Multimodality Cardiac Imaging: Its Use in the Era of Value-based Reimbursement

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Cedars-Sinai Heart Institute
Professor of Medicine
UCLA School of Medicine

ACC DC
2015
Can Cardiac Imaging in CAD Provide Value?
Challenges
DISCLOSURE

Daniel S. Berman, M.D.
declares the following relationships:

Consultant: Spectrum-Dynamics
Molecular-Dynamics

Royalties: Cedars-Sinai Medical Center
Value-based Cardiac Imaging in CAD: Noninvasive Imaging

- The exciting:
  - Technology: always improving
- The realistic:
  - Proven value will be required for its use
Value-based Cardiac Imaging in CAD
Nuclear Cardiology, Cardiac CT and CMR

• Technologic improvements
• Value-based imaging
  – Prevention
  – Acute coronary syndromes
  – Stable ischemic heart disease
  – Heart failure
• Challenges
Value-based Cardiac Imaging in CAD
Nuclear Cardiology

- Instrumentation/software
  - Automatic quantitation
  - Increased resolution
    - SPECT: CZT
    - PET: Flurpiridaz
  - Decreased radiation
- Assessments: Adding to Perfusion and Viability
  - Anatomy and function: CAC scanning
  - Coronary flow reserve
  - Molecular imaging
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ML vs TPD alone

Machine learning
Arsanjani...Slomka
JNC 2013
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Automated assessment with machine learning will become routine

ML vs TPD alone

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Arsanjani...Slomka
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Berman

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Nakazato, et al JNC 2015
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Berman, Maddahi, et al JACC 2012
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*Nakazato et al JNC 2014
Einstein et al JNC 2014
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- Stress-only
- CZT (~1 mSv)*
- Reconstruction methods

*Nakazato et al JNC 2014
Einstein et al JNC 2014
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Adding CAC to PET/SPECT: Increases diagnostic certainty
Detects subclinical atherosclerosis

- Anatomy and function: CAC scanning
- Coronary flow reserve
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M. Di Carli
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Murthy: Circ, 2011
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CFR: Adds prognostic information to perfusion defect
Increases certainty; identifies diffuse disease

– Anatomy and function: CAC scanning
– Coronary flow reserve
– Molecular imaging

Murthy: Circ, 2011
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Distinguishing Stable from Active Atherosclerosis
Identifying the Vulnerable Patient

Fibroatheroma: Stable Plaque
Narula & Willerson, JACC (ed)

TCFA with Cap Rupture
Narula & Virmani, 1999

Berman
Distinguishing Stable from Active Atherosclerosis
Identifying the Vulnerable Patient

Current paradigm: Revascularize when: stenosis and ischemia
Potential paradigm: Revascularize the lesion likely to rupture

Narula & Willerson, JACC (ed) Narula & Virmani, 1999
F-18 Sodium Fluoride PET Identifies Ruptured and High-Risk Coronary Plaques

- 40 AMI
  - 93% uptake in culprit plaque at ICA
- 40 Stable angina
  - 45% uptake in plaques with high risk features (IVUS)

Joshi…Newby
Lancet 2013
F-18 Sodium Fluoride PET Identifies Ruptured and High-Risk Coronary Plaques

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- 40 Stable angina
  - 45% uptake in plaques with high risk features (IVUS)

Fluride F-18: Potential to alter treatment paradigm in SIHD

Joshi…Newby
Lancet 2013
Berman
Value-based Cardiac Imaging in CAD
Cardiac CT

• Instrumentation/software
  – Full coverage single beat
  – Higher temporal resolution 66 msec
  – Lower radiation <1 mSv
  – Model based interactive reconstruction

• Assessments
  – Plaque
  – Perfusion
  – Flow
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  – Plaque characteristics
    - Positive remodeling
    - Lipid core
    - Spotty calcification
    - Volume
  – Plaque
  – Perfusion
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  – Spectral CT
  – Model based iterative reconstruction

• Assessments
  – Plaque
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CT perfusion:
Predicts:
  Stenosis on ICA
  Rochitte, EHJ 2013
  Ischemia on SPECT
  Cury, JCCT 2015
Value-based Cardiac Imaging in CAD

Cardiac CT

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  – Flow
  \( \text{FFR}_{\text{CT}} \)
    - Uses rest CCTA
      - Computational fluid dynamics
      - No additional radiation
      - No adenosine
Cardiac MR in CAD

- Anatomy & morphology
- Function & wall motion
- Perfusion
- Coronary plaque
- Coronary MRA
- Viability

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Diagnostic accuracy of CMR perfusion for ischemic stenosis with FFR as reference: meta-analysis

Per patient (n=650): 90% sensitivity; 87% specificity
Per vessel (n=1073): 89% sensitivity; 86% specificity

Li M, et al JACCi 2014

Berman
Biograph mMR
Simultaneous, whole-body molecular MR (PET/MR)
Value-based Cardiac Imaging in CAD

• Technologic improvements
• Applications
  – Prevention
  – Acute coronary syndromes
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• Challenges
Value-based Cardiac Imaging in CAD

• Value = quality/cost*
  – Quality ≈ outcomes (e.g., MACE, QOL)
  – Cost: total costs related to episode of care*

• Future:
  – Value will be the driver;
    • Tests/procedures that add value will be “purchased” by third party carriers

*The “Value equation: health care outcomes achieved per dollar spent; Review article: Sarwar et al RadioGraphics 2015
Value-based Cardiac Imaging in CAD

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• Challenges
CT Coronary Artery Calcium (CAC)

• CAC: a marker of CAD
  – Burden of coronary atherosclerosis
• Integrated lifetime effect of all risk factors
  – Overcomes the limitations of FRS
  – Consistent evidence: incremental prognostic value

<1 mSv
(~ mammogram)
Single breath
No contrast
Novel Risk Markers for Cardiovascular Risk Assessment in Intermediate-Risk Subjects

Figure. Receiver Operator Characteristic Curves Showing Area Under the Curve for Incident Coronary Heart Disease and Incident Cardiovascular Disease in Intermediate-Risk MESA Participants

A. Incident coronary heart disease

- Framingham Risk Score (FRS) alone (reference)
- FRS plus coronary artery calcium
- FRS plus carotid intima-media thickness
- FRS plus brachial flow-mediated dilation
- FRS plus C-reactive protein
- FRS plus family history
- FRS plus ankle-brachial index

B. Incident cardiovascular disease

A, Receiver operator characteristic curves showing area under the curve for FRS alone, 0.623; FRS plus coronary artery calcium, 0.784 (P<.001); FRS plus intima-media thickness, 0.652 (P=.01); FRS plus flow-mediated dilation, 0.639 (P=.06); FRS plus high-sensitivity C-reactive protein, 0.640 (P=.03); FRS plus family history, 0.675

Yeboah JAMA 2012 - MESA
Novel Risk Markers for Cardiovascular Risk Assessment in Intermediate-Risk Subjects

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= FRS + CAC

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Consistent findings in multiple population-based studies

Berman
Yeboah JAMA 2012 - MESA
CAC may lead to better treatment / lifestyle

- More targeted preventive treatment
- Improvement in risk factor profile\(^1\)
- Intensification of Rx\(^2\)
- Better adherence to Rx\(^3,5\)
- Dietary modifications\(^4\)
- Increased exercise\(^4\)

\(^1\) Rozanski et al, JACC 2011 (EISNER Study)
\(^2\) Nasir K et al, Circ Cardiovasc Qual Outcomes 2010 (MESA)
\(^3\) Kalia NK et al, Atherosclerosis. 2006
\(^4\) Orakzai RH et al, Am J Cardiol 2008
\(^5\) Taylor A et al, JACC 2008
Imaging for Prevention
Coronary Calcium Screening

• Outcomes: ↑↑
• Costs: ↑
• Value: probably ↑
Value-based Cardiac Imaging in CAD

• Technologic improvements
• Applications
  – Prevention
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  – Heart failure
• Challenges
Rest or rest/stress MPI for Chest Pain in ED

49 M in ED

ERASE Trial (2002): 20% reduction in unnecessary admissions

- Can be performed in any patient
- Particularly useful in known CAD/ high CAC
Coronary CTA

- Sensitivity and specificity for CAD: ~ 95%/90%
- Higher than all other modalities
  - Per patient
  - Per vessel
  - Per segment
- Very high negative predictive value for events
Coronary CTA

- Sensitivity and specificity for CAD: ~ 95%/90%
- Higher than all other modalities
  - Per patient
  - Per vessel
  - Per segment
- Very high negative predictive value for events
Primary Outcome - Length of Hospital Stay

Hoffman, et al ACC 2012
Coronary CTA in Suspected ACS

– Reduces length of stay and time to diagnosis*
– Safely increases direct ED discharge rates
– No increase in costs of care**

• Consistent results in three large RCTs:
  Goldstein, et al JACC 2011
  Litt, et. al. NEJM, 2012
  Hoffman, et al ACC 2012
Position Statement

Investigational and Not Medically Necessary:

Coronary computed tomography angiography (CCTA) or coronary magnetic resonance angiography (MRA) is considered investigational and not medically necessary for all other indications, including, but not limited to, the following:

- Screening for coronary artery disease (CAD), either in asymptomatic individuals or as part of a preoperative evaluation; or
- Diagnosis of CAD, in individuals with acute or non-acute symptoms, or after a coronary intervention; or
- As a technique to evaluate cardiac function.
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Imaging for Acute Chest Pain
Coronary CTA

- Outcomes: no $\Delta$ or $\uparrow^*$
- Costs: $\downarrow^{**}$
- Value: $\uparrow$

* Length of stay and time to diagnosis: quality measures
**Large proportion of ED CCTAs are completely normal: potential to reduce subsequent ED visits not yet developed
Value-based Cardiac Imaging in CAD

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Noninvasive Imaging for CAD

Suspected CAD: Stable

Pre-test likelihood of CAD

Low-to-Intermediate (15-85%)

Stress imaging

• Most common approach
• Could be performed without imaging
Noninvasive Imaging for CAD
Suspected CAD: Stable

Pre-test likelihood of CAD

Low-to-Intermediate (15-85%)

Coronary CTA

• Growing as initial test
Prognostic Value of CCTA CAD Extent / Severity

23,854 patients w/o known CAD (57±13 years), 2.3 year f/u

Source: CONFIRM Min et al. J Am Coll Cardiol 2011
Consistent findings in all populations studied to date

23,854 patients w/o known CAD (57±13 years), 2.3 year f/u

Source: CONFIRM Min et al. J Am Coll Cardiol 2011
Long-term Prognosis For Normal CCTA

“Warranty Period” of a Normal CT: at least 7 years

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Follow-up (yr)</th>
<th>Imaging Equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ostrom (ACM)</td>
<td>2538</td>
<td>6.5</td>
<td>EBCT</td>
</tr>
<tr>
<td>CONFIRM (ACM)</td>
<td>1000</td>
<td>&gt;4</td>
<td>&gt;64-row CT</td>
</tr>
<tr>
<td>Andreini (MACE)</td>
<td>1304</td>
<td>4.3</td>
<td>64-row CT</td>
</tr>
<tr>
<td>Hadamitzky (MACE)</td>
<td>1584</td>
<td>5.6</td>
<td>16-/ 64-row CT</td>
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6426 patients, ~5.5 yr f/u

- CONFIRM >5 year f/u anticipated for ~10,000 patients 4/13

Source: Ostrom et al. JACC 2008; Min et al. J Am Coll Cardiol 2011; Andreini et al. JACC CVImaging 2012; Hadamitzky et al. (In press)
Long-term Prognosis For Normal CCTA

“Warranty Period” of a Normal CT: at least 7 years

- Ostrom (ACM): 2538 patients, 6.5 yr f/u, EBCT
- CONFIRM (ACM): 1000 patients, >4 yr f/u, >64-row CT
- Andreini (MACE): 1304 patients, 4.3 yr f/u, 64-row CT
- Hadamitzky (MACE): 1584 patients, 5.6 yr f/u, 16- / 64-row CT

6426 patients, ~5.5 yr f/u

- CONFIRM >5 year f/u anticipated for ~10,000 patients 4/13

“Warranty Period” of a normal CCTA: likely at least 7 years

Source: Ostrom et al. JACC 2008; Min et al. J Am Coll Cardiol 2011; Andreini et al. JACC CVImaging 2012; Hadamitzky et al. (In press)
Scot-Heart Trial

Trial:
• 4146 patients with suspected angina due to CHD
• Randomized to CCTA vs standard of care
• Follow-up: median 1.7 years

Conclusions:
• Changes and clarifies the diagnosis: 1 in 4
• Alters subsequent investigations: 1 in 6
• Changes treatments: 1 in 4
• May reduce fatal and non-fatal MI

Newby et al Lancet 2015
CTCA and Clinical Outcome

1.7 Years of Follow-up

CHD Death and Non-Fatal MI

- Standard Care
  - HR 0.62 [0.38-1.01], P=0.053

- CTCA

CHD Death, Non-Fatal MI and Non-fatal Stroke

- Standard Care
  - HR 0.64 [0.41-1.01], P=0.056

- CTCA

CTCA Standard Care

Follow Up (years)

CTCA Standard Care

Follow Up (years)

Proportion of patients with an event (%)
Trial: PROMISE Trial

- 10,003 symptomatic patients with no prior CAD referred for noninvasive testing
- Likelihood of CAD (Diamond-Forrester): 53%
- Randomized to CCTA or functional testing
  - (nuclear, echo, CMR)
- Follow-up: median 25 months
- Primary endpoint: death, MI, hosp, for UA, procedural complications (n=315, 3.1%; death or MI: 216, 2.1%)

Conclusions

- CTA no difference in clinical outcomes
- CTA strategy: lower rate of invasive catheterization without obstructive CAD

Primary Endpoint:
Death, MI, Unstable Angina, Major Complications

CTA: Functional
Hazard Ratio: 1.04
(95% CI: 0.83, 1.29)
P = 0.750


# at risk
<table>
<thead>
<tr>
<th></th>
<th>Baseline (0)</th>
<th>6 Mo.</th>
<th>12 Mo.</th>
<th>18 Mo.</th>
<th>24 Mo.</th>
<th>30 Mo.</th>
<th>36 Mo.</th>
<th>42 Mo.</th>
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<tr>
<td>CTA</td>
<td>4996</td>
<td>4703</td>
<td>4362</td>
<td>3551</td>
<td>2652</td>
<td>1705</td>
<td>902</td>
<td>269</td>
</tr>
<tr>
<td>Functional</td>
<td>5007</td>
<td>4536</td>
<td>4115</td>
<td>3331</td>
<td>2388</td>
<td>1518</td>
<td>832</td>
<td>258</td>
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Noninvasive Imaging for CAD
Suspected-known CAD

Risk-assessment

• All modalities validated for prognosis across multiple clinical presentations
• Evidence base for coronary CTA now extensive
• How to manage patients based on test results not yet established
  – Necessary to prove value
“What should I do about it?”

Level of risk

Very Low  Low  Borderline  Can’t tell  Medium  High

Assure  Prevent  + Stress  + Stress or cath  + Cath

Berman
Suspected CAD

Hypothesis: Value of Coronary CTA Depends on Pre-test Likelihood of CAD
Low-to Intermediate

- Outcomes: no $\Delta$
- Costs: ↓
- Value: ↑
Suspected CAD
Hypothesis: Value of Coronary CTA Depends on Pre-test Likelihood of CAD

Low-to Intermediate  High

• Outcomes: no \( \Delta \)
• Costs: ↓
• Value: ↑

• Outcomes: no \( \Delta \)
• Costs: ↑
• Value: ↓
Coronary CTA is less useful in several settings

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<th>Condition</th>
<th>CCTA</th>
<th>MPI</th>
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<tbody>
<tr>
<td>High CAC</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Renal failure</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Morbidly obese</td>
<td>-</td>
<td>+</td>
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Noninvasive Imaging for CAD

Suspected CAD

Pre-test likelihood of CAD

Intermediate to High (50-100%)

Ischemia Testing* (+ CAC)

*Possibly without imaging if patient can exercise
SPECT: Risk Increases as a Function of Stress Perfusion Abnormality

- Men and women
- Sx and Asx
- Diabetics
- Obese
- Renal Failure
- Arrhythmia
- High CAC Score
- Known CAD
  - MI
  - PCI
  - CABG

Data from over 50,000 patients

Risk* adjusted or unadjusted

Risk vs. Extent/Severity of Perfusion Defects

*Adjusted or unadjusted
Post-SPECT Cardiac Mortality and Rx Given Early Revascularization vs Medical Therapy

10,627
F/U: 1.9 ± 0.6 yrs
Risk adjusted

* p<0.001

Hachamovitch, et al. (Cedars-Sinai) Circulation 2003
Ischemia on MPI Predicts Benefit from Revascularization

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<td>No Known CAD</td>
<td>Circulation 2003</td>
</tr>
<tr>
<td>No Known CAD + EF</td>
<td>JNC 2006</td>
</tr>
<tr>
<td>Elderly</td>
<td>Circulation 2010</td>
</tr>
<tr>
<td>Prior revascularization</td>
<td>EHJ 2010</td>
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<tr>
<td>Prior MI</td>
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Hachamovitch, et al
ISCHEMIA Trial

International Study of Comparative Health Effectiveness with Medical and Invasive Approaches

Study Chair: Judith Hochman
Principal Investigator: David Maron

Sponsor: NHLBI

Berman
ISCHEMIA Trial

≥10% Ischemia*
LVEF ≥35%

Blinded CCTA
Exclude LM/NCA

RANDOMIZE

Cath
(Revasc+ OMT)

No Cath
(OMT)

• 3-6 yr. F/U

*SPECT, PET, echo, CMR
Core lab verification

• 8,000 stable CAD patients
• 3-6 yr. F/U

• 3-6 yr. F/U

• 3-6 yr. F/U

Berman
Suspected/Known Stable CAD
Hypothesis: Value of **Ischemia Testing** Depends on Pre-test Risk
Intermediate-to-high

- Outcomes: ↑
- Costs: ↓
- Value: ↑

- Diamond-Forrester: needs update
Yearly Prevalence of Abnormal and Ischemic SPECT Myocardial Perfusion Imaging Studies between 1991 and 2009

% Prevalence

Yearly Prevalence of Abnormal and Ischemic SPECT Myocardial Perfusion Imaging Studies between 1991 and 2009

% Ischemia
% Abnormal SPECT

N=39,515
Rozanski, et al JACC 2012 (Cedars-Sinai)
How could <10% of patients without known CAD currently undergoing SPECT have ischemia?
Diamond-Forrester Classification (DFC) overestimates likelihood of angiographically “significant” CAD by CCTA*.

Overall Obstructive CAD prevalence in patients with NonAng, AtypAng, and TypAng (n=8106)

expected by using DFC and CASS

Observed in CONFIRM

Ob-CAD prevalence (%)

0%
20%
40%
60%
80%
100%

51%
18%

Cheng, et al Circulation 2011 (CONFIRM)

* In patients referred for CCTA
Obstructive CAD identified by invasive coronary angiography correlates poorly with FFR

Tonino et al. JACC 2010
Obstructive CAD identified by invasive coronary angiography correlates poorly with FFR.

FAME: 57% of lesions with >50% stenosis had FFR <0.80

Tonino et al. JACC 2010
Suspected/Known Stable CAD
Hypothesis: Value of Ischemia Testing Depends on Pre-test Risk

Low
  • Outcomes: No $\Delta$
  • Costs: ↑
  • Value: ↓

Intermediate-to-high
  • Outcomes: ↑
  • Costs: ↓
  • Value: ↑

• Diamond-Forrester: needs update
• Min risk score: Am J Med 2015—potential for adoption
Value-based Cardiac Imaging in CAD

• Technologic improvements
• Applications
  – Prevention
  – Acute coronary syndromes
  – Stable ischemic heart disease
  – Heart failure:
• Challenges
Value-based Cardiac Imaging in CAD

• Technologic improvements

• Applications
  – Prevention
  – Acute coronary syndromes
  – Stable ischemic heart disease
  – Heart failure: PET, CMR

• Challenges
Value-based Cardiac Imaging in CAD

- Technologic improvements
- Applications
  - Prevention
  - Acute coronary syndromes
  - Stable ischemic heart disease
  - Heart failure
- Challenges
Can Cardiac Imaging in CAD Provide Value?

Challenges

- Must improve outcomes or reduce costs
- Imaging tests cannot improve outcomes unless they result in improved therapy
Can Cardiac Imaging in CAD Provide Value?

Challenges

- Must improve outcomes or reduce costs
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F-18-Fluorodeoxyglucose Positron Emission Tomography Imaging-Assisted Management of Patients With Severe Left Ventricular Dysfunction and Suspected Coronary Disease
A Randomized, Controlled Trial (PARR-2)

- 430 pts; HF + CAD; LV EF <35%
- Randomized to Standard care vs PET guided care
- Overall result: Death, MI, Rehosp at 1 y: p=0.15
  - Subset result: Appropriate action taken on PET findings: p=0.019
  - Subset result: Ottawa 5 (experienced PET centers): p=0.005
- Caveat: Imaging trial results depend on: test accuracy, incorporation of results into care, effectiveness of therapy

Beanlands et al JACC 2007
JNM 2010

Courtesy Pam Douglas
Value-based Cardiac Imaging in CAD

- Technology/assessments will improve across modalities and clinical settings
- Applications providing value will dominate
- Value
  - Will depend on the clinical setting
  - Requires linkage to therapeutic change
  - Evidence will be required
Thank you very much