Imaging of Cardiovascular Elasticity

Third International Conference on the Ultrasonic Measurement and Imaging of Tissue Elasticity

Lake Windermere, Cumbria, United Kingdom

Cardiovascular Deformation Imaging.
part 1: vascular

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Content

1. Elasticity Imaging
2. Mechanical properties of arteries: Why and What?
3. Sources for deformation
4. Non-invasive vascular elasticity Imaging
5. Invasive vascular elasticity Imaging
   - Validation in Phantoms
   - Ex-vivo validation
   - In vivo validation
   - Patient studies
6. Three dimensional vascular elasticity imaging
7. Conclusion

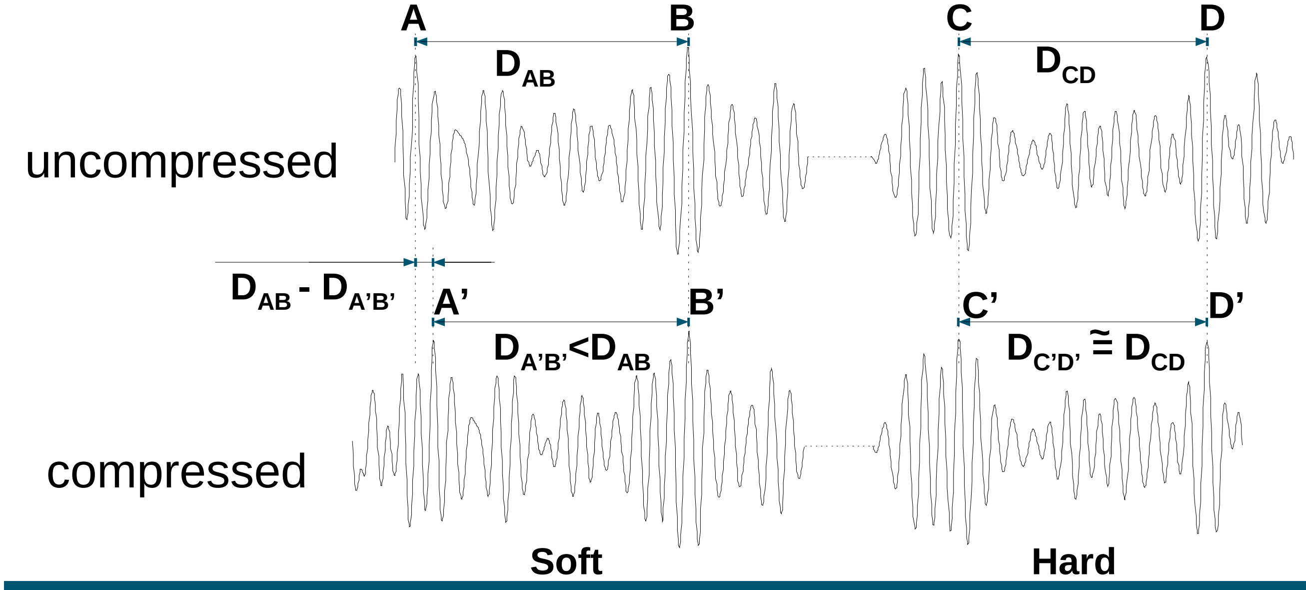
1. Elasticity Imaging

- Elastography: assessment of strain of tissue as a result of a controlled deformation. The response of the tissue is function of its mechanical properties.
- Strain Imaging: assessment of strain of tissue as a result of a physiologic deformation (blood pressure, muscle contraction). The strain is related to the mechanical properties or the function of the tissue.
- Different methods to detect strain:

  1. rf or envelope based elastography.
  2. TDI based strain/strain-rate imaging.
  3. Sonoelasticity Imaging.

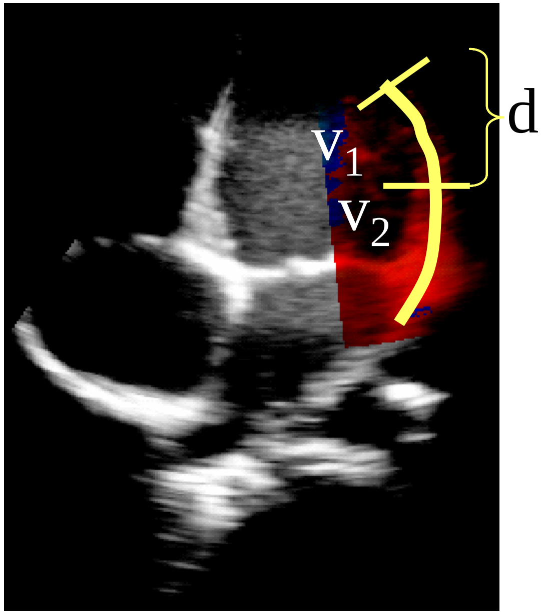
RF or Envelope based elastography.

- Classical way of doing elastography as described in patent (1991).
- Cross-correlation analysis of windowed ultrasound signals.
- Finite difference to determine strain from time delays.



TDI based strain/strain-rate Imaging

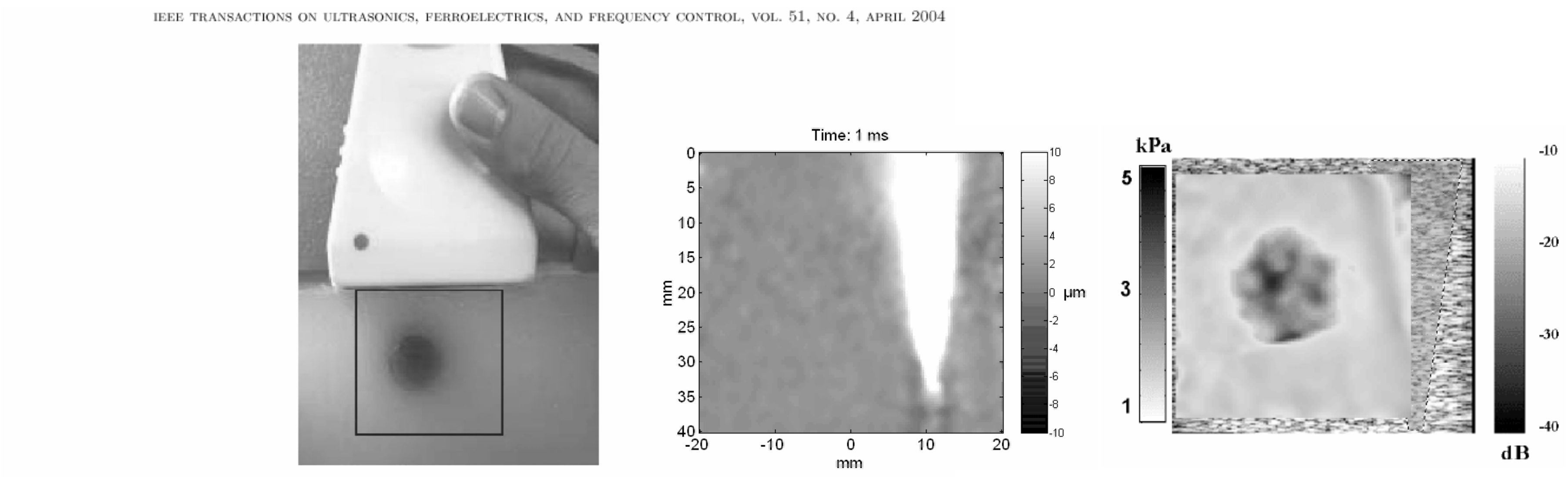
- Method was first applied in cardiac imaging.
- Difference of tissue velocity in different regions along the ultrasound beam results in strain-rate.
- Strain-rate is converted to strain using integration.



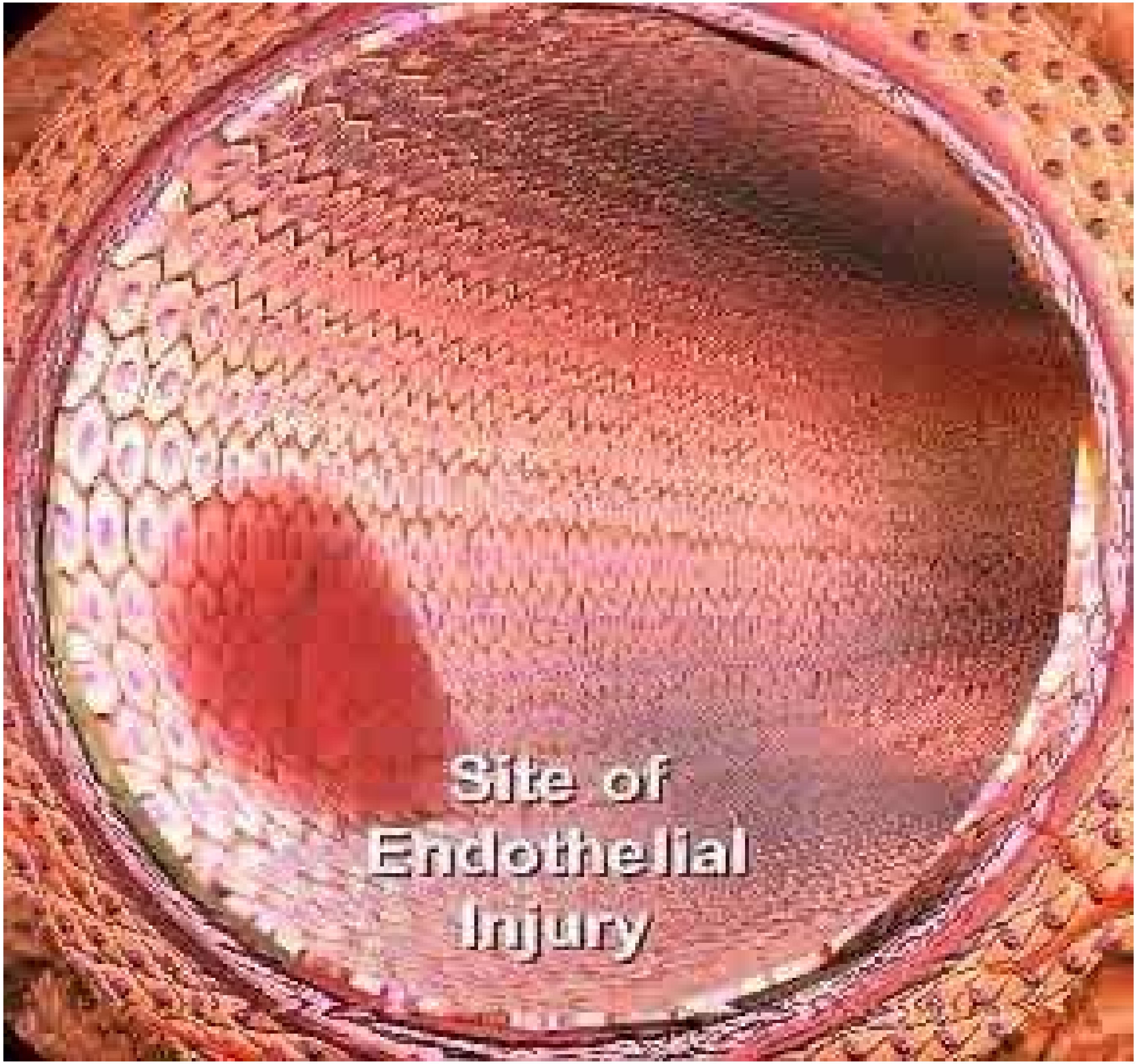
$$SR = (V2-V1)/d$$

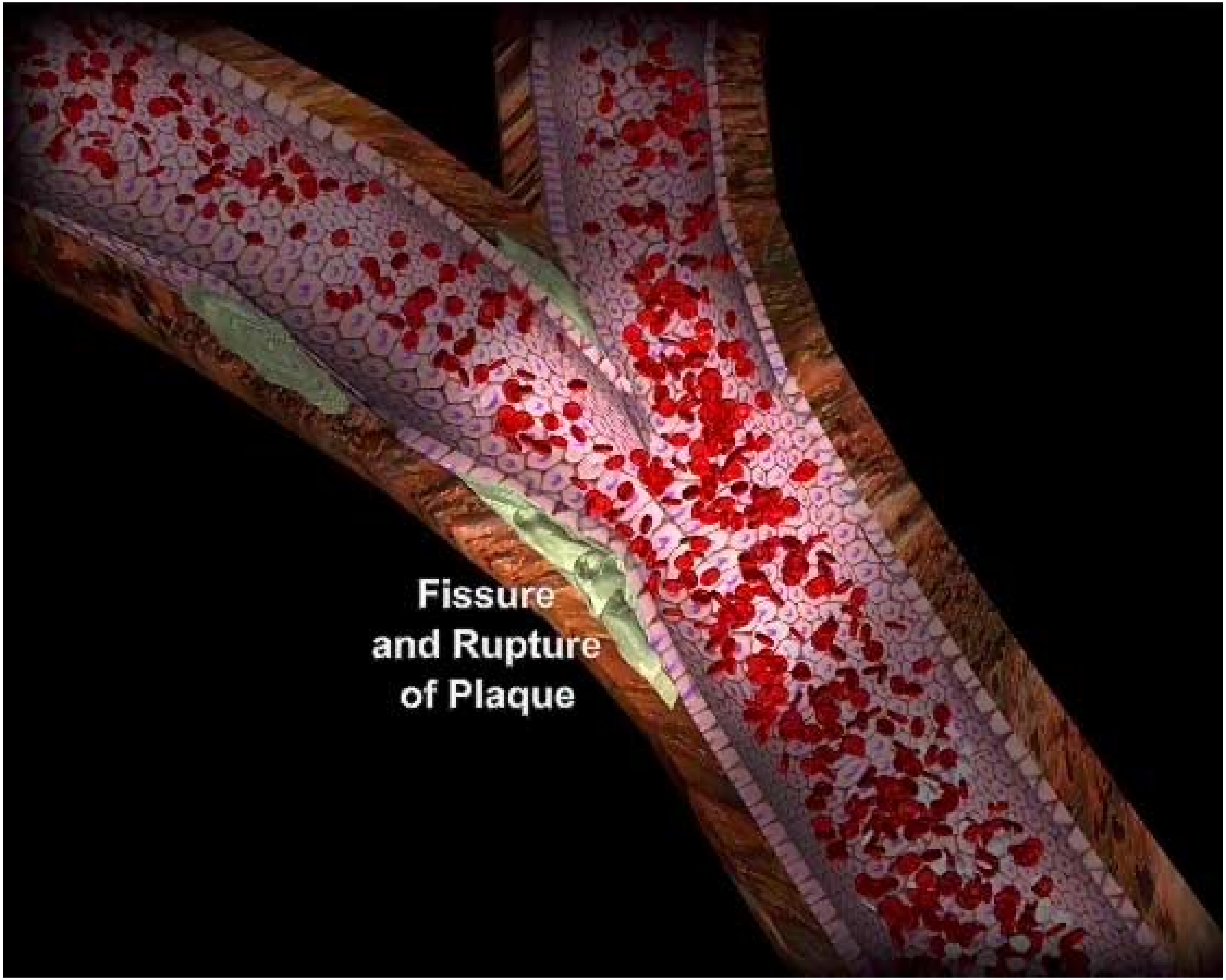
Sonoelasticity

- A low frequency vibration is applied
- A small tissue inhomogeneity causes a disturbance in the shear wave.
- Supersonic Shear Imaging (SSI) is ‘updated’ version.

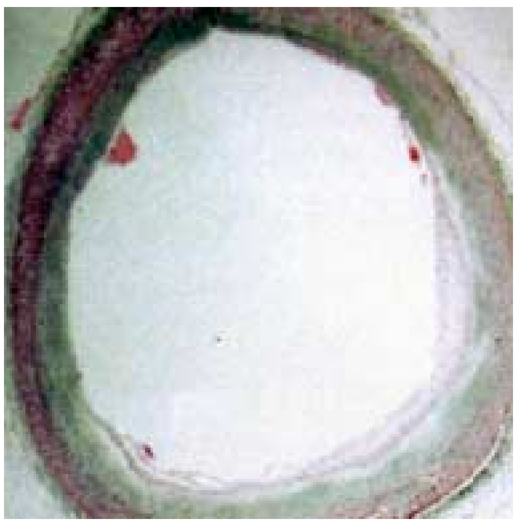


Bercoff et al, IEEE UFFC. 2004


Site of
Endothelial
Injury

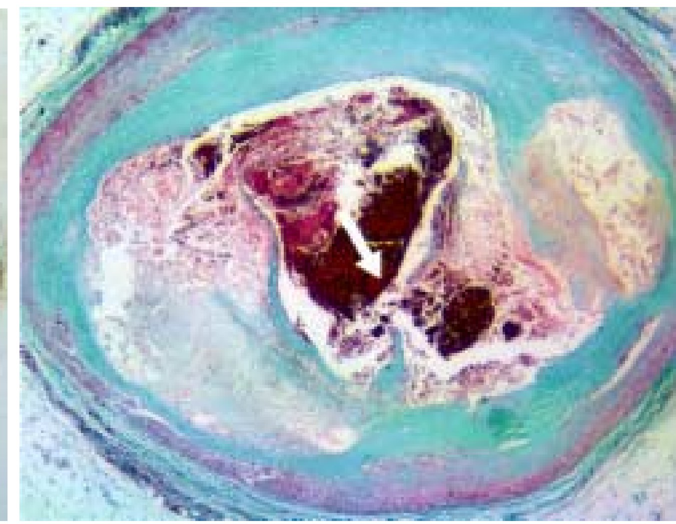

Fissure
and Rupture
of Plaque

The way into the catastrophe



Small plaque

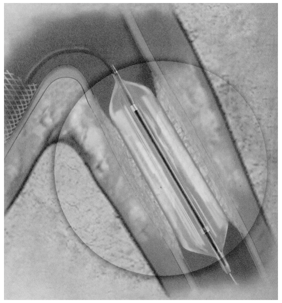
Big plaque



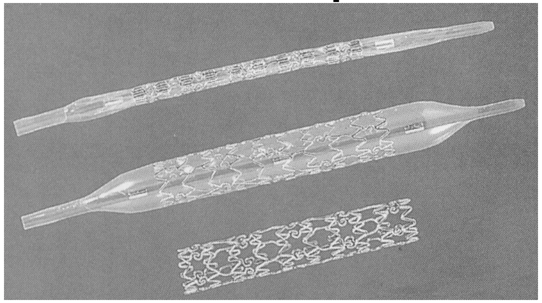
Infarction

2. Mechanical properties of arteries

- Why do we need mechanical properties:
  1. Composition of the vessel wall and plaque
  2. Vulnerability of a plaque
  3. Effect of interventional procedures



PTCA



Stent

  4. Effect of pharmaceutical treatment
  5. Age of thrombus
- What can we image in arteries and veins using elasticity imaging methods:

Composition

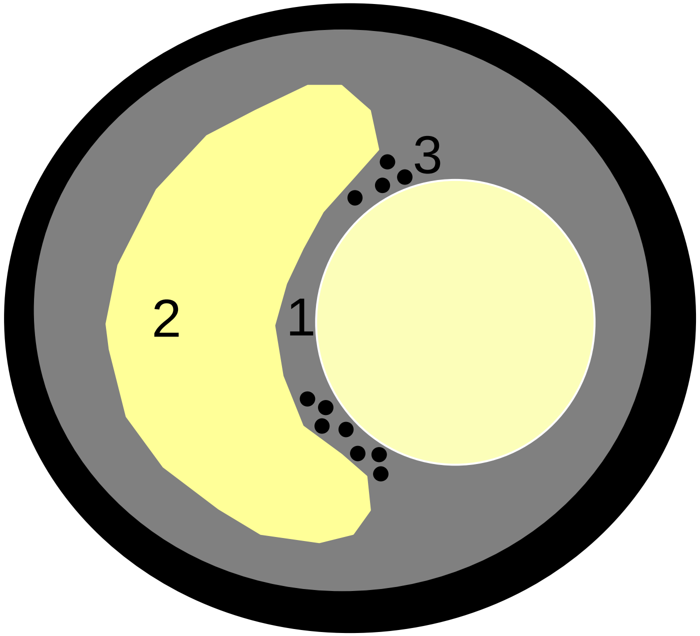
- The main components of atherosclerotic plaques have different mechanical properties *(Lee et al, Arteriosclerosis Thromb. 1992)*

Tissue type	Modulus
non-fibrous	41 kPa
fibrous	82 kPa
calcified	355 kPa

- Caps with increased macrophage density are weaker than non-inflamed caps *(Lendon et al, atherosclerosis. 1991)*

Plaque vulnerability

- Plaque vulnerability is associated with:
  1. Thin fibrous cap
  2. Big lipid pool
  3. Inflammation (macrophage infiltration)
  4. High stress regions



Age of thrombus

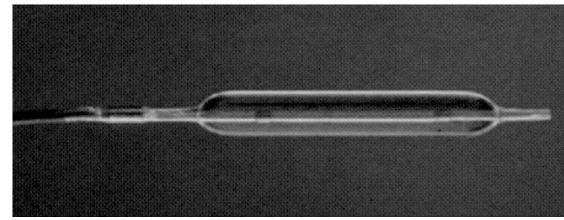
- The age of a thrombus is the parameter that determines the strategy to dissolve it.

Pharmaceutical treatment

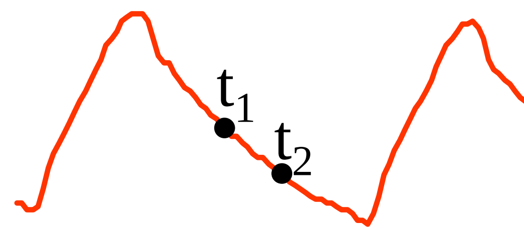
- Several therapies (like statin treatment) stabilize the plaque and does not affect the size of it.
- Interventional strategies are mechanical in nature and will affect the mechanical properties of the vessel wall and plaque.

3. Sources for deformation in vascular applications

- Balloon



- Intraluminal pressure

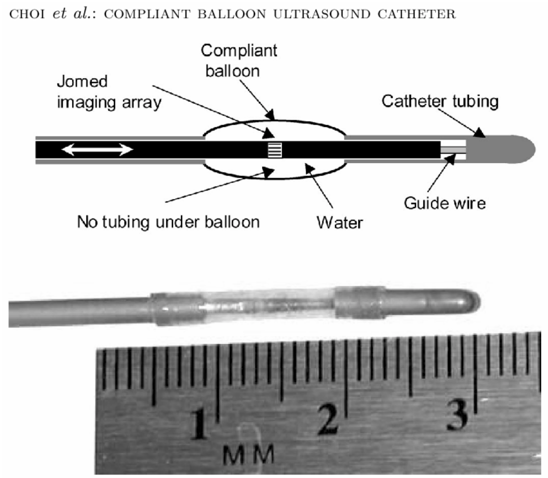


- Deformation from outside

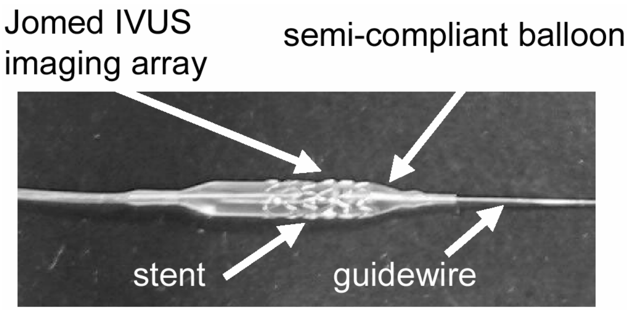
Balloon

- Two types of balloon are used:

1. Compliant balloon
   - Optimal relation between pressure and applied stress.
   - Minimum cause of damage.



Choi et al, IEEE UFFC. 2002

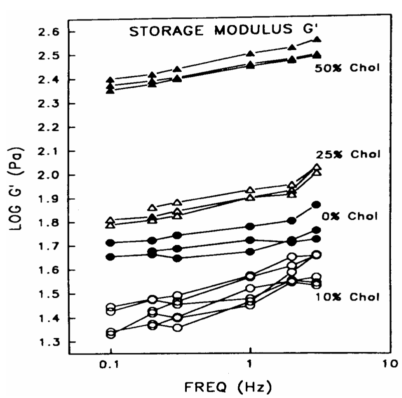


Choi et al, Proc IEEE Ultras Symp. 2002

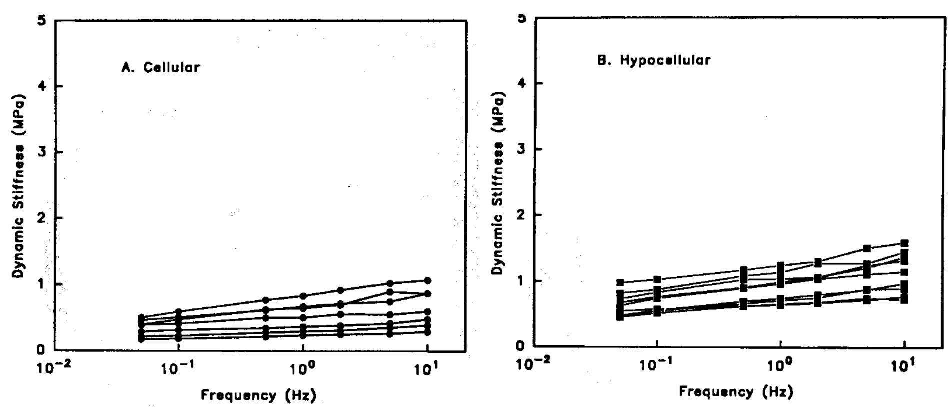
2. Non-compliant balloon
   - Stress in tissue is unknown due to ‘shielding’ of the balloon.
   - Used for monitoring interventional procedures

Intraluminal pressure

- Minimal invasive since it is already present.
- Excellent relation between pressure and applied stress.
- Dynamic (or semi-dynamic) instead of static excitation. However, ratio remains the same.
- Non-controllable.
- Acquisitions are disturbed by motion.



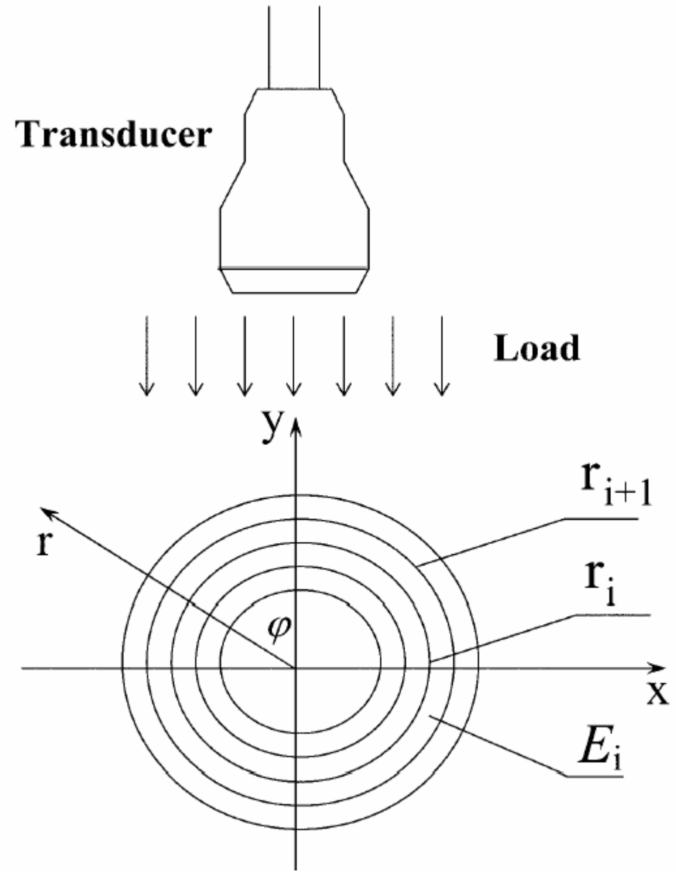
Loree et al, Arteriosclerosis Thromb. 1994



Lee et al, Circulation. 1991

Deformation from outside

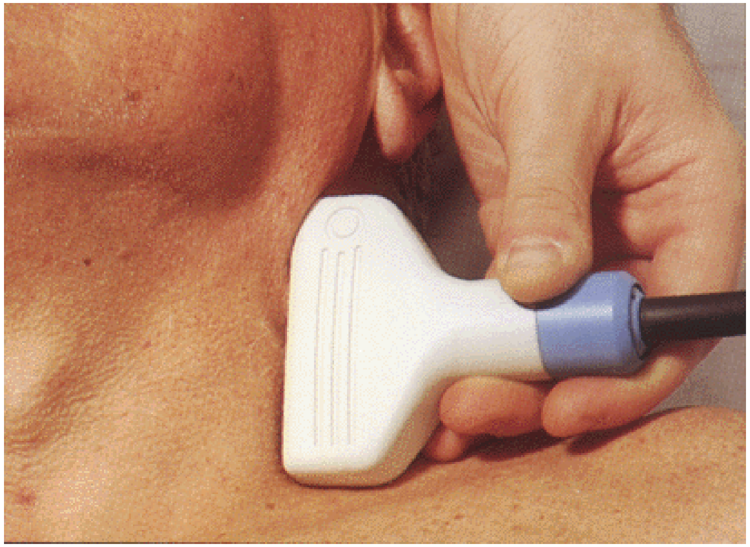
- Only for superficial arteries
- Especially suited for clotted arteries (thrombosis).
- Correction needed for misalignment of ultrasound beam and radial strain vector.



Aglyamov et al, IEEE UFFC. 2004

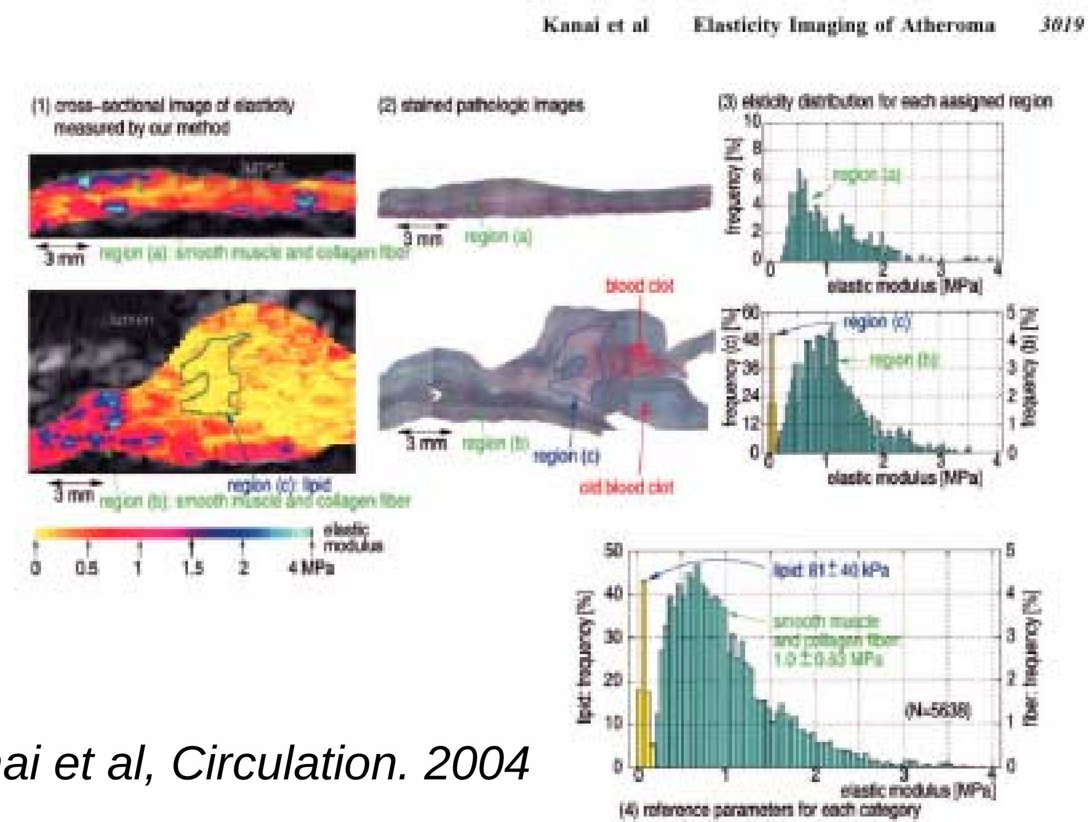
4. Non-invasive vascular elasticity imaging

- Assessment of plaque composition in superficial arteries.
- Assessment of thrombus stiffness/age
- Arteries suitable for non-invasive approach:
  - Carotid artery
  - Femoral artery



Assessment of plaque composition I

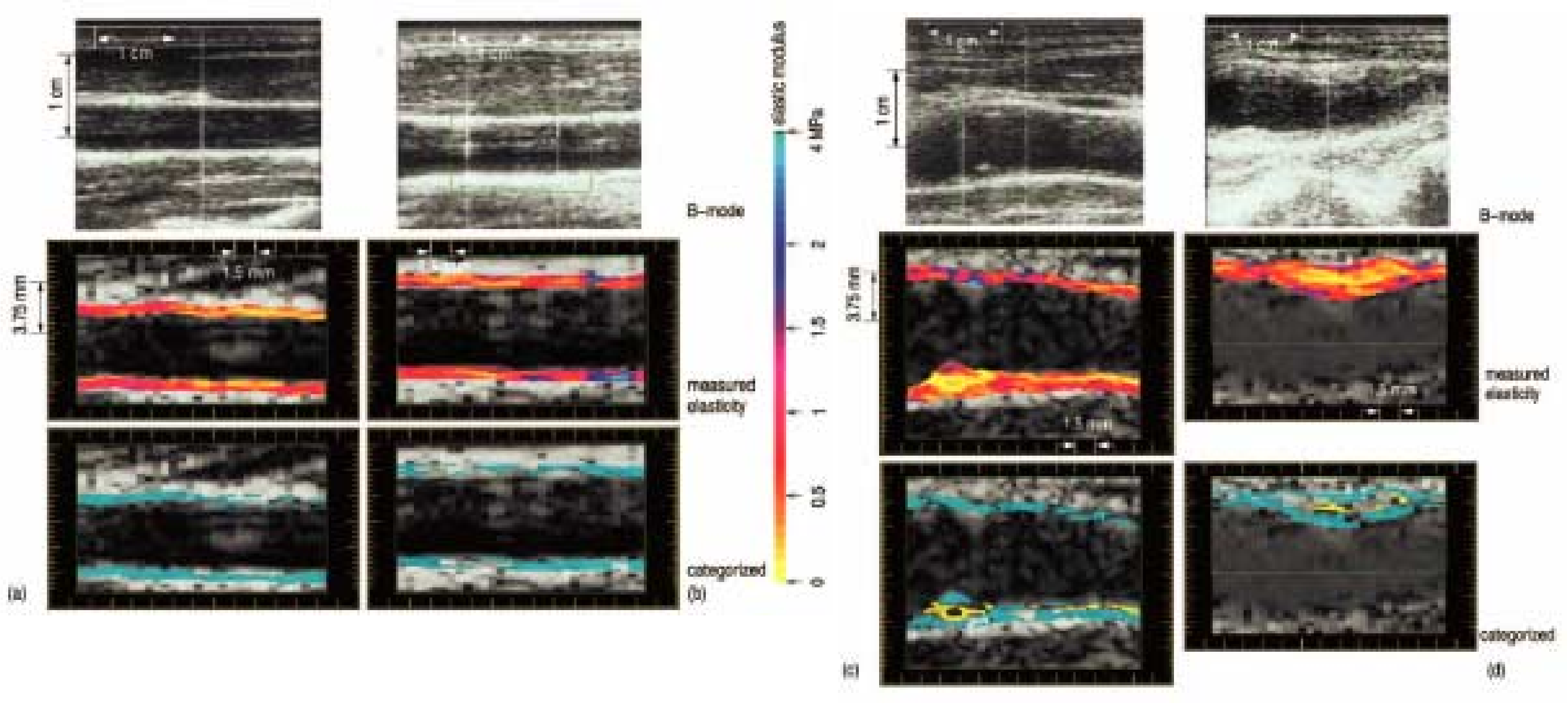
- Parallel orientation of the transducer and artery: *in vitro validation.*



Kanai et al, Circulation. 2004

Assessment of plaque composition II

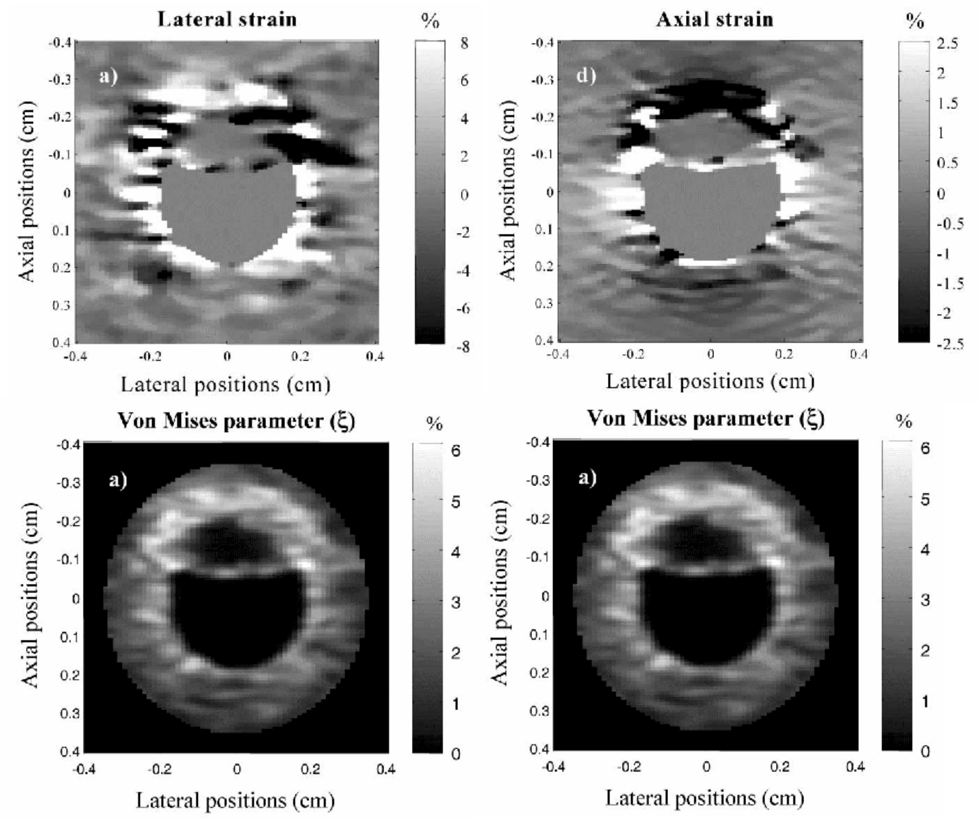
- Parallel orientation of the transducer and artery: *in vivo application.*



Kanai et al, Circulation. 2004

Assessment of plaque composition III

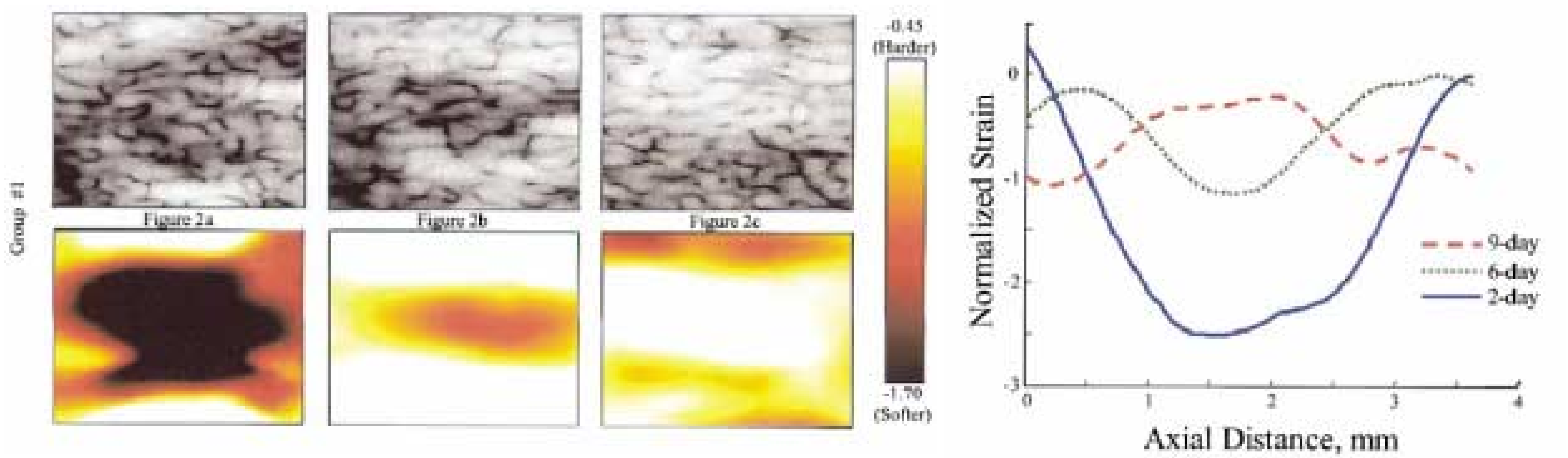
- Transducer orientation perpendicular to vessel axis
  simulations.



Maurice et al, IEEE Med Imag. 2004

Assessment of thrombus stiffness I

- Force is applied externally with the transducer.
- Evaluation of technique in vivo in rat model.

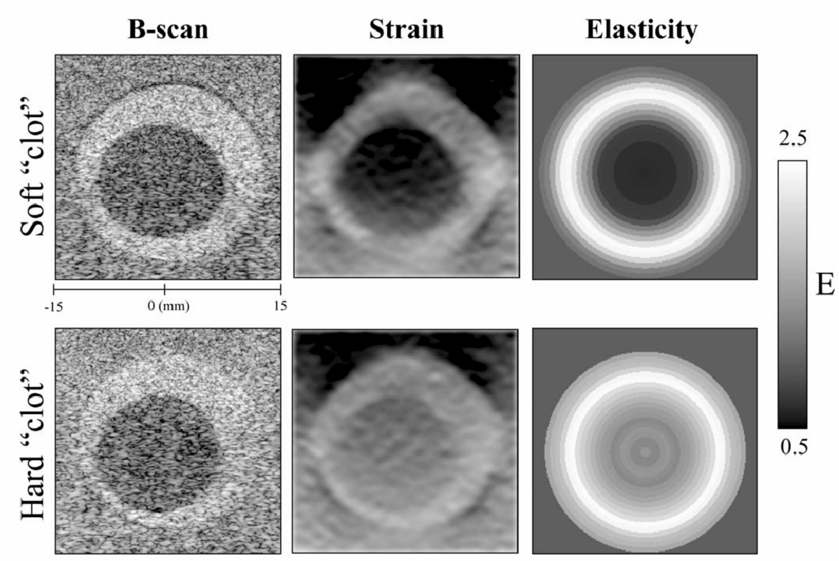


Emelianov et al, Ultras Med Biol. 2002

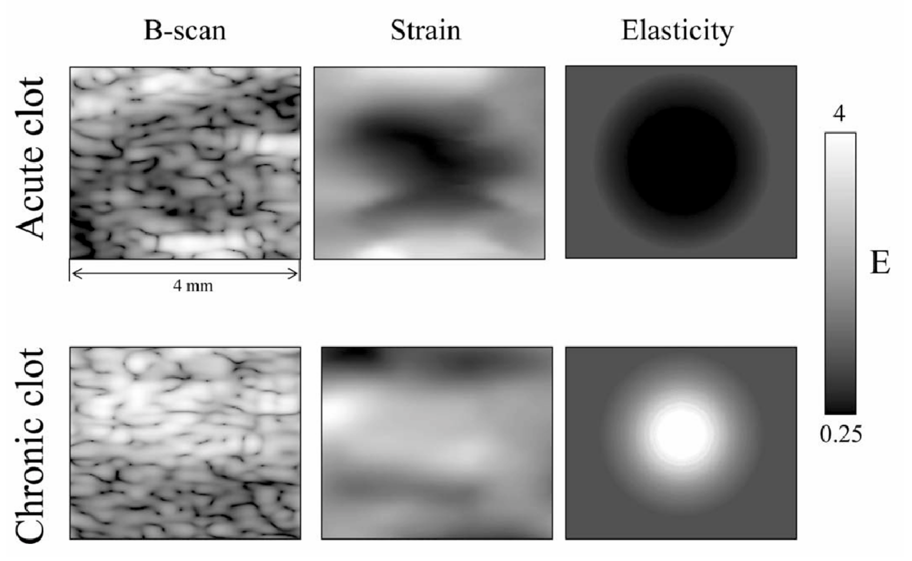
Assessment of thrombus stiffness II

- Layered cylinder model is used to estimate E.

Phantom



Rat model in vivo



Aglyamov et al, IEEE UFFC. 2004

5. Invasive vascular elasticity Imaging

- Using an intravascular catheter.
- Pulsatile pressure or balloon is used as force.
- Assessment of strain in larger vessels (diam >2mm).
- Especially used in coronary arteries.

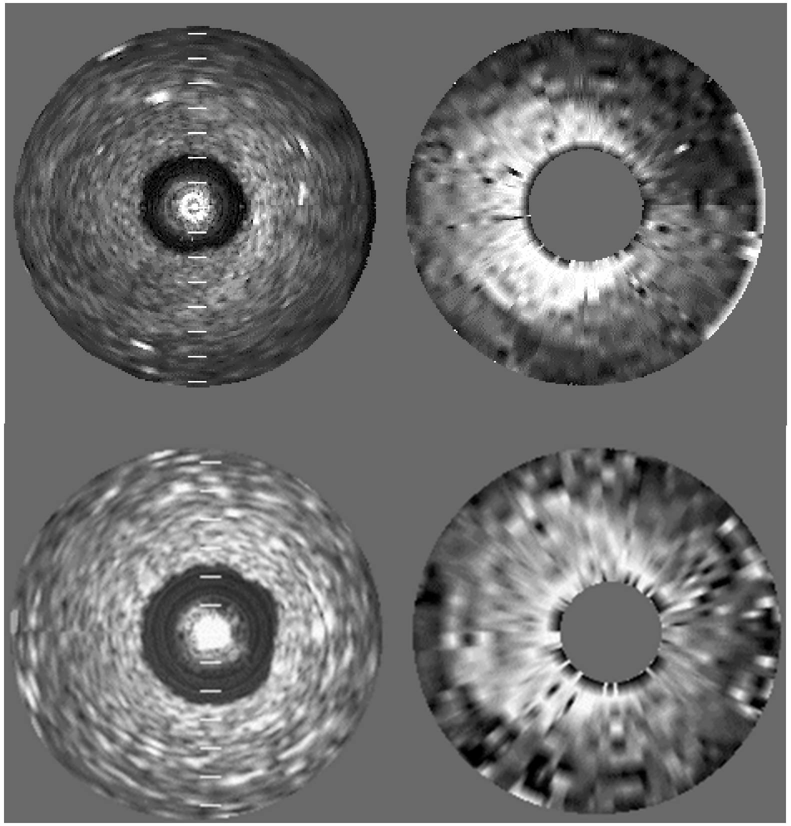
Validation in Phantoms

- Phantom studies:
  1. Flexible geometries and moduli
  2. Thick walled vessels to develop techniques
  3. Testing Influence of echogenicity
  4. Homogeneous phantoms allow theoretical studies (catheter position, SNR_E)

- Performed by various groups using different catheters and deformation sources

Validation in Phantoms

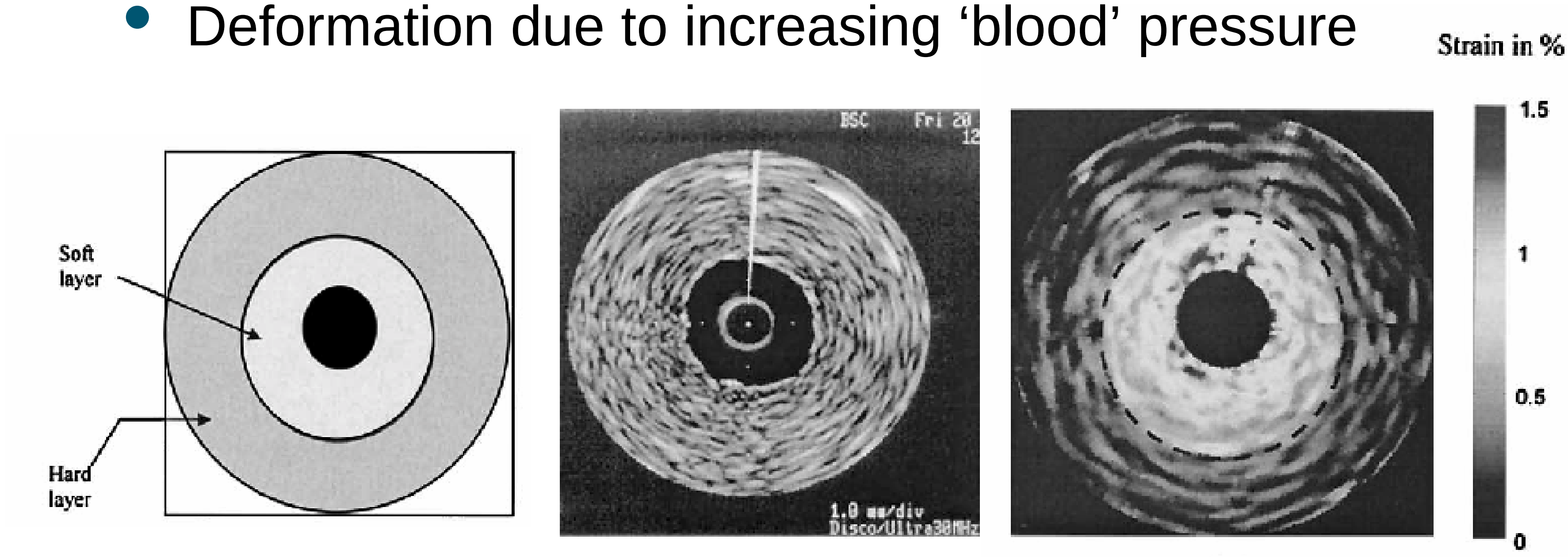
- Modified single element catheter using ‘blood’ pressure.



de Korte et al, Ultras Med Biol. 1997

Validation in Phantoms

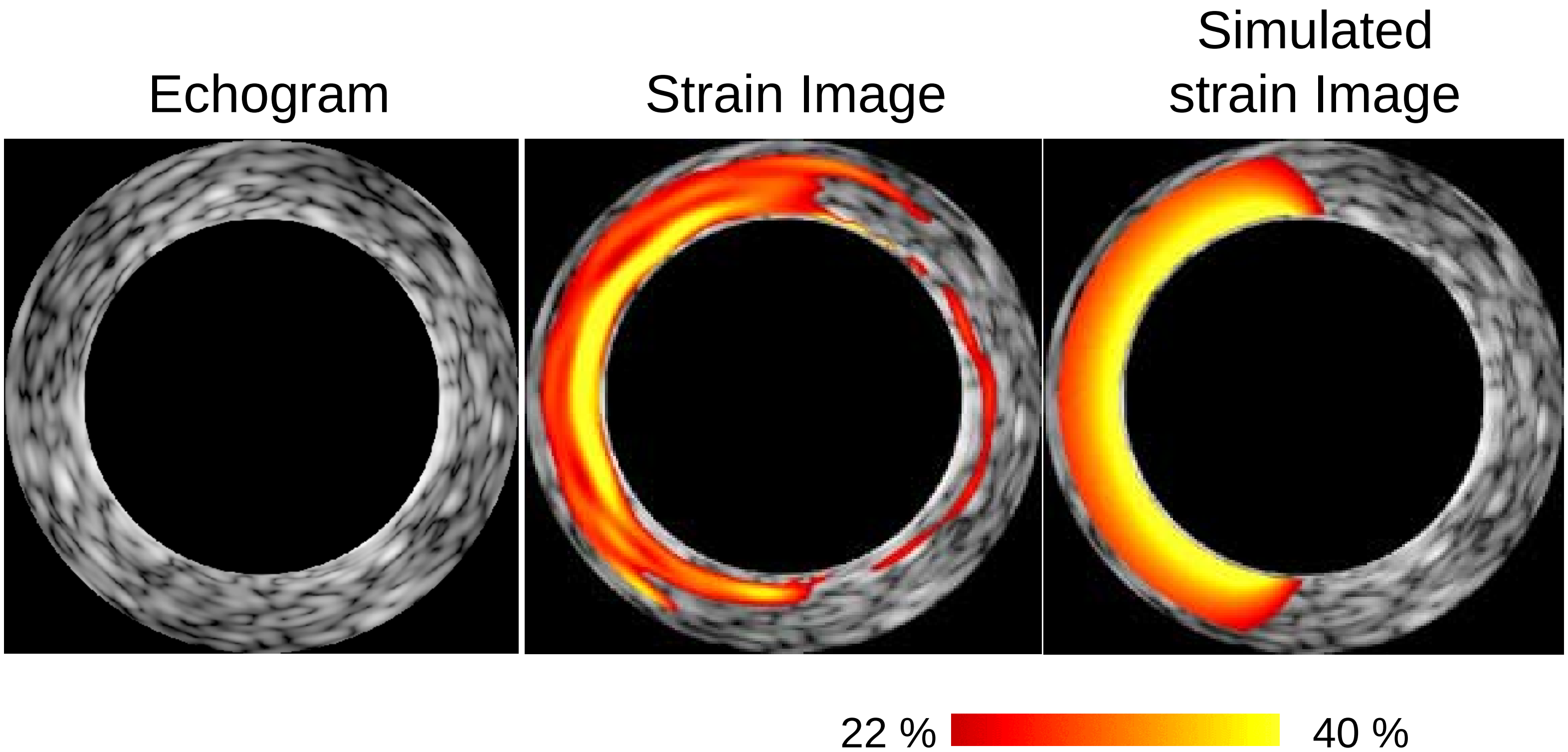
- Single element catheter connected to commercial IVUS system
- Deformation due to increasing ‘blood’ pressure



Brusseau et al, Ultras Med Biol. 2002

Validation in Phantoms

- Array catheter integrated with balloon



Courtesy M. O'Donnell et al, Ann Arbor, USA

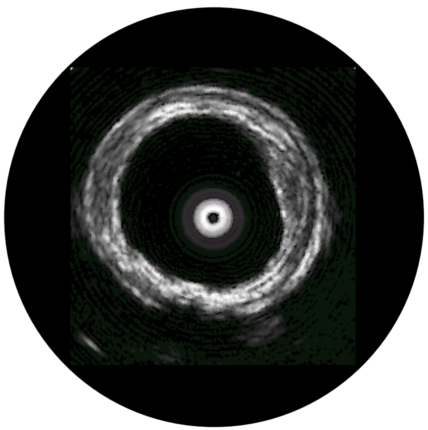
Ex-vivo validation

- Validation studies:
  1. Provides answer to question if technique works on real specimen
  2. Allows correlation with histology
  3. Provides tissue characterization properties
  4. Provides vulnerable plaque detection properties

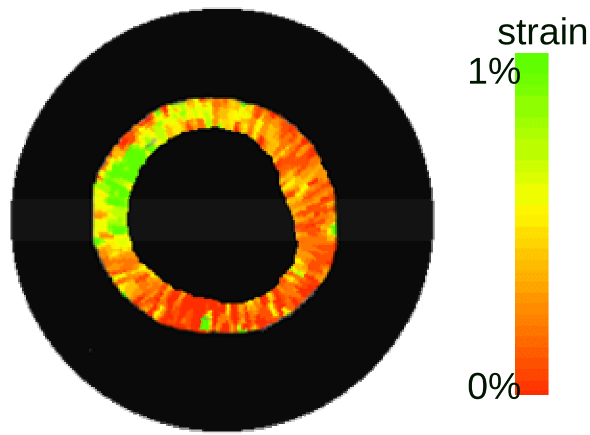
- Performed by various groups using different catheters and deformation sources

Ex-vivo validation: feasibility I

- Single element catheter and intraluminal pressure.
- Fibrous plaque in human femoral



IVUS



Elastogram

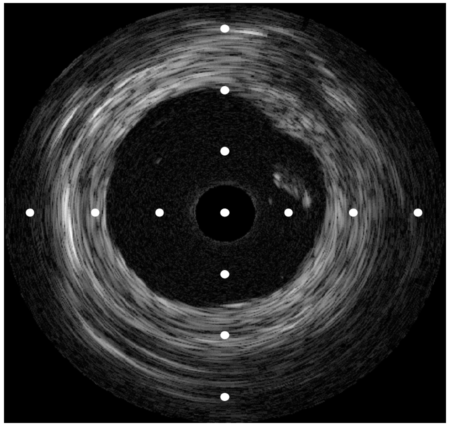
Hematoxylin Eosin

Elastic van Gieson

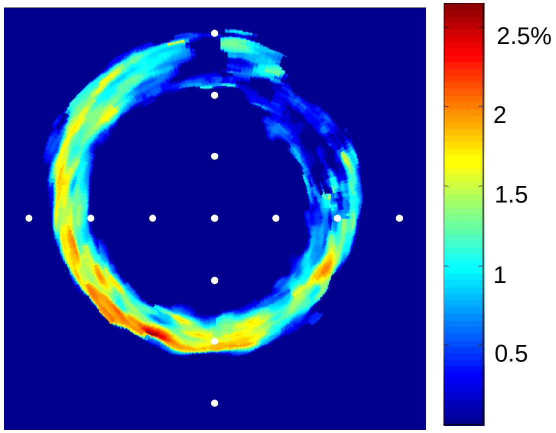
de Korte et al, Ultras Med Biol. 1997

Ex-vivo validation: feasibility II

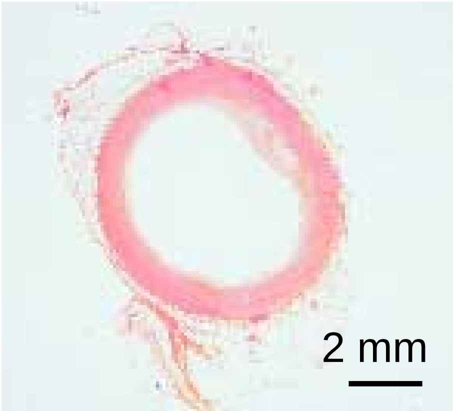
- Single element connected to commercial system.
- Fibrous plaque in carotid artery.



Echogram



Elastogram

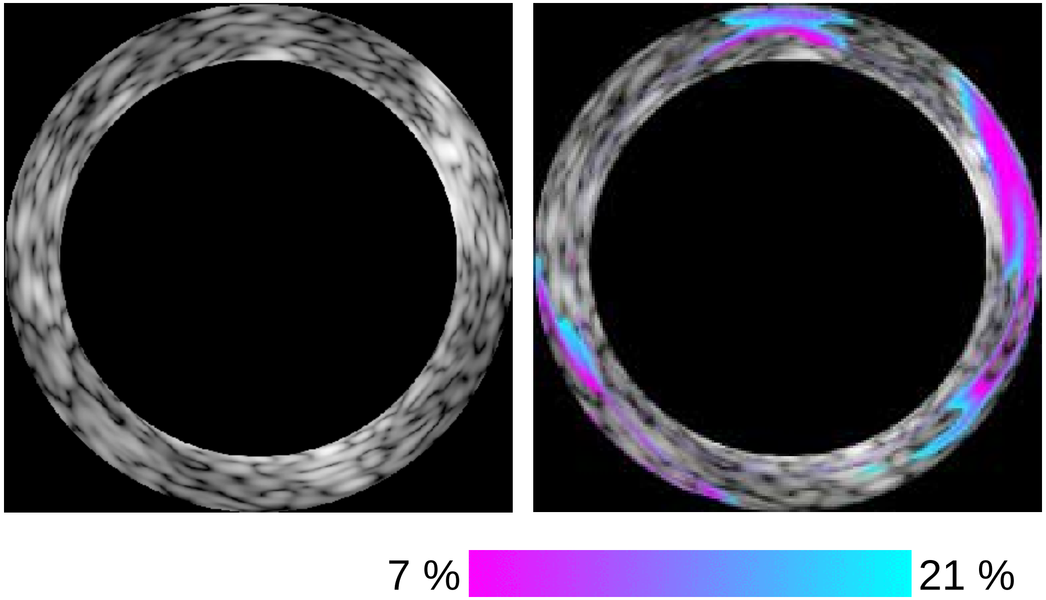


Histological section

Brusseau et al, Ultras Med Biol. 2002

Ex-vivo validation: feasibility III

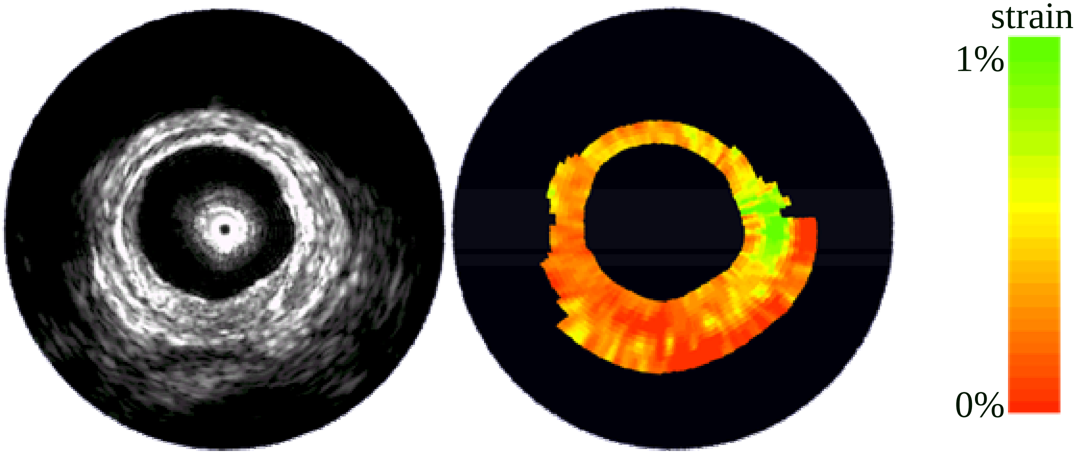
- Array catheter with integrated balloon.
- Fibrotic plaque in human femoral artery.
- Strain values higher than 21% are not shown



Courtesy M. O'Donnell et al, Ann Arbor, USA

Ex-vivo validation: validation I

- Single element catheter and intraluminal pressure

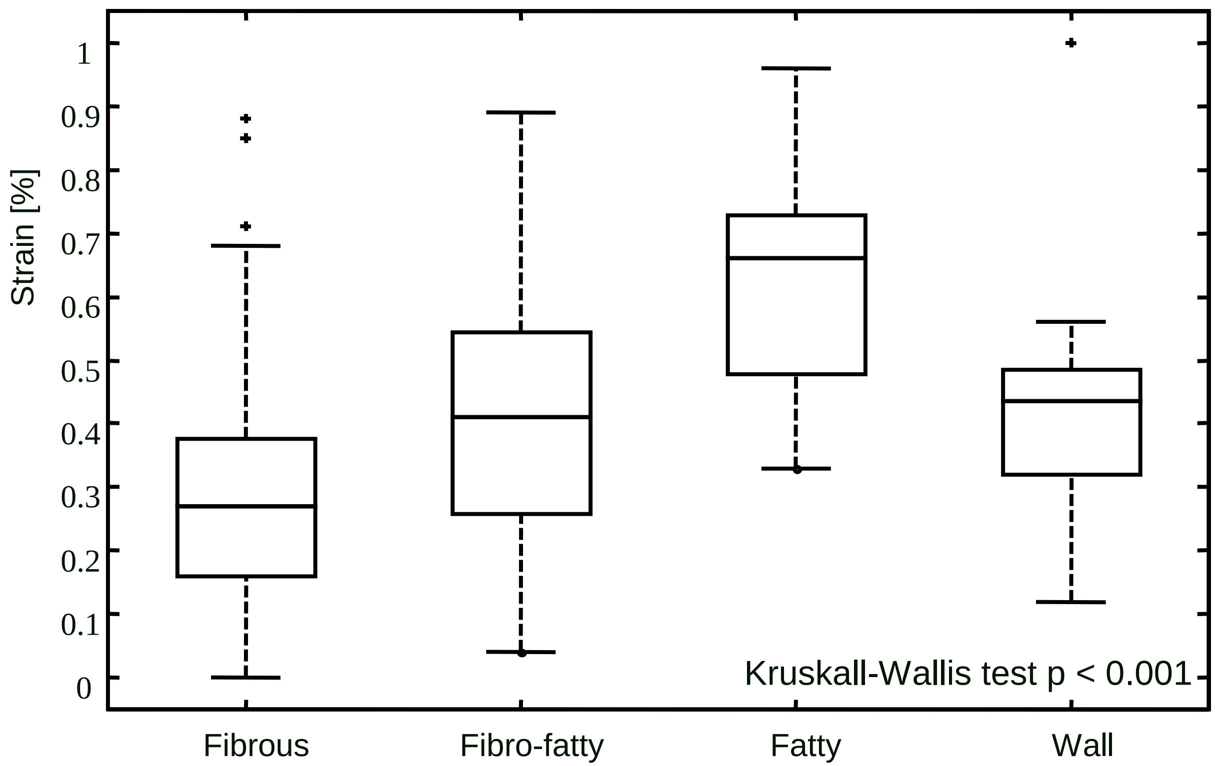


Picrosirius-red   Alpha-actin   Anti-CD68 antibody

de Korte et al, Circulation. 2000

Ex-vivo validation: validation II

- Human femoral (n=9) and coronary (n=4) arteries with 125 regions segmented in 45 cross-sections



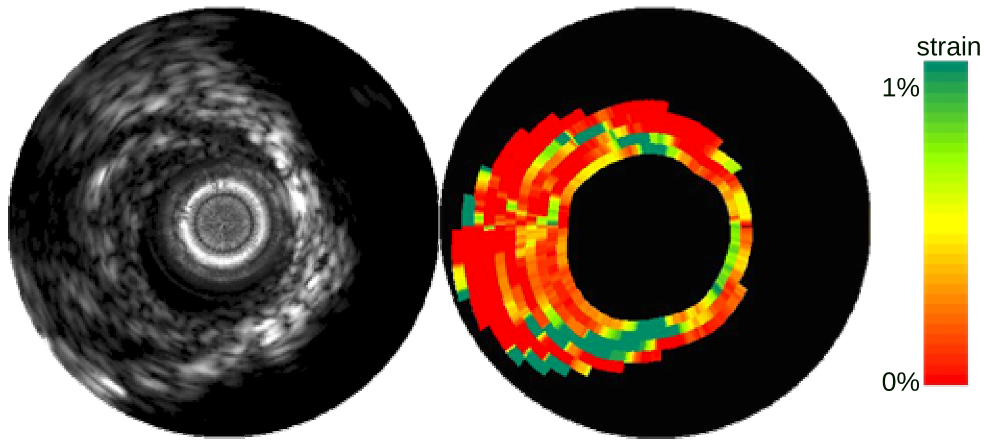
Differences between groups using Wilcoxon test

	Fibro-Fattty	Fatty
Fibrous	0.004	0.001
Fibro-Fatty		0.058

de Korte et al, Circulation. 2000

Ex-vivo validation: validation III

- Annular array catheter and intraluminal pressure

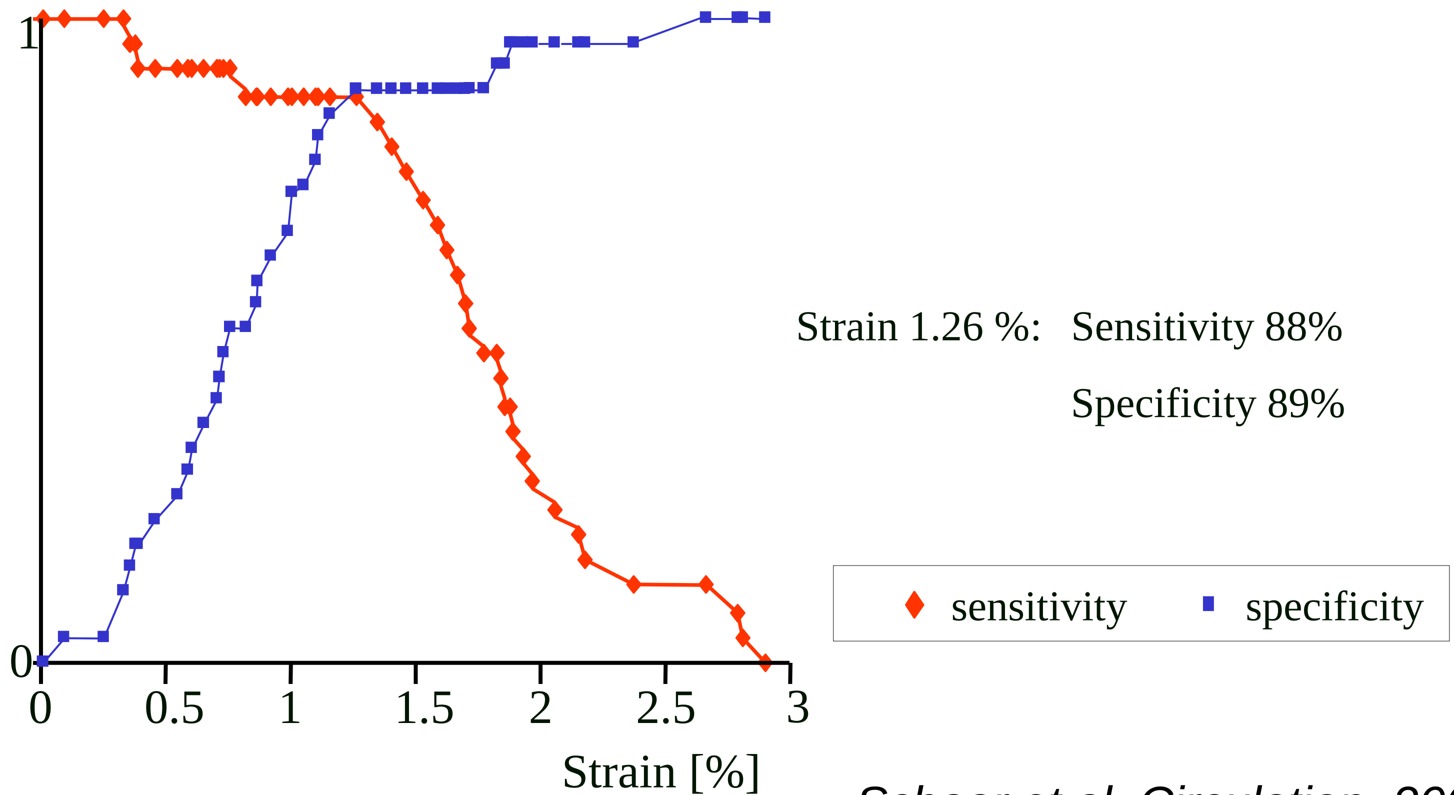


Picrosirius-red Alpha-actin Anti-CD68 antibody

Schaar et al, Circulation. 2003

Ex-vivo validation: validation IV

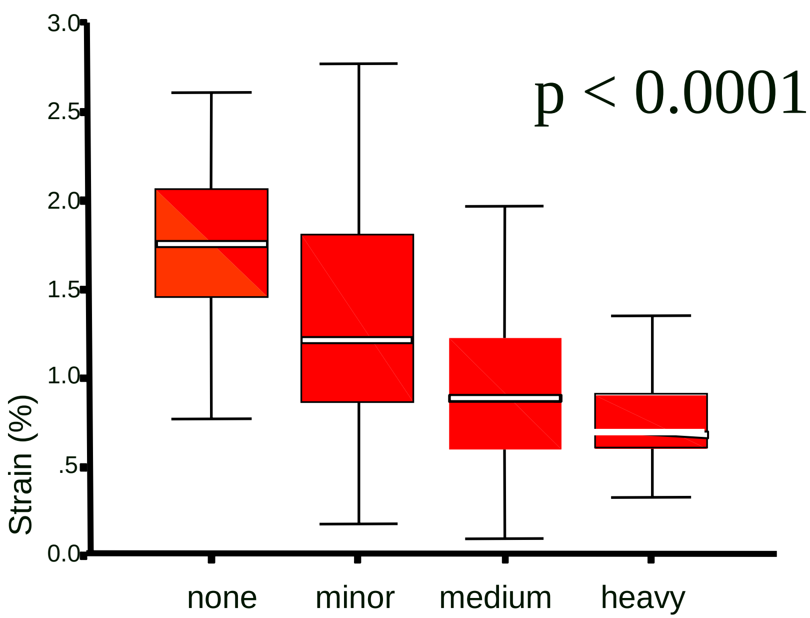
- Sensitivity/specificity analysis to determine optimal threshold



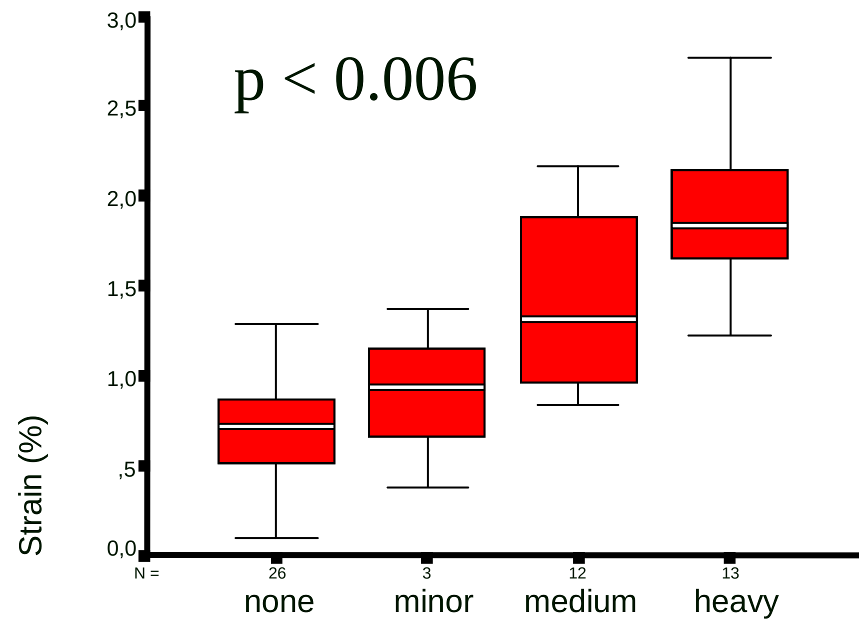
Schaar et al, Circulation. 2003

Ex-vivo validation: validation V

- Relation between strain value in high strain spot and plaque composition



Smooth muscle cells

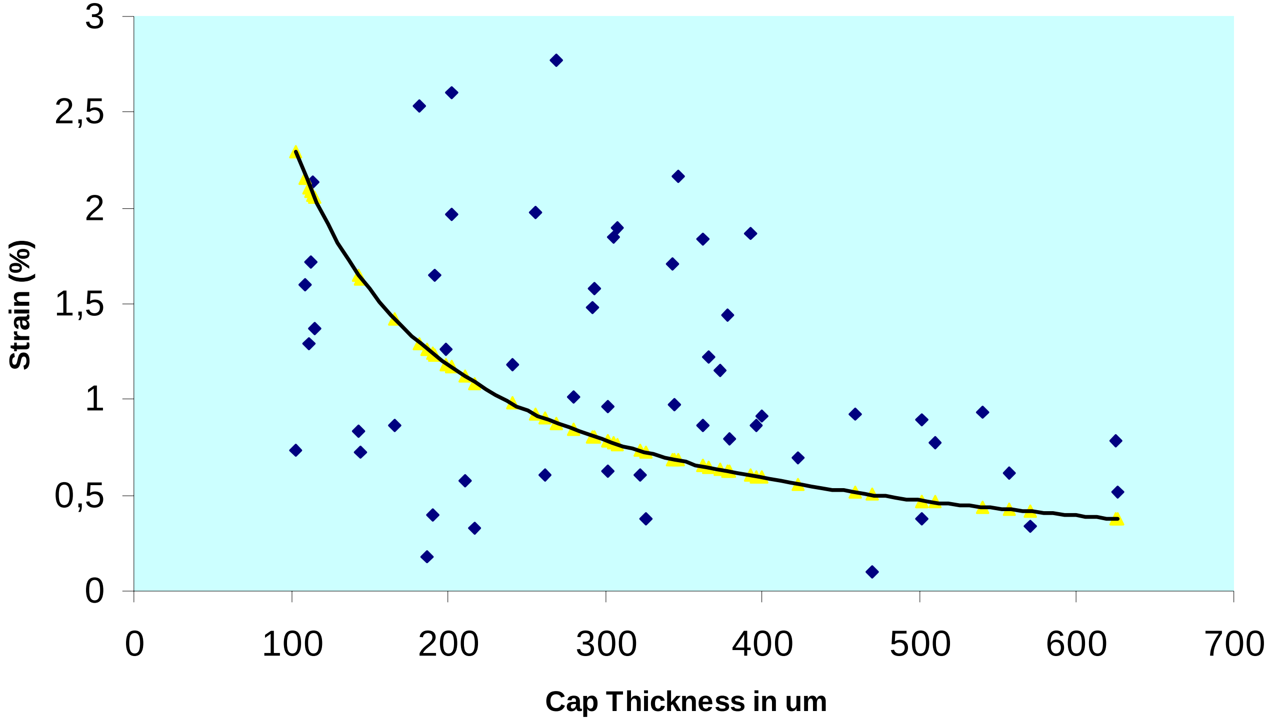


Macrophages

Schaar et al, Circulation. 2003

Ex-vivo validation

- Relation between strain value in high strain spot and cap thickness

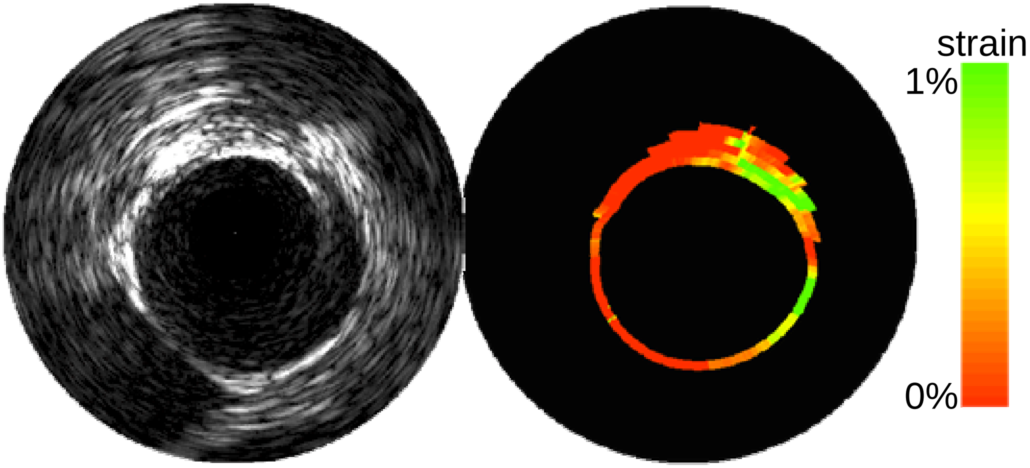


Schaar et al, Circulation. 2003

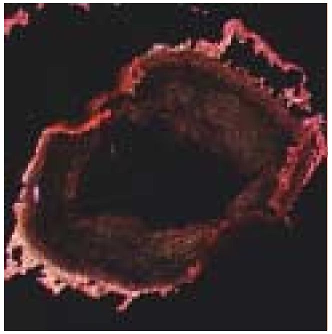
In vivo validation I

- Array catheter using intraluminal pressure as force.
- Yucatan Pig atherosclerotic model
- Acquisitions in femoral and iliac artery
- Histologic analysis for:
  1. Plaque composition
  2. Vulnerable plaque markers

In vivo validation II



Elastic-von Giesson



Picro-Sirius red
Polarized light

Acid Phosphatase

de Korte et al, Circulation. 2002

In vivo validation III

- Relation between strain and plaque type

Mean strain value in total plaque area

Tissue	Strain [%] mean	Strain [%] std
Normal segments (n=6)	0.21	0.09
Early fatty lesion (n=9)	0.46*	0.17
Early fibrous lesion (n=3)	0.24	0.03
Advanced fibrous lesion (n=6)	0.22	0.04

* P=0.007

de Korte et al, Circulation. 2002

In vivo validation IV

- Relation between strain and vulnerable plaque markers.

Presence of a high strain spot

	fat	no fat
↑ e	9	3
↓ e	0	12

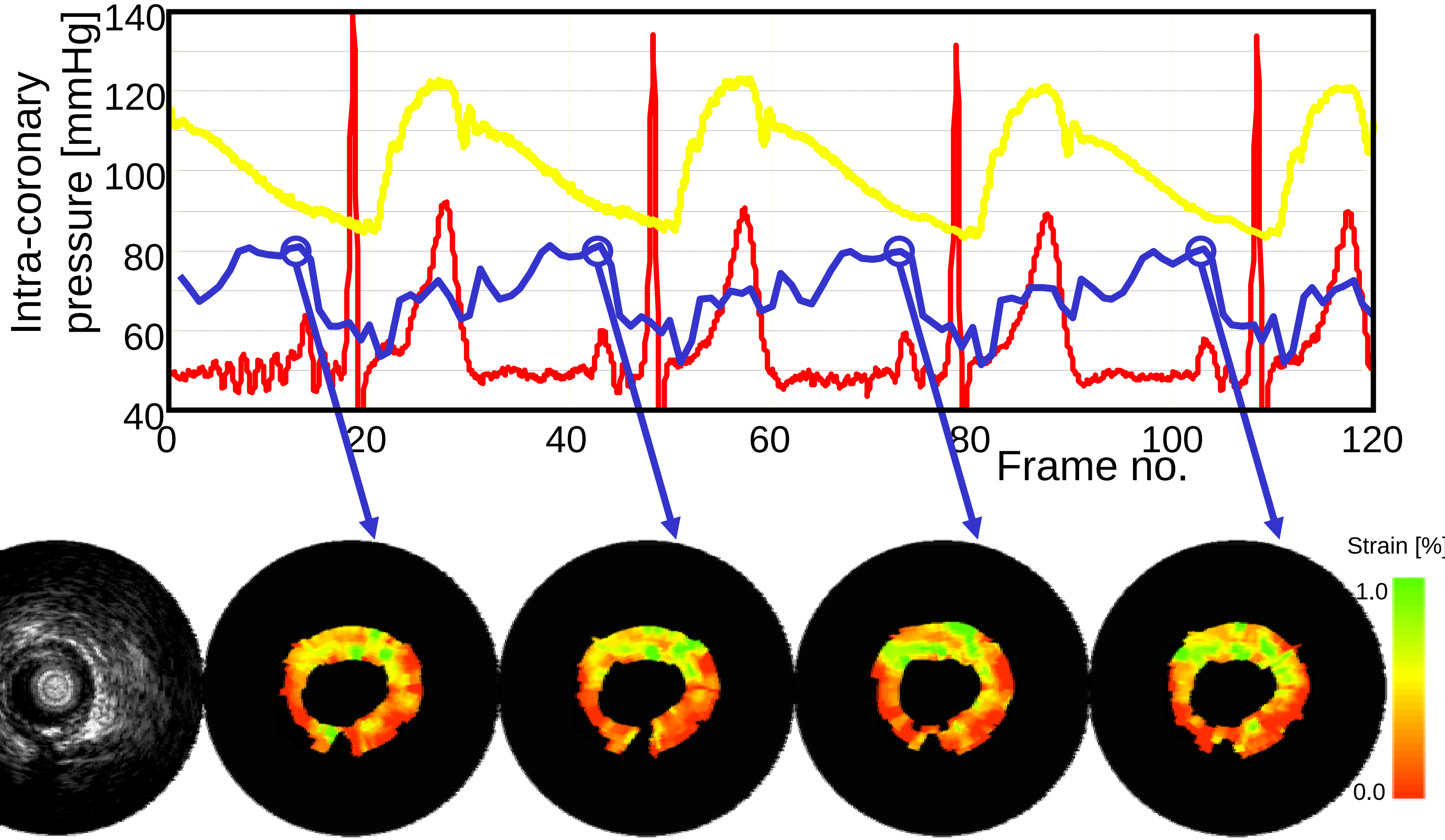
	MΦ	no MΦ
↑ e	11	1
↓ e	1	11

de Korte et al, Circulation. 2002

Patient studies

- Patients referred for Percutaneous Coronary intervention
- Pre intervention IVUS assessment of the culprit lesion using array catheter connected to commercial IVUS echo system.
- Due to contraction of the heart the catheter will have in-plane and out-of-plane motion:
  Find phase of heart-cycle with minimal motion.

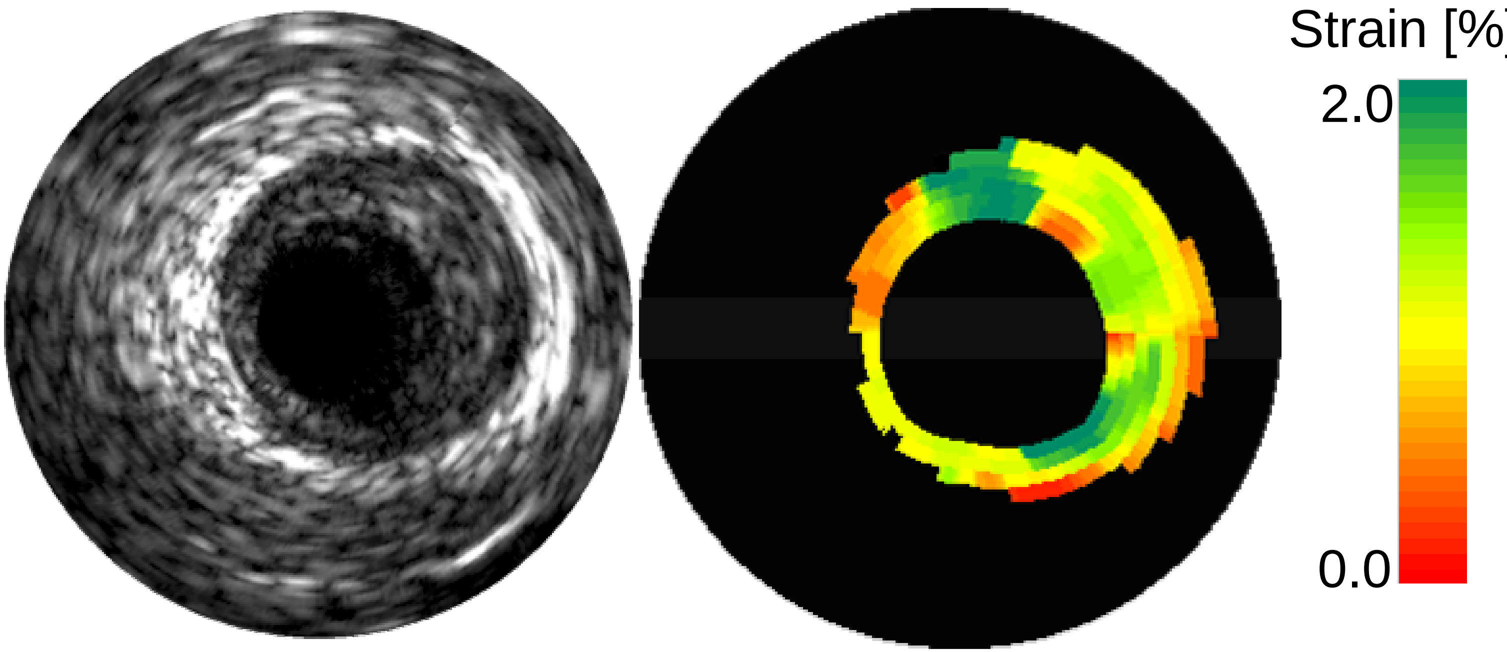
Patient studies II



de Korte et al, Eur Heart J. 2002

Patient studies III

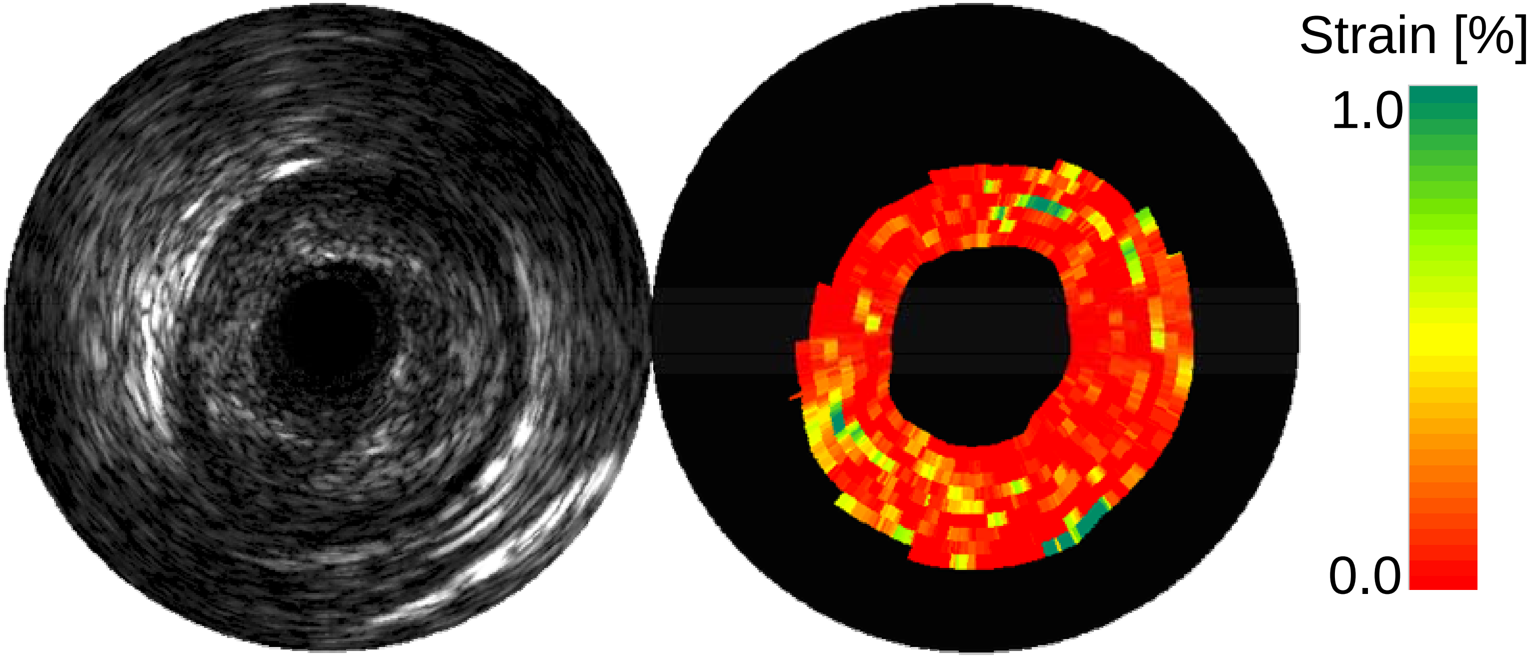
- Coronary artery in patient with unstable angina pectoris



de Korte et al, WCU Proceedings. 2003

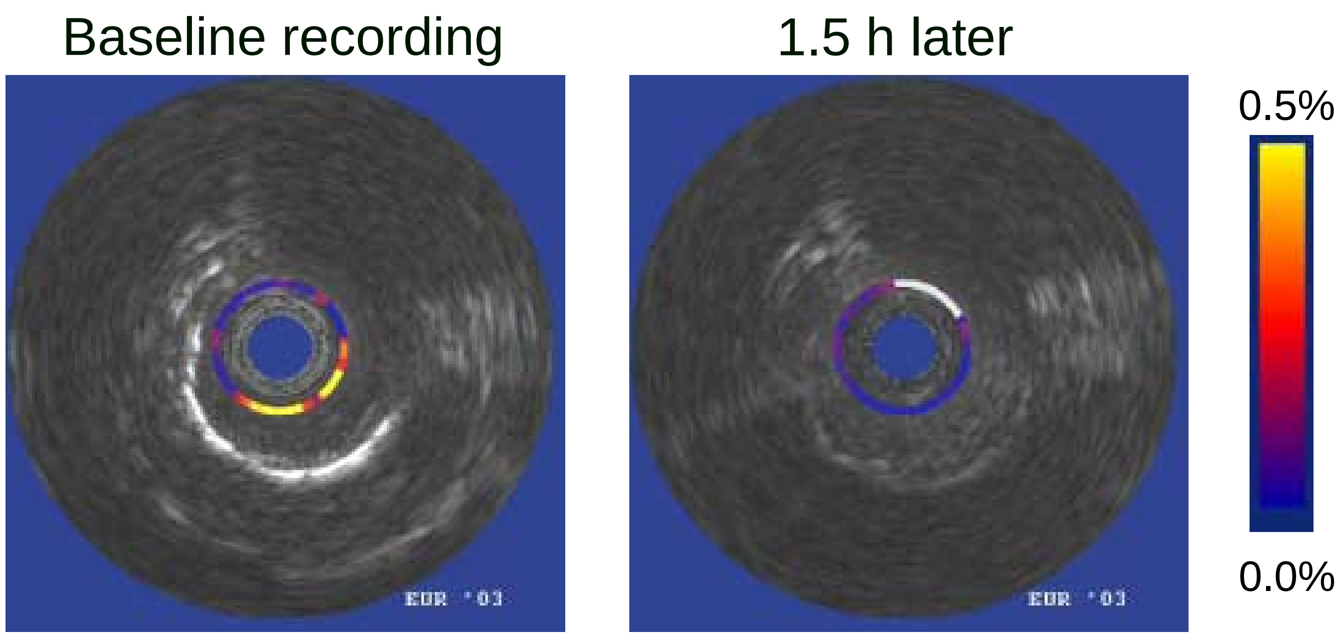
Patient studies IV

- Coronary artery in patient with stable angina pectoris



Assessment of thrombus stiffness I

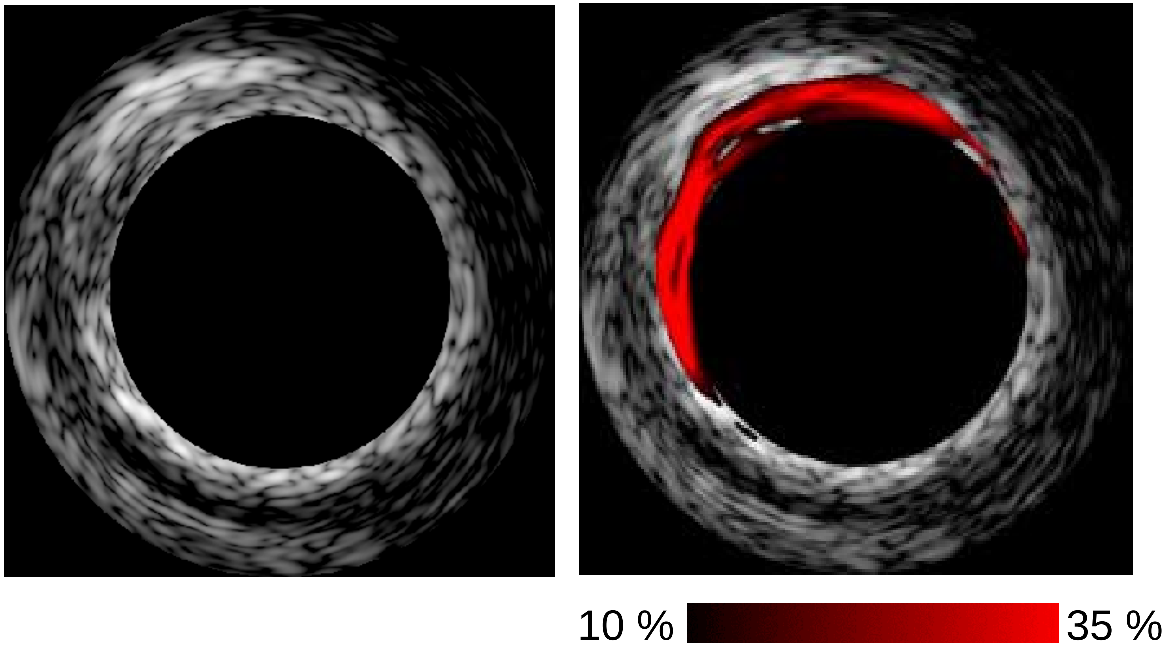
- Using an intravascular array catheter as imaging device and the pulsatile pressure as force.



Courtesy J.A. Schaar et al, ErasmusMC, Rotterdam The Netherlands

Assessment of thrombus stiffness II

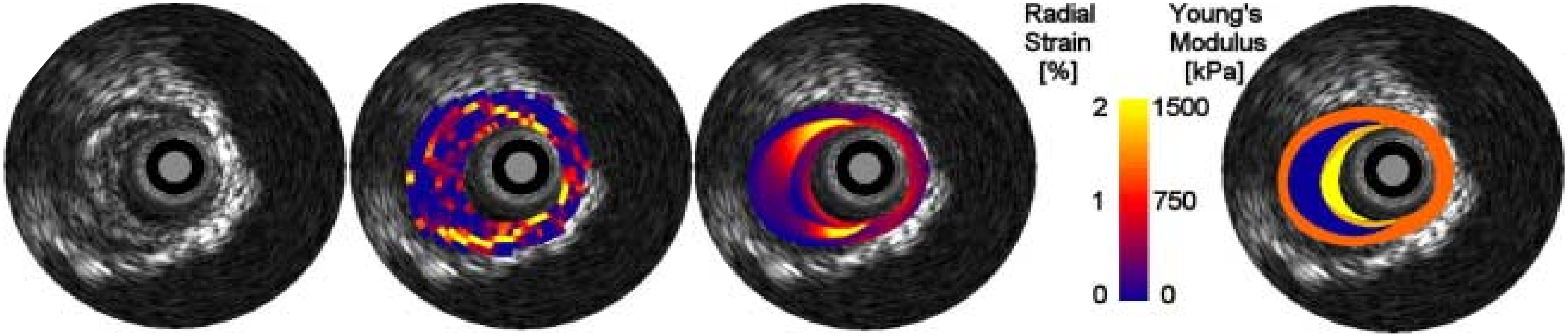
- Using an intravascular array catheter as imaging device covered by balloon as force.



Courtesy M. O'Donnell et al, Ann Arbor, USA

Young's modulus reconstruction

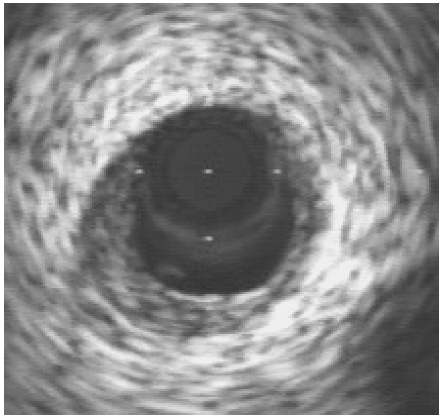
- Creation of FEM using the IVUS geometry
- Parameter variation for E of cap, lipid pool and vessel wall
- Variation of cap thickness



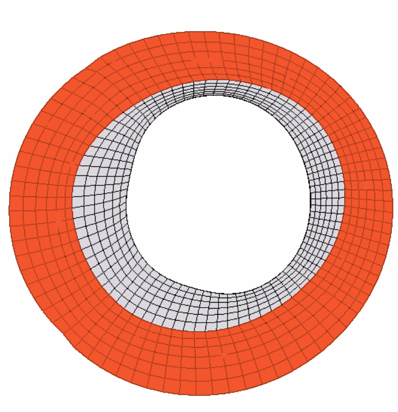
Baldewsing et al, Ultras Imag. 2004

Strain calculation using Deformable Images

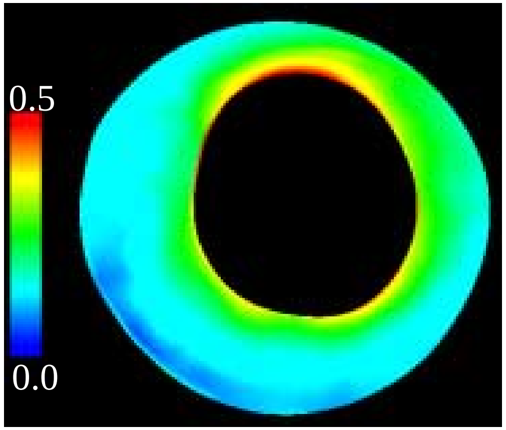
- Deformation map from Forward FE model to Template to generate synthetic Target image.
- deformation map from Forward FE model to Template to generate synthetic Target image.



Template Image



Deformed Mesh



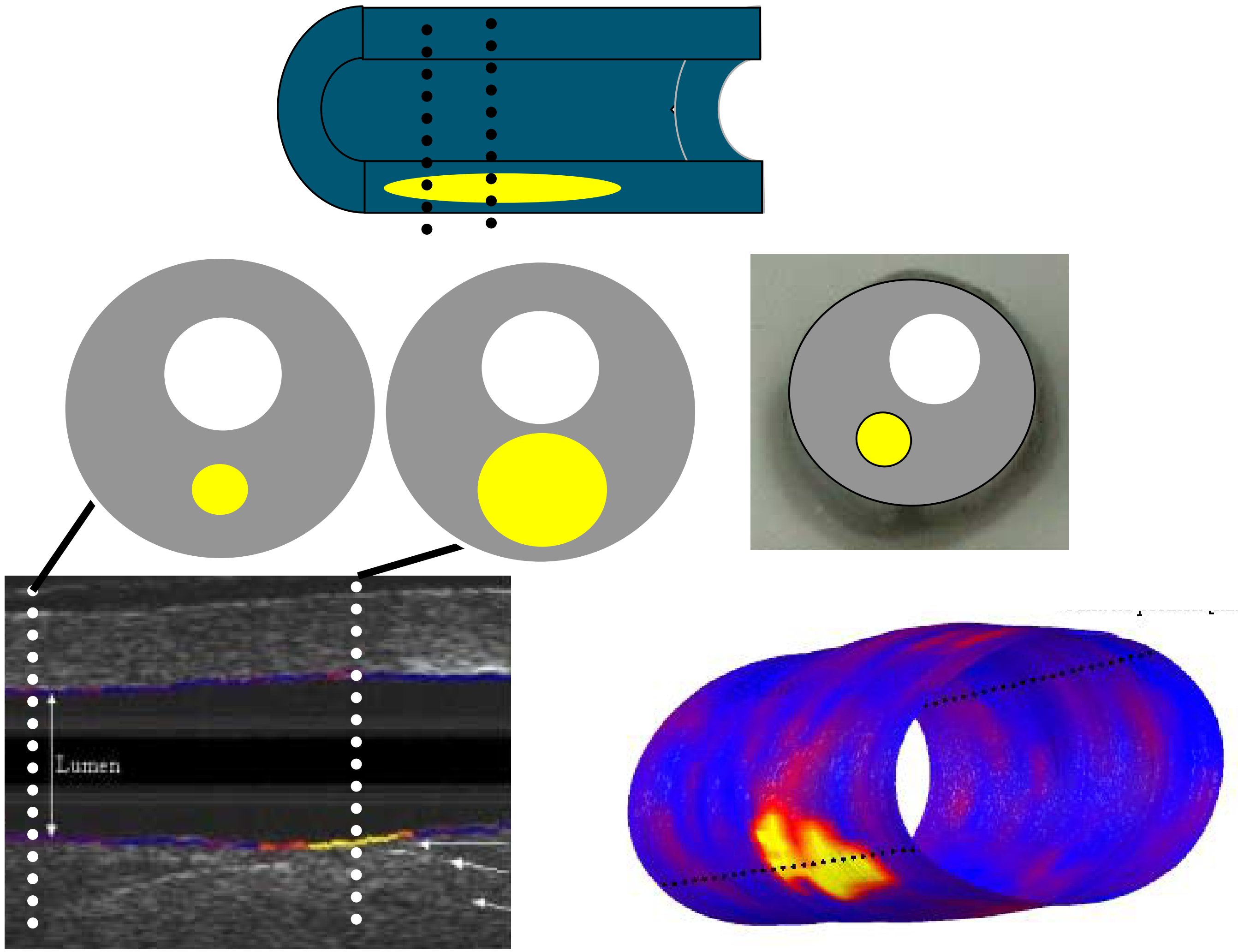
1st principal Green-Lagrange strain

Courtesy Veress et al, Univ Utah, UT, USA

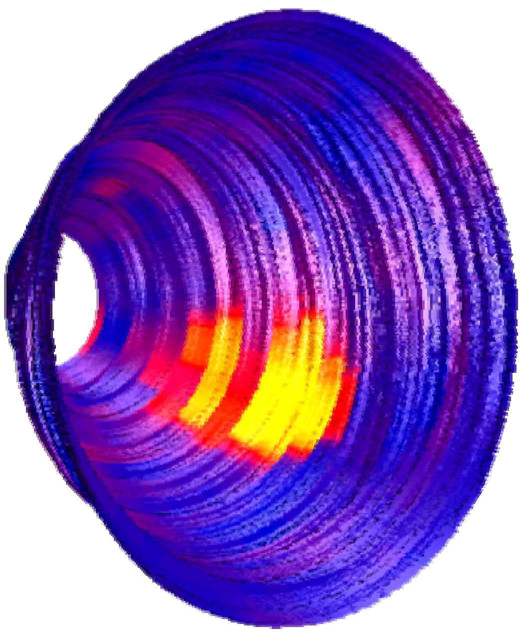
6.Three dimensional vascular elasticity imaging

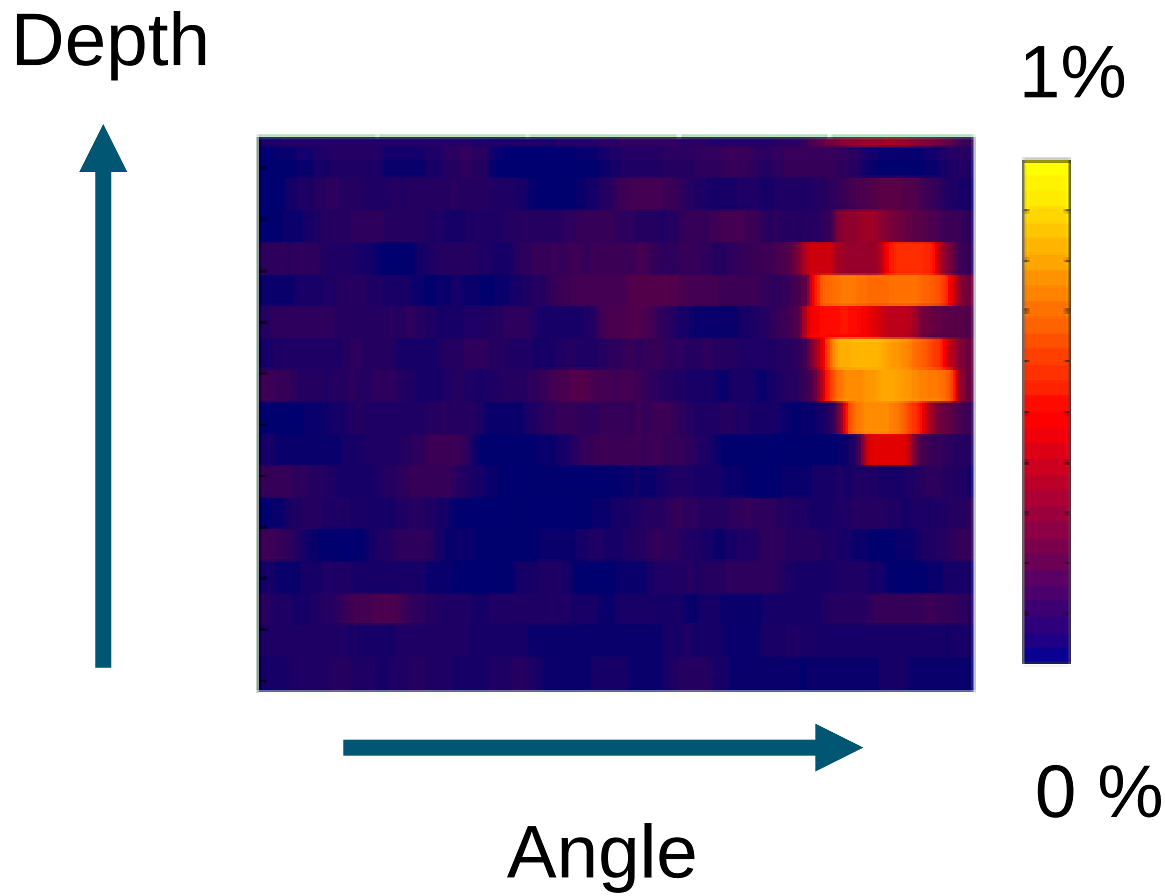
- One cross-section does not represent whole artery.
- For follow-up studies, 3D information is crucial.
- Image formation of 3D artery with strain in the wall is complicated.
- Palpogram reveals strain at lumen vessel-wall boundary: most important identifier vulnerable plaque.
- In coronary artery: performing a pullback decreases out-of-plane motion.
- Each heartbeat a palpogram is calculated: depending on pullback speed a resolution of 0.5 or 1.0 mm is obtained.

Phantom experiment I

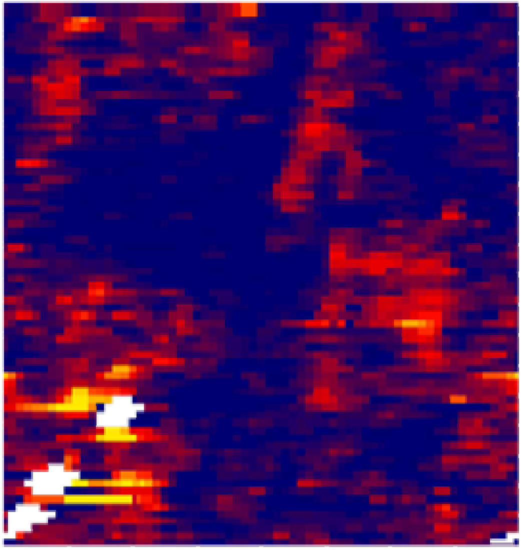


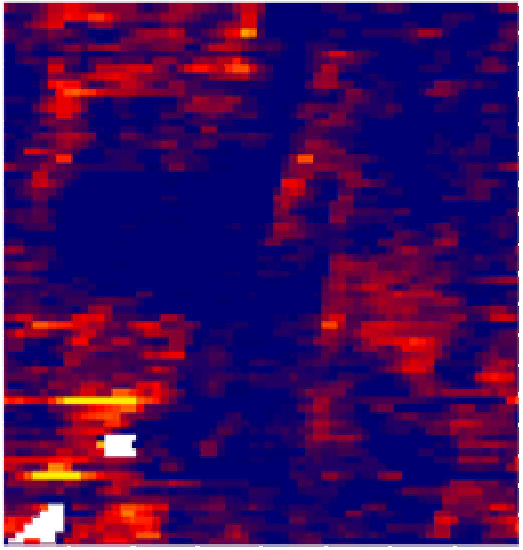
Phantom experiment II

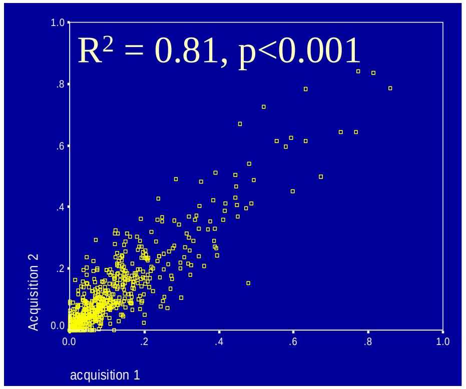


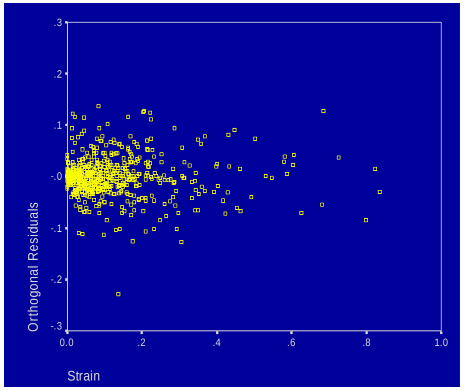


In vivo reproducibility: atherosclerotic rabbit model

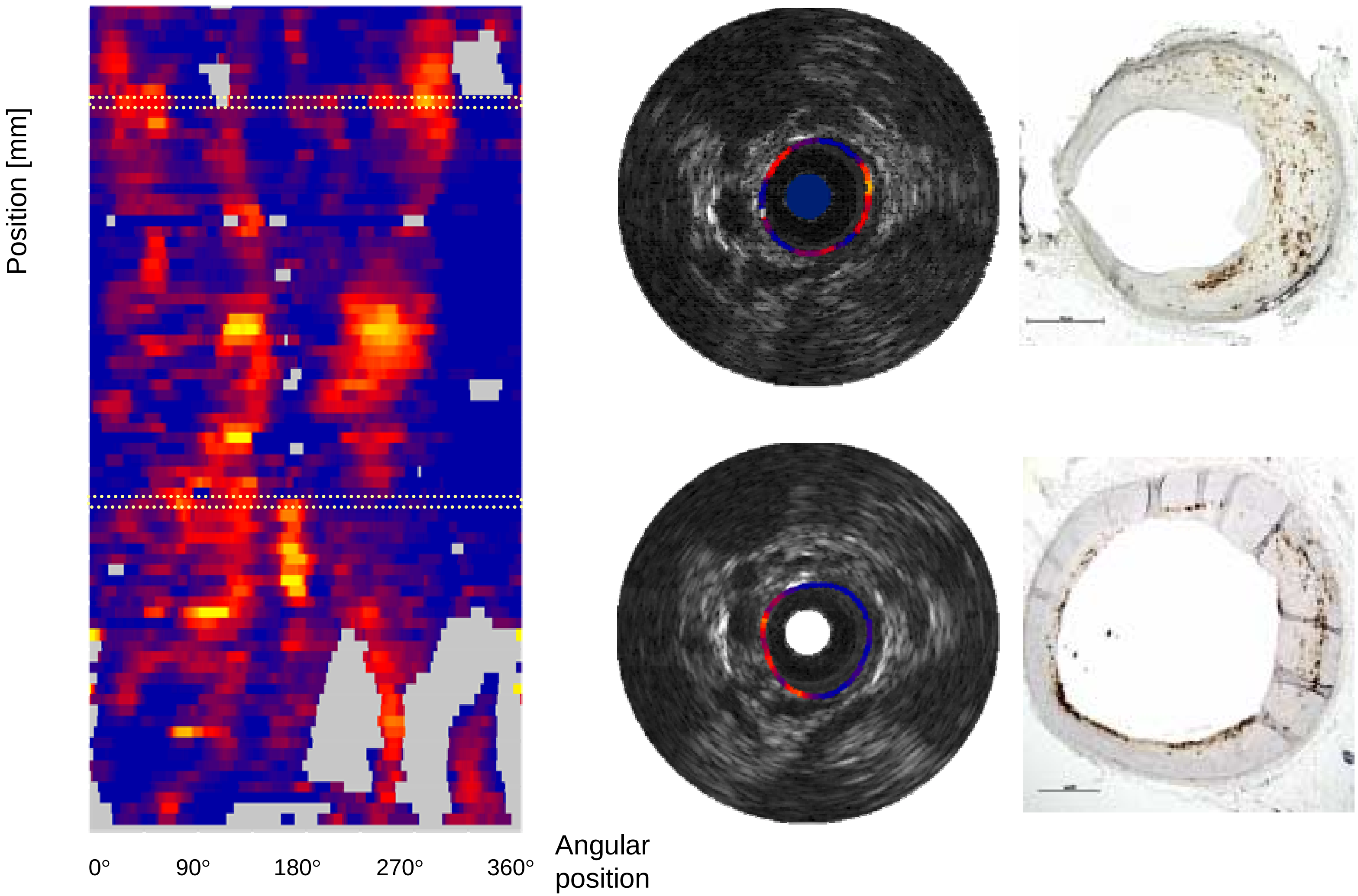




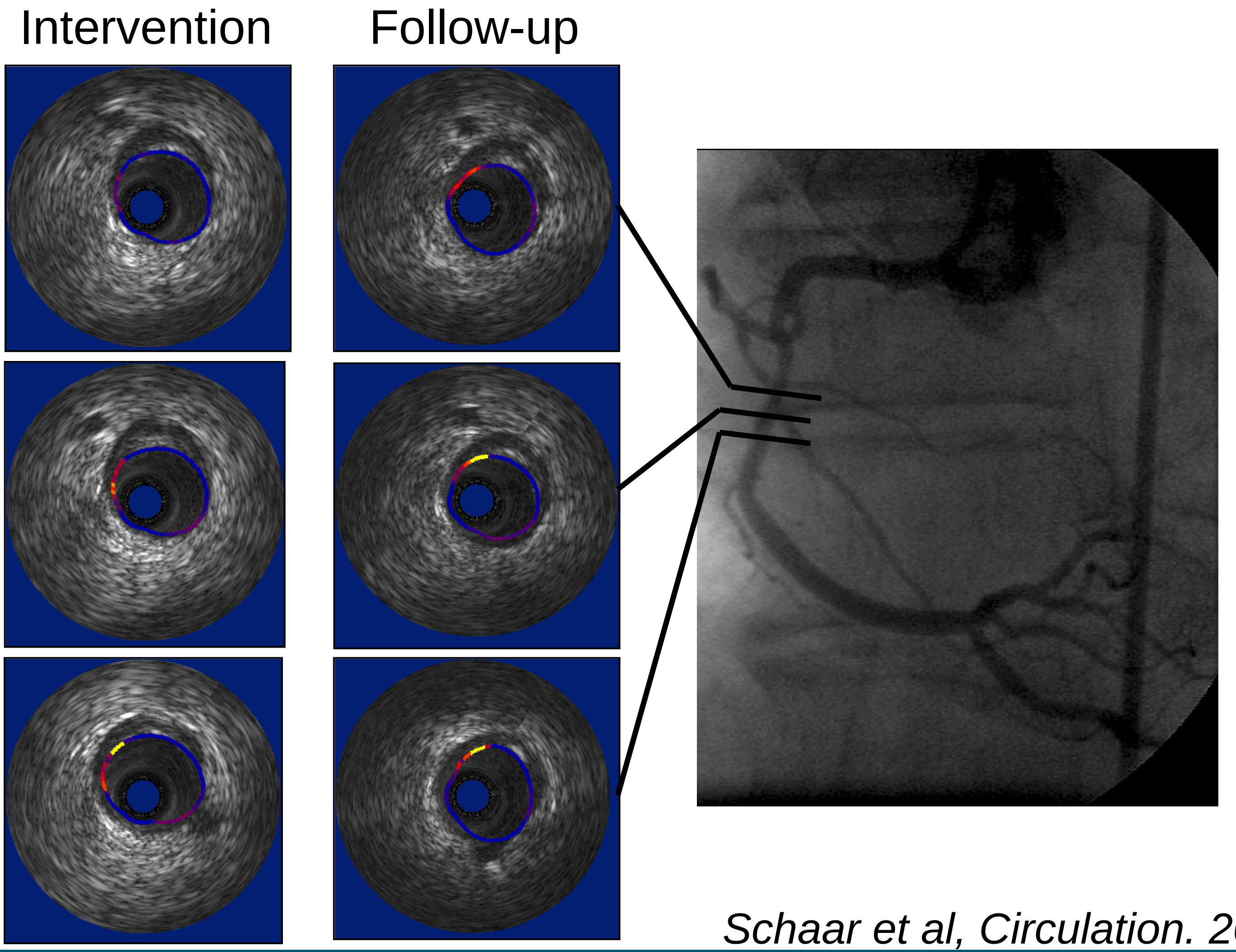




In vivo validation: atherosclerotic rabbit model



In vivo validation: follow up in patient



Schaar et al, Circulation. 2002

Conclusions

- (Intra)vascular elasticity imaging reveals information to identify thrombus age and plaque composition.
- (Intra)vascular elastography is validated in phantoms, in vitro and in vivo.
- Intravascular elastography is a powerful technique to identify the vulnerable plaque.
- Three dimensional intravascular elastography opens possibilities to perform longitudinal studies.

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