### Perspectives in Vulnerable Plaque Imaging

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#### The Limits of Opening Arteries NYTimes March 28, 2004

- A changing notion of how heart attacks occur ought to lower expectations for the traditional methods used to prevent arteries from clogging shut. It has long been customary for cardiologists to treat narrowing arteries by either enlarging and holding open the restricted channel or performing bypass surgery to carry blood around the narrowed section. The problem is, the vast majority of heart attacks are now known to originate in sections of artery that have not yet narrowed.
- As described in an article by Gina Kolata in last Sunday's Times, the old view of the progression of cardiovascular disease held that fatty deposits, or plaques, accumulate in the arteries slowly over decades, much as sludge builds up in a pipe, until one day the opening becomes so narrow that no blood can get through, and the patient suffers a heart attack. The newer view, which has taken hold in recent years but is little known to the public, is that heart attacks occur when an area of plaque ruptures and causes a blood clot to form, abruptly blocking the flow. In perhaps 75 to 80 percent of these cases, the plaque was not obstructing an artery, would not have been treated or bypassed and produced no symptoms.
- Experts agree that artery-opening methods -- like bypass surgery, or insertion of a balloon to mash down plaque and a wire-cage stent to keep the channel open -- can alleviate crushing chest pain and save some lives. But patients should not assume that their cardiovascular problems are "fixed" by such procedures, and

patients without symptoms whose arteries are narrowing should be wary about undergoing these procedures to ward off a potential heart attack. They

may have hundreds of vulnerable plaques elsewhere that are more apt to burst and trigger a heart attack than are the more stable plaques in the narrow section. Most such patients might better be treated with drugs to lower their cholesterol levels, control their blood pressure and prevent blood clots, or should adopt a healthier life style by giving up smoking, eating hearthealthy foods and exercising.

• This profound change in thinking about cardiovascular problems makes us yearn for the day when there can be much wider testing of one therapy against another to identify those that work best from those that may be oversold.





### "Vulnerable plaque" events post-PCI

Of 3747 consecutive patients in the NHLBI Dynamic PCI Registry, 216 (5.8%) required additional non-TLR for clinical plaque progression at 1 year.

	Different artery	Same artery as PCI site		
		Proximal	Distal	
LAD	35	7	8	
LCX	32	5	7	
RCA	21	12	12	



(Glaser et al. Circulation 2005;111:143-9)



### Three Vessel IVUS Imaging in 24 Pts with ACS and Positive Tn

#### • 50 ruptured plaques

- 9 culprit lesion
- 41 nonculprit lesion
- 19 pts had at least 1 nonculprit plaque rupture (79%)
  - 17 pts had 1 plaque rupture in a second artery
  - 3 pts had plaque ruptures in all 3 arteries





Rioufol et al Circulation 2002;106:804-808



## How common are vulnerable plaques?





Number of thin-cap fibroatheromas in patients dying with MI, sudden death, or noncardiac causes and studied at necropsy using cross-sectional analysis





(Burke et al. J Am Coll Cardiol 2003;41:1874-86-)



### Number of thin-cap fibroatheromas in 50 patients studied at necropsy using Iongitudinal analysis

	All pts	Pts with ≥1 ruptured plaque	Pts with ≥1 TCFA or ruptured plaque	Pts with CV death
# of patients	50	14	20	33
# of ruptured plaques	19 (0.38/pt)		19 (0.95/pt)	15 (0.45/pt)
# fibroatheromas	193			
# TCFAs	23 (0.46/pt)	15 (1.21/pt)	23 (1.15/pt)	18 (0.55/pt)



(Cheruvu et al. J Am Coll Cardiol 2007;50:940-9)



### Ruptured plaques in patients with MI and stable angina

#### % of patients

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(Hong et al Circulation 2004;110:928-33)







#### PROSPECT: Imaging Summary Per patient incidence of VH-TCFAs



Lesions/patient per coronary tree ■ 0 ■ 1 ■ 2 ■ 3 ■ ≥4





### Location of 82 TCFAs in 34 patients with AMI and 17 patients with stable angina and three vessel OCT

In 34 AMI patients, there were 50 TCFAs (1.5/patient), 16 in the infarct related artery and 34 in the non-infarct related artery Length of artery imaged beginning at the coronary ostium (mm)

LAD	72±24mm
LCX	56±30mm
RCA	97±31mm



## Are vulnerable plaque locations predictable?







Spatial Distribution of Advanced Coronary Lesions



(Cheruvu et al. J Am Coll Cardiol 2007;50:940-9)



## Angiographic location of acute coronary occlusions





(Wang et al. Circulation 2004;110:278-84)





Location of 82 TCFAs in 34 patients with AMI and 17 patients with stable angina and three vessel OCT: Vulnerable plaques tend to cluster in predictable "hot spots" within the proximal segments of the LAD and LCX and the entire length of the RCA



## When vulnerable plaques rupture, do they always cause events?





## Symptoms in 254 patients with 300 plaque ruptures in 257 arteries





Maehara et al J Am Coll Cardiol 2002;40:904-10



### Ruptured plaques in patients with MI and stable angina

#### % of patients

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(Hong et al Circulation 2004;110:928-33)



### Comparison of Culprit & Non-Culprit Rupture Sites in ACS Patients and Rupture Sites in Non-ACS Patients





Fuji et al. Circulation 2003;108:2473-8



### Are all non-culprit events in the first year post-PCI related to vulnerable plaques? Or are some related to incomplete revascularization at the time of initial PCI?





### **Angiographic Occult Stenoses**

- On pre-intervention IVUS, 404 patients with 436 arteries had 500 lesions with an IVUS minimum lumen area <4.0mm<sup>2</sup>
- 28% (140/500) had an angiographic DS<50%</li>



(Maehara et al. Am J Cardio 2003;91:1335-8)











### Are all vulnerable plaques thin-cap fibroatheromas?

#### **Different Types of Vulnerable Plaque**



### Who should be studied?

- Primary preventions
  - All patients?
  - High risk patients?
  - Invasive vs non-invasive diagnosis?
- Secondary prevention
  - Just the PCI artery?
  - All arteries?
- How often should a patient be restudied?
- What is the risk of multivessel invasive imaging?
- What is the cost?





# What is the temporal stability of vulnerable plaques?

- How quickly do they form?
- How often do they heal spontaneously?
- How often do they rupture without causing events?
- What is the impact of modern medical therapy: ASA, clopidogrel, statin?





#### Conclusion

- I make the assumption that we will be able to detect TCFAs. After all, we are smart people, and a lot of money and time is being spent on this problem.
- However, that does not mean that this will become a clinical reality.



