**IVUS vs CCTA**

- IVUS has better spatial resolution, but at 20-fold increased cost and allows only 1-2 segment evaluation.
- CCTA is inexpensive, non-invasive, and allows evaluation of all coronary segments.
Plaque burden and CTA

- Large non-calcified
- Plaque areas with positive remodeling

Madaj, Karlsberg, Karpman, Budoff
- Acad Rad 2012

Figure 1. A large nonculified plaque (arrow) in the proximal left anterior descending artery.
Glagov Hypothesis: Coronary Remodeling

Progression

Artery can compensate for up to 40% plaque volume (lumen size remains constant)

Artery at maximum expansion: lumen narrows

Normal vessel
Minimal CAD
Moderate CAD
Severe CAD

Vulnerable Plaque with Spotty Calcification (<90 degree arc)
Virmani et al. Pathology of the Vulnerable Plaque

A

C16

Lp

Th

B
Napkin Ring Sign
The risk for an acute coronary event was 22% in subjects with PR and LAP. An ACS developed in 11% of subjects with either of the 2 features. Only 0.5% of the patients without either feature had an acute coronary event, providing a strong negative predictive
Plaque Progression with CT Angiography
Semi-Automated CTCA Vessel/Plaque Analysis – QAngioCT (Research)
REPRODUCIBILITY – 50 scans

**Graph B**

- **Total plaque volume (mm³)** vs **Total plaque volume (mm³) observer 1 first time**
- **R² Linear = 0.994**
- **P < 0.001**
Plaque Analysis

- Diameter Stenosis – \( \frac{x-y}{100} \)
Plaque Analysis – Area Stenosis

\[
\text{Area Stenosis} = \frac{(A1 - A2)}{100}
\]
Other Plaque Parameters Measured

- Plaque Burden Area = (Vessel wall Area – Luminal Area)
Remodelling Index

Mean Reference Area (A1)  Vessel wall area at maximum stenosis (A2)

RI – A2/A1 (Positive Remodelling if > 1.05)
Prospect MSCT vs IVUS Study

Figure 3. Association Between Mean Low-Density Lipoprotein Cholesterol Levels and Median Change in Percent Atheroma Volume for Several Intravascular Ultrasound Studies
Plaque Progression with CTA

- Reducing radiation doses with Cardiac CT angiography have allowed for serial studies
- Excellent correlation with IVUS plaque volumes has increased confidence in using a less invasive measure
- Quantitation of CTA plaque has improved with better workstations
Annualized plaque progression between patients with or without diabetes by multivariable linear regression models (n=64)
Changes of CCTA-measured plaque volumes (in mm$^3$) over 12 months.

We evaluated 100 patients with serial CCTA over 1 year, 60 on statin therapy, 40 on placebo

<table>
<thead>
<tr>
<th>Plaque Measures</th>
<th>Placebo (n=40)</th>
<th>Statin (n=60)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Plaque Volume</td>
<td>31.0</td>
<td>-33.3</td>
<td>0.0006</td>
</tr>
<tr>
<td>Non-calcified Plaque Volume</td>
<td>13.8</td>
<td>-47.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low Attenuation Plaque</td>
<td>5.9</td>
<td>-12.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calcified Plaque Volume</td>
<td>29.3</td>
<td>10</td>
<td>0.133</td>
</tr>
</tbody>
</table>
Effects of statin therapy on coronary artery plaque volume and high-risk plaque morphology in HIV-infected patients with subclinical atherosclerosis: a randomised, double-blind, placebo-controlled trial
5-Lipoxygenase Inhibitor VIA-2291
Budoff Et al 2012
6 Month F/U – Budoff 2012
Changes of CCTA-measured plaque volumes (in mm$^3$) over 6 months.

<table>
<thead>
<tr>
<th>Plaque Measures</th>
<th>Placebo (n=17)</th>
<th>VIA 2291 (n=39)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrotic Core Plaque Volume</td>
<td>5.9±20.7</td>
<td>-9.7±33.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fibrofatty Plaque Volume</td>
<td>11.1±13.3</td>
<td>-0.9±2.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Fibro-calcified Plaque Volume</td>
<td>-0.1±6.22</td>
<td>-14.3±6.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Calcified Plaque Volume</td>
<td>3.9±3.2</td>
<td>0.2±0.4</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Budoff Circulation 2011 – 5-Lipoxygenase Inhibitor
Garlic 4 – REGRESSION OF PLAQUE

Baseline

Follow-up

% TPV = 34.2%
% NCP = 33.8%
% LAP = 8.4%
% DC = 0.08%

% TPV = 30.0%
% NCP = 27.4%
% LAP = 3.7%
% DC = 0.44%
Garlic – Matsumoto 2016

- Total Plaque
- Soft Plaque
- Low Att Plaque
- Calcium

AGE
Placebo
Testosterone Trial (5U01AG030644)

- A double blind placebo controlled study to assess 170 participants with dual CT angiograms over 1 year to evaluate for plaque progression
EFFECT OF TESTOSTERONE REPLACEMENT ON CORONARY PLAQUE VOLUME

Effect of Testosterone on Coronary Artery Plaque Volume

- Noncalcified: Placebo (n=65), Testosterone (n=73)
  - Mean Change from Baseline: p=0.003

- Total: Placebo (n=65), Testosterone (n=73)
  - Mean Change from Baseline: p=0.006

- Low Attenuation: Placebo (n=65), Testosterone (n=73)
  - Mean Change from Baseline: p=0.14

- Fibrous Fatty: Placebo (n=65), Testosterone (n=73)
  - Mean Change from Baseline: p=0.11

- Fibrous: Placebo (n=65), Testosterone (n=73)
  - Mean Change from Baseline: p=0.01

- Dense Calcium: Placebo (n=65), Testosterone (n=73)
  - Mean Change from Baseline: p=0.51
Demonstrated a difference in over 800 participants undergoing CCTA for plaque volume and composition among HIV + and HIV – patients.

Will study 550 patients over 5 years for repeat measures.
REPRIEVE STUDY

PRIMARY: Effect of pitavastatin on non-calcified coronary plaque volume measured on serial coronary computed tomography angiography (CCTA).

SECONDARY:
1. High risk plaque features on CCTA.
2. Serum markers immune activation, inflammation, and CVD risk.
3. Relative contributions to coronary plaque progression.

FISH OILS and PLAQUE

Plaque regression in each group:
- PTV: 24%
- PTV/EPA: 50%

Correlation between percent change in EPA/AA ratio and percent change in plaque volume:
- R = -0.332
- P < 0.001
Serial Studies with CTA

- Ongoing studies are using serial CT angiography to track the cardiovascular effects of different agents (ie – statins, oral hypoglycemics, fish oils)

- This non-invasively replaces IVUS with more segments evaluable
## TABLE 4 Cardiac Events After CTA-2

<table>
<thead>
<tr>
<th>Univariable</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariable</strong></td>
<td><strong>Multivariable</strong></td>
</tr>
<tr>
<td><strong>HR (95% CI)</strong></td>
<td><strong>HR (95% CI)</strong></td>
</tr>
<tr>
<td>Age</td>
<td>0.99 (0.94-1.06)</td>
</tr>
<tr>
<td>Male</td>
<td>1.32 (0.24-24.55)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.59 (0.39-10.70)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.13 (0.24-4.27)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>0.86 (0.22-4.06)</td>
</tr>
<tr>
<td>BMI &gt;25 kg/m²</td>
<td>5.58 (1.46-26.52)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>2.35 (0.62-9.51)</td>
</tr>
<tr>
<td>Previous ACS</td>
<td>6.26 (1.15-116.32)</td>
</tr>
<tr>
<td>Statin use</td>
<td>1.11 (0.27-7.44)</td>
</tr>
<tr>
<td>Chest pain at CTA-2</td>
<td>3.09 (0.65-11.73)</td>
</tr>
<tr>
<td>HRP at CTA-1</td>
<td>4.40 (1.08-16.67)</td>
</tr>
<tr>
<td>HRP at CTA-2</td>
<td>9.07 (2.38-43.11)</td>
</tr>
<tr>
<td>Plaque progression</td>
<td>61.32 (11.24-1,137.73)</td>
</tr>
</tbody>
</table>

Abbreviations as in Tables 1 and 2.
Conclusions

• % TPV change on CCTA is significantly associated with % SPV change on IVUS
• CCTA can be used as a non-invasive imaging modality as opposed to IVUS
• CCTA may allow more wide use to assess drug efficacy on atherosclerosis progression in primary and secondary prevention populations