling: > 80% binding
    - High unbound Tc-99m pertechnetate levels with recent transfusion, renal failure, heparin therapy, some chemotherapy, other medications

- **Dosimetry**
  - Organ receiving largest radiation dose: Heart

- **Image acquisition**
  - Patient supine
  - ECG gating
    - 16-32 frames per R-R interval
  - Planar images: LEAP/high-resolution collimator
  - Matrix: 64 x 64
  - Each image acquired for 300K counts or 5 min
  - Anterior view: 45° shallower than best septal LAO
    - Shows anterolateral and apical LV; right atrium and right ventricle
  - Best septal view LAO: Angle chosen that best shows septum between right and left ventricles
    - Shows septal, anterolateral, posterolateral LV
  - Left lateral/LPO: 45° greater than best septal LAO
    - Shows inferior, apical, anterolateral LV
  - Caudal angulation ± slanted collimator: May help separate ventricular from atrial blood pool
  - Image processing
    - Evaluate raw images (cine) for study quality: Counts, labeling, gating, views
  - Region of interest (ROI) analysis
    - ROIs drawn around LV: End systole, end diastole, and background
    - Manual, automatic, or semiautomatic ROI placement available
    - Avoid drawing background over spleen or aorta; EF will be spuriously high
    - Avoid drawing background over empty stomach or outside body; EF will be spuriously low
    - Background ~ 1/3 size of end diastole

**Artifacts and Quality Control**

- Heart must be in regular rhythm for optimal imaging

- Irregular heartbeats rejected
  - Optimal: ≤ 10% irregular beats
  - Ejection fraction results less reliable if ≥ 30% irregular beats

**DIFFERENTIAL DIAGNOSIS**

**Ischemic Dilated Cardiomyopathy**

- Cardiovascular
  - Regional wall motion abnormalities in coronary artery distribution most common

**Nonischemic Dilated Cardiomyopathy**

- Toxic cardiomyopathy induced by chemotherapy
  - Serial LVEFs most common MUGA indication
- Also: Stress-induced, infectious, genetic, peripartum, sarcoid, autoimmune, cirrhosis, end-stage renal disease

**DIAGNOSTIC CHECKLIST**

**Image Interpretation Pearls**

- Compare qualitative estimation of LVEF with quantitative calculation
- Reprocessing may be necessary if discrepancy
- Comparison with previous studies important: ROIs should be similar
- Reprocessing may be necessary if discrepancy

**Reporting Tips**

- Cardiac morphology
  - Chamber sizes
  - Ventricular wall thickness
  - Pericardial silhouette
  - Filling defects
- Systolic function
  - Qualitative
    - Global LV function
    - Regional LV function
    - Hypo/akinesis, aneuryism
  - Ejection fraction
    - Qualitative: Estimate from cine loop
    - Quantitative: ROI analysis of counts and calculation
      - LVEF (%): \[
        \frac{\text{End diastolic counts} - \text{background counts} - \text{end systolic counts} - \text{background counts}}{\text{end diastolic counts} - \text{background counts}} \times 100
      \]
    - Phase image: Shows sequence of contraction of atria and ventricles
    - Amplitude image: Shows magnitude of contraction of atria and ventricles
- Right ventricular EF
  - Qualitative and quantitative analysis as with LVEF

**SELECTED REFERENCES**

Left Ventricular Function

(Left) Anterior MUGA shows right atrium, right ventricle, anterolateral left ventricle, and left ventricular apex. (Right) Anterior graphic of the heart shows right atrium, right ventricle, anterolateral left ventricle, and left ventricular apex.

(Left) Left anterior oblique MUGA shows septum, anterolateral left ventricle, and posterolateral left ventricle. Also called the best septal view, this image is commonly obtained at 45°. Caudal tilt can also assist in obtaining best view of septum. (Right) Left anterior oblique graphic of the heart shows right ventricle, septum, and left ventricle.

(Left) Left posterior oblique MUGA shows inferior, apical, and anterolateral left ventricle. Note splenic activity, normal physiologic uptake on Tc-99m pertechnetate RBC studies. (Right) Left posterior oblique graphic of the heart shows inferior, apical, and anterolateral left ventricle.
Left Ventricular Function

(Left) Anterior MUGA shows a large photopenic defect surrounding the heart. (Right) Left anterior oblique MUGA in the same patient shows the photopenic defect around the heart, a large pericardial effusion.

(Left) Left anterior oblique MUGA shows a filling defect in the left ventricular apex. The differential diagnosis includes mass lesions and thrombus. Note that medical devices such as pacemakers and postmastectomy tissue expanders can cause artifactual filling defects on MUGA; however, these tend to be in different locations depending on the angle of imaging. (Right) This MUGA shows dilated left ventricle and LV dyskinesis apparent on end-systolic images, a small LV aneurysm.

(Left) This MUGA demonstrates dilated left ventricle and global hypokinesis, evidenced by minimal excursion between end diastole and end systole in a patient with chemotherapy-induced cardiomyopathy. (Right) This MUGA shows severe biventricular enlargement in a patient with viral-induced cardiomyopathy.
Myocardial Infarction and Ischemia

KEY FACTS

DIAGNOSTIC CHECKLIST

- Raw images
  - May identify artifacts, extracardiac tracer uptake (cancer, infection, bowel), infiltration
- Study quality
  - Comment if excessive motion, poor radiotracer uptake/infiltration, technical error
- Artifacts
  - Motion, scatter, reconstruction, attenuation
- Adequacy of stress modality
  - Exercise or pharmacologic
- Perfusion images: Qualitative analysis
  - LV chamber size: Normal vs. dilated
  - 17 segment model: Describe stress/rest perfusion
  - Transient ischemic dilatation (TID): Dropout of endocardial border on stress
- Perfusion images: Quantitative analysis
  - 17 segment model: Each segment scored on 5-pt scale
  - Summed difference score: < 4 = normal; 4-8 = mildly abnormal; 9-13 = moderately abnormal; > 13 = severely abnormal
  - TID ratio: 1.12-1.36 positive for TID
- Gated images: Ejection fraction and wall motion
  - Brightening and endocardial excursion = normal
  - Hypokinesis/akinesis if photopenia, lack of endocardial excursion
  - Lower limits of normal EF for MPI: 45%
  - EF overestimated if small heart size
- Conclusion
  - Positive or negative for inducible ischemia
  - Positive or negative for myocardial infarction (± peri-infarct ischemia)
    - Consider possibility of hibernating myocardium, need for viability study
  - LV function: EF and wall motion

(Left) Short axis view of the left ventricle on CT shows vascular territories supplying the myocardium. The left anterior descending artery supplies the anterior and septal walls. The left circumflex artery supplies the lateral wall. The right coronary artery supplies the inferior and inferoseptal walls. (Right) Drawing of short axis 17-segment model shows bull’s-eye view of the heart for quantitative analysis.

(Left) Short axis MPI shows decreased activity in the inferolateral wall on rest, which is more pronounced on stress images, signifying inferolateral infarction with peri-infarct ischemia. Note the perfusion defect appears flat. (Right) Vertical long axis MPI shows inferior wall before attenuation correction on SPECT/CT. After attenuation correction, counts in the inferior wall are no longer artifactually decreased by diaphragmatic/soft tissue attenuation in this obese patient.
Myocardial Infarction and Ischemia

IMAGING

General Features

- Best diagnostic clue
  - Myocardial perfusion imaging (MPI)
    - Usually Tc-99m-based perfusion agent that localizes to myocardium
      - Radiotracer injected at rest, then image
      - Radiotracer injected at stress, then image
      - Rest and stress images compared
  - Myocardial ischemia: Perfusion defect evident on stress images, normal perfusion on rest images
  - Acute myocardial infarction (AMI): Perfusion defect on MPI with injection within 2 hrs of pain episode
  - Chronic myocardial infarction: Fixed perfusion defect on rest and stress images
  - Hibernating myocardium: Fixed perfusion defect on rest/stress images, normal on viability images

- Location
  - Anterior/septal wall: Left anterior descending (LAD) artery
  - Lateral wall: Circumflex artery
  - Inferior wall: Posterior descending artery (PDA)
    - Right coronary artery (RCA) in 85% (right dominant)
    - Continuation of circumflex in 15% (left dominant)
  - Apex: Usually from LAD, but variable

Imaging Recommendations

- Protocol advice
  - Patient preparation
    - Review for contraindications to stress test, pregnancy
    - Mostly required for stress portion of test
      - NPO for 4 hrs prior to stress test
      - No caffeine 12 hrs prior to pharmacologic stress
  - Radiopharmaceutical
    - Tc-99m sestamibi or Tc-99m tetrofosmin
      - Dose: 10-40 mCi (370 MBq to 1.4 GBq)
      - 1-day protocol: Up to 40 mCi (1.4 GBq) (10 mCi [370 MBq] for rest, 30 mCi [1.1 GBq] for stress)
      - 2-day protocol (patients > 250-275 lbs): 25-30 mCi (925 MBq to 1.1 GBq) for both rest and stress, 1 day apart
      - Dosimetry: Colon (sestamibi) and gallbladder wall (tetrofosmin) receive largest radiation dose
      - 6 hrs t1/2
    - Thallium-201 chloride
      - Dose: 2-4 mCi (74-148 MBq)
      - Rest images on dual-tracer MPI
      - Stress-rest images on TI-201 only MPI
      - Redistribution imaging for viability
      - Long t1/2 (73 hrs) leads to higher dose than Tc-99m-based agents
      - Dosimetry: Kidneys receive largest radiation dose
      - Rb-82
      - Dose: 2D PET: 40-60 mCi (1.4-2.2 GBq); 3D PET: 10-20 mCi (370-740 MBq) BGO system; 30-40 mCi (1.1-1.4 GBq) LSO system
      - Generator produced
      - 75 sec t1/2
      - Cost-effective PET tracer for high-volume centers

- Pharmacologic stress utilized due to short t1/2
- Dosimetry: Kidneys receive largest radiation dose
  - N-13 ammonia
    - Dose: 15-25 mCi (555-925 MBq)
    - PET perfusion agent
    - Cytoplron produced (on-site due to 9.8 min t1/2)
    - Dosimetry: Urinary bladder receives largest radiation dose

- Image acquisition: Tc-99m sestamibi and Tc-99m tetrofosmin
  - Patient position: Supine, upright/semiupright
  - Injection to imaging time: 15-60 min
  - Time between rest/stress injections: 30 min to 4 hrs
  - Collimator: Low energy, high resolution
  - 180° planar acquisition: Preferred if no attenuation correction (better spatial resolution, higher contrast, less attenuation)
  - SPECT and SPECT/CT: Preferred in obese patients, allows attenuation correction
  - Matrix: 64 x 64
  - Step and shoot or continuous acquisition
  - 60-64 projections; 20-25 sec per projection
  - ECG gate stress only or rest and stress
  - 8 frames/cycle standard
  - 140 keV with 15-20% window

- Image acquisition: TI-201
  - Similar to Tc-99m-based tracers, except
    - 70-80 keV with 15-20% window
    - 64 projections
    - Stress-rest MPI: Image 10 min after injection for stress images; rest (redistribution) images at 3-4 hrs
    - Rest only for dual-tracer MPI: Image 10 min after injection for rest images; utilize Tc-99m-based radiotracer for stress
    - Viability: Image 10 min after injection for rest images; redistribution (viability) images at 3-4 hrs

- Image acquisition: Rb-82 and N-13 ammonia PET/CT
  - Rb-82: Image acquisition starts 1-1.5 min after injection, 5-10 min acquisition
  - N-13 ammonia: Image acquisition starts 4-5 min after injection, 10-15 min acquisition
  - Attenuation correction from CT for large patients

- Image processing
  - Reconstruction using filtered backprojection or iterative reconstruction
  - Stress images usually displayed on top row, rest images on bottom row

Artifacts and Quality Control

- Motion artifact
  - Hurricane sign: Counts outside epicardial border on short axis
  - Blurred endocardial border
  - Lateral wall blurring

- Scatter artifact
  - Counts scatter into inferior wall due to high bowel activity

- Reconstruction artifact
  - Photopenia in inferior wall from high bowel activity
  - Photopenia at 11 o’clock position on short-axis views on rest and stress
Myocardial Infarction and Ischemia

**Attenuation**
- Soft tissue attenuation causing fixed defects
- Misregistration of attenuation correction map and perfusion data

**DIFFERENTIAL DIAGNOSIS**

**Myocardial Infarction**
- Normal apical thinning
- Left ventricular hypertrophy: Fixed lateral wall defect
- Soft tissue attenuation of photons: Breast (anterior wall), diaphragm (inferior wall)
- Septal hypokinesis common in absence of MI, especially after coronary artery bypass graft surgery
- Decreased activity in lateral wall on N-13 ammonia PET can be seen in healthy controls
- Myocardial hibernation: Myocardium with little/no perfusion, but viable due to anaerobic glycolysis
  - 25% of fixed defects are viable on viability studies

**Myocardial Ischemia**
- Artifactual perfusion defects on stress only (e.g., bowel activity on stress images, shift of overlying soft tissue)
- Left bundle branch block: Functional septal reversibility with exercise stress (false-positive)

**Other Vascular Disease**
- Vasospastic disease (Prinzmetal angina)
- Microvascular disease (e.g., diabetes mellitus, syndrome X)

**PATHOLOGY**

**General Features**
- Etiology
  - Ruptured coronary artery plaque disrupts myocardial blood supply
    - Myocardial necrosis begins in 20-30 min, spreading from subendocardial to epicardium
  - Risk factors
    - Hyperlipidemia, diabetes mellitus, hypertension, obesity, cigarette smoking, family history

**CLINICAL ISSUES**

**Demographics**
- Age
  - Men: Usually > 45 yrs
  - Women: > 55 yrs

**DIAGNOSTIC CHECKLIST**

**Consider**
- Myocardial infarction
  - Fixed perfusion defect, regional wall motion abnormality
  - Peri-infarct ischemia can cause chest pain
- Myocardial ischemia
  - Reversible perfusion defect on rest and stress images, no regional wall motion abnormality

**Reporting Tips**
- Raw images
  - Review to identify artifacts, extracardiac radiotracer uptake (breast/lung cancer, lymphoma, infection)

**Study quality**
- Comment if excessive motion, poor radiotracer uptake/infiltration, technical error

**Artifacts**
- Describe if present: Motion, scatter, reconstruction, attenuation

**Adequacy of stress modality**
- Exercise: Discuss percent age-predicted max heart rate achieved
- Vasodilators: If infused and radiotracer injected per protocol, assume adequate stress

**Perfusion images**
- Qualitative analysis
  - LV chamber size: Normal vs. dilated
  - 17 segment model: Describe perfusion defects on stress and rest using these segments
  - Transient ischemic dilatation (TID): Dropout of endocardial border on stress
- Quantitative analysis
  - Computer generation of segmental perfusion scores in each of 17 segments on a 5-point scale at stress and rest (0 = normal, 4 = absent)
  - Summed stress score (SSS): Analysis of resting and stress-induced perfusion defects
  - Summed rest score (SRS): Analysis of resting perfusion defects
  - Summed difference score (SDS): SSS minus SRS; a measure of stress-induced ischemia
  - SDS: < 4 = normal; 4-8 = mildly abnormal; 9-13 = moderately abnormal; > 13 = severely abnormal
  - TID ratio: 1.12-1.36 correlates with multivessel disease
  - TID = endocardial volume at stress / endocardial volume at rest

**Gated images**
- Wall motion
  - Normal if brightening and endocardial excursion on gated slice images
  - Hypokinesia/akinesia if photopenia, lack of endocardial excursion
- Ejection fraction
  - Lower limits of normal for MPI: 45%
  - Overestimated if small heart size

**Conclusion**
- Positive or negative for inducible ischemia
- Positive or negative for myocardial infarction (± peri-infarct ischemia)
  - Consider possibility of hibernating myocardium, need for viability study
  - LV function: EF and wall motion

**SELECTED REFERENCES**

Cardiac

Myocardial Infarction and Ischemia

(Left) Short axis MPI shows transient ischemic dilatation. Note normal endocardial border on rest, which appears to enlarge on stress. This high-risk finding is due to reversible subendocardial ischemia and suggests multivessel disease. Note also the anterior and inferior perfusion defects at stress. (Right) Vertical long axis MPI views (same patient) show enlarged endocardial border and severe stress-induced perfusion defects involving the anterior wall, inferior wall, and apex. Resting images below are normal.

(Left) Short axis MPI views in an obese patient show heterogeneous myocardium due to poor counts. The top row is prior to CT attenuation correction. The bottom row is after CT attenuation correction. (Right) Short axis MPI shows high activity in adjacent bowel. Note the adjacent inferior wall shows decreased counts on rest and normal counts on stress. The bowel activity caused decreased counts in the inferior wall due to reconstruction artifact.

(Left) Short axis MPI shows extracardiac activity extending from the left ventricle due to patient motion, called the hurricane sign. With motion correction, the hurricane sign disappeared. (Right) 3D MPI rendering of the left ventricle at end systole shows a dilated left ventricle with dyskinesis at the inferoseptum, an apical aneurysm.
Myocardial Infarction and Ischemia

(Left) Short axis MPI shows multivessel coronary disease. Anteroseptal and inferolateral perfusion defects are more evident on stress compared with rest images. (Right) Horizontal long axis MPI in the same patient shows lateral inducible ischemia.

(Left) Short axis MPI bull’s-eye computer analysis in the same patient shows multivessel inducible ischemia in the anteroseptum, apical, and inferolateral walls on stress imaging. (Right) Short axis MPI bull’s-eye computer analysis in the same patient at rest shows virtually normal perfusion.

(Left) 3D view of MPI raw images shows normal myocardial radiotracer uptake. (Right) 3D view of MPI raw images in the same patient who presented for follow-up MPI shows normal myocardial uptake and a large photopenic defect surrounding the heart, a pericardial effusion.
Myocardial Infarction and Ischemia

(Left) Short axis MPI shows high counts in the bowel due to normal radiotracer excretion. Note the relatively diminished perfusion in the inferior wall on repeat image, confirming artifactual scatter of counts into the inferior wall. (Right) Vertical long axis MPI shows anterior inducible ischemia. Note high counts in bowel on stress images (hidden by computer processing). Coronary artery catheterization showed no inferior wall disease, suggesting reconstruction artifact reduced counts in this area on stress images.

(Left) Short axis MPI shows decreased counts in the left ventricle on stress that appear to improve on rest. (Right) Short axis MPI in the same patient with arms up during both rest and stress acquisitions show similar perfusion patterns. Note that the images must be obtained with similar patient positioning to avoid introduction of artifacts.

(Left) Sagittal MPI raw images in an 86-year-old woman with atypical chest pain show normal myocardial uptake. (Right) Sagittal MPI raw images in the same patient show abnormal uptake in the left breast, a possible breast cancer. Mammographic correlation is necessary for this finding.
**TERMINOLOGY**
- Myocardial viability evaluation
  - Detection of myocardial hibernation or stunning vs. necrosis/infarction in patients with ischemic cardiomyopathy

**IMAGING**
- Tc-99m/Tl-201 myocardial perfusion scintigraphy
  - Viability present in 25% of regions called infarction
  - Viability present in up to 50% of patients with infarcted segments
- Perfusion-PET mismatch
  - Myocardial uptake of radioactive glucose analog compared with myocardial uptake of perfusion radiotracer (Tc-99m perfusion agent or Tl-201)
  - Anaerobic glucose utilization in underperfused myocardium = viability
- Tl-201 SPECT viability
  - Rest-redistribution mismatch

**TOP DIFFERENTIAL DIAGNOSES**
- Myocardial hibernation
  - Chronic myocardial dysfunction due to chronically decreased myocardial perfusion (chronic total occlusions)
  - Regions of abnormal perfusion will show F-18 FDG utilization or redistribution on Tl-201
- Myocardial stunning
  - Temporary myocardial dysfunction due to short-term underperfusion or lack of perfusion to myocardium
  - Regions of abnormal perfusion will show F-18 FDG utilization or redistribution on Tl-201
- Myocardial infarction
  - Myocardial necrosis and remodeling (scar)
  - Regions of abnormal perfusion will show lack of F-18 FDG utilization or lack of redistribution on Tl-201

(Left) Vertical long axis F-18 FDG PET viability shows normal perfusion in the anterior wall with associated glucose metabolism. This confirms glucose is an available substrate for hypoperfused inferior wall, which does not show viability on PET. (Right) Horizontal long axis F-18 FDG PET viability shows hypoperfused septum with glucose utilization, signifying viability. Note that the normally perfused lateral wall is not utilizing glucose, signifying free fatty acids are being utilized.

(Left) Short axis F-18 FDG PET viability shows hypoperfused septum that is utilizing glucose, signifying viability. Note the inferior myocardial infarction that is not viable. (Right) Vertical long axis F-18 FDG PET viability shows inferior wall perfusion and glucose metabolism mismatch. This suggests that the inferior wall will improve in contractility after revascularization.
TERMINOLOGY

Definitions
- Myocardial viability evaluation
  - Detection of myocardial hibernation or stunning vs. necrosis/infarction in patients with ischemic cardiomyopathy
    - Myocardial hibernation
      - Chronic myocardial dysfunction due to chronically decreased myocardial perfusion
    - Myocardial stunning
      - Temporary myocardial dysfunction due to short-term underperfusion or lack of perfusion to myocardium
- Regions of hibernating/stunned myocardium likely to show improved contractility after revascularization

IMAGING

Nuclear Medicine Findings
- Tc-99m/Tl-201 myocardial perfusion scintigraphy
  - Viability present in 25% of regions called infarction
  - Viability present in up to 50% of patients with infarcted segments
- F-18 FDG PET viability
  - Perfusion-PET mismatch
    - Myocardial uptake of radioactive glucose analog compared with myocardial uptake of perfusion radiotracer (Tc-99m perfusion agent or Tl-201)
    - Anaerobic glucose utilization in underperfused myocardium = viability
- TI-201 SPECT viability
  - Rest-redistribution mismatch
    - Myocardial uptake of TI-201 at rest compared with delayed myocardial uptake (redistribution)
    - Delayed myocardial uptake in regions of underperfused myocardium = viability
    - > 10% increase in tracer uptake on redistribution images = viability
    - Comparison of TI-201 uptake in underperfused segments to normally perfused segments
      - ~ 90% of segments with > 80% uptake of normal segments show functional improvement after revascularization
      - ~ 55% of segments with 50-60% uptake of normal segments show functional improvement after revascularization

Imaging Recommendations
- Protocol advice
  - F-18 FDG PET viability
    - Patient preparation
      - Obtain resting myocardial perfusion SPECT prior to F-18 FDG PET scan
      - Fast 6-12 hrs prior to F-18 FDG PET scan
      - F-18 FDG PET performed in presence of elevated insulin level (postprandial/post insulin administration)
      - Oral glucose loading (25-100 g) followed by blood glucose check at 45-90 min
      - Administer 1-5 units of insulin (sliding scale) depending on blood glucose level
    - Radiopharmaceutical
      - 5-15 mCi (185-555 MBq) F-18 FDG
      - Injection after glucose load/insulin administration
    - Dosimetry
      - Critical organ: Urinary bladder
    - Image acquisition
      - Imaging performed at ~ 60 mins after F-18 FDG injection
      - CT for attenuation correction
      - 3-10 min imaging time
    - Image processing
      - Match F-18 FDG PET images with myocardial perfusion SPECT images using dedicated myocardial perfusion scintigraphy software
- TI-201 viability
  - Patient preparation
    - None
  - Radiopharmaceutical
    - 2-4 mCi (74-148 MBq) TI-201
  - Dosimetry
    - Critical organ: Testes, thyroid
  - Image acquisition
    - 10 min after injection; 4 &/or 24 hr images
    - LEAP collimator
    - SPECT/CT with CT for attenuation correction
    - Long imaging times recommended to enhance counting statistics on TI-201 rest imaging
  - Image processing
    - Match rest images to redistribution images using dedicated myocardial perfusion scintigraphy software

Artifacts and Quality Control
- F-18 FDG PET viability
  - Severe type-II diabetes mellitus
    - Can have no F-18 FDG myocardial uptake despite insulin
    - TI-201 preferred
  - Attenuation correction
    - Misregistration of attenuation map can cause artificially increased or decreased counts
    - Attenuation correction recommended to decrease artificial perfusion defects in inferior (diaphragm), anterior (breast) walls
  - SPECT perfusion
    - Overlapping bowel activity can add to counts in inferior wall, mimicking normal perfusion
- TI-201 viability
  - Poor count statistics/artifacts due to obesity
    - Use attenuation correction
  - Movement during imaging
    - Motion correct or reimage
  - SPECT perfusion
    - Overlapping bowel activity can add to counts in inferior wall, mimicking normal perfusion
    - Attenuation correction recommended to decrease artificial perfusion defects in inferior (diaphragm), anterior (breast) walls
  - Attenuation correction
Myocardial Viability

- Misregistration of attenuation map can cause artifactually increased or decreased counts
  - Improper imaging time
  - Inadequate time for redistribution on Tl-201 imaging (image at both 4 and 24 hr after injection to increase sensitivity for viability)

**DIFFERENTIAL DIAGNOSIS**

**Myocardial Hibernation**
- Chronic myocardial dysfunction due to chronically decreased myocardial perfusion (chronic total occlusions)
- Regions of abnormal perfusion will show F-18 FDG utilization or redistribution on Tl-201

**Myocardial Stunning**
- Temporary myocardial dysfunction due to short-term underperfusion or lack of perfusion to myocardium
- Regions of abnormal perfusion will show F-18 FDG utilization or redistribution on Tl-201

**Myocardial Infarction**
- Myocardial necrosis and remodeling (scar)
- Regions of abnormal perfusion will show lack of F-18 FDG utilization or lack of redistribution on Tl-201

**PATHOLOGY**

**Microscopic Features**
- Myocardial viability requires
  - Sarcolemmal membrane integrity
  - Preserved metabolic activity
  - Adequate myocardial perfusion

**CLINICAL ISSUES**

**Presentation**
- Most common signs/symptoms
  - Heart failure
    - Regional &/or global wall motion abnormalities
    - Fatigue
    - Dyspnea
    - Physical activity limitations
  - Chronic total occlusions
    - Chest pain in up to 50%
    - ~ 12% heart failure

**Demographics**
- Age
  - 50-59 yrs: 8 per 1,000
  - 60-89 yrs: 66-79 per 1,000
- Epidemiology
  - USA: 5.1 million people have heart failure (2006)
  - Chronic total occlusions: 33-52% prevalence in patients with coronary artery disease

**Natural History & Prognosis**
- Patients with viable myocardium
  - Benefit from revascularization
  - If untreated, risk of cardiac death or nonfatal MI is increased
- Patients with nonviable myocardium
  - Increased morbidity and mortality with revascularization

- Viability testing most important in patients with heart failure
  - 50% of patients with heart failure: Death within 5 years
  - Revascularization: Decreases morbidity and mortality where viable myocardium is present

**TREATMENT**

- Revascularization with coronary artery bypass grafting
  - Older patients
  - Left main coronary artery disease
  - Diabetes mellitus
  - Triple vessel disease
- Revascularization with catheterization and percutaneous coronary intervention
  - Younger patients
  - Normal renal function
  - Lower risk coronary artery disease

**DIAGNOSTIC CHECKLIST**

**Consider**
- F-18 FDG PET viability
  - If no F-18 FDG activity in heart, consider improper patient preparation
- Tl-201 viability
  - Consider using Tl-201 in patients with severe type-II diabetes mellitus
    - Lack of F-18 FDG uptake can be due to severe insulin resistance
  - False-negative Tl-201 scans often due to imaging too early after tracer injection
    - If 4 hr images negative, repeat at 24 hrs
    - 24 hr images most sensitive
- CT attenuation correction for F-18 FDG PET/CT and SPECT/CT tracers to reduce soft tissue artifacts
  - Note that misregistration of attenuation map can cause artifacts as well

**SELECTED REFERENCES**

Myocardial Viability

(Left) Horizontal long axis F-18 FDG PET viability shows matched perfusion and glucose metabolism defects in the apex, signifying nonviable myocardial infarction. (Right) Vertical long axis F-18 FDG PET viability shows a large apical myocardial infarction that is not metabolizing glucose.

(Left) Short axis F-18 FDG PET viability shows an enlarged right ventricle and an anterolateral perfusion defect. Note only blood pool activity, which may signify poor patient preparation or anterolateral nonviability. In highly insulin-resistant patients, the heart may not take up glucose despite viability. (Right) Vertical long axis F-18 FDG PET viability shows decreased anterior and apical perfusion. The anterior wall shows glucose metabolism, whereas the apex does not.

(Left) Short axis F-18 FDG PET viability shows abnormal inferolateral perfusion with a high level of glucose metabolism consistent with myocardial viability. Note the normal septum is not utilizing glucose but is still utilizing free fatty acids as an energy substrate. (Right) Horizontal long axis F-18 FDG PET viability shows viable, underperfused lateral wall.
Right-to-Left Shunt

**TERMINOLOGY**
- Right-to-left shunt: Abnormal shunting of blood through cardiovascular and pulmonary system, bypassing the pulmonary capillary circulation
  - Can allow venous to arterial emboli, causing ischemia to multiple organs (e.g., brain, bowel)

**IMAGING**
- Tc-99m MAA pulmonary perfusion scan
  - Abnormal uptake within brain and kidneys confirms shunting of Tc-99m MAA administered intravenously
  - Tc-99m MAA should localize only in brain and kidneys with shunt
  - Must be differentiated from extrapulmonary uptake of free Tc-99m pertechnetate
    - Tc-99m can dissociate from MAA (resulting in free Tc-99m pertechnetate) due to lack of quality control in pharmacy and radiotracer handling

**DIAGNOSTIC CHECKLIST**
- Always scrutinize VQ scans for unexpected incidental uptake within brain or kidneys
- If uptake in kidneys, must look for brain or thyroid/salivary uptake
- Brain images: Most sensitive indicator of right-to-left shunt
- Nuclear medicine findings are not specific for location of shunt

(Left) Anterior VQ scan shows normal uptake within lungs. There is no extrapulmonary uptake (brain or renal) to suggest a right-to-left shunt. (Right) VQ scan shows expected uptake within the lungs on both anterior and posterior projections. Unexpected uptake within the kidneys bilaterally suggests either right-to-left shunt or free pertechnetate.

(Left) VQ scan shows unexpected uptake within both brain and bilateral kidneys confirming presence of a right-to-left shunt. (Right) VQ scan shows unexpected uptake within both kidneys and thyroid tissue consistent with free pertechnetate rather than a right-to-left shunt.
Right-to-Left Shunt

TERMINOLOGY

Definitions
- Right-to-left shunt: Abnormal shunting of blood through cardiovascular and pulmonary system, bypassing pulmonary capillary circulation
  - Can allow venous to arterial emboli, causing ischemia to multiple organs (e.g., brain, bowel)

IMAGING

Nuclear Medicine Findings
- Tc-99m MAA pulmonary perfusion scan
  - Abnormal uptake within brain and kidneys confirms shunting of Tc-99m MAA administered intravenously
    - Tc-99m MAA should localize only in brain and kidneys with shunt
  - Must be differentiated from extrapulmonary uptake of free Tc-99m pertechnetate
    - Tc-99m can dissociate from MAA (resulting in free Tc-99m pertechnetate) due to lack of quality control in pharmacy and radiotracer handling
    - Free Tc-99m pertechnetate is also visualized in thyroid gland, salivary glands, and gastric mucosa
  - May be incidental finding on V/Q scan for suspected pulmonary embolism

Protocol Advice
- Radiopharmaceutical
  - Tc-99m MAA
  - Use reduced MAA particle count (100,000-200,000) in case of suspected shunt, pulmonary hypertension, pregnancy, or pediatric patient
    - If shunt present, particles bypass pulmonary capillary bed initially and become trapped in brain/kidneys
    - Makes critical organs (brain, kidneys) at risk of unanticipated radiation exposure
  - IV injection in upper extremity sufficient
    - Can inject indwelling line but not through port or any filtered line because will filter out MAA particles

- Dose
  - Adults: 1-4 mCi (37-148 MBq) of Tc-99m MAA, ~ 200,000-700,000 particles
  - Children: 0.03 mCi/kg with minimum of 0.4 mCi

- Dosimetry
  - Adults: Largest radiation dose to lungs 0.067 mGy; effective dose 0.011 mSv
  - Pediatrics (5 year old): Largest radiation dose to lungs 0.21 mGy; effective dose 0.038 mSv

- Image acquisition
  - LEAP collimator
  - In addition to anterior/posterior planar images of lungs, posterior images of kidneys and anterior/posterior of brain
  - Brain images: Most sensitive indicator of right-to-left shunt

- Image processing
  - Can quantitate degree of shunt if desired
    - Right-to-left shunt % = (systemic counts/whole-body counts x 100%) / [(whole-body counts - lung counts)/whole-body counts] x 100%

DIFFERENTIAL DIAGNOSIS

Intracardiac Right-to-Left Shunts
- Adults
  - Atrial septal defect or patent foramen ovale
- Children
  - Atrial septal defect, patent foramen ovale, ventricular septal defect, or more complex congenital defects

Extracardiac Right-to-Left Shunts
- Pulmonary
  - Arteriovenous malformation (AVM)
    - Enlarge with time, most typically do not present until adulthood
    - May be single or multiple, simple or complex
  - Hereditary hemorrhagic telangiectasia (a.k.a. Osler-Weber-Rendu) syndrome: Multiple systemic AVMs
- Anomalous systemic venous return
  - Left superior vena cava (if communication with left atrium)

Acquired Shunts
- Hepatopulmonary syndrome (develop pulmonary AVMs)
- Post-traumatic/surgical

Free Tc-99m Pertechnetate
- Tc-99m pertechnetate can dissociate from MAA (resulting in free Tc-99m pertechnetate) due to lack of quality control in pharmacy and radiotracer handling
- Free Tc-99m pertechnetate also demonstrates uptake within kidneys
- Also shows uptake within thyroid & salivary glands, gastric mucosa

DIAGNOSTIC CHECKLIST

Image Interpretation Pearls
- Always scrutinize VQ scans for unexpected incidental uptake within brain or kidneys
- If uptake in kidneys, must look for brain or thyroid/salivary uptake
  - If brain uptake also noted, consistent with right-to-left shunt
  - If thyroid/salivary, gastric mucosa uptake also noted, free Tc-99m pertechnetate rather than shunt

- Nuclear medicine findings are not specific for location of shunt

SELECTED REFERENCES