YESTERDAY

- Functional Imaging constituted 95%+ of all work ups for CAD
- Performance of nuclear, stress echo and ETT were adequate, as intermediate and high risk patients were being tested
- LOW threshold to send to cardiac catherization
<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Sensitivity % (range)</th>
<th>Specificity % (range)</th>
<th># Studies</th>
<th># Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMT</td>
<td>68 (70-94)</td>
<td>77 (43-97)</td>
<td>132</td>
<td>24,027</td>
</tr>
<tr>
<td>Planar MPI</td>
<td>79 (70-94)</td>
<td>73 (43-97)</td>
<td>6</td>
<td>510</td>
</tr>
<tr>
<td>SPECT</td>
<td>88 (73-98)</td>
<td>77 (53-96)</td>
<td>8</td>
<td>628</td>
</tr>
<tr>
<td>Stress echo</td>
<td>76 (40-100)</td>
<td>88 (80-95)</td>
<td>10</td>
<td>1174</td>
</tr>
</tbody>
</table>

* NEJM Vol. 344, No. 24 June 14, 2001
TODAY

• More statins, preventive therapies, changing prevalence of obstructive disease
• Less smoking, more diabetes, more women being studied
• More COURAGE to treat medically
Rozanski JACC 2013

Frequency (% Ischemia and % Abnormal SPECT) over years from 1991 to 2009.
“CAC scanning, with or without treadmill exercise electrocardiography, could serve as potentially low-cost alternative to more expensive imaging tests for the initial workup of relatively lower-risk diagnostic patients.”
DATA TAKEN FROM “THE DAWN OF A NEW ERA - NON-INVASIVE CORONARY IMAGING” R. ERBEL HERZ 1996; 21, 75-77
The best predictor of a life threatening illness is the early manifestation of a life threatening illness

Sir Geoffrey Rose
Cardiac Epidemiologist
Known for “The Rose Principle”
Coronary Artery Scanning

- SEVERE CALCIFICATION
Global cardiovascular risk (Framingham risk score) + Consideration of family history of cardiovascular disease and lifestyle factors (e.g., strenuous exercise)

Risk classification:
- Low
- Low-intermediate
- Intermediate
- High

Coronary artery calcium score

Risk reclassification:
- Low (CAC=0)
- Intermediate (CAC=1-100)
- High (CAC>100)

Consider statin therapy
CTA vs Functional Meta Analysis AHA 2013

Diagnostic accuracy

• Nieman K et al. Heart. 2009;95:1669-75.

Outcome

2012;28:675-84.
Diagnostic accuracy - Nielson EHJI 2014

Sensitivity: CCTA 98% vs. XECG 67%, (p < 0.001)
Sensitivity: CCTA 99% vs. SPECT 73%, (p = 0.001)
Specificity: CCTA 82% vs. XECG 46%, (p < 0.001)
Specificity: CCTA 71% vs. SPECT 48%, (p = 0.14)
Obstructive CAD at Cath: NCDR 2005-2007

- 376,430 pts without CAD/MI or prior PCI/CABG
- Undergoing diagnostic cath to R/O CAD
- 59% of patients with positive stress tests had no obstructive CAD on invasive angio (False positive), 73% with equivocal test result

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>No Stress Test</th>
<th>Positive Stress Result</th>
<th>Equivocal Stress Result</th>
<th>Negative Stress Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>376,430</td>
<td>16%</td>
<td>68%</td>
<td>4%</td>
<td>12%</td>
</tr>
<tr>
<td>No CAD</td>
<td>233,518 (62%)</td>
<td>65%</td>
<td>59%</td>
<td>73%</td>
<td>72%</td>
</tr>
<tr>
<td>CAD</td>
<td>142,912 (38%)</td>
<td>35%</td>
<td>41%</td>
<td>27%</td>
<td>28%</td>
</tr>
</tbody>
</table>

Patel MR, Peterson ED, Dai D, Brennan JM, Redberg RF, Anderson HV, Brindis RG, Douglas PS. NEJM. 2010 Mar 11;362(10):886-95
Non-Invasive Functional Testing Prior to Angiography

CONVERSELY, 70% of all CCTA had obstructive disease, still 30% false positives

Data from an analysis of more than 385,000 patients at over 1,100 US hospitals

PATEL M NCDR AHJ 2014

Cury et al, JCCT 2014.
Figure 3. Sensitivity and specificity of noninvasive imaging techniques.
CCTA indicates coronary computed tomography angiography; CMR, cardiac magnetic resonance; ECHO, echocardiography; PET, positron emission tomography; and SPECT, single-photon computed emission tomography.
• So Anatomical Testing is more accurate than Functional Testing
• What about CV outcomes?
# CTA vs Functional Meta Analysis

## Myocardial infarction

<table>
<thead>
<tr>
<th>Study</th>
<th>Coronary CTA MI</th>
<th>Total</th>
<th>FT MI</th>
<th>Total</th>
<th>Coronary CTA OR (95% CI)</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPECT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min-2008</td>
<td>8</td>
<td>1930</td>
<td>43</td>
<td>7709</td>
<td>0.74 (0.35, 1.58)</td>
<td>12.11</td>
</tr>
<tr>
<td>Shreibati</td>
<td>17</td>
<td>8803</td>
<td>575</td>
<td>131768</td>
<td>0.44 (0.27, 0.72)</td>
<td>50.68</td>
</tr>
<tr>
<td>Cheezum</td>
<td>0</td>
<td>252</td>
<td>0</td>
<td>241</td>
<td>(Excluded)</td>
<td>0.00</td>
</tr>
<tr>
<td>Subtotal test for OR=1: p=0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.50 (0.33, 0.75)</td>
<td>62.79</td>
</tr>
<tr>
<td>Heterogeneity: $I^2=23.0%$, p=0.254</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XECG</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nielsen</td>
<td>0</td>
<td>251</td>
<td>3</td>
<td>244</td>
<td>0.14 (0.01, 2.70)</td>
<td>2.49</td>
</tr>
<tr>
<td>Shreibati</td>
<td>17</td>
<td>8803</td>
<td>195</td>
<td>60868</td>
<td>0.60 (0.37, 0.99)</td>
<td>34.72</td>
</tr>
<tr>
<td>Subtotal test for OR=1: p=0.02</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.57 (0.35, 0.93)</td>
<td>37.21</td>
</tr>
<tr>
<td>Heterogeneity: $I^2=0.0%$, p=0.338</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall test for OR=1: p&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.53 (0.39, 0.72)</td>
<td>100.00</td>
</tr>
<tr>
<td>Heterogeneity: $I^2=0.0%$, p=0.502</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nielson EHJI 2014
SPARC STUDY
Hlatky JACC April 2014

P<0.0001

CTA (N=590)  |  SPECT (N=565)  |  PET (N=548)

- NonFatal MI
- Death
- Total
“CTA may be a better diagnostic tool and may play a key role in prognostic stratification”
Death or Non-fatal MI

CTA: Functional
Hazard Ratio: 0.88
(95% CI: 0.67, 1.15)
P-value: 0.348

12 Months
HR 0.66; p=0.049

Percent with event

Months since randomization

# at risk
CTA Baseline (0) 6 Mo. 12 Mo. 18 Mo. 24 Mo. 30 Mo. 36 Mo. 42 Mo.
4996 4739 4409 3599 2686 1732 918 276
Functional 5007 4563 4148 3365 2415 1540 846 262
## PROMISE TRIAL

### Catheterization Without Obstructive CAD ≤90 days

<table>
<thead>
<tr>
<th></th>
<th>CTA (n=4996)</th>
<th>Functional (n=5007)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive catheterization without obstructive CAD — N (%)</td>
<td>170 (3.4%)</td>
<td>213 (4.3%)</td>
<td>0.022</td>
</tr>
<tr>
<td>Invasive catheterization</td>
<td>609 (12.2%)</td>
<td>480 (9.1%)</td>
<td></td>
</tr>
<tr>
<td>With obstructive CAD (% of caths.)</td>
<td>439 (72.1%)</td>
<td>193 (47.5%)</td>
<td></td>
</tr>
<tr>
<td>Revascularization</td>
<td>311 (6.2%)</td>
<td>158 (3.2%)</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>72</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>
PROMISE TRIAL
Primary Endpoint – Death, MI, and UA

Anatomic Testing
- Abnormality vs. Normal: Hazard Ratio (95% CI)
  - Severe Abnormalities: 10.13 (5.15, 19.92)
  - Moderate Abnormalities: 7.67 (3.83, 15.37)
  - Mild Abnormalities: 2.94 (1.64, 5.26)
  - Normal

Functional Testing
- Abnormality vs. Normal: Hazard Ratio (95% CI)
  - Severe Abnormalities: 3.88 (2.58, 5.85)
  - Moderate Abnormalities: 2.65 (1.46, 4.83)
  - Mild Abnormalities: 0.94 (0.47, 1.89)
  - Normal

Coronary CTA: Obstructive CAD >70%

C-Index: 0.72 (95% CI: 0.68, 0.77) 0.64 (95% CI: 0.59, 0.69) p=0.014
## Net Reclassification Index (NRI)

<table>
<thead>
<tr>
<th>FRS plus Test Results vs. FRS Alone</th>
<th>Anatomical Testing</th>
<th>Functional Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of Events correctly Reclassified</td>
<td>Proportion of Non-events correctly Reclassified</td>
<td>NRI (95% Bootstrap CI)</td>
</tr>
<tr>
<td><strong>Death/MI/UA</strong></td>
<td>0.18</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>CV death/MI/UA</strong></td>
<td>0.32</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>CV death/MI</strong></td>
<td>0.41</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Reclassification is based on the change (continuous) in the estimated risk probability.
• Discriminatory ability of coronary CTA was significantly better than functional testing (c-index: 0.73 (95% CI: 0.69, 0.77) vs. 0.64 (95% CI: 0.59, 0.69); p=0.011).

• Net Reclassification Index: CCTA 0.70 (95%: 0.52, 0.89) and Functional 0.40 (95%: 0.24, 0.56).

• **CCTA provided higher discrimination, reclassification and more robust event prediction**
• 4,146 patients (mean age: 57 years, 56% male) who presented with chest pain due to suspected coronary artery disease

• Changes in diagnosis occurred in 25% of patients receiving CTCA and only 1% of pts receiving standard protocol (P < .001).

• after 3 years, the proportion of patients with events was reduced by 50% in the CTCA group (~2.5% vs ~1.7%, P = .015).
Future of Cardiac Imaging

- More emphasis on early atherosclerosis and aggressive medical/lifestyle management
- Less emphasis on obstruction and stenting
- Continued decline, probably rapidly, of functional testing – concerns of cost, accuracy and radiation
So, we can continue what we are doing...

CT ANGIOGRAM = LARGE SOFT PLAQUE, INSTITUTE STATIN, ASPIRIN LIFESTYLE...

Or with CTA
We can do better!!

FUNCTIONAL TEST RESULT = NORMAL STUDY, Reassure patient

CT ANGIOGRAM = LARGE SOFT PLAQUE, INSTITUTE STATIN, ASPIRIN LIFESTYLE....
Why is CTA-Superior?

• Superior test performance
  – ↓ false negative test results/untreated CAD
  • ↓ coronary events

• Better detection of non-obstructive CAD
  • Improved preventive treatment and adherence
  – Longer ‘warranty’ period with fewer repeat tests
  • ↓ hospitalizations during follow up
Stable chest pain pathway

2. Diagnostic testing for people in whom stable angina cannot be diagnosed or excluded by clinical assessment alone.

- Estimated likelihood of CAD 10 to 29%
  - CT calcium scoring
    - score is zero
      - Investigate other causes of chest pain**
    - score is 1-400
      - 64-slice (or above) CT coronary angiography
      - Significant CAD
        - Treat as stable angina
      - Uncertain
      - Investigate other causes of chest pain**
  - Follow pathway for 61-90% CAD

- Estimated likelihood of CAD 30-60%
  - Appropriate functional imaging test (see box 5 overleaf). If reversible myocardial ischaemia found, treat as stable angina. If not, investigate other causes of chest pain**
  - Reversible myocardial ischaemia
    - Yes
      - Treat as stable angina
    - Uncertain
Testing and Costs Go Down after implementation of NICE – BMJ 2015

**Figure 1** Mean costs of investigations per patient pre-CG95 (Clinical Guideline 95) and post-CG95.

**Figure 2** Mean number of investigations per patient preimplementation and postimplementation of CG95 (Clinical Guideline 95).
SYMPTOMATIC ALGORITHM

Determine Probability of Coronary Artery Disease

Low Pretest Probability (0-50%)
- CT ANGIOGRAM

Intermediate Pretest Probability (50-80%)
- FUNCTIONAL TESTING

High Pretest Probability
- CARDIAC CATHETERIZATION
UK NICE Guidelines 2016

Offer 64-slice (or above) CT coronary angiography if:

- clinical assessment (see recommendation 1.3.3.1) indicates typical or atypical anginal chest pain, or
- clinical assessment indicates non-anginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves.

Additional diagnostic investigations

1. Offer non-invasive functional imaging (see section 1.3.6) for myocardial ischaemia if 64-slice (or above) CT coronary angiography has shown CAD of uncertain functional significance or is nondiagnostic. [2016]

2. Offer invasive coronary angiography as a second-line investigation when the results of non-invasive functional imaging are inconclusive. [2016]
What About FFR-CT?

LAD stenosis 70-90%

FFR 0.94

FFR<sub>CT</sub> 0.93

FFR<sub>CT</sub> Model
Per-Patient Diagnostic Performance vs. CT

- CT (>50%)
- FFR<sub>CT</sub> (≤ 0.80)

<table>
<thead>
<tr>
<th>Metric</th>
<th>CT (53%)</th>
<th>FFR&lt;sub&gt;CT&lt;/sub&gt; (81%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>53</td>
<td>81</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Specificity</td>
<td>81</td>
<td>79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PPV</td>
<td>40</td>
<td>65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>94</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>NPV</td>
<td>92</td>
<td>93</td>
<td></td>
</tr>
</tbody>
</table>

Platform Study – Douglas et al

Usual Care Cohort

Patients With Suspected CAD → Usual Care Path → Invasive Coronary Angiography (ICA)

Obstructive CAD → Revascularization

No Obstructive CAD

CTA/FFR<sub>CT</sub>-guided Cohort

Patients With Suspected CAD → CTA/FFR<sub>CT</sub> → Invasive Coronary Angiography (ICA)

Obstructive CAD → Revascularization

No Obstructive CAD → No Need for ICA

**CONSERVE Trial – ESC 2016**

**Study Design**

Stable Patients with Suspected CAD
Referred to ACC/AHA Guideline-Indicated Non-emergent ICA

RANDOMIZE

- **Direct Catheterization Strategy (ICA)**
  - MD Discretion

- **Selective Catheterization Strategy (CCTA)**
  - MD Discretion
Primary Endpoint (Clinical)

### MACE Rates

<table>
<thead>
<tr>
<th></th>
<th>Direct ICA</th>
<th>Selective ICA</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.6% (33/719)</td>
<td>33 (4.6%)</td>
<td>36 (4.6%)</td>
</tr>
<tr>
<td>4.6% (36/784)</td>
<td>33 (4.6%)</td>
<td>36 (4.6%)</td>
</tr>
</tbody>
</table>

Hazard Ratio for MACE (p=0.99)

<table>
<thead>
<tr>
<th>Event</th>
<th>Overall</th>
<th>Direct ICA</th>
<th>Selective ICA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE (primary)</td>
<td>69 (4.6%)</td>
<td>33 (4.6%)</td>
<td>36 (4.6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Non-fatal MI</td>
<td>4 (0.3%)</td>
<td>2 (0.3%)</td>
<td>2 (0.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>UA</td>
<td>17 (1.1%)</td>
<td>8 (1.1%)</td>
<td>9 (1.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Urgent / emergent revascularization</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>-</td>
</tr>
<tr>
<td>CV hospitalization</td>
<td>64 (4.3%)</td>
<td>31 (4.3%)</td>
<td>33 (4.2%)</td>
<td>1.00</td>
</tr>
<tr>
<td>CV Death</td>
<td>3 (0.2%)</td>
<td>1 (0.1%)</td>
<td>2 (0.3%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Stroke</td>
<td>4 (0.3%)</td>
<td>2 (0.3%)</td>
<td>2 (0.3%)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
## CONSERVE RESULTS

### Per-Patient Resource Utilization and Costs

<table>
<thead>
<tr>
<th>Per-Patient</th>
<th>Direct ICA</th>
<th>Selective ICA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA (Index + Downstream)</td>
<td>1.02</td>
<td>0.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-78% reduction</td>
<td></td>
</tr>
<tr>
<td>Revascularization</td>
<td>0.17</td>
<td>0.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-41% reduction</td>
<td></td>
</tr>
<tr>
<td>Non-invasive testing (Index + Downstream)</td>
<td>0.15</td>
<td>1.17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-invasive testing (Downstream)</td>
<td>0.15</td>
<td>0.17</td>
<td>0.27</td>
</tr>
<tr>
<td>CV hospitalizations</td>
<td>0.04</td>
<td>0.04</td>
<td>0.95</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>3.04</td>
<td>2.82</td>
<td>0.018</td>
</tr>
<tr>
<td>Cardiovascular Costs* (USD)</td>
<td>6,746</td>
<td>3,338</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-60% reduction</td>
<td></td>
</tr>
</tbody>
</table>

*Costs include all components of resource utilization during the trial period*
Conclusions

- Compared to Direct ICA, Selective ICA demonstrated at 12 months:
  - No differences in MACE
  - Lower rates of ICA
  - Lower rates of coronary revascularization
  - Lower cardiovascular costs

- For ACC / AHA guideline-indicated ICA, Selective ICA informed by CCTA was associated with identical clinical outcomes while reducing ICA by nearly 80%.
Current CCTA dose is significantly reduced

Multicenter study of 449 patients undergoing CCTA after implementation of a standardized image acquisition protocol that employed prospective gating, reduced tube voltage, lower tube current and reduced Z-axis coverage.

Source: Labounty, Leipsic, Earls, Min et al. AJC 2010
Conclusions

• With increasing accuracy and decreasing radiation exposure, CT angiography will become the dominant method to evaluate coronary artery disease.

• For Preventive-minded physicians, the ability to see atherosclerosis will enhance patient selection and improve adherence.