Aims of Noninvasive Imaging in Cardiology

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Imaging Techniques

- Morphology
- Function
- Subclinical Atherosclerosis
- Diagnosis
- Risk Stratification
- Prognosis
Every year, five billion imaging tests are performed worldwide
Half of these are cardiovascular examinations

*Picano E. BMJ 2004;328:578*

At least one-third of all examinations are partially or totally inappropriate
(risks and costs outweigh benefits)

*FDA, 2010*
From 23,887 patients referred for elective coronary intervention, only 44% had undergone any kind of stress testing in a 90-day period prior to the intervention.

Lin G et al. JAMA 2008;300:1765
Which Cardiac Diseases to Image? With which Techniques?

1. Valvular Diseases
   - Congenital Heart Diseases
   - ECHO / MRI / Cardiac CT

2. Ischemic Heart Disease
   - Cardiomyopathies
   - NM: SPECT/PET
     - Endothelial Function
     - Intima-media thickness

3. Vulnerable Plaque
Comparative efficacy of Imaging Techniques in CHD

2,560 pts (British ROBUST-study) - SPECT
Sensitivity: 91% / Specificity: 87%

Ischemic Heart Disease

Possibilities of different techniques

Coronary Anatomy
CT, MRI

Myocardial Perfusion / Integrity of the cell membrane
SPECT, PET, MRI, CT

Myocardial Cell Metabolism
PET, MRI

Myocardial Perfusion/Coronary Flow Reserve
PET, SPECT, MRI, ECHO

Ventricular Function: Wall Motion, Systolic Thickening, LVEF (All)
DIAGNOSIS
ECHOCARDIOGRAPHY

- Non invasive
- No radiation
- Portable equipment
- Versatile
- Practical knowledge for all cardiologists
- Clinical applications in all cardiac diseases
- Dx: anatomical, functional and hemodynamic
Noninvasive angiography
High Negative Predictive Value
Adequate Diagnostic Accuracy
Attention! Coronary Arteries without epicardial stenosis
See Calcium Score
CT vs. MPI:

✓ **Angio-CT**: high sensitivity and NPV (97-99%) Highly reliable test for excluding CAD in pts with low-to-intermediate probability of CAD

✓ **MPI** if high-to-intermediate probability of CAD
Assessment of the relationship between stenosis severity and distribution of coronary artery stenoses on multislice computed tomographic angiography and myocardial ischemia detected by single photon emission computed tomography

Balaji K. Tamarappoo, PhD, MD, Ariel Gutstein, MD, Victor Y. Cheng, MD, Ryo Nakazato, MD, Heidi Gransar, MS, Damini Dey, PhD, Louise E. J. Thomson, MBChB, FRACP, Sean W. Hayes, MD, John D. Friedman, MD, Guido Germano, PhD, Piotr J. Skomka, PhD, and Daniel S. Berman, MD
Approach to patients with suspected CAD

Yerramasu A et al. JNC 2010
Myocardial Perfusion Imaging_MRI

- Mainly if resting ECG abnormalities or an inability to exercise
  - Advantage: no radiation
  - Perfusion / Stress imaging of ventricular function with dobutamine (high accuracy for detecting ischemia due to excellent LV endocardial visualization)

Value for identifying inducible myocardial ischemia and contractile reserve indicative of potential for recovering systolic thickening after revascularization

Hundley WG et al. Circulation 2010;121:2462
Necrois

- ECHO: segmental wall motion abnormalities at rest

- MRI vs. SPECT: LGE is more reliable in detecting subendocardial scar
  Ibrahim T et al. JACC 2007;49:208
  ........and also improves the detection of RV infarction
  Kumar A et al. JACC 2006;48:1969

Hundley WG et al. Circulation 2010;121:2462
Takotsubo Cardiomyopathy: A Unique Cardiomyopathy With Variable Ventricular Morphology

R. Todd Hurst, MD,* Abhiram Prasad, MD,† J. Wells Askew III, MD,† Partho P. Sengupta, MBBS,* A. Jami Tajik, MD* Scottsdale, Arizona; and Rochester, Minnesota

Table 1. Proposed Mayo Clinic Criteria for Diagnosis of Takotsubo Cardiomyopathy

1. Transient hypokinesis, akinesis, or dyskinesis of the left ventricular mid segments, with or without apical involvement. Regional wall motion abnormalities extend beyond a single coronary vascular bed.* A preceding physical or emotional stressor is often present.

2. No obstructive coronary disease or acute plaque rupture (determined angiographically).†

3. New electrocardiographic abnormalities (ST-segment elevation, T-wave inversion, or both) or modest elevation in cardiac troponin level.

4. No pheochromocytoma or myocarditis. For such patients, the diagnosis of takotsubo cardiomyopathy should be made cautiously, and a clear, stressful, precipitating event must be sought.
Rest
3 months later

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>3 m later</th>
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<tr>
<td>LVEF</td>
<td>39%</td>
<td>74%</td>
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<tr>
<td>EDV</td>
<td>97</td>
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<td>ESV</td>
<td>59</td>
<td>21</td>
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<tr>
<td>SV</td>
<td>38</td>
<td>60</td>
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Takotsubo Cardiomyopathy
Rest

3 months later

Longitudinal Left Ventricular Strain in Stress Cardiomyopathy

Stanton T et al. JACC Img
2010;3:867
## VIABILITY

<table>
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<tr>
<th></th>
<th>No. Studies</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
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<td><strong>F18-FDG PET</strong></td>
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<td><strong>TI-201</strong></td>
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<td>55</td>
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<td><strong>Technetium</strong></td>
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<tr>
<td><strong>Dobutamine stress-echo</strong></td>
<td>32</td>
<td>81</td>
<td><strong>80</strong></td>
<td>85</td>
<td>77</td>
</tr>
</tbody>
</table>

*Bax J et al. Curr Probl Cardiol 2001;26:142*

**MRI_LGE:** Information of the transmural extent of scar
**BUT:** it can not distinguish hibernating myocardium from normally perfused myocardium in regions of nontransmural hyperenhancement.
Male, 49 y, typical chest pain, normal ECG at rest. Ca score: Left main CA: 20, LAD 59, Cx 34, T: 113
Stress test: Chest pain, ST

<table>
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<tr>
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<td>35</td>
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<td>SV</td>
<td>70</td>
<td>65</td>
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<tr>
<td>TID</td>
<td>1.30</td>
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Incremental Prognostic Power of Single-Photon Emission Computed Tomographic Myocardial Perfusion Imaging in Patients With Known or Suspected Coronary Artery Disease

Salvador Borges-Neto, MD, Linda K. Shaw, MS, Robert H. Tuttle, MSPH, John H. Alexander, MD, William T. Smith IV, MD, Marianna Chambless, BS, R. Edward Coleman, MD, Robert A. Harrington, MD, and Robert M. Califf, MD

Am J Cardiol 2005;95:182–188

FIGURE 3. Kaplan-Meier cardiovascular event-free survival curves demonstrating risk represented by SSS values 0 to 4, 5 to 14, and ≥15.
Prognosis CT vs. MPI

Primary end-point: all cause death
2-year survival rates: 97% after both tests
Annual mortality rates predicted by:
CT: 0.2-11%
MPI: 0.2-12%

The prognostic potential of CT is similar to that of MPI

541 patients, 2 years FU

Annualized mortality and non-fatal MI

Obstructive CAD: 4.8%
None or mild CAD: 1.8%
Abnormal vs. Normal MPI: 3.8% vs. 1.1%
Combined use of MSCT and MPI resulted in significantly improved prediction of the composite hard end-point of all-cause mortality and non-fatal MI.

Van Werkhoven J. JACC 2009;53:623
Review of 27 622 pts:

- Presence of any coronary artery calcium confers a 4-fold increased risk of cardiac death or non-fatal MI ($p < 0.0001$) compared with the absence of calcium

*Greenland P et al. JACC 2007;49:378*

- Risk of 0.4% in pts without any coronary artery calcium
1. 17.5% of pts were reclassified as having significant CAD as defined by a coronary Ca score >100

Thompson R et al. JNC 2005;12:392

2. 760 pts with normal Rb-82 PET/CT 64.1%, subclinical CAD based on an abnormal CACS

Clinical value for treatment

3. 22.4% with CACS > 400

Bybee K et al. JNC 2010;17:188
DILATED CARDIOMYOPATHY
Dilated Cardiomyopathy

**Etiology / Function:** Echo, SPECT, PET, CT, MRI

1. Ventricular dyssynchrony + viability: Echo, SPECT, MRI
2. Coronary venous anatomy: CT, MRI
3. Cardiac Repair Assessment: Stem cells Transplant Rejection
4. Adrenergic Innervation: SPECT, PET
Dilated Cardiomyopathy

Perfusion

Function
Synchronism
Synchronism Assessment

✓ High variability in TDI measurement by echo (interobserver variability) (PROSPECT Trial, 498 pts, 53 centers worldwide)

  Chung E et al. Circulation 2008; 117:2608

✓ By phase analysis_SPECT: CRT Responders have an histogram bandwidth and a phase standard deviation significantly higher than non-responders

✓ Cutoff point of 135º for histogram bandwidth yielded a sensitivity and specificity of 70% for prediction of CRT response

✓ Cutoff point of 43º for phase standard deviation yielded a sensitivity and specificity of 74% for prediction of CRT response

  Henneman M et al. JNM 2007;48:1104
Myocardial Iodine-123
Meta-iodobenzylguanidine Imaging
and Cardiac Events in Heart Failure

Results of the Prospective ADMIRE-HF (AdreView
Myocardial Imaging in Heart Failure) Study

Arnold F. Jacobson, MD, PhD,* Roxy Senior, MD,† Manuel D. Cerqueira, MD,‡
Nathan D. Wong, PhD,§ Gregory S. Thomas, MD, MPH,§ Victor A. Lopez, BS,§
Denis Agostini, MD, PhD,‖ Fred Weiland, MD,¶ Harish Chandna, MD,# Jagat Narula, MD, PhD,§
on behalf of the ADMIRE-HF Investigators

Princeton, New Jersey; London, United Kingdom; Cleveland, Ohio; Irvine, California; Caen, France;
Roseville, California; and Victoria, Texas

961 patients
NYHA functional class: II – III / LVEF ≤ 35%
Follow-up: 2 years
Event Rate: 38% (H/M < 1.60) vs. 15% (H/M ≥ 1.60)
The quantitation of sympathetic innervation of the myocardium with \( ^{123} \text{I} \text{MIBG SPECT} \) is a strong predictor of cardiac events in patients with HF and depressed LVEF, independently of BNP and LVEF values.
Cardiac Sympathetic Denervation Assessed With 123-Iodine Metaiodobenzylguanidine Imaging Predicts Ventricular Arrhythmias in Implantable Cardioverter-Defibrillator Patients

Mark J. Boogers, MD,* † C. Jan Willem Borlefs, MD,* Maureen M. Henneman, MD,* Rutger J. van Rommel, MD,* Jan van Ramshorst, MD,* Eric Boersma, Ph.D,§ Petra Dibbers-Schneider, MSc; † Marcel P. Stokkel, MD, Ph.D, † Ernst E. van der Wall, MD, Ph.D,* Martin J. Schalij, MD, Ph.D,* Jeroen J. Bax, MD, Ph.D*
Leiden, Utrecht, and Rotterdam, the Netherlands

Results
One-hundred sixteen heart failure patients referred for ICD therapy were enrolled. During a mean follow-up of 23 ± 15 months, appropriate ICD therapy (primary end point) was documented in 24 (21%) patients and appropriate ICD therapy or cardiac death (secondary end point) in 32 (28%) patients. Late 123-I MIBG SPECT defect score was an independent predictor for both end points. Patients with a large late 123-I MIBG SPECT defect (summed score >26) showed significantly more appropriate ICD therapy (52% vs. 5%, p < 0.01) and appropriate ICD therapy or cardiac death (57% vs. 10%, p < 0.01) than patients with a small defect (summed score ≤26) at 3-year follow-up.

Conclusions
Cardiac sympathetic denervation predicts ventricular arrhythmias causing appropriate ICD therapy as well as the composite of appropriate ICD therapy or cardiac death. (J Am Coll Cardiol 2010;55:2769–77) © 2010 by the American College of Cardiology Foundation
Boogers M et al. JACC 2010;55:2769
SUBCLINICAL ATHEROSCLEROSIS
- Systemic atheromatosis Rx/US
- Calcium Score CT
- Carotid intima – media thickness US
- Endothelial function US
- High-sensitivity CRP
- Coronary flow reserve PET, MRI

Are We Getting Nearer to Screening for Atherosclerosis?
Shlomo Stern
*Circulation* 2008;117;122-126
Guidelines for the Ultrasound Assessment of Endothelial-Dependent Flow-Mediated Vasodilation of the Brachial Artery
A Report of the International Brachial Artery Reactivity Task Force
Mary C. Corretti, MD, FACC,* Todd J. Anderson, MD,† Emelia J. Benjamin, MD, MSc,‡ David Celermajer, MD,*§ Francois Charbonneau, MD,¶ Mark A. Creager, MD,‖ John Deanfield, MD,¶ Helmut Drexler, MD,** Marie Gerhard-Herman, MD,¶ David Herrington, MD, MHS,¶ Patrick Vallance, MD,¶† Joseph Vita, MD,¶ Robert Vogel, MD*
Baltimore, Maryland; Calgary, Alberta and Montreal, Quebec, Canada; Boston, Massachusetts; Sydney, Australia; London, United Kingdom; Hannover, Germany; and Winston-Salem, North Carolina

**Postdilation – basal x 100% basal**
Normal > 5%
Carotid intima-media thickness (CIMT)

- Inter- (but NOT intra-) observer variability
- Lack of a universal standardized protocol
- Normal Value: 0.5 – 1.2 mm
- Plaque > 1.2

Good for screening: noninvasive, quantitative, and correlates with clinical outcome
O’Leary D, Bots M. Eur Heart J 2010;31:1682
Carotid intima-media thickness (CIMT)

PROGNOSTIC VALUE:

  (Systematic review and meta-analysis), 37 197 subjects, mean FU: 5.5 years
  For an absolute CIMT difference of 1.1 mm
  Future risk of MI increases by 10-15% and stroke risk increases by 13-18%

- CIMT and CAC:
  Newman A et al. Am J Cardiol 2008;101:186
  559 subjects. CIMT & CAC, similar HR for total cardiovascular events and CHD. CIMT, more strongly related to stroke

MESA (Multi-Ethnic Study of Atherosclerosis)
6814 adults, mean FU: 3.9 years
- CAC was a better predictor of incident cardiovascular events than was CIMT (AUC: 0.81 vs. 0.78)
- CIMT was more predictive of stroke
VULNERABLE PLAQUE
Vulnerable Plaque

- Plaque size / volume (CT, MRI)
- Positive remodeling (CT, MRI)
- Thin fibrous cap (CT, MRI)
- Inflammation & Intraplaque neovascularization:
  - Metabolism assessment with PET-radiotracers (F18-FDG)
  - Targeted contrast agents (MRI, CT, US)
With CT:
- Very low CT density (below 30 HU)
- Predominance of non-calcified plaque
- Pronounced positive remodeling

Motoyama S et al. JACC 2007;50:319
JACC 2009;54:49
Achenbach S, Raggi P. Eur Heart J 2010;31:1442

Kate G et al. JNC 2010
MPI problems: multivessel disease, subclinical atherosclerosis, attenuation artifacts

CCTA problems: to detect functionally relevant lesions in distal coronary segments, diagonal branches and in vessels with heavy calcification

INTEGRATION ALLOWS:
- To detect balanced ischemia
- To enhance risk predictions
- To detect the culprit lesion
However, the clinical usefulness in terms of impact on treatment strategy and subsequently on outcome by hybrid imaging remains to be determined in prospective and long-term studies.


What do cardiologists look for?

- ACCURATE INFORMATION (BOTH ANATOMICAL AND FUNCTIONAL)
- EARLY DIAGNOSIS (ASAP...)
- MOLECULAR DIAGNOSIS
Thank You!

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