Ultrasound Tissue Characterisation

Geoff Vince

Cleveland Clinic Foundation and Volcano Corp

Angioplasty Summit

Seoul, Korea

How much disease? Pick a number

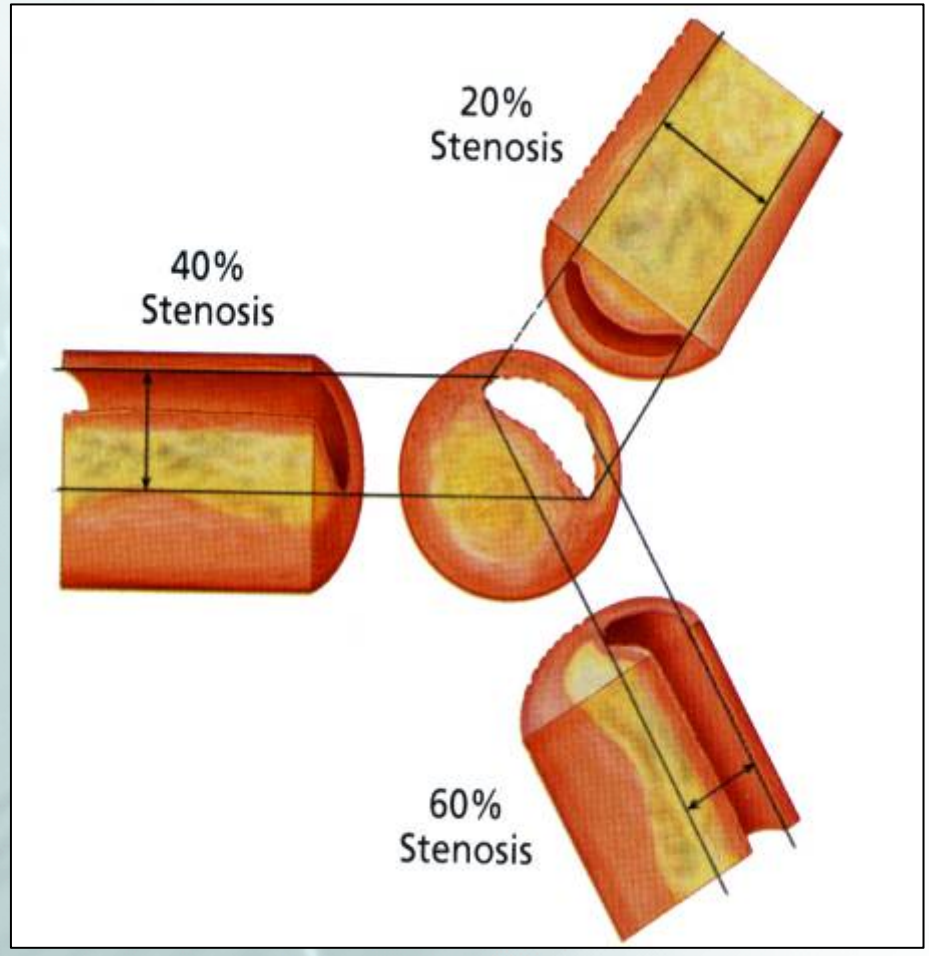
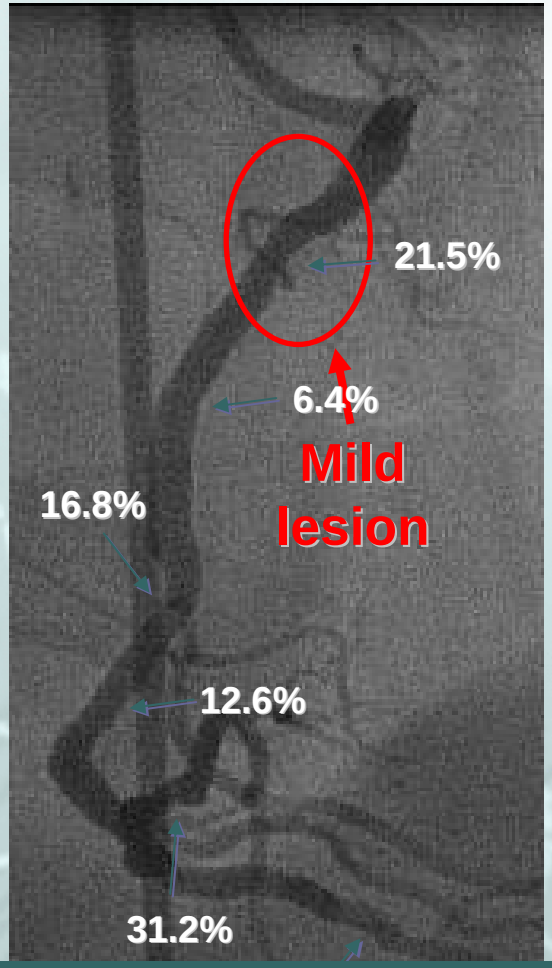


Image courtesy of S.E. Nissen, MD

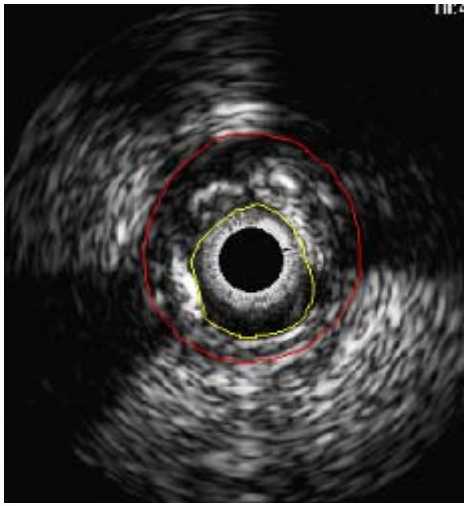
Gray Scale IVUS

62. y.o. ♂ with NSTEMI, LAD stented



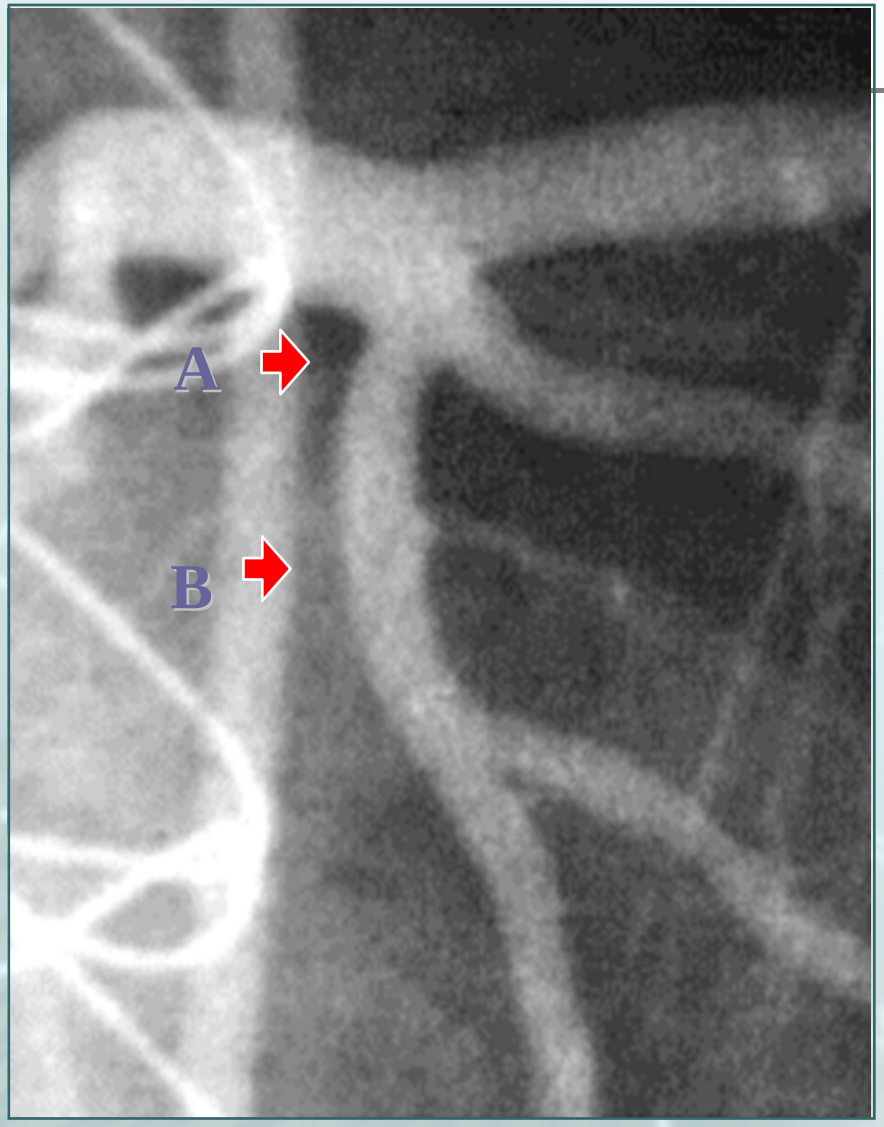
QCA
RVD 4.64 mm
MLD 3.64 mm
DS 21.5%

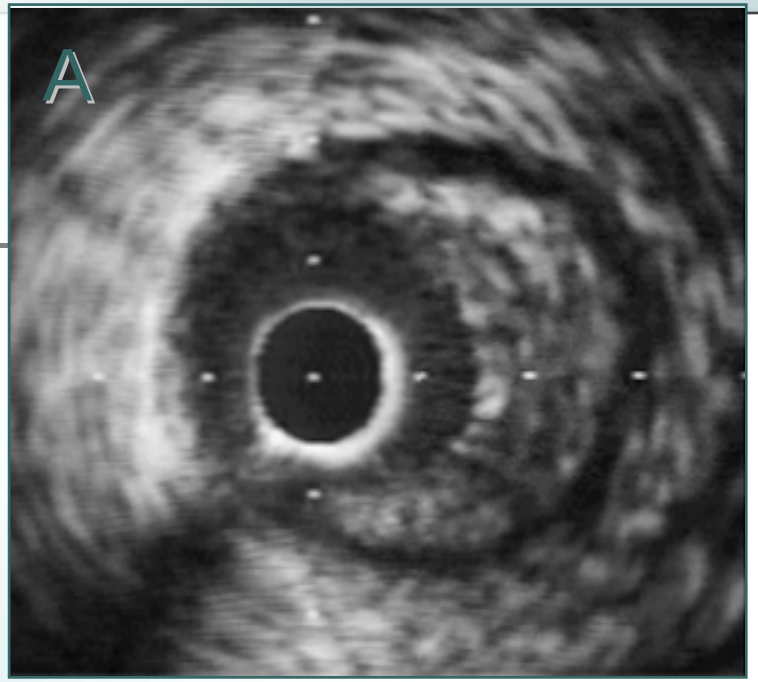
MLA 2.95 mm²

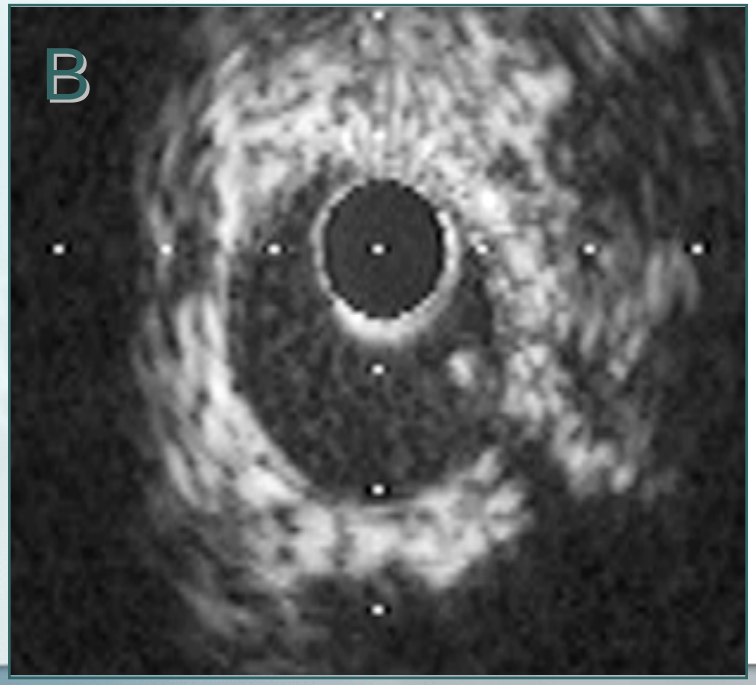


Angiographic mild lesion (21.5%) by QCA is actually ***severe*** by IVUS

Lumen vs. Vessel Wall

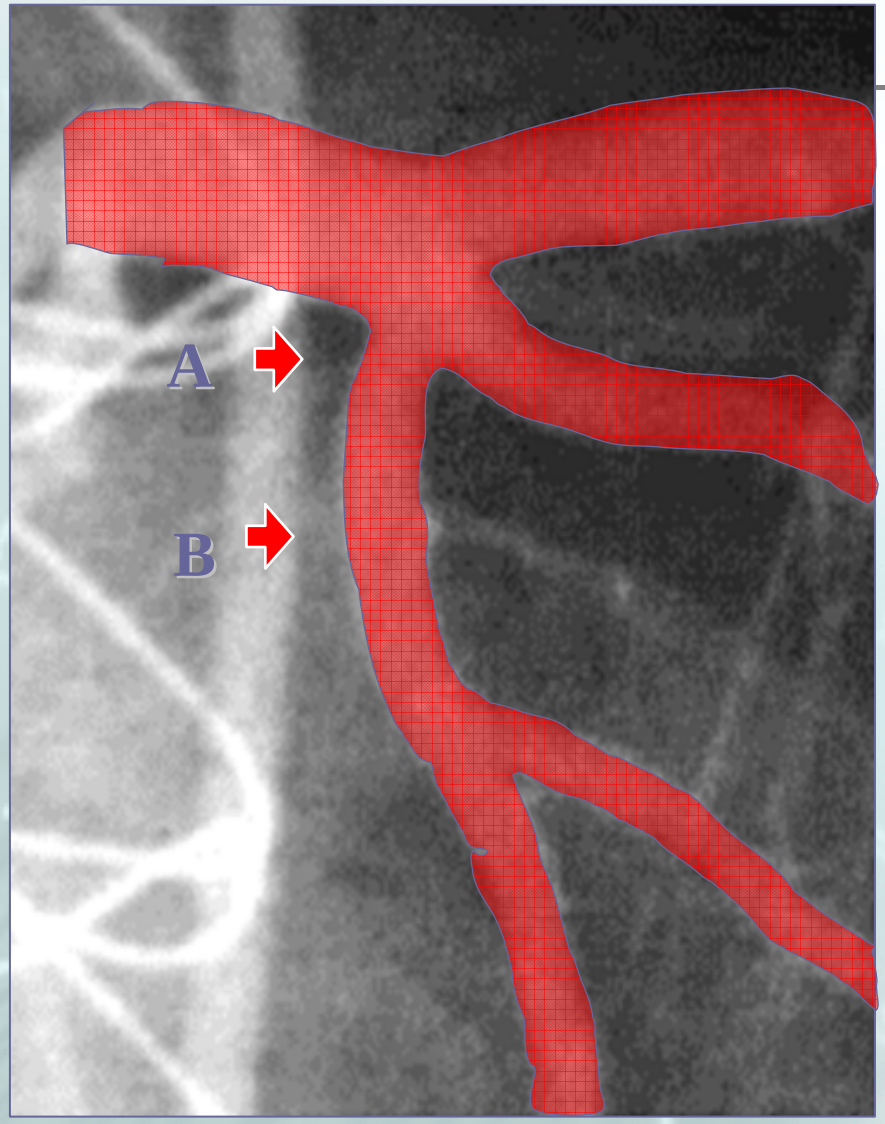


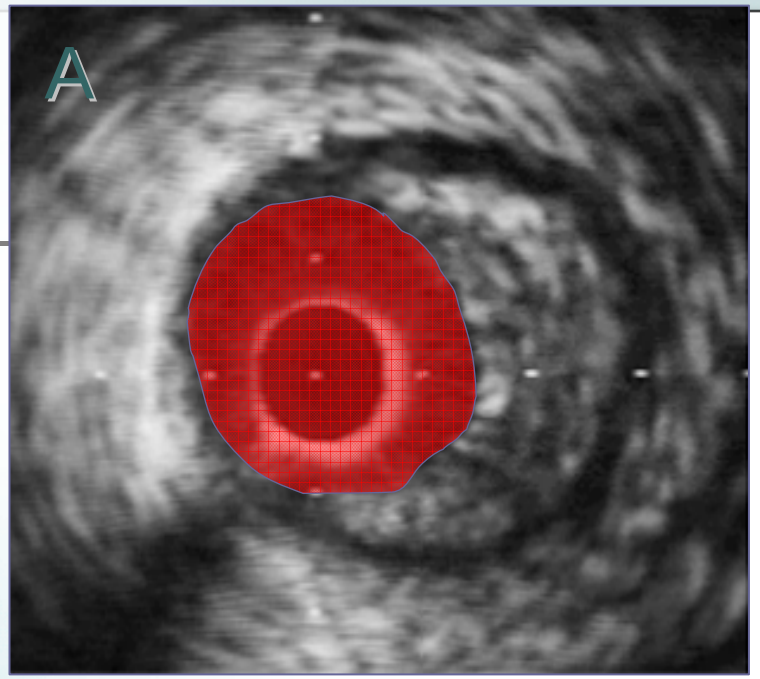


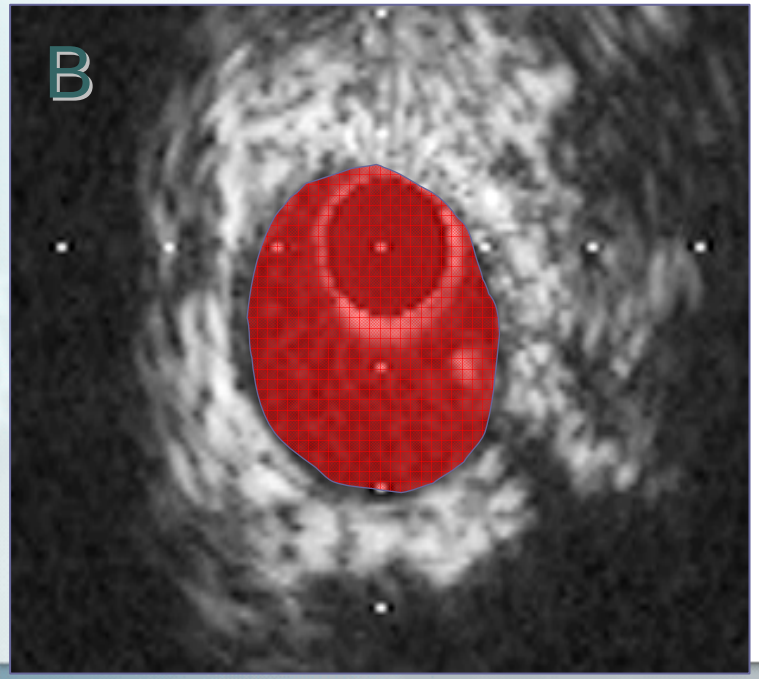


Slide courtesy of S.E. Nissen

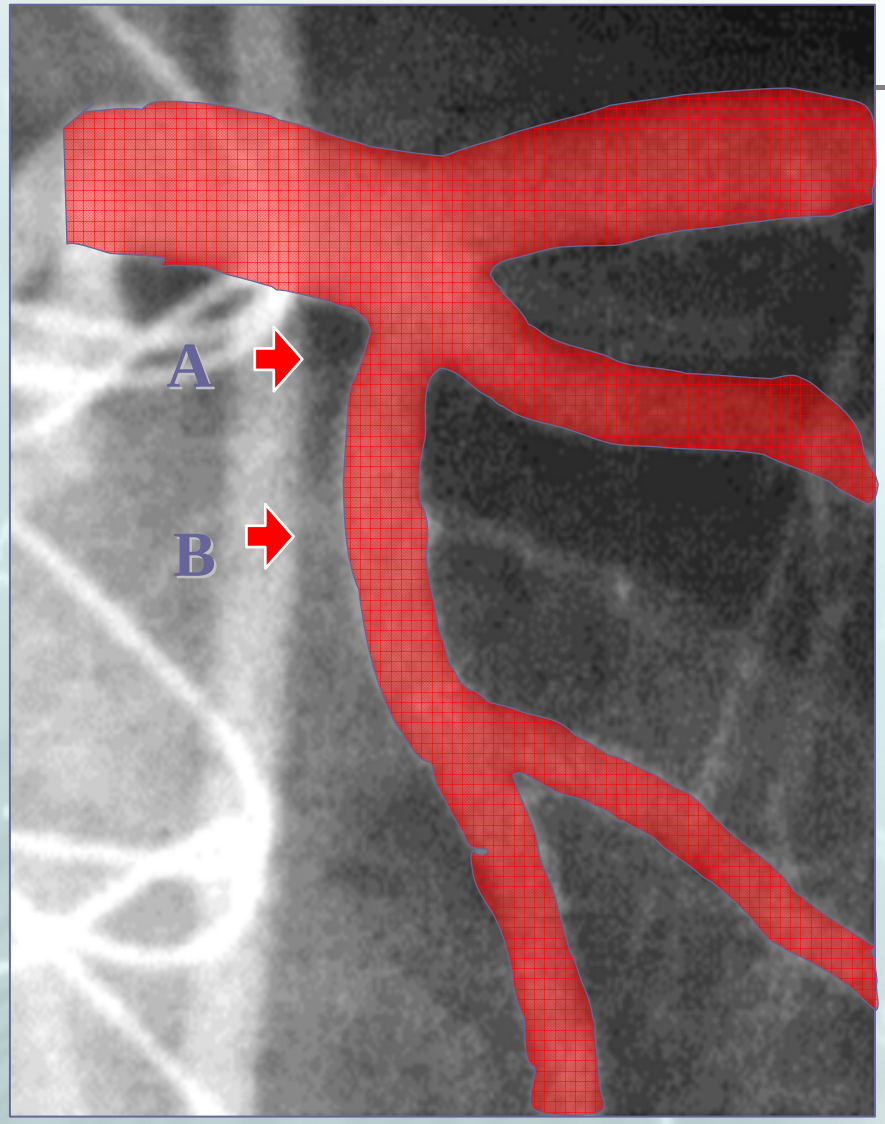
Lumen vs. Vessel Wall

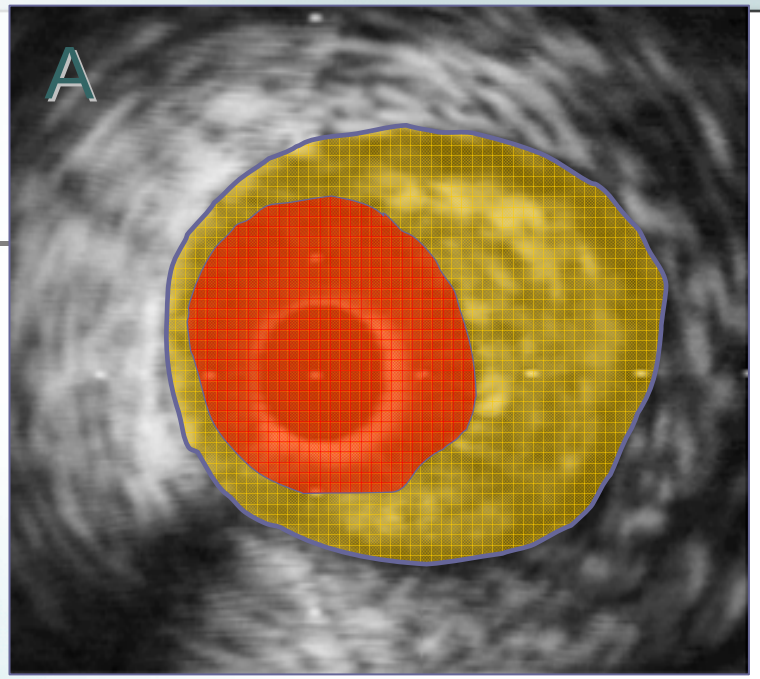


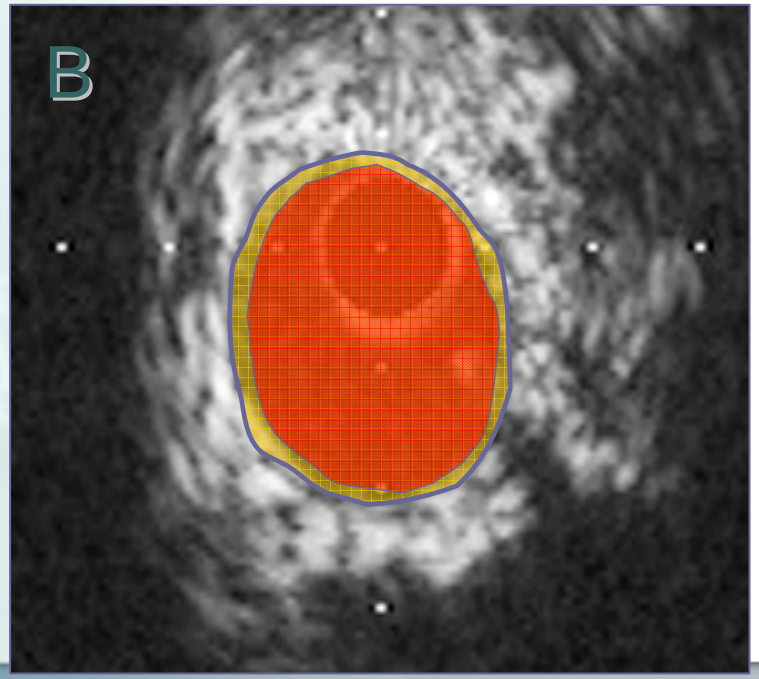




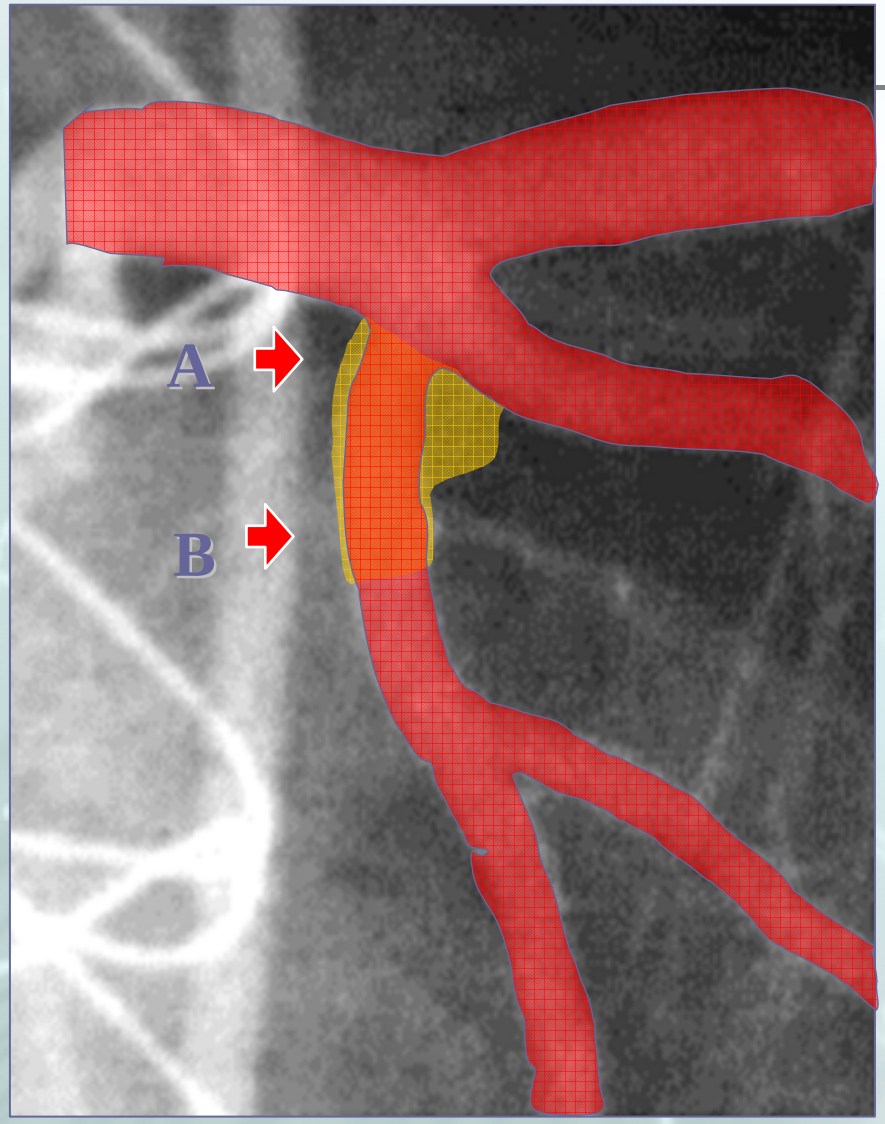
Lumen vs. Vessel Wall

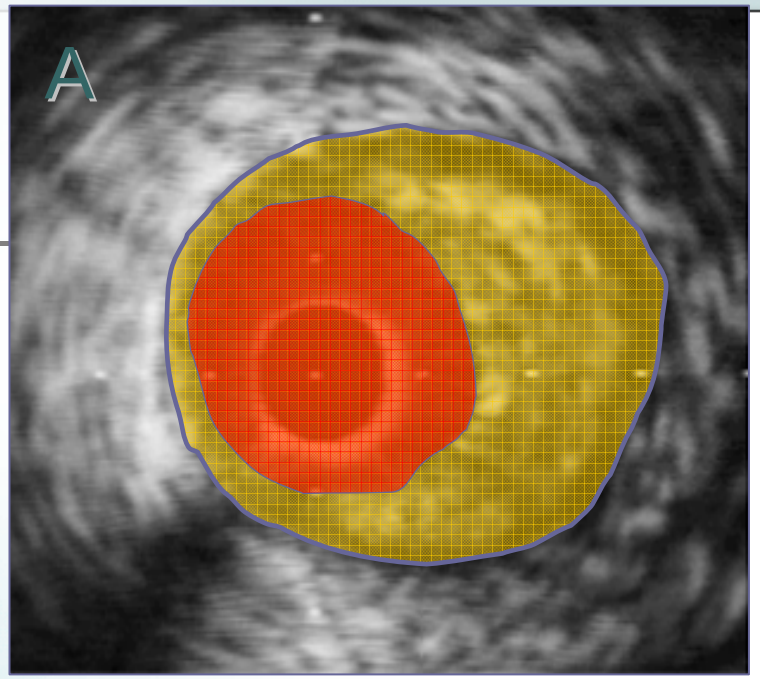


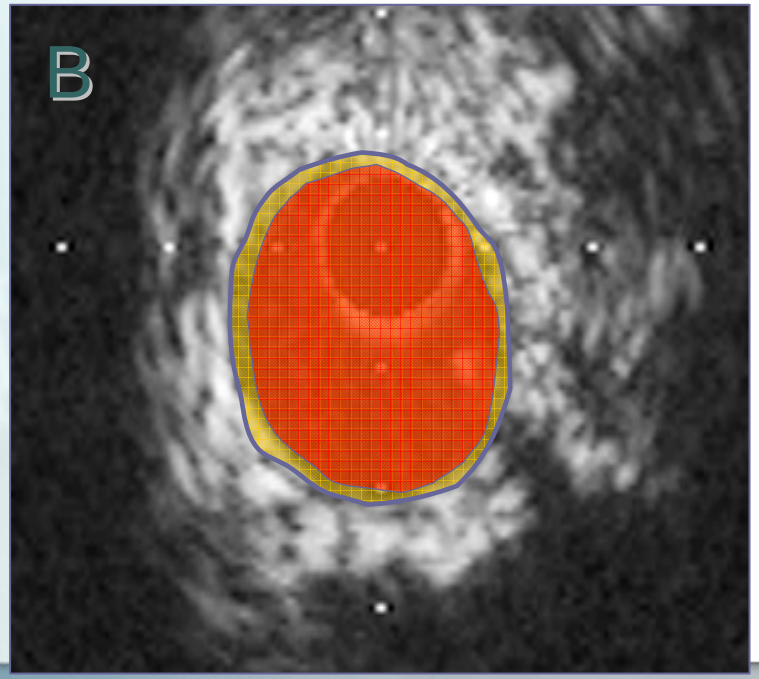




Lumen vs. Vessel Wall







Angiography

- If flow is not limited why do we care?
  - Correlation between positive remodelling and unstable presentation
    - Virmani
    - Schoenhagen
  - Can’t see remodelling on an angiogram!!

Angiography

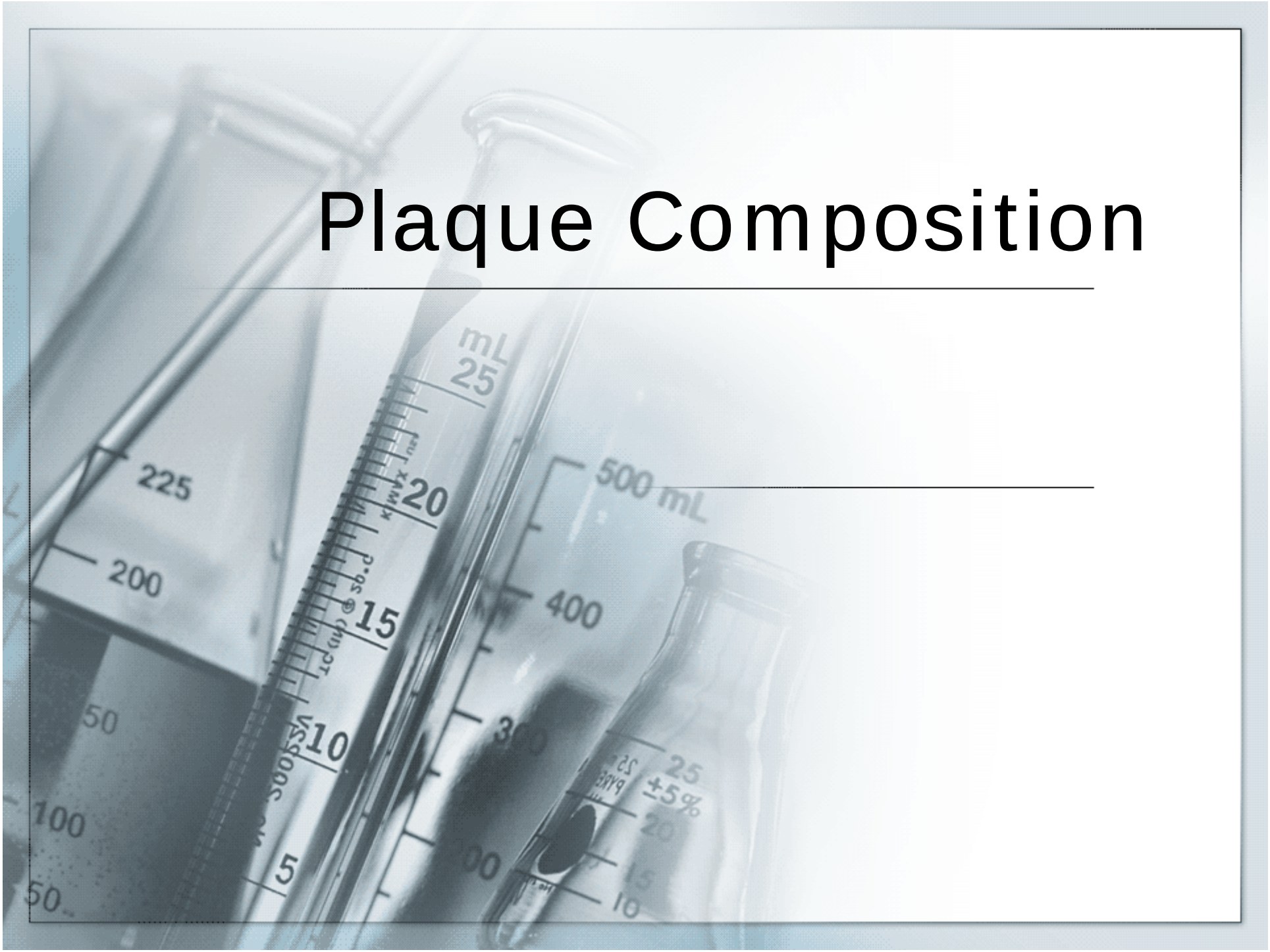
- If flow is not limited why do we care?
  - Correlation between positive remodeling and unstable presentation
  - 68% of MIs are caused by plaques that are less than 50% occluded
  - Insignificant or not visible on an angiogram!!

Angiography

- If flow is not limited why do we care?
  - Correlation between positive remodeling and unstable presentation
  - 68% of MIs caused by plaque that are less than 50% occluded
  - 6% of PCI patients will have clinical plaque progression requiring nontarget lesion PCI by 1 year.” Glaser, 2005
- Can’t detect these plaques on an angiogram!!

Not just size?

Plaque Composition



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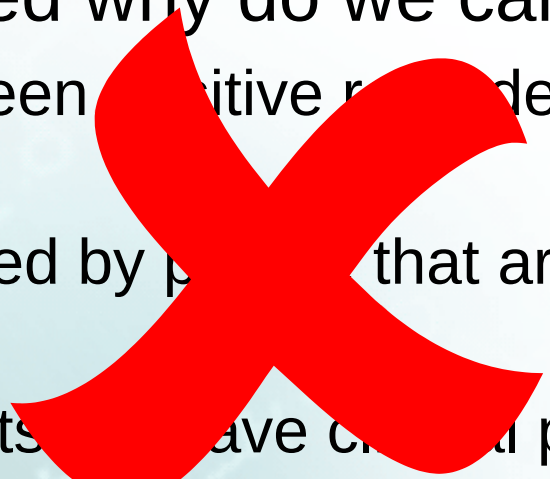
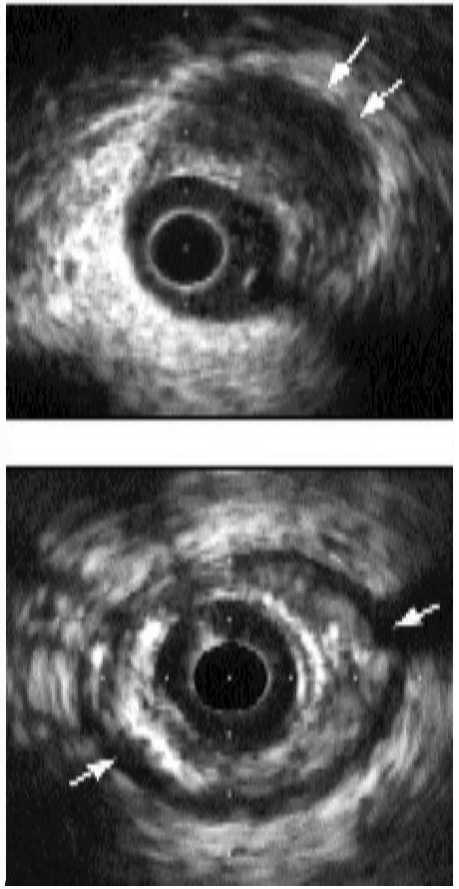


Coronary Imaging

Previous histological studies have demonstrated that the discrimination of lipid is inconsistent using greyscale images alone.

- Palmer *et al.* Eur Heart J., 1999
- Peters *et al.* J Am Soc Echocardiogr., 1994
- Peters *et al.* Circulation, 1994

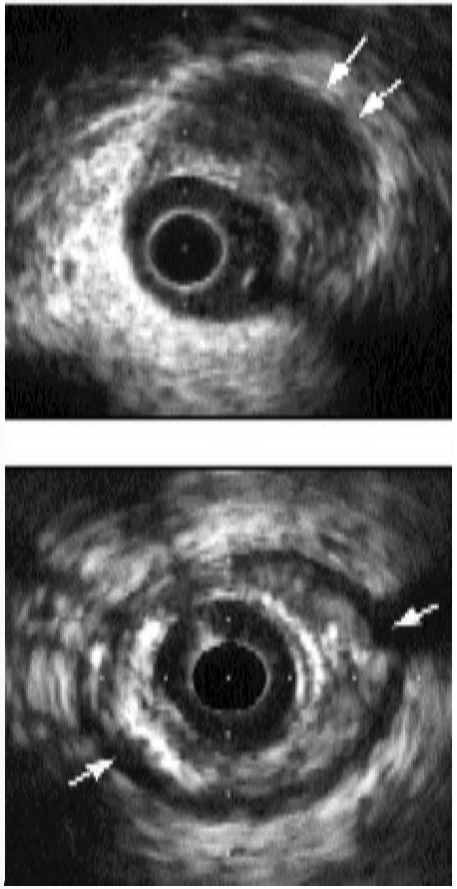
- Grayscale IVUS interpretation is not reliable; qualitative; and subjective.



Images Courtesy of CCF IVUS Core Lab

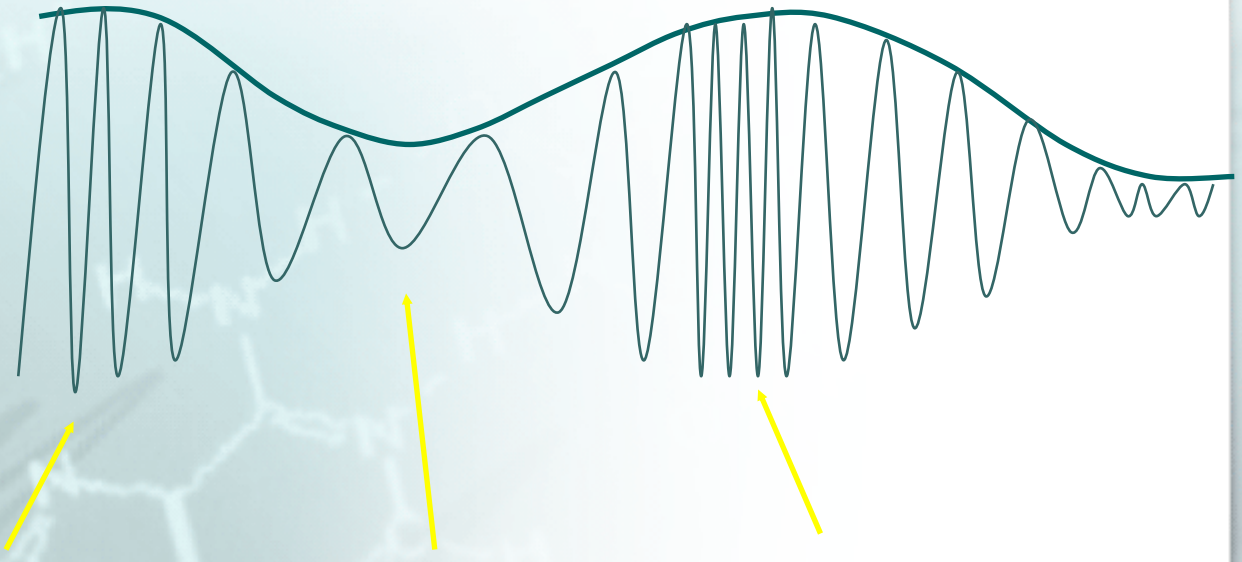
Echolucent vs Echogenic

- These two plaques are different!
- Is there additional information available?



Images Courtesy of CCF IVUS Core Lab

VH IVUS ™



Virtual Histology

$$E_{contours} = \int_0^1 \left(\alpha(s)E_L(s) + \beta(s)E_M(s) + \gamma(s)E_P(s)\right)ds$$

E_L uses 4 terms

1) Transverse curvature

$$\left|V_{(n-1)\bmod N} - 2V_{n\bmod N} + V_{(n+1)\bmod N}\right|^2$$

2) Transverse rigidity (keeps line straight)

$$\left|V_{(n-1)\bmod N} - V_{n\bmod N}\right| + \left|V_{n\bmod N} + V_{(n+1)\bmod N}\right|$$

3) Radial RF Gradient

$$\frac{\min_{RF} - G_{RF}}{\max_{RF} - \min_{RF}}$$

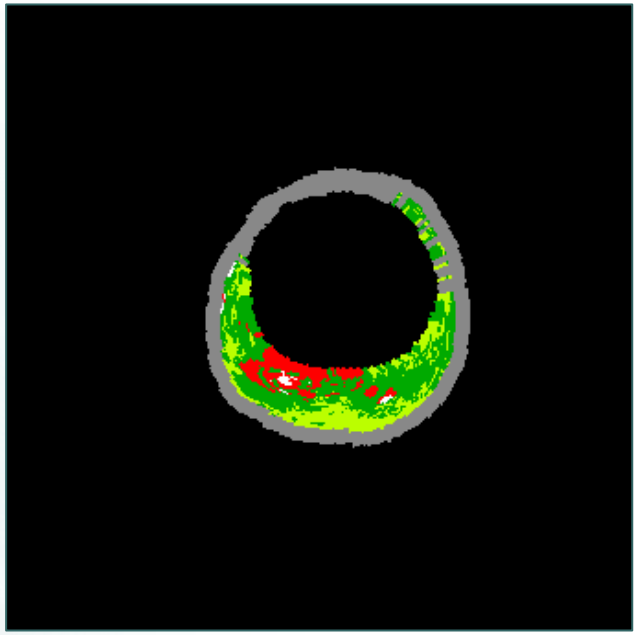
4) Radial pre-process VH Gradient

$$\frac{\min_{VH} - G_{VH}}{\max_{VH} - \min_{VH}}$$

Each term in the 3 energy calculations has a separate weight and each of E_L, E_M, and E_P have weights

VH IVUS ™

- Use frequency information to determine plaque composition.
  - Fibrous Tissue
  - Fibro-Fatty
  - Necrotic Core
  - Dense Calcium



Currently over 2000 systems worldwide

Technology licenced to Volcano Corporation

Accuracy and Validation

Quantitative

VH Plaque Component	Predictive Accuracy	Sensitivity %	Sensitivity CI	Specificity %	Specificity CI
FT (*n* = 471)	93.5%	95.7%	94 – 98	90.9%	88 – 94
FF (*n* = 130)	94.1%	72.3%	65 – 80	97.9%	97 – 99
NC (*n* = 132)	95.8%	91.7%	87 – 96	96.6%	95 – 98
DC (*n* = 156)	96.7%	86.5%	81 – 92	98.9%	98 – 100

Nair, et al.,In press, EuroIntervention, 2007

Quantitative

TRUTH TABLE

Histology Interpretation	VH Plaque Component	VH Interpretation: FT	FF	NC	DC	TOTAL
	FT (*n* = 471)	**451**	14	3	3	471
	FF (*n* = 130)	27	**94**	8	1	130
	NC (*n* = 132)	6	1	**121**	4	132
	DC (*n* = 156)	5	1	15	**135**	156
	TOTAL	489	110	147	143	**889**

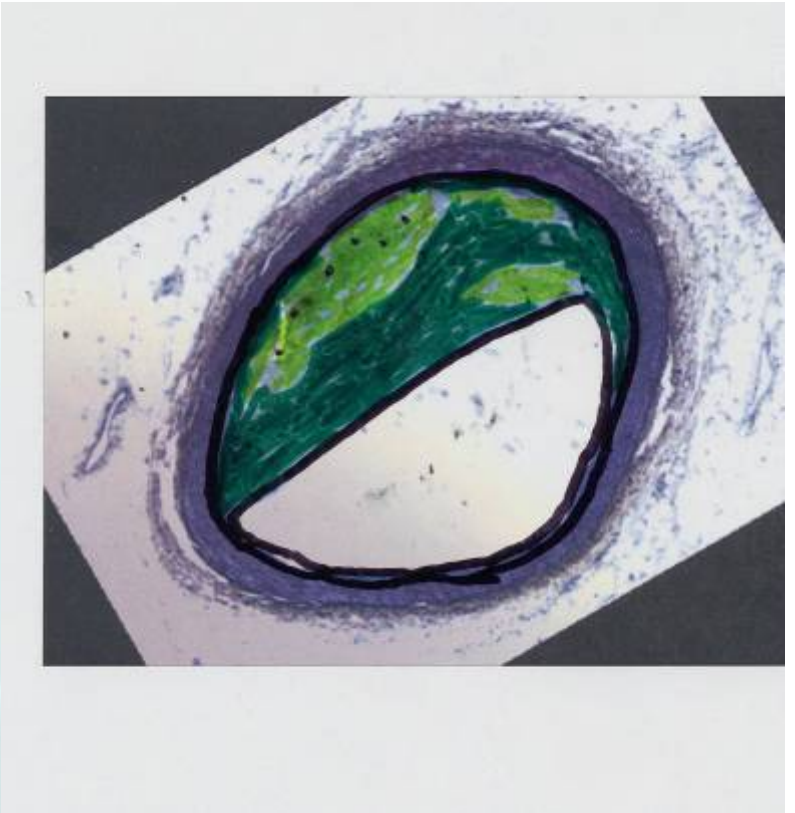
In press, EuroIntervention, 2007

Gold Standard

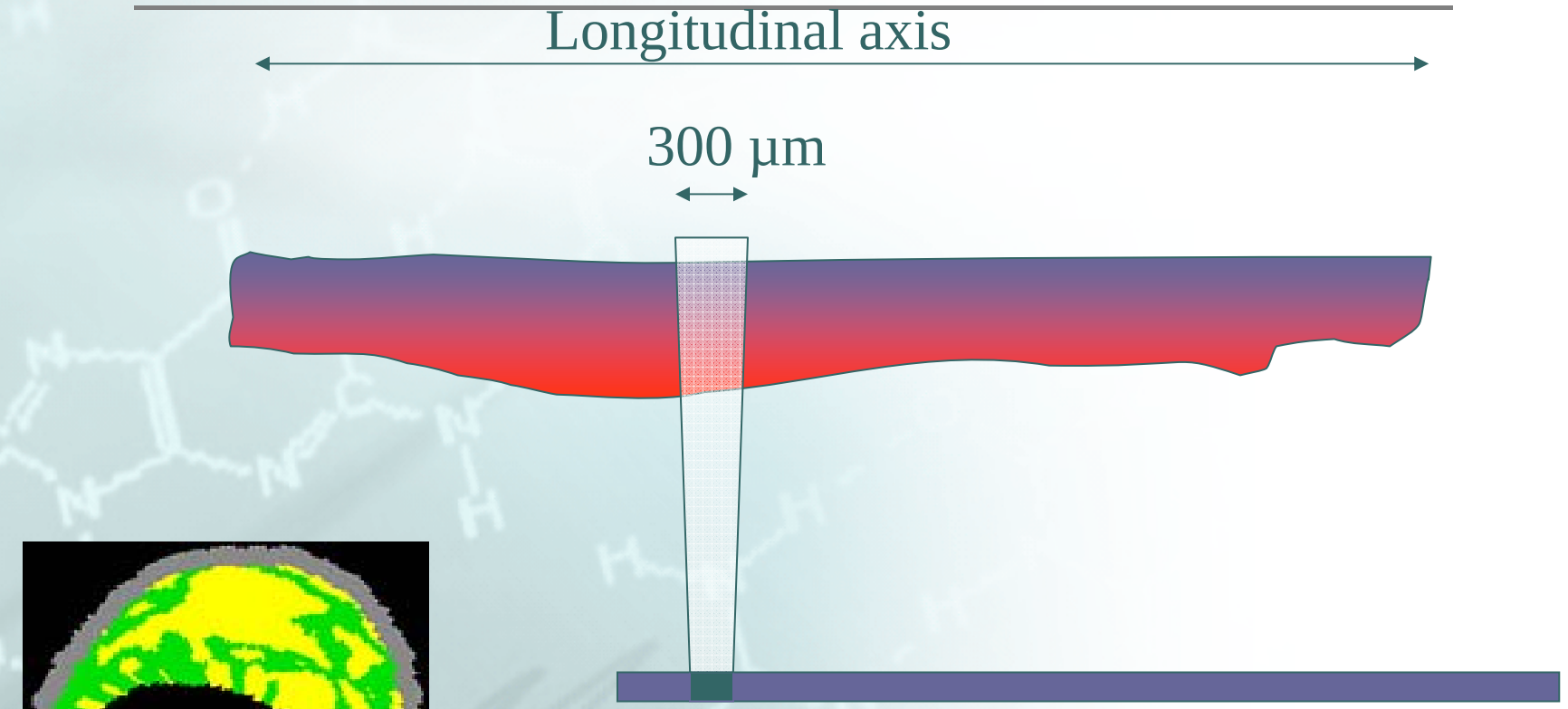
- The histology is the truth
- Pathologists are our gold standard
- How does the phenotype of the plaque agree determined by VH compare to that determined by a pathologist?

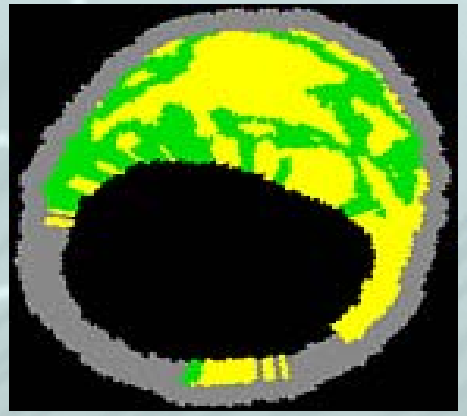
Method

- Four pathologists shown the same slides (n = 30)
  - Dr Renu Virmani (CVPath, USA)
  - Dr Massimo Sangiorgi/ Alessandro Mauriello (Rome, Italy)
  - Dr Rene Rodriquez (CCF, USA)
  - Dr Hiro Hao (Osaka, Japan)
- High quality digital images of histology were printed.
- Transparent film was taped over page.
- Borders drawn with black permanent marker
- Pathologist asked to review corresponding slide and draw her version of VH on the transparent film using coloured markers.
- Green – fibrous; Lime green – fibrofatty; Red – necrotic core; purple – calcium
- Pathologist was not shown the Grayscale or VH

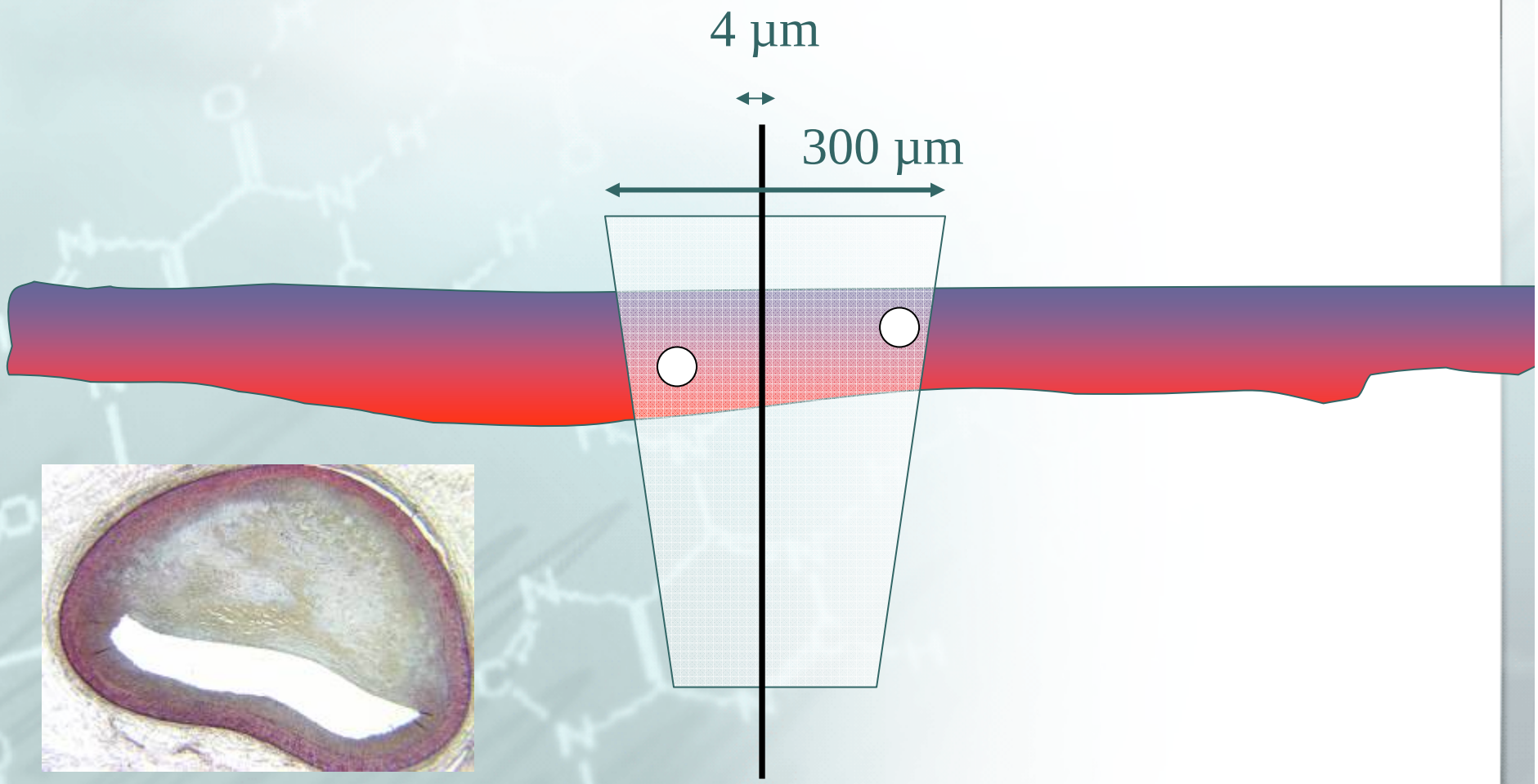


VH slice thickness





Histology slice thickness



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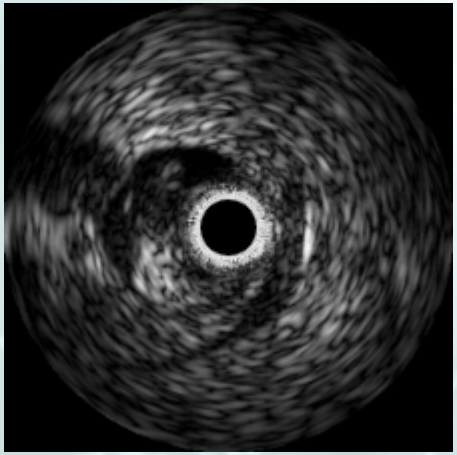

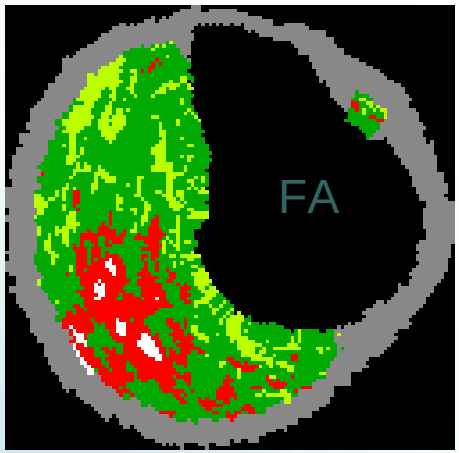

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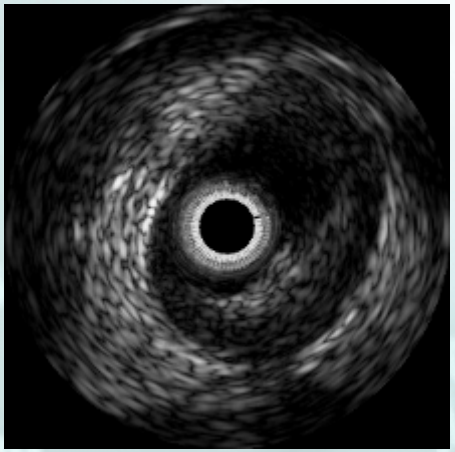

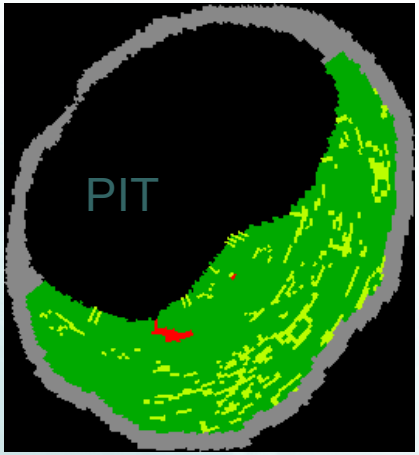

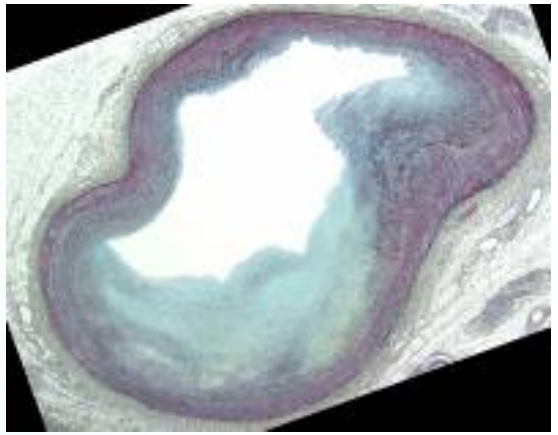

PIT

FT

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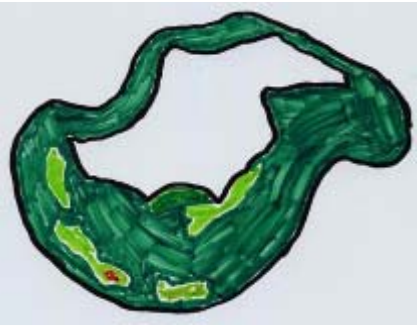

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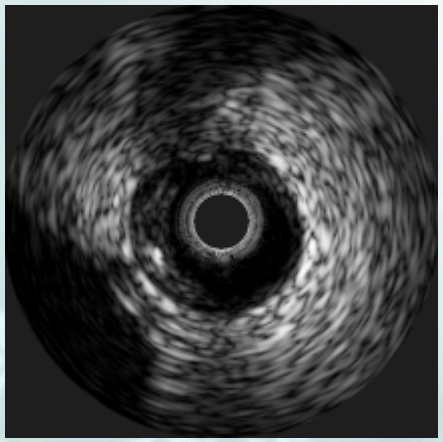

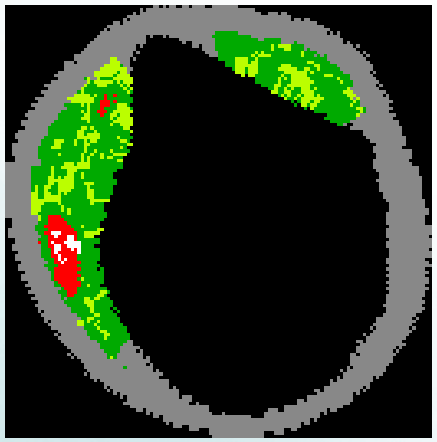

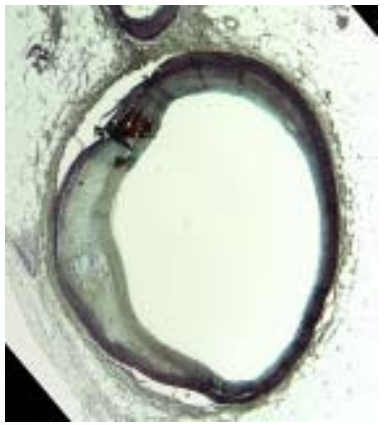

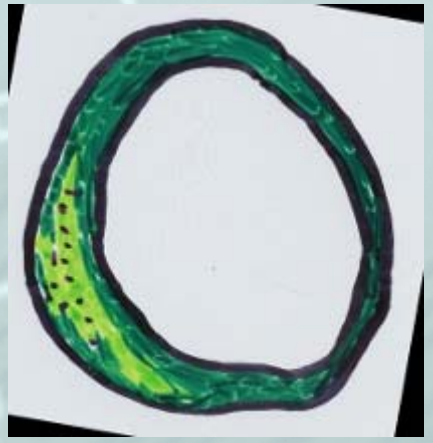

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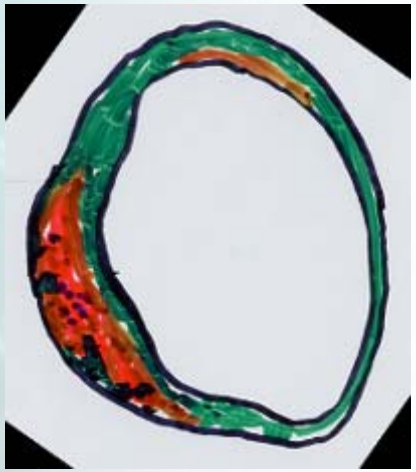

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Pathology agreement

- All pathologists agree with each other: 27%
- 75% agreement (3 out of 4): 72%
- 50% agreement (2 out of 4): 96%

- If VH agrees with a pathologist 75% of the time is it accurate?
- If VH agrees with a pathologist 50% of the time is it accurate?
- Completing study – watch this space !!!

PROSPECT

- Partnership with ABBOTT/GUIDANT Corporation
- Natural History Study
- Product
  - Eagle Eye Gold, Grayscale, VH™ IVUS, & Palpography
- Site/Investigator
  - Greg Stone Primary Investigator (US)
  - Patrick Serruys & Bernard deBruyne (EU)
- Number of Patients
  - 700 – enrollment complete

PROSPECT Baseline Analysis

- Enrollment complete, but key follow-up is still pending
- In the first 250 patients:
  - Angio alone misses lesions
    - 32% of angiographic mild lesions were severe by IVUS
    - IVUS Identified 328 lesions in the proximal vessels not seen by angio alone
- Data pending patient follow-up to study lesion progression

Summary

- Angiography can significantly underestimate the degree of vessel stenosis and provides little information on composition
- Plaque compositional analysis by evaluation of Grayscale IVUS is subjective and qualitative
- VH IVUS accurately determines plaque composition
- However, we need to correlate plaque composition to clinical events (PROSPECT and SPECIAL trials)