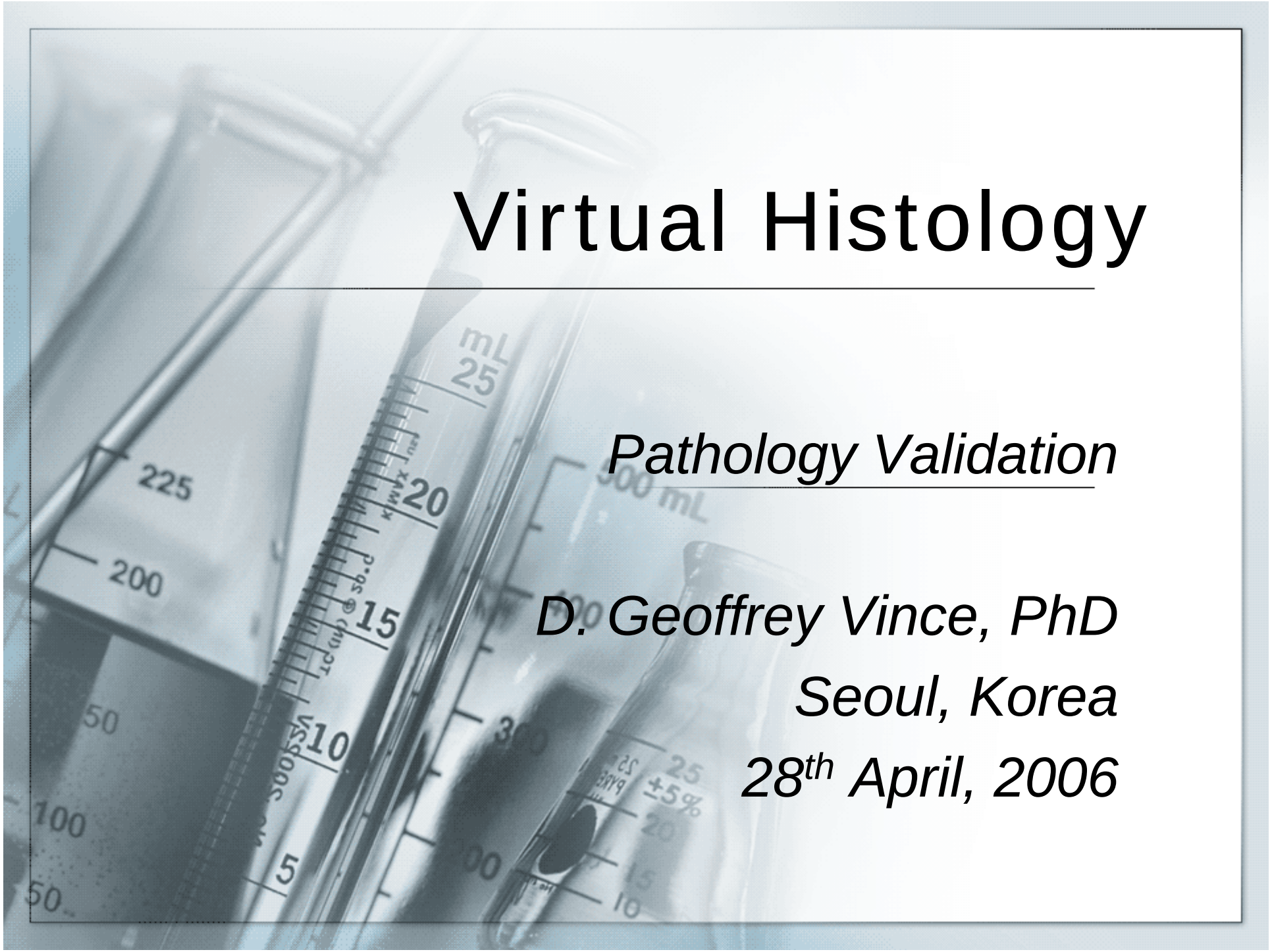


Virtual Histology

Pathology Validation

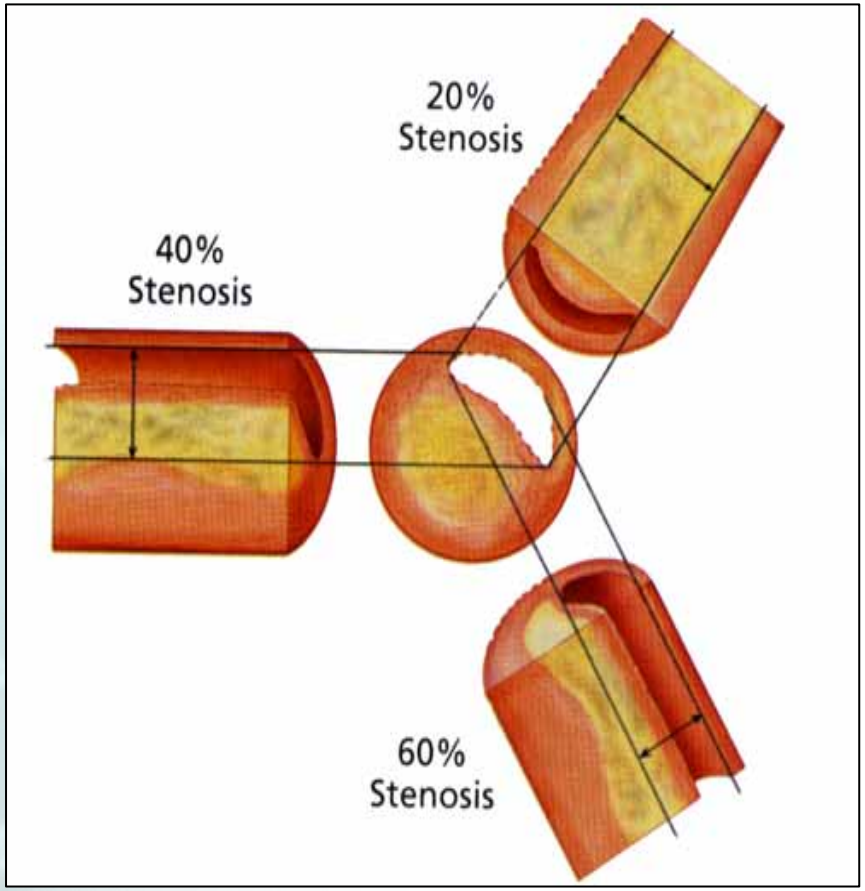
D. Geoffrey Vince, PhD

Seoul, Korea

28th April, 2006

Coronary Imaging

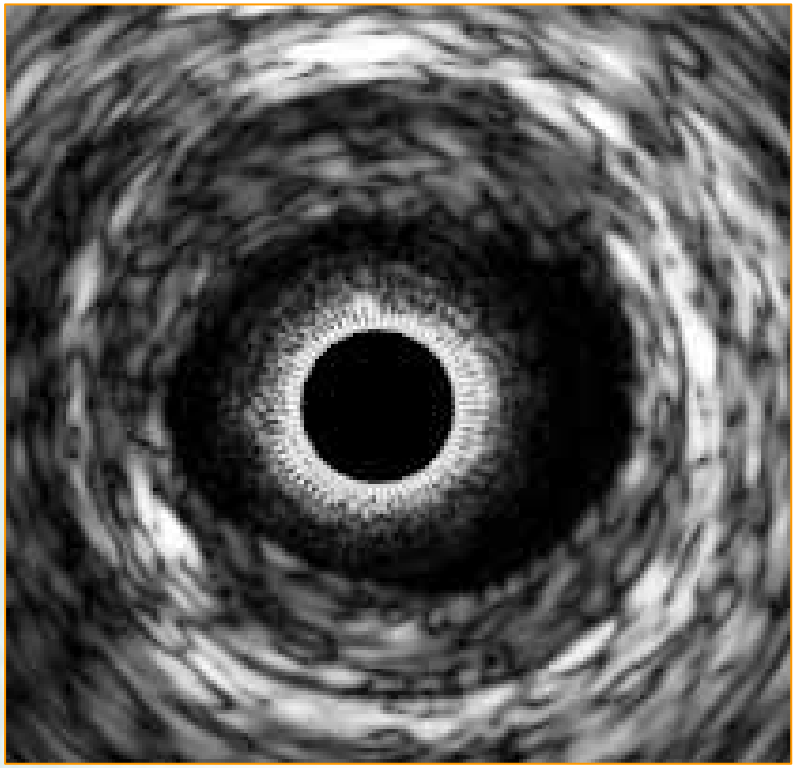
- Angiography is the current “gold-standard” in interventional imaging
- Angiography underestimates the degree of stenosis
  - Glagov remodelling
  - Vessel foreshortening



Nissen SE. *Cleveland Clinic Journal of Medicine. 66(8):479-85, 1999 Sep*

Coronary imaging

- IVUS can provide accurate information on:
  - Lumen area
  - Lesion length (pullback)
  - Plaque size
  - Vessel size
- However…

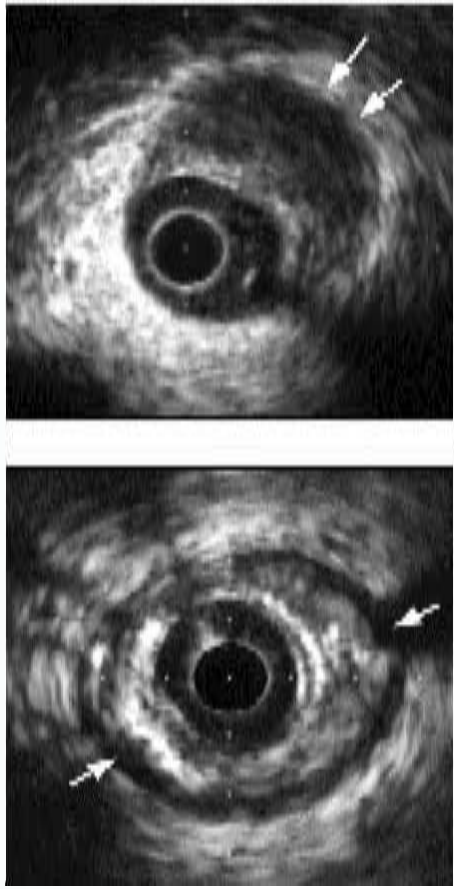


Coronary Imaging

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

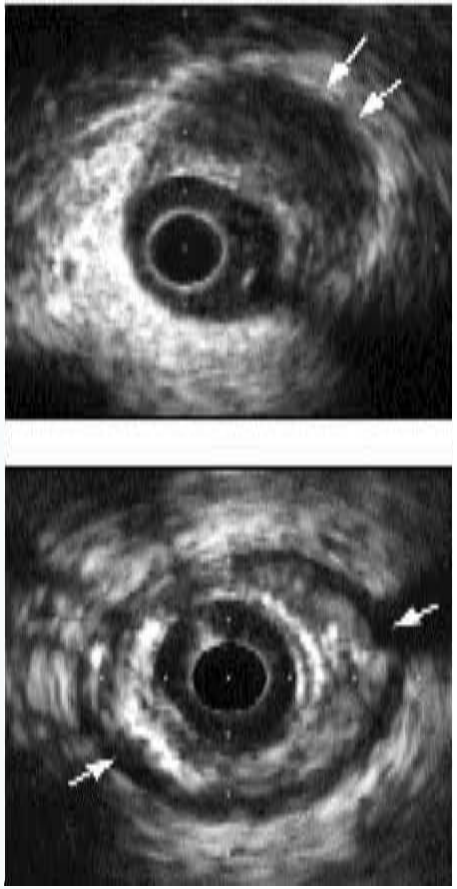
- Grayscale IVUS interpretation is not reliable; qualitative; and subjective.



Images Courtesy of CCF IVUS Core Lab

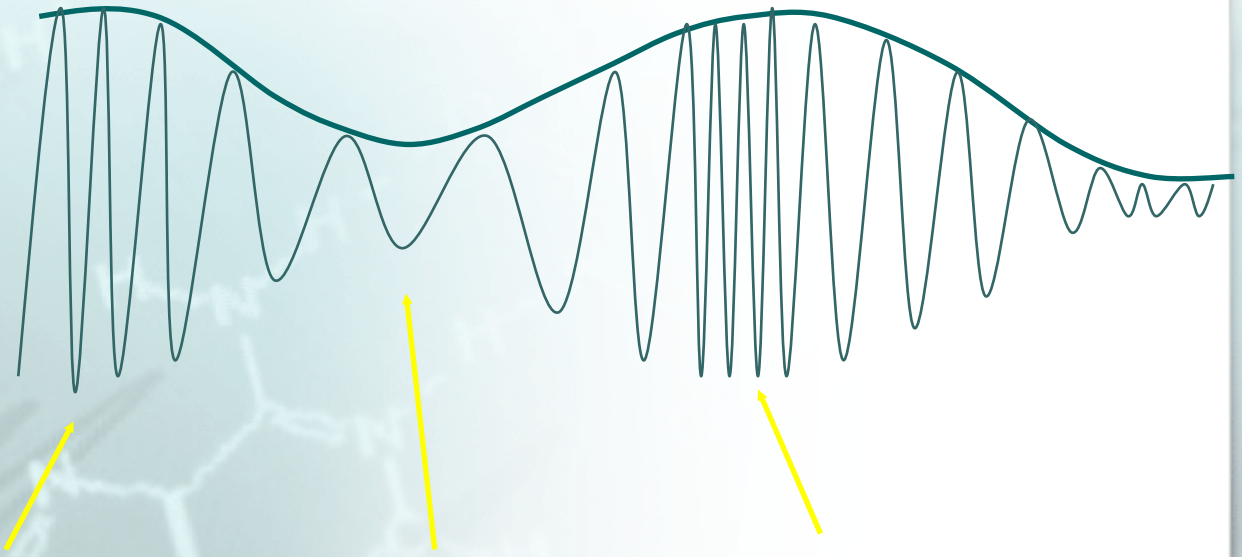
Echolucent vs Echogenic

- 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

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

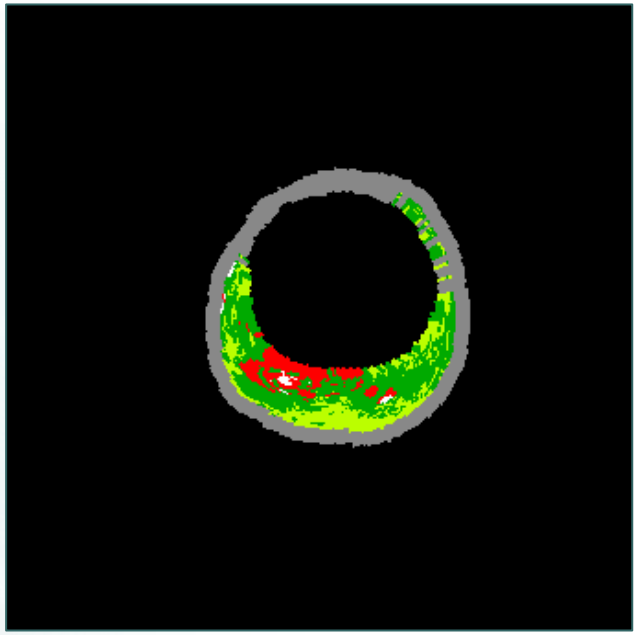
4) Radial pre-process VH Gradient

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

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

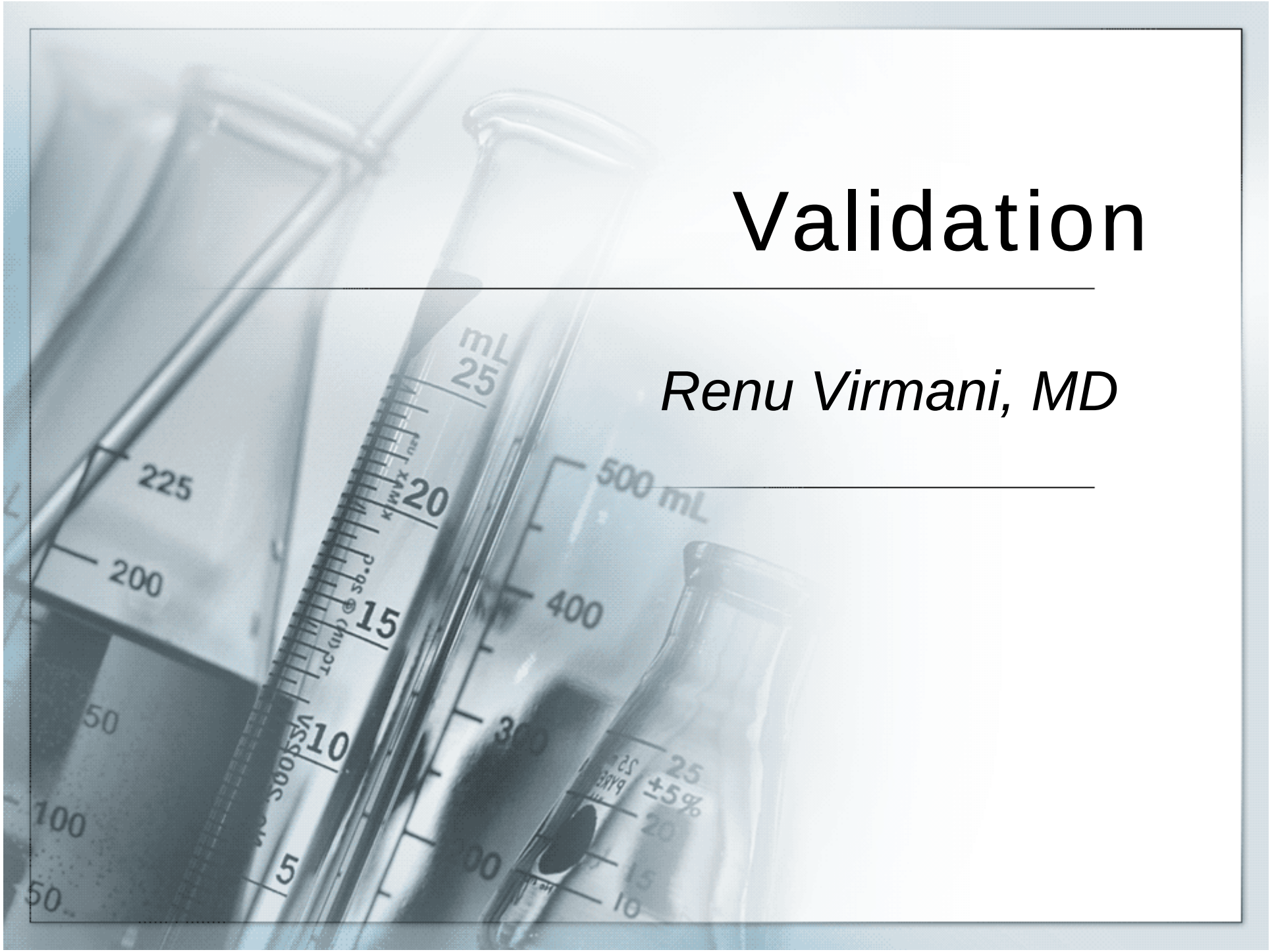
VH IVUS ™

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



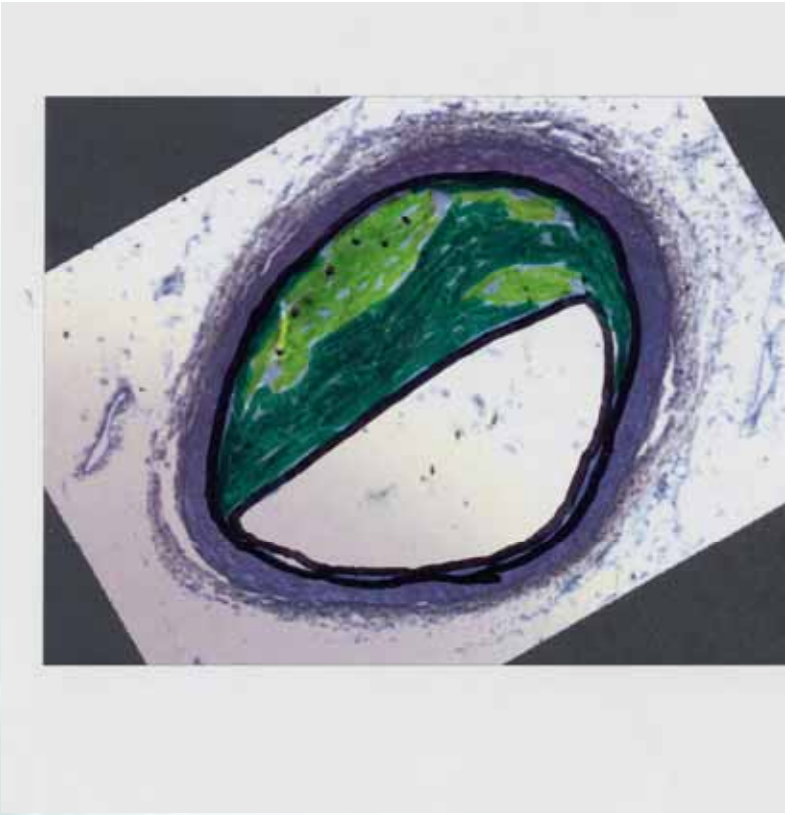
Validation

Renu Virmani, MD



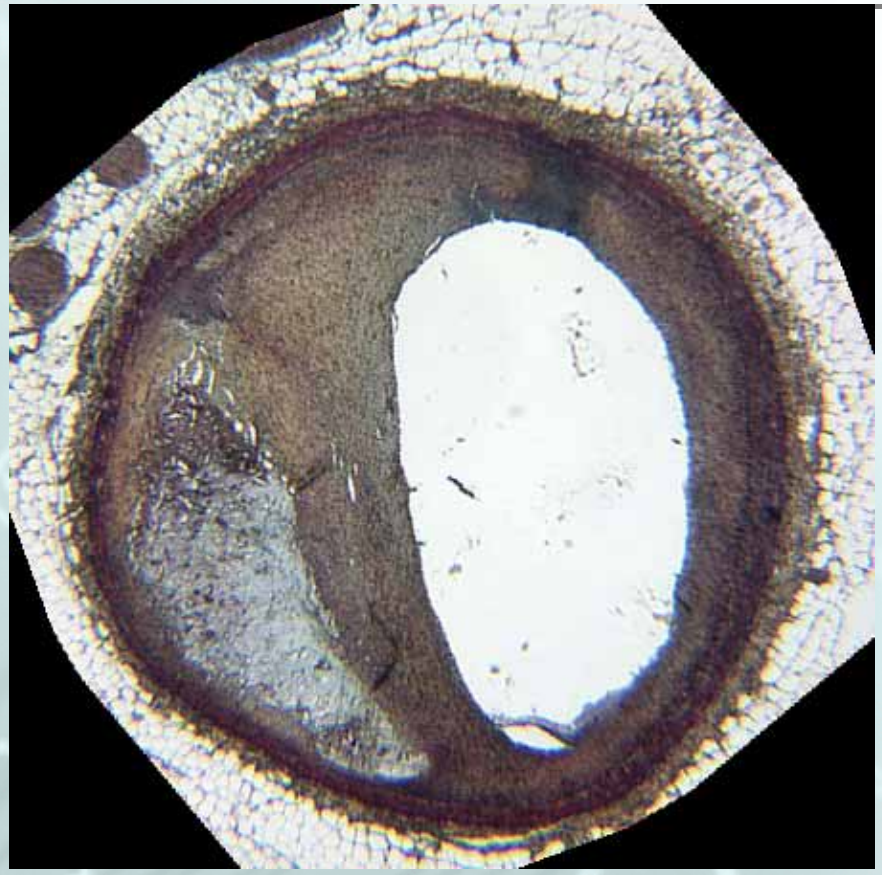
Method

- High quality digital images of histology were printed.
- Transparent film was taped over page.
- Borders drawn with black permanent marker
- Dr Virmani 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
- Dr Virmani was not shown the Grayscale or VH

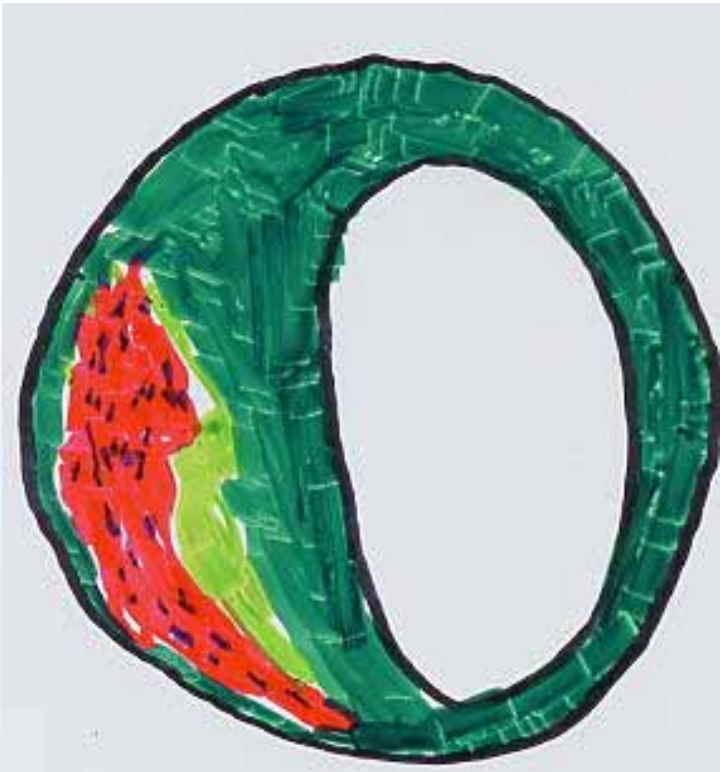


CCF 04037 B1

Histology

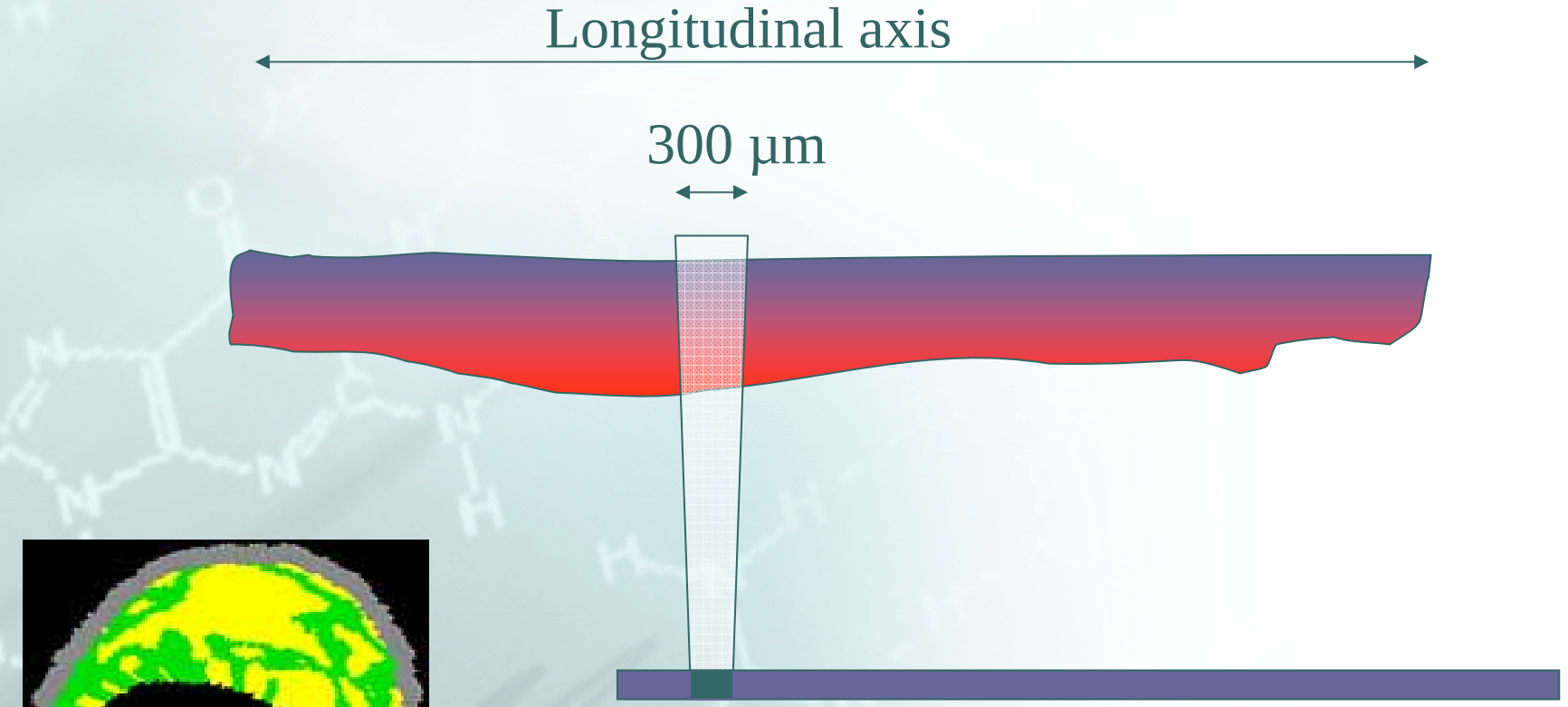


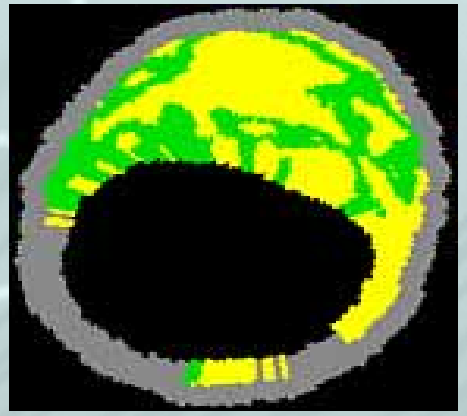
Virmani VH



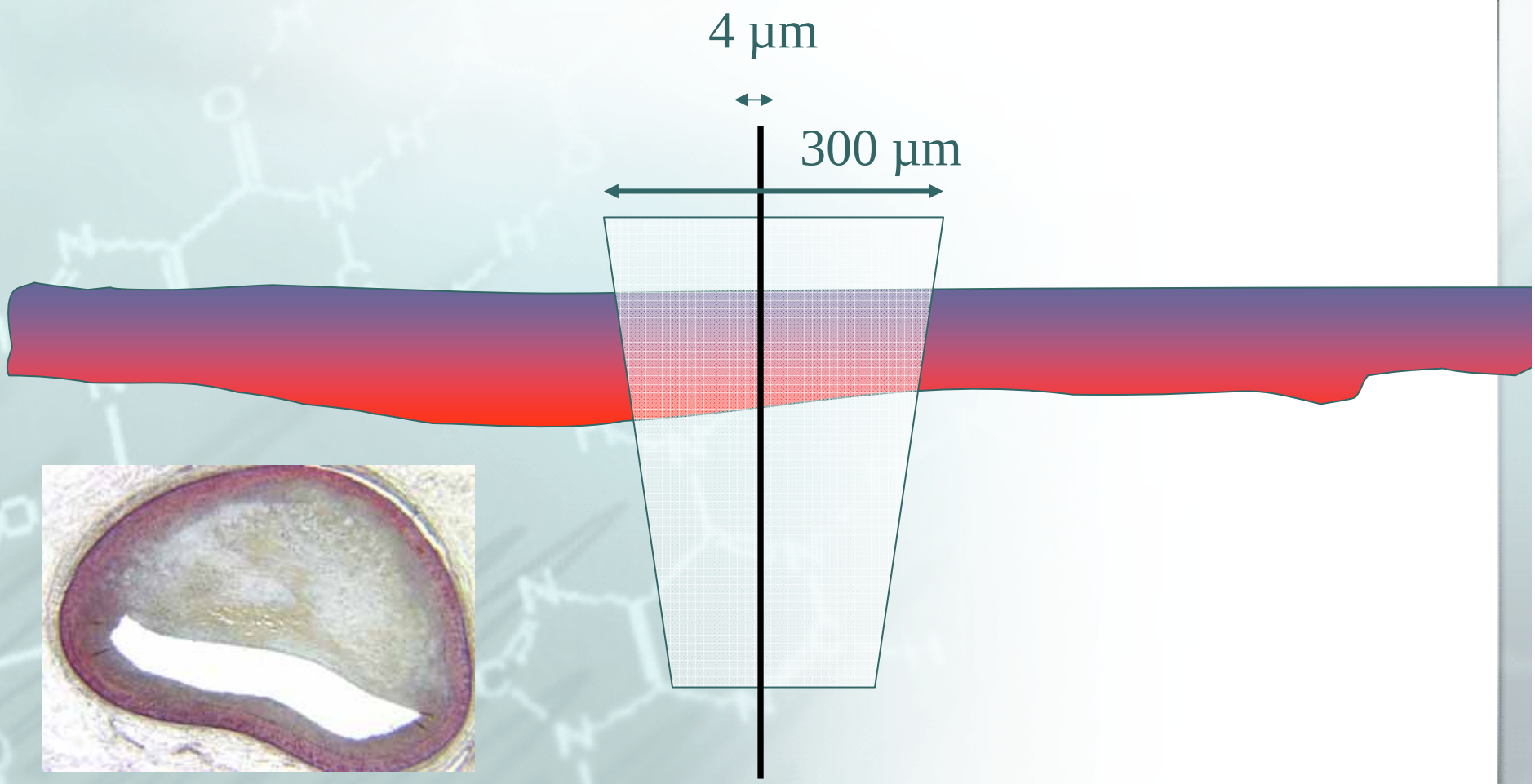
- Notes:
  - Fibroatheroma
  - Low likelihood of rupture
  - Speckled calcium

VH slice thickness



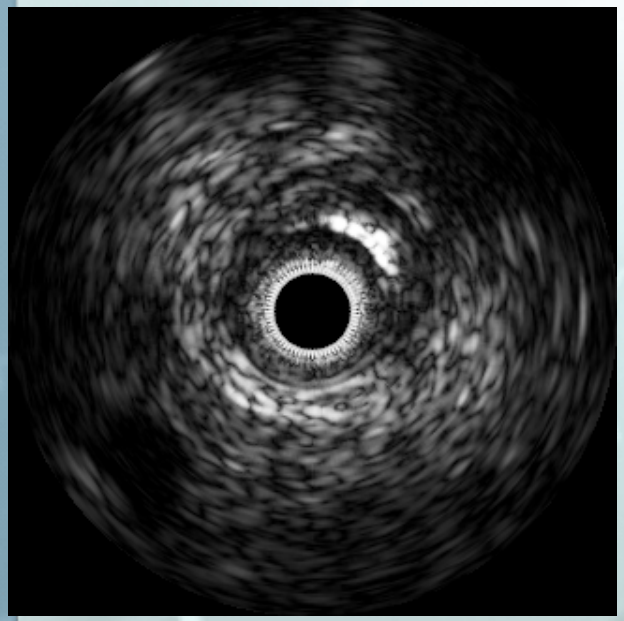


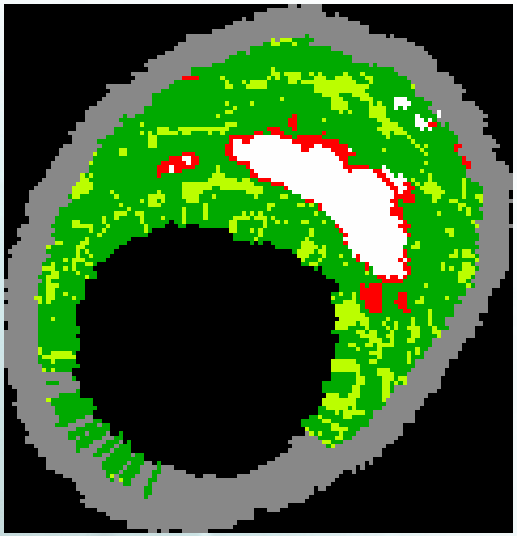
Histology slice thickness



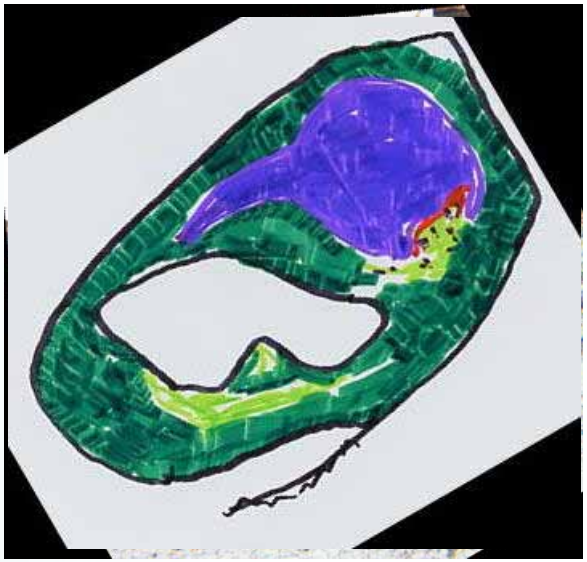
CCF 04038 B4, FCa

IVUS





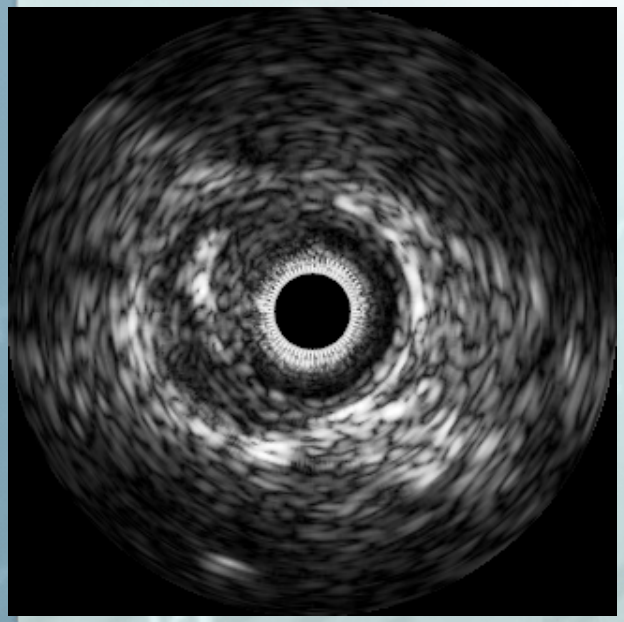
Histology

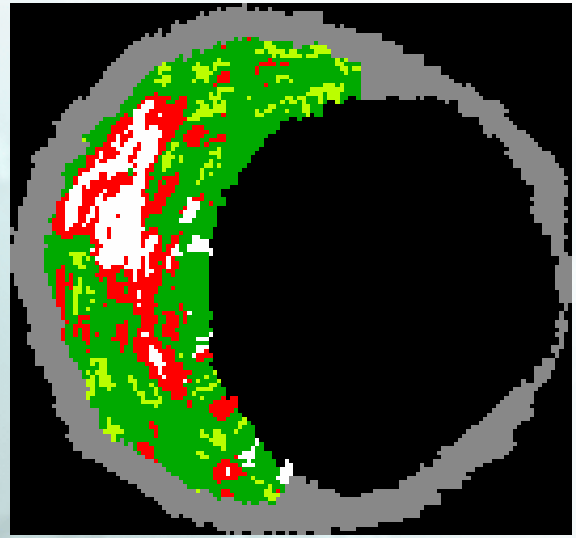


CCF 04042 B6, Ca FA

Histology

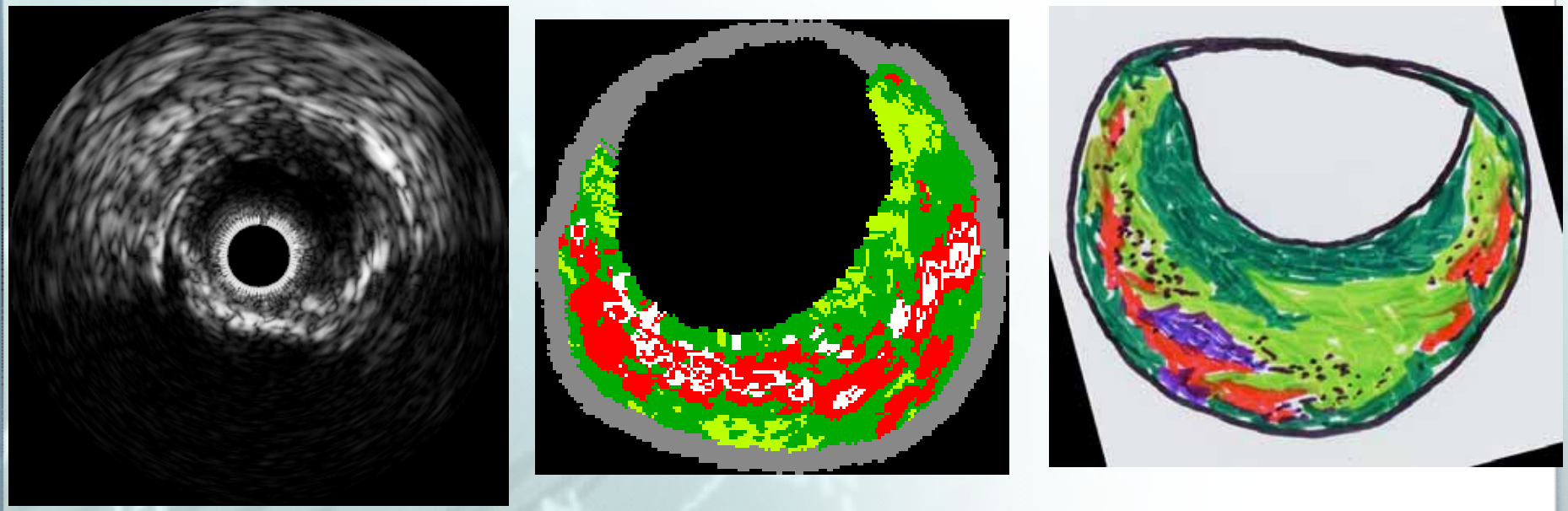
IVUS





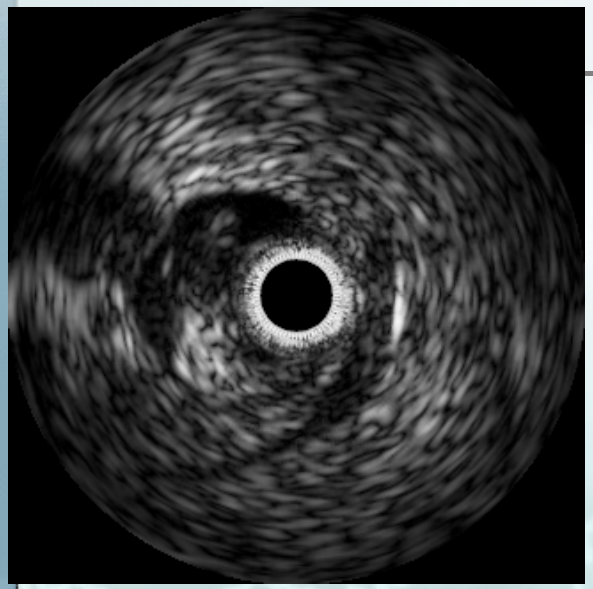
CCF 04075 B6, Ca FA

IVUS **Histology**



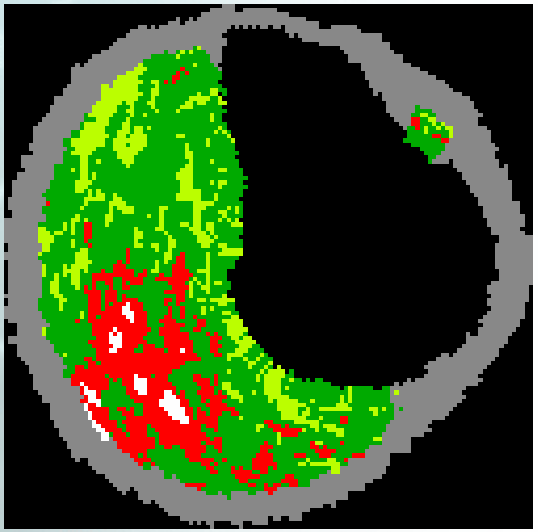
CCF 04106 B2, FA

IVUS

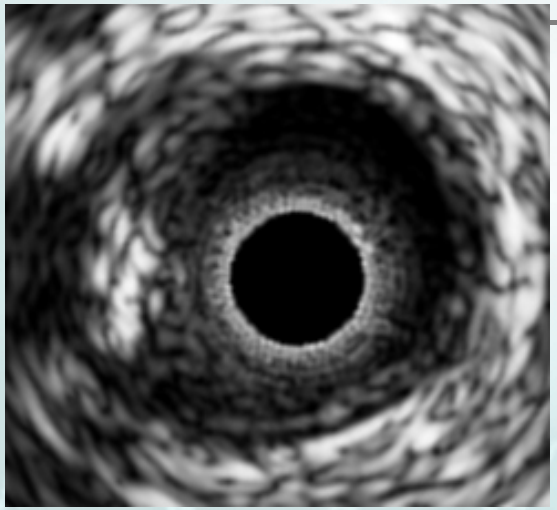


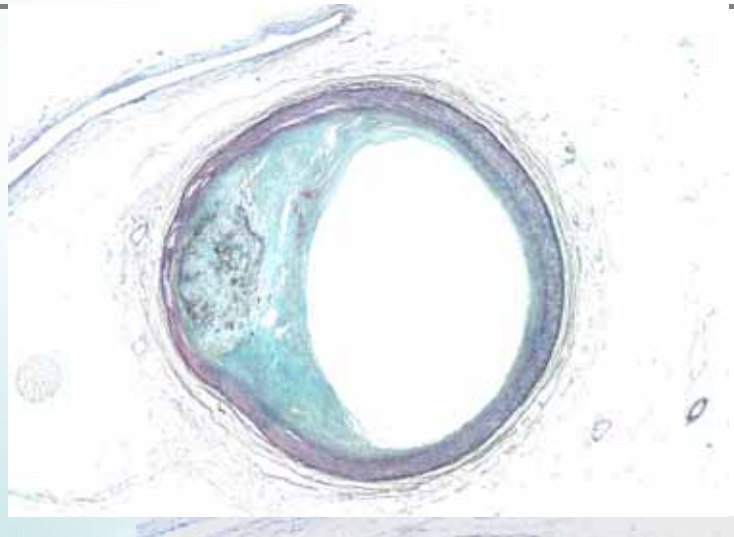
Histology

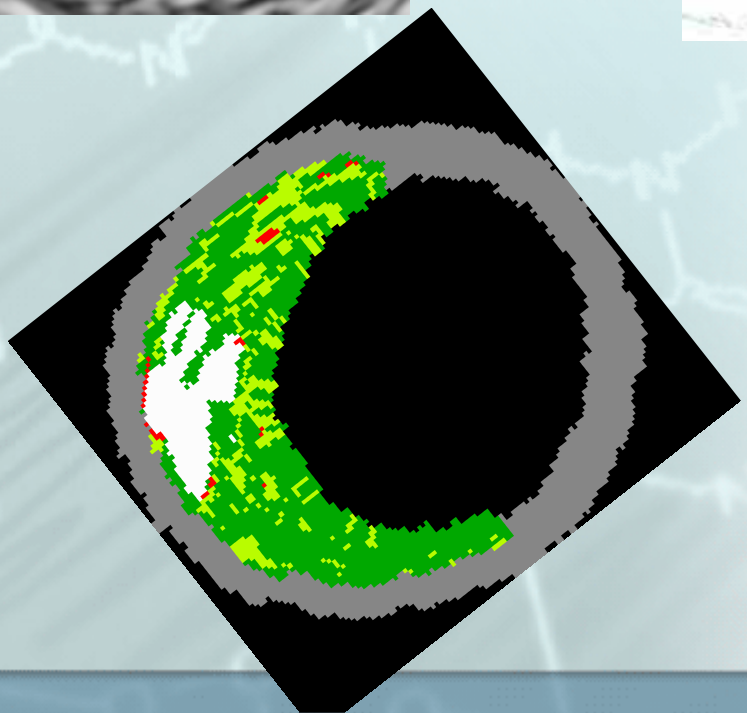
VH IVUS 2.0

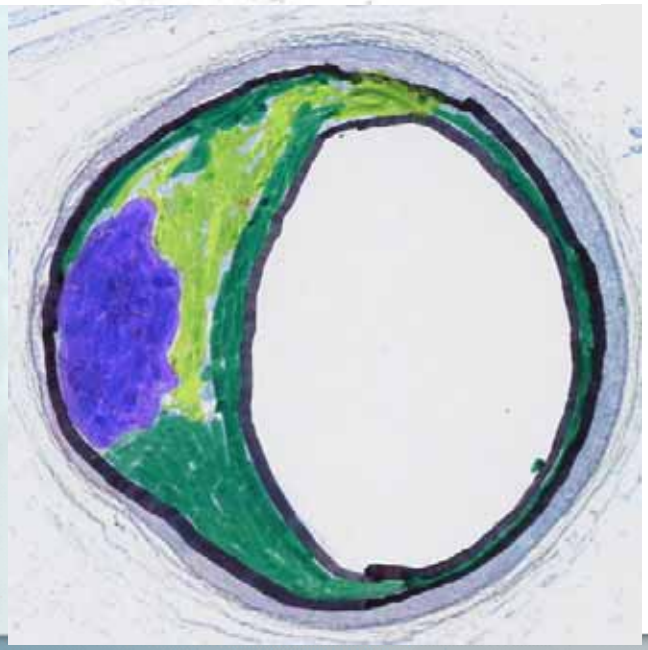


Fibrocalcific Plaque









How do we use this information?

- Need natural history studies to assess disease progression
  - PROSPECT – USA and EU
  - SPECIAL – Japan

Clinical Trial Aims

- PROSPECT (US and EU)
  - Identify the VH IVUS features of plaques which lead to a clinical event within a year
  - At the end of the study, we hope to say “If you see this kind of a plaque, there is a X % likelihood of that plaque to cause a thrombotic clinical event within a year”
- SPECIAL (Japan)
  - Identify the VH features of plaques which cause a silent clinical event within year
  - At the end of the study, we hope to say “If you see this kind of a plaque, there is an X% likelihood of that plaque to cause a silent thrombotic event within a year”