Stenosis, Physiology and Medications are not enough: Vulnerable Plaque Must be identified

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What to treat/prevent?

Angiographic stenosis → Interventionalists

Angina on exertion → Improves quality of life

AMI or SCD → Enormous benefit

Potentially
SCD in USA

- 1000/day
- 1/1000 person year
- Men x3 > women
- 75% at home
- Etiology: 75% CAD ↔ Vulnerable Plaque
Can VP be identified?
Vulnerable Plaque

- Large lipid
- Thin fibrous cap
- High MΦ density
- Positive remodeling
- Inc vasa vasorum
## Intravascular Diagnostics for VP

<table>
<thead>
<tr>
<th>Modality</th>
<th>Resolution</th>
<th>Penetration</th>
<th>Cap</th>
<th>Lipid</th>
<th>Inflam</th>
<th>Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVUS</td>
<td>100 µm</td>
<td>good</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>Angioscopy</td>
<td>100 µm</td>
<td>poor</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>OCT</td>
<td>10 µm</td>
<td>poor</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Thermography</td>
<td>-</td>
<td>poor</td>
<td>-</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Spectroscopy</td>
<td>-</td>
<td>poor</td>
<td>+</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>IV MR</td>
<td>160 µm</td>
<td>good</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

Suh, Jang. Circ Img 2011
### OCT: Ex Vivo Study Results

<table>
<thead>
<tr>
<th></th>
<th>SENS</th>
<th>PPV</th>
<th>SPEC</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fibrous</strong></td>
<td>.87</td>
<td>.88</td>
<td>.97</td>
<td>.96</td>
</tr>
<tr>
<td><strong>Calcific</strong></td>
<td>.95</td>
<td>1.0</td>
<td>1.0</td>
<td>.95</td>
</tr>
<tr>
<td><strong>Lipid</strong></td>
<td>.92</td>
<td>.81</td>
<td>.94</td>
<td>.97</td>
</tr>
</tbody>
</table>

Interobserver $k = 0.88$, Intraobserver $k = 0.91$

Yabushita, .. Jang, Bouma, Tearney. Circulation 2002
Fibrous Cap Thickness
Histology vs OCT

\[ y = 0.98x - 16.52 \]
\[ r = 0.92, \ p < 0.001 \]

Macrophage Study

Low Mφ

High Mφ

OCT

250 µm

CD68

massachusetts general hospital heart center
## AMI v ACS v SAP

<table>
<thead>
<tr>
<th></th>
<th>AMI</th>
<th>ACS</th>
<th>SAP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=20/30/35)</td>
<td>(n=20/24/--)</td>
<td>(n=17/31/20)</td>
</tr>
<tr>
<td>LRP (%)</td>
<td>90/93/--</td>
<td>75/71/--</td>
<td>58/42/--</td>
</tr>
<tr>
<td>FCT (µm)</td>
<td>47/49/--</td>
<td>54/79/--</td>
<td>103/196/--</td>
</tr>
<tr>
<td>TCFA (%)</td>
<td>72/83/77</td>
<td>50/46/--</td>
<td>20/3/25</td>
</tr>
<tr>
<td>MΦ (%)</td>
<td>5.7±1.4</td>
<td>5.9±2.1</td>
<td>4.2±1.7</td>
</tr>
</tbody>
</table>

TCFA (Thin Cap FibroAtheroma)

Stable Plaque

TCFA

Ruptured Plaque
Must VP be identified?
The PROSPECT Trial (700 ACS pts)

3-vessel imaging post PCI: Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

IVUS

Virtual histology

Palpography (n=~350)

Meds rec
Aspirin
Plavix 1yr
Statin
Repeat biomarkers
@ 30 days, 6 months

F/U: 1 mo, 6 mo,
1 yr, 2 yr,
±3-5 yrs

MSCT
Substudy
N=50-100

Repeat imaging
in pts with events
# PROSPECT: MACE

## 3-year follow-up, hierarchical

<table>
<thead>
<tr>
<th>Event</th>
<th>All (n)</th>
<th>Culprit lesion related (n)</th>
<th>Non culprit lesion related (n)</th>
<th>Indeterminate (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death</td>
<td>1.9% (12)</td>
<td>0.2% (1)</td>
<td>0% (0)</td>
<td>1.7% (11)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>0.3% (2)</td>
<td>0.3% (2)</td>
<td>0% (0)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>MI (STEMI or NSTEMI)</td>
<td>2.7% (17)</td>
<td>1.7% (11)</td>
<td>1.0% (6)</td>
<td>0.2% (1)</td>
</tr>
<tr>
<td>Rehospitalization for unstable or progressive angina</td>
<td>15.4% (101)</td>
<td>10.4% (69)</td>
<td>10.7% (68)</td>
<td>0.8% (5)</td>
</tr>
<tr>
<td>Composite MACE</td>
<td>20.4% (132)</td>
<td>12.9% (83)</td>
<td>11.6% (74)</td>
<td>2.7% (17)</td>
</tr>
<tr>
<td>Cardiac death, arrest or MI</td>
<td>4.9% (31)</td>
<td>2.2% (14)</td>
<td>1.0% (6)</td>
<td>1.9% (12)</td>
</tr>
</tbody>
</table>

Rates are 3-yr Kaplan-Meier estimates (n of events)
PROSPECT: Implications

• The relatively low prevalence of high-risk lesions (~1 in 5 pts), coupled with the fact that when they become symptomatic they usually present with angina and not death or MI, suggests that 3-vessel imaging to identify and prophylactically stent these lesions is not warranted in ACS patients who are revascularized and treated with optimal medical therapy.

• Similarly, if a high risk non ischemia-producing lesion happens to be found (e.g. 3 year event rate >10%), since most patients present with angina, prophylactic DES cannot be recommended.
TCFA

Stable Plaque

TCFA

Ruptured Plaque

Study Date
April 2000

5 years later
No MACE
Frequency of AMI

- 59 cases with acute thrombus
  
  41 Rupture → 4 AMI (19%)
  
  18 Erosion → 2 AMI (11%)

Majority of plaque disruptions are silent!

Burke A. NEJM 1997
Summary

- Can TCFA be identified? Yes
- Must VP be identified? ??

However.....
one study
one modality
MGH OCT Registry

- Target #: 3000 - 5000 patients
- Follow up: 5 years
- Start: June 1, 2010
- Sites: 20

http://www.massgeneral.org/octregistry
Participating PIs and Institutions

Australia
- OC Raffel: Brisbane
- H Lowe: Sydnesy
- P Balis: Melburn

China
- B Yu: Harbin Med Univ.
- S Lee: Univ. of Hong Kong

USA
- IK Jang: MGH
- A Prasad: Mayo
- S Sharma: Mt. Sinai

Japan
- K Mizuno: Tokyo
- S Uemura: Nara Univ.
- K Kakuta: Tsuchiura Kyodo
- T Ito: Iwate

Korea
- SY Choi: Ajou
- YS Jang: Yonsei
- SJ Kim: Kyung Hee
- JM Cho: EW
- SJ Park: Asan

Singapore
- S Chia: National Heart Center
Enrollment Overview

- 503 patients have been enrolled into the Registry from 6 countries

# Patients Enrolled by Country

Cumulative Enrollment Over Time*

- Singapore
- Australia
- USA
- Japan
- Korea
- China

- Aug-10
- Sep-10
- Oct-10
- Nov-10
- Dec-10
- Jan-11
- Feb-11
- Mar-11
Number of vessels imaged

# of Vessels Imaged

- 36%
- 37%
- 27%

1
2
3
Thank You

MGH history book to commemorate bicentennial

As part of the MGH’s bicentennial celebrations, a commemorative book covering the hospital’s unique beginnings and illustrious history will be published in 2011. "Something in the Ether: A Bicentennial History of Massachusetts General Hospital, 1811 to 2011," was written by author and publisher Webster Beil. Much of the content was drawn from interviews with longtime MGH staff and countless hours of research of historical records and archival material. The book is scheduled to be released in March and will be available at the MGH General Store and select booksellers.

(Continued on page 2)