**Coronary Atherosclerotic Plaque Imaging with ECG-gated CT**

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**ECG-gated MDCT**

1. Detection of coronary artery stenosis / occlusion  
2. Coronary calcium scoring  
3. Evaluation of atherosclerotic plaque  
4. Evaluation of stent patency  
5. Postoperative evaluation of bypassed vessels  
6. Myocardial imaging  
7. Evaluation of myocardial function  
8. Coronary artery anomalies

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**Coronary Atherosclerosis**

Stary, Circulation 1995  
Fayad, Circ Res 2001

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**Imaging Modality**

- IVUS: Clinical gold standard  
  - Characterization: soft, fibrotic, calcified  
- Angioscopy  
- MRI  
  - Coronary MRA, Wall imaging  
  - New contrast media: ex. USPIO (macrophage)  
- CT  
  - Coronary calcium scoring  
  - Coronary CTA

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**CT Density**

Rule of thumb:  
The CT value of water is 0 and air -1020. The relative values of the other tissues are calculated relative to that of water:  

This is the so-called CT number in Hounsfield unit (HU)
CT for Coronary Atherosclerosis

- Coronary Calcium Scoring
  - EBCT method (since 1990)
  - Relatively large data
  - No contrast agent / low radiation
  - Indirect assessment of noncalcified plaque
- Coronary CT angiography
  - New technique
  - Lumen + wall change
  - Contrast-enhanced / high radiation
  - Limited data available

Coronary Calcium Scoring

Clinical impact

- Evidence of coronary atherosclerosis
- Correlates with total plaque burden
- Possible indicator for future myocardial events in asymptomatic high risk persons

Interpretation of Ca. Score

<table>
<thead>
<tr>
<th>EBCT Score (Agatston Method)</th>
<th>Interpretation</th>
<th>Age- and sex-specific (score percentiles)</th>
<th>Risk Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-11</td>
<td>Nonminimal plaque</td>
<td>0-25</td>
<td>Small risk</td>
</tr>
<tr>
<td>11-100</td>
<td>Some plaque present</td>
<td>26-50</td>
<td>Moderate risk</td>
</tr>
<tr>
<td>111-400</td>
<td>Moderate plaque burden</td>
<td>51-75</td>
<td>Increased risk</td>
</tr>
<tr>
<td>401-1000</td>
<td>Severe plaque burden</td>
<td>75-90</td>
<td>High risk</td>
</tr>
<tr>
<td>&gt; 1000</td>
<td>Vary severe plaque burden</td>
<td>&gt; 90</td>
<td>Very high risk</td>
</tr>
</tbody>
</table>

Prognostic Value of Ca. Score: EBCT Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>No.</th>
<th>F/U (mo)</th>
<th>CAC in pts with events</th>
<th>CAC in pts without events</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arad</td>
<td>1177</td>
<td>43</td>
<td>764 ± 935</td>
<td>135 ± 432</td>
<td>14.3</td>
</tr>
<tr>
<td>Raggi</td>
<td>632</td>
<td>32</td>
<td>303 ± 441</td>
<td>92 ± 240</td>
<td>12.5</td>
</tr>
<tr>
<td>Park</td>
<td>967</td>
<td>77</td>
<td>395 ± 571</td>
<td>195 ± 378</td>
<td>4.4-</td>
</tr>
</tbody>
</table>

Prognostic Value of CAC Screening

- 10,377 asymptomatic subjects
- 5 y follow-up, death rate = 2.4%
- CAC was independent predictor of mortality (p<.001)
- 5-y risk-adjusted survival was 95% for score > 1,000, 99% for score < 10.
- Risk-adjusted relative risk value for CAC, compared with CAC < 10 : 1.7, 2.5, 4.0 for >100, >400, >1000

Shaw et al. Radiology 2003;228:826-833
ACC/AHA Consensus (2000)

1. A negative EBCT test makes the presence of atherosclerotic plaque, including unstable plaque, very unlikely.
2. A negative test is highly unlikely in the presence of significant luminal obstructive disease.
3. Negative tests occur in the majority of patients who have angiographically normal coronary arteries.
4. A negative test may be consistent with a low risk of a cardiovascular event in the next 2 to 5 years.
5. A positive EBCT confirms the presence of a coronary atherosclerotic plaque.
6. The greater the amount of calcium, the greater the likelihood of occlusive CAD, but there is not a 1-to-1 relationship, and findings may not be site specific.
7. The total amount of calcium correlates best with the total amount of atherosclerotic plaque, although the true “plaque burden” is underestimated.
8. A high calcium score may be consistent with moderate to high risk of a cardiovascular event within the next 2 to 5 years.

Suggested Guidelines for CAC Scoring (Partner’s HealthCare System 2002)

• Not recommended for asymptomatic low-risk subjects
• Positive test might be valuable in determining actual risk (apparently intermediate → actually high risk)

Ca. Scoring: Problems

• Interscan, interobserver, intraobserver variability
• Is it OK to use EBCT data in interpreting MDCT?
• What is the best score?
  – Agaston vs. Volume vs. Mass
• No standardized imaging technique
• No Korean Reference Data
• Noncalcified vulnerable plaque

CT for Coronary atherosclerosis

• Coronary Calcium Scoring
  – EBCT method (since 1990)
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Plaque Imaging
Plaque Characterization

**MDCT vs IVUS**
- Schroeder, JACC 2001
  - 15 pts
  - >40% stenosis
  - 34 out of 40 plaque

**MDCT vs Histology**
- Becker, Eur Radiol 2003
  - 11 human cadaver hearts
  - 50 by macroscopic exam, 40 by CT
  - 33 lesions direct comparison
  - CT number
    - Lipid-rich (VI, Va): 47 ± 9 HU
    - Fibrous-rich (Vb, Vc): 104 ± 28 HU
  - Failed to detect type I-III lesions

**Detection of Nonstenotic Plaque**
- Seg. Based Comparison: 16-CT vs IVUS (n = 22)
  - Noncalcified Plaque
    - Sens, 78%; Spec, 87%.
  - Calcified Plaque
    - Sens, 94%; Spec, 94%.
  - Underestimation of plaque volume by MDCT (24 vs 43 mm³, p < .001)

**MDCT vs Histology**
- Schroeder et al. JCAT 2004
  - 12 human hearts
  - Histology (Stary classification) vs CT (density)

**CT Density**
- Rule of thumb:
  - The CT value of water is 0 and air ~1000. The relative values of the other tissues are calculated relative to that of water.
  - This is the so-called CT number in Hounsfield unit (HU).
Vulnerable Plaque

- By Little (1990) and Muller (1992)
- Lesion prone to thrombosis
- Sudden thrombotic occlusion (Falk, Circulation, 1995)
  - Often occurs in area of moderate pre-existing atherosclerosis
  - Plaque progression: result of episodic thrombosis and organization
  - Risk of plaque rupture correlates only weakly with the degree of stenosis
- Identifying a plaque prone to thrombosis will predict the majority of AMI and sudden death.

Vulnerable Plaque: Diagnosis

Major Criteria
- Active inflammation
- Thin cap with a large lipid core
- Endothelial denudation with superficial platelet aggregation
- Fissured plaque
- Stenosis > 90%

Minor Criteria
- Superficial calcified nodule
- Glistening yellow on angiography
- Intraplaque hemorrhage
- Endothelial dysfunction
- Outward remodeling

What is Vulnerable Plaque?

- Large lipid-rich area with thin fibrous cap
- Large lipid core is associated with plaque vulnerability and MI (Virmani, Arterioscler
  Thromb Vasc Biol 2000)
  - 80% of ruptured plaque: necrotic cores larger than 1.0 mm²
  - 90%: lipid core greater than 10% of plaque area

Detection of Vulnerable Plaque

- 30 patients with heart rate < 66/min
- All patients underwent 3 vessel IVUS
- Coronary CTA
  - Reconstructed at mid-diastole, 1mm/0.3mm
  - Cross-sectional MPR image in 0.2mm interval
- Two radiologists blind to the IVUS result, independently
- Lipid Core: low density area in vessel wall
  - CT number <60HU / Area > 5 mm²
- Nine segment model
  - LM, pLAD, mLAD, dLAD, pLCx, mLCx, pRCA, mRCA, dRCA

Detection of Lipid-core: AMC

- 30 patients with heart rate < 66/min
- All patients underwent 3 vessel IVUS
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Seo JB 2004 KRS, RSNA
Case 1: Stenotic Segment
49/M AMI, mLAD
36 mm from LAD-LCx bifurcation

Case 2: Nonstenotic Segment
72/M AMI, pRCA
32 mm from RCA ostium

Results
- Assessable: 230/270 segments
  - 25 segment: poor CT image quality
  - 15 segment: failure of IVUS
- IVUS: 22 lipid cores (13 with stenosis, 9 without)
- Detection of hypoechoic (lipid-rich) plaque

<table>
<thead>
<tr>
<th></th>
<th>Reader 1</th>
<th>Reader 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>73%</td>
<td>68%</td>
</tr>
<tr>
<td>Specificity</td>
<td>92%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Interobserver agreement: kappa 0.608

* Ten concordant false positive lesions: IVUS misdiagnosis?

CT Detection of Lipid Core

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>All seg.</td>
<td>10% (22/230)</td>
<td>73% 86% 92%</td>
<td>90%</td>
</tr>
<tr>
<td>Stenotic seg.</td>
<td>31% (13/42)</td>
<td>85 69 69 76</td>
<td></td>
</tr>
<tr>
<td>Nonstenotic seg.</td>
<td>5% (9/188)</td>
<td>56 67 96 92</td>
<td></td>
</tr>
<tr>
<td>Left main</td>
<td>7% (2/30)</td>
<td>100 100 89 86</td>
<td></td>
</tr>
<tr>
<td>LAD segments</td>
<td>10% (8/87)</td>
<td>100 78 92 86</td>
<td></td>
</tr>
<tr>
<td>LCx segments</td>
<td>8% (4/50)</td>
<td>25 50 89 94</td>
<td></td>
</tr>
<tr>
<td>RCA segments</td>
<td>11% (7/63)</td>
<td>57 57 95 95</td>
<td></td>
</tr>
</tbody>
</table>

* Interobserver agreement (Kappa): 0.608

False Positive Lesions
- 17 FP lesions in reader 1 / 21 in reader 2 results
- 10 false positive lesions on CT are concordant between two readers

- IVUS: gold standard but subjective
- False positive on CT or IVUS misdiagnosed lesion?
- No histopathologic correlation
Conclusion

• When compared with IVUS, ECG-gated CT with dedicated postprocessing method showed reasonably high accuracy and interobserver agreement in detecting lipid-rich plaque.

• ECG-gated cardiac CT may be used as a noninvasive tool to detect vulnerable, lipid-rich, necrotic core in coronary arterial wall.

Plaque Characterization

• Leber AW, JACC, 2004
  – 37 patient with HR < 65/min
  – 58 vessels analyzable on MDCT / 68 IVUS

<table>
<thead>
<tr>
<th>IVUS</th>
<th>Accuracy</th>
<th>CT Number (HU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoechoic (lipid-rich)</td>
<td>62/80 (78%)</td>
<td>49 ± 22</td>
</tr>
<tr>
<td>Hyperechoic (fibrous)</td>
<td>87/112 (78%)</td>
<td>91 ± 22</td>
</tr>
<tr>
<td>Calcified</td>
<td>150/158 (95%)</td>
<td>391 ± 156</td>
</tr>
<tr>
<td>Exclude plaque</td>
<td>484/525 (92%)</td>
<td></td>
</tr>
</tbody>
</table>

Detection of Vulnerable Nonstenotic Plaque

• Caussin et al. Am J Cardiol 2004
  – 21 patients with ACS
  – CT detection of vulnerable components
    • Rich lipid area / plaque disruption / eccentricity, arterial remodeling, calcification
  – Goldstandard; IVUS

Plaque in Mildly-Stenotic Seg.

• 46 LCA segments in 14 pts.
• 37 segments (80.4%) assessable
• Plaque presence / calcification / distribution / positive remodeling
• ROC analysis

Listing 2 Intravascular Ultrasound (IVUS) Versus Computed Tomography (CT)

<table>
<thead>
<tr>
<th>IVUS</th>
<th>CT</th>
<th>Sensivity</th>
<th>Specificity</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remodeling</td>
<td>7 (7%)</td>
<td>0 (0%)</td>
<td>100%</td>
<td>90%</td>
</tr>
<tr>
<td>Hypoechoic</td>
<td>19 (95%)</td>
<td>19 (95%)</td>
<td>100%</td>
<td>95%</td>
</tr>
<tr>
<td>Echolucency</td>
<td>19 (95%)</td>
<td>19 (95%)</td>
<td>100%</td>
<td>95%</td>
</tr>
<tr>
<td>Calcified</td>
<td>7 (72%)</td>
<td>0 (0%)</td>
<td>100%</td>
<td>92%</td>
</tr>
<tr>
<td>Plaque area</td>
<td>20 (2%)</td>
<td>0 (0%)</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Density</td>
<td>20 (2%)</td>
<td>0 (0%)</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>CT tissue index, MDCT normalized</td>
<td>18 (17%)</td>
<td>18 (17%)</td>
<td>85%</td>
<td>80%</td>
</tr>
</tbody>
</table>

IVUS comparison: 32 vessels / 18 pts

<table>
<thead>
<tr>
<th>IVUS</th>
<th>CT</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque CSA</td>
<td>8.1 mm²</td>
<td>7.3</td>
</tr>
<tr>
<td>Lumen CSA</td>
<td>8.4 mm²</td>
<td>9.4</td>
</tr>
<tr>
<td>EEM CSA</td>
<td>16.4 mm²</td>
<td>16.7</td>
</tr>
<tr>
<td>% vessel obstruction</td>
<td>50.4 %</td>
<td>41.1</td>
</tr>
</tbody>
</table>
Accuracy of 64-Slice Computed Tomography to Classify and Quantify Plaque Volumes in the Proximal Coronary System

A Comparative Study Using Intravascular Ultrasound

- Leber et al. 2006 JACC
- 19 pts / 36 vessel
- Correct detection:
  - 54/65 (83%) noncalcified
  - 50/63 (94%) mixed
  - 41/43 (95%) calcified
  - 7/10 (70%) lipid pool
- Plaque volume:
  - $r^2 = 0.69$
  - Underestimation of mixed/noncalc+ plaque
  - Overestimation of calc plaque

Limitations of CT Angiography

- Limited data available
- Limited temporal resolution
  - motion artifact (RCA)
  - heart rate control
- Limited spatial resolution
  - One pixel: 0.3x0.3x0.4-6mm
- Time consuming; dedicated software
- Influence of intracoronary attenuation on coronary plaque measurement (Cademartiri, Eur Radiol, 2005)

New Software for Plaque Characterization of Quantification

Plaque Characterization

Courtesy of Dennis Foley, M.D.

Quantification

CT Angiography for Plaque Imaging

- Non-invasive / repeated study
- Lumen + wall
- Objective assessment
  - Software dependent
- Ongoing technical improvement
Perspective

• Future studies
  – Accuracy / limitation
  – Clinical impact
  – Research
    • Pathogenesis
    • Monitoring of drug effect

Plaque Monitoring

• 53/M / Regression of plaque (avostatin therapy)
• Johnson KM, AJR, 2006