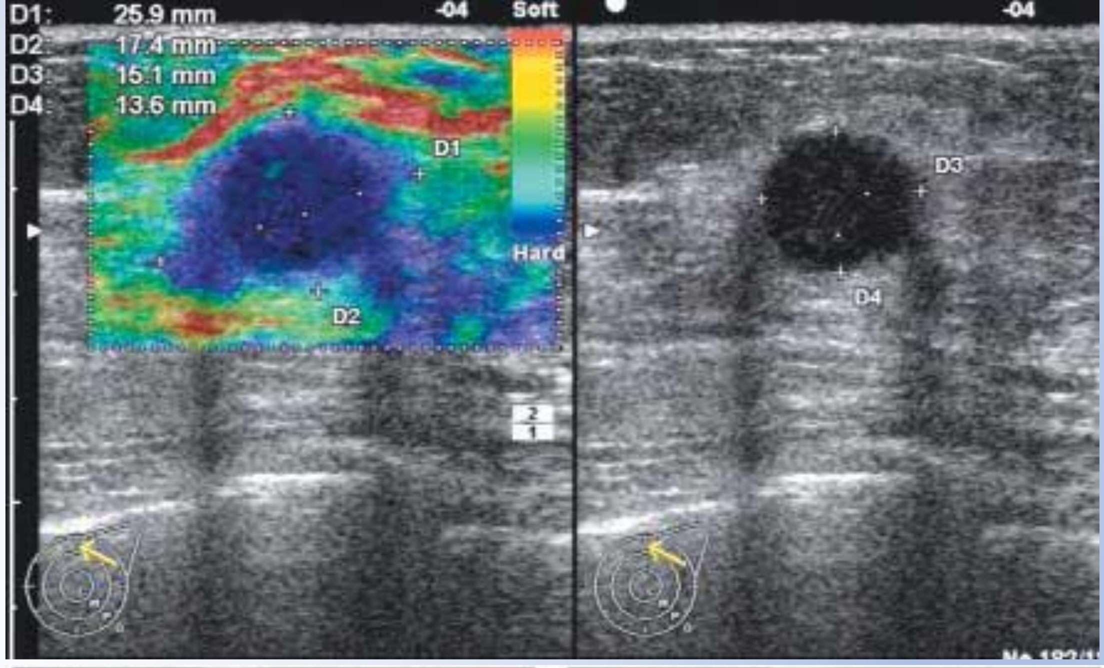
Elastography

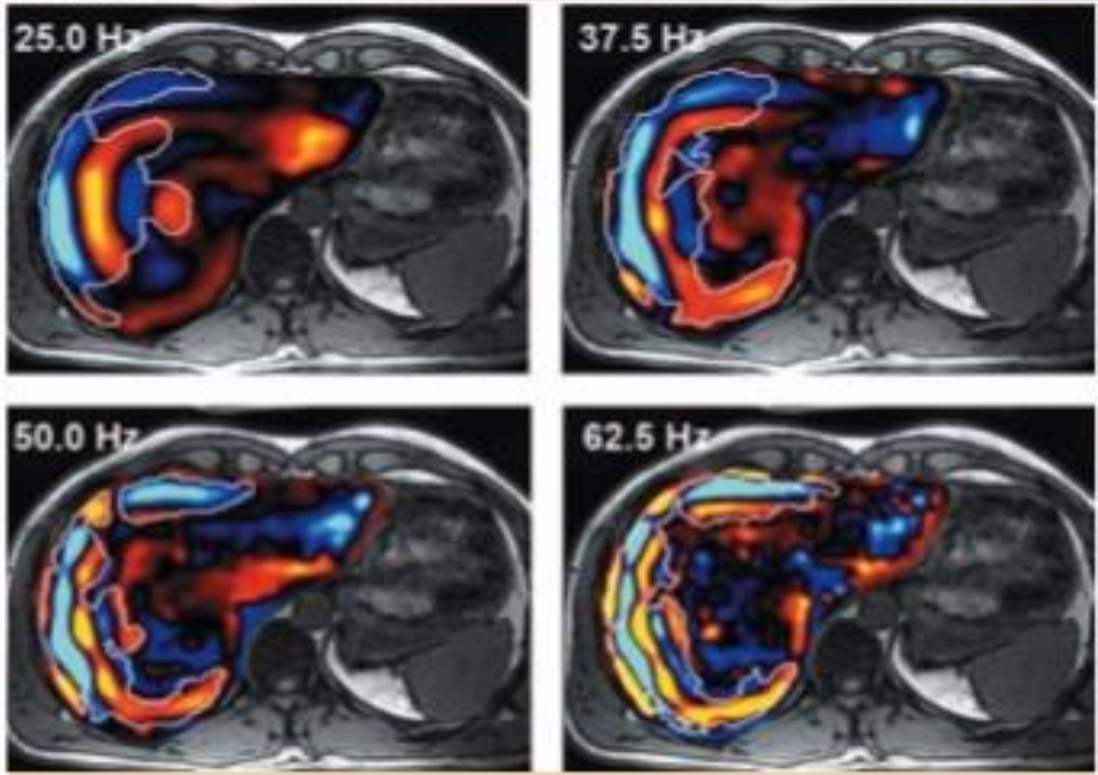
Lecture 13

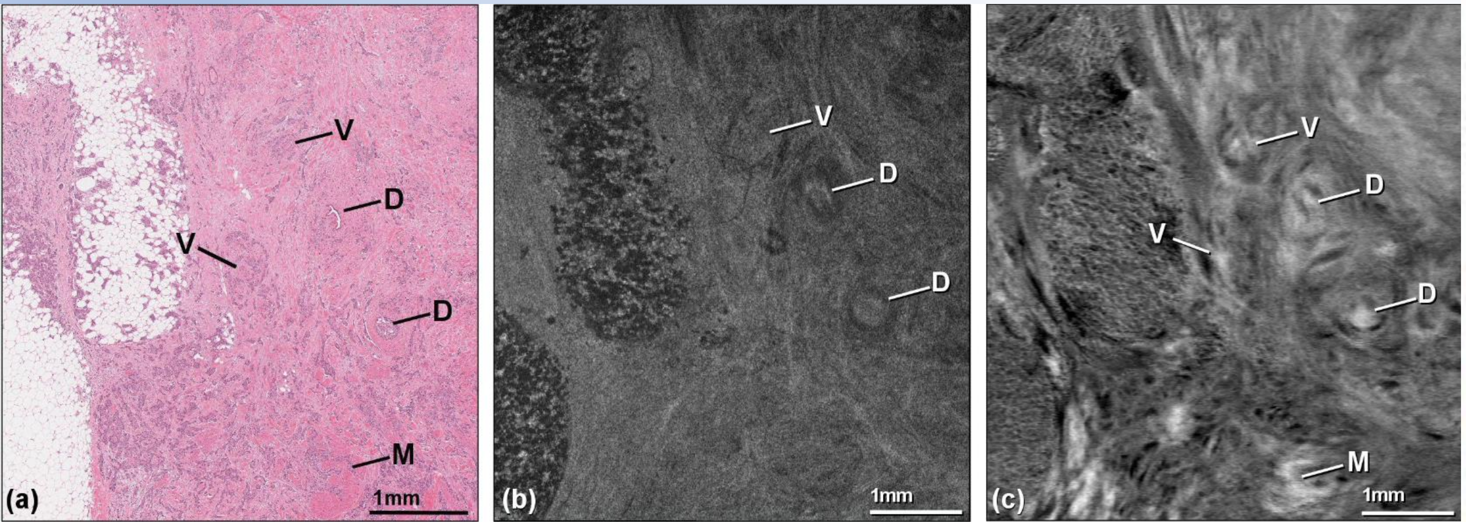
Elastography

- Mechanical property imaging of tissue
- Imaging modality – Ultrasound, MRI, OCT, etc
- Non-invasive, convenient, precise, (low-cost)

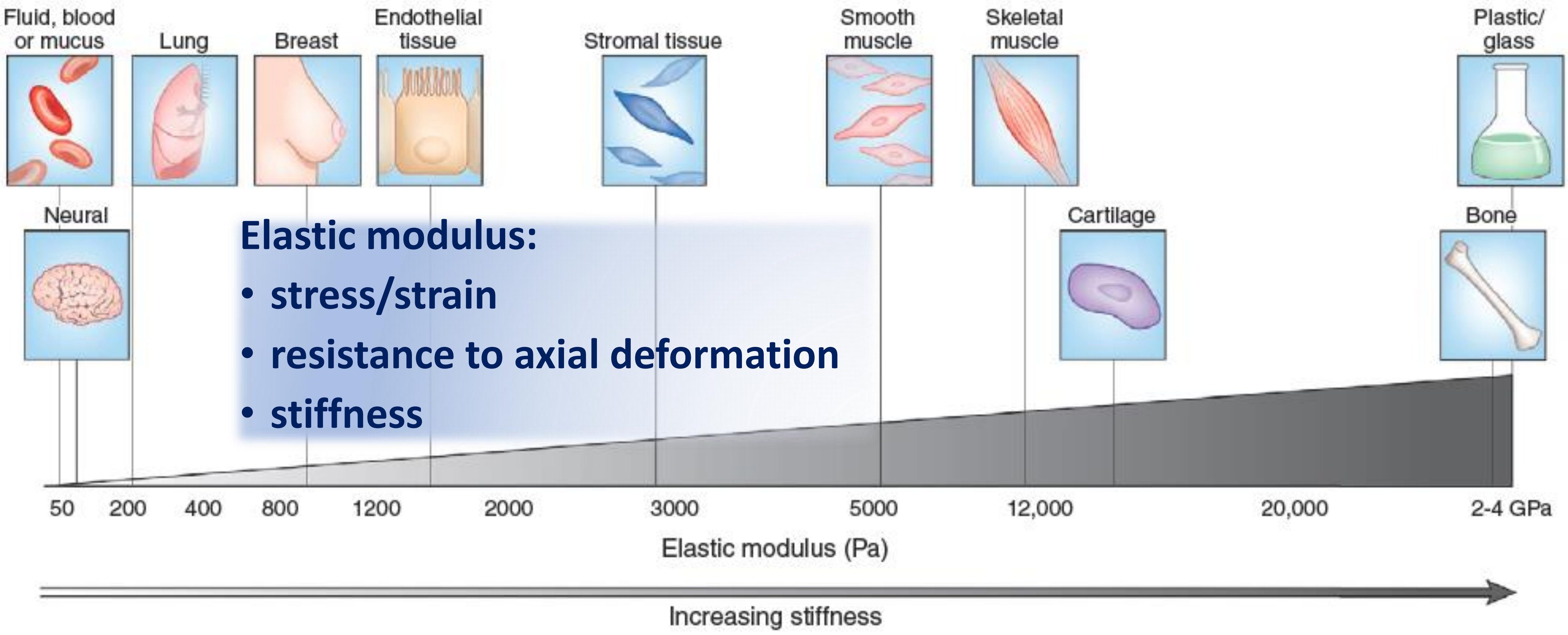


Disease pathophysiology
Diagnosis
Treatment





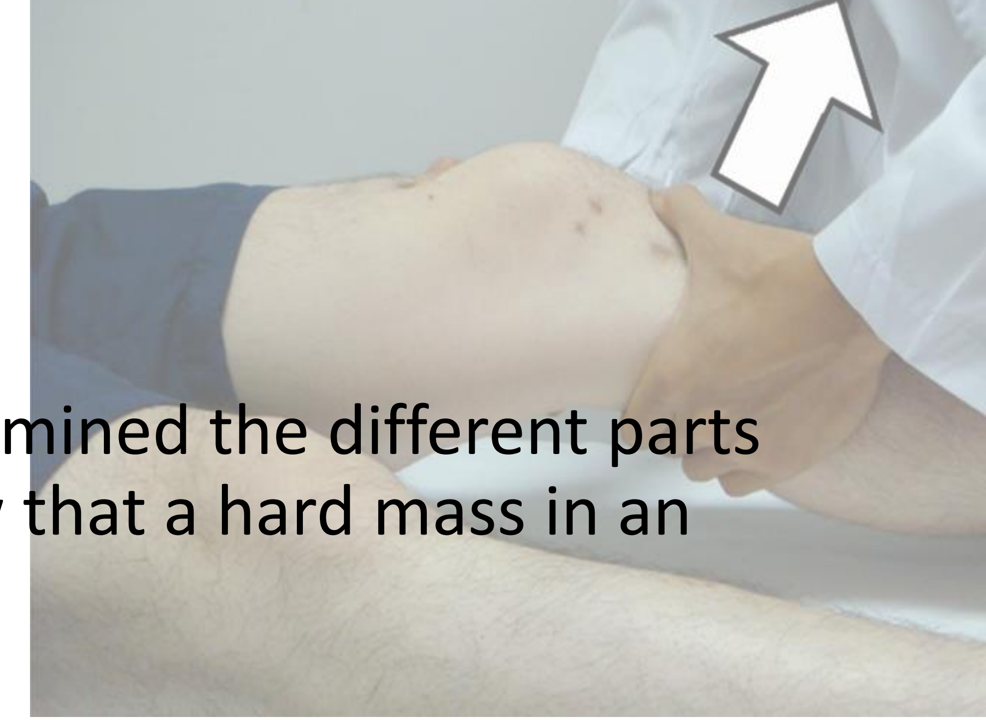
Elastic property of Tissue



Elastic modulus:

- **stress/strain**
- **resistance to axial deformation**
- **stiffness**

Diagnosis with Elasticity



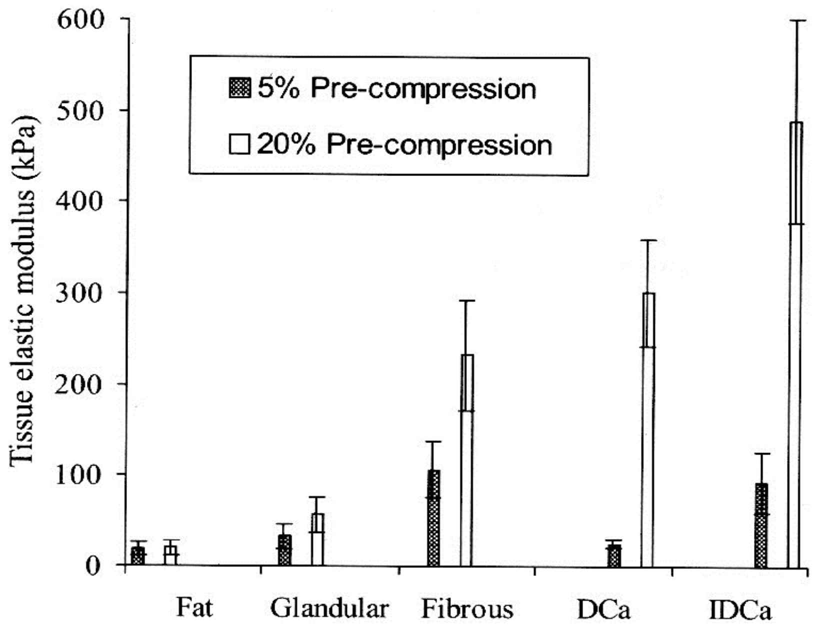
- In old Egypt, 5 000 years ago, physicians examined the different parts of the body to evaluate elasticity, they knew that a hard mass in an organ is pathologic.

- In Greek ancient age, for Hippocratic medicine, palpating was an essential time of physical examination.

- In 21st century, imaging take preeminent place in medicine and Elastography could be considered as an « imaging palpation »

Diagnosis with Elasticity

- Disease changes tissue elasticity
- Palpation: Used for centuries – low resolution, not depth resolved, highly subjective
- Elasticity can vary by up to four orders of magnitude

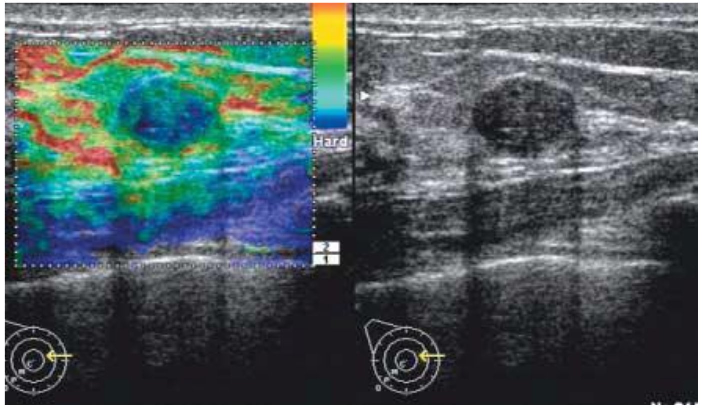


Ex) Compression test on 142 breast tissue samples

38 fat
31 glandular tissue
18 fibrous tissue
23 intraductal carcinoma
32 infiltrating ductal carcinoma

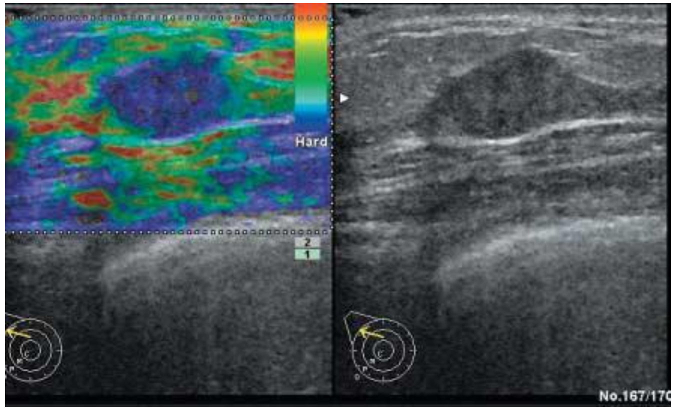
US elastography - breast cancer diagnosis

Fibroadenoma

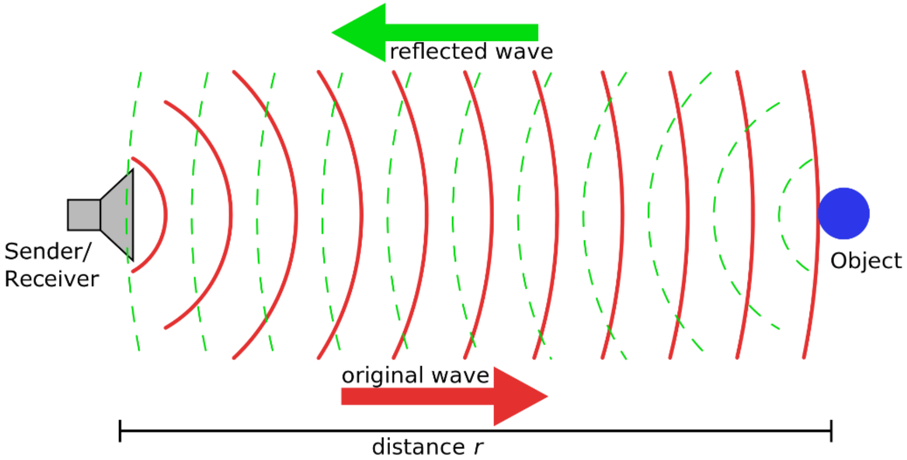


Benign Benign

Invasive ductal carcinoma



Malignant Benign



Results of study

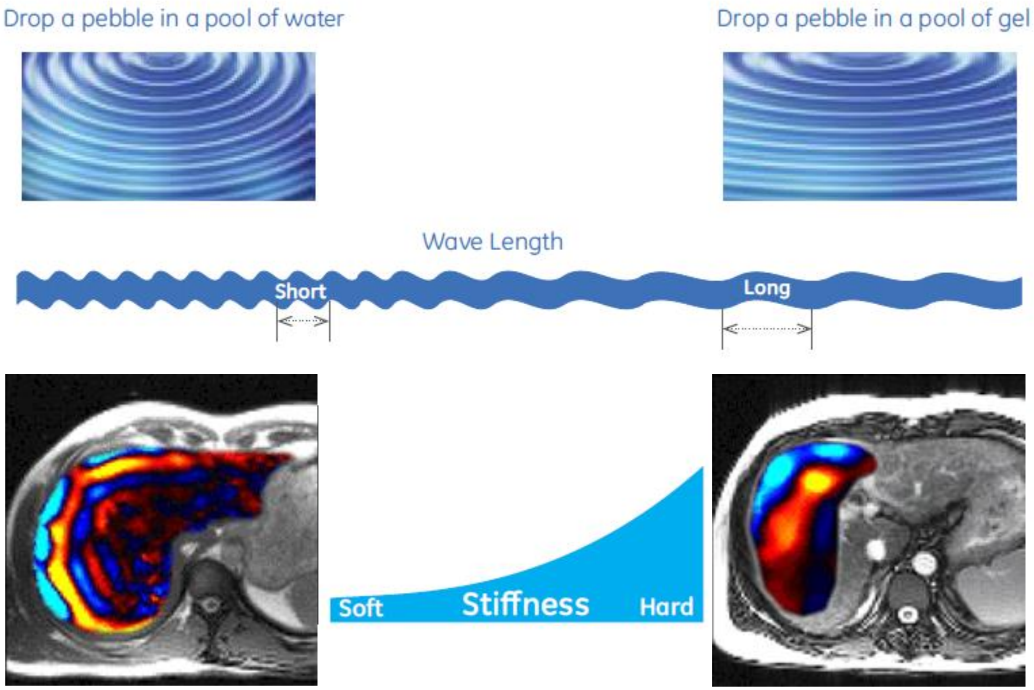
296 solid lesions from 232 patients

- Sonography – 72.6% accuracy
- Elastography – 88.2% accuracy

Features of US elastography

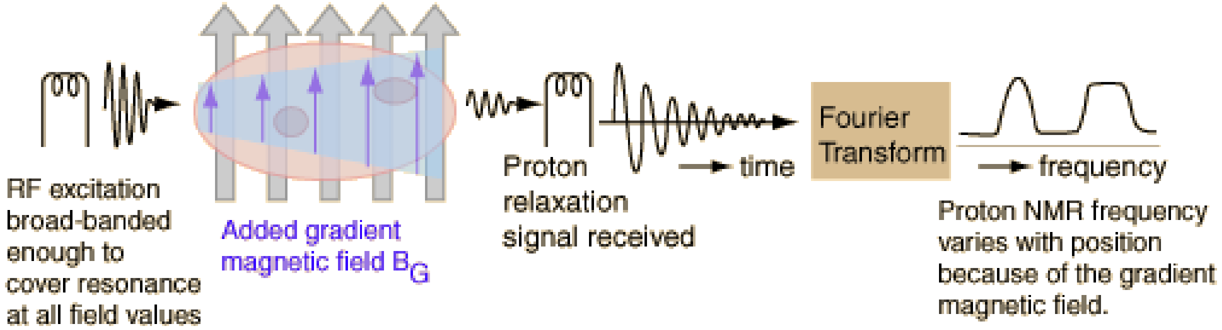
- Deep penetration
- Poor resolution
- Commercially available

MR elastography – diseased liver diagnosis



Healthy liver

Cirrothic liver



Results of study

141 solid lesions from 232 patients

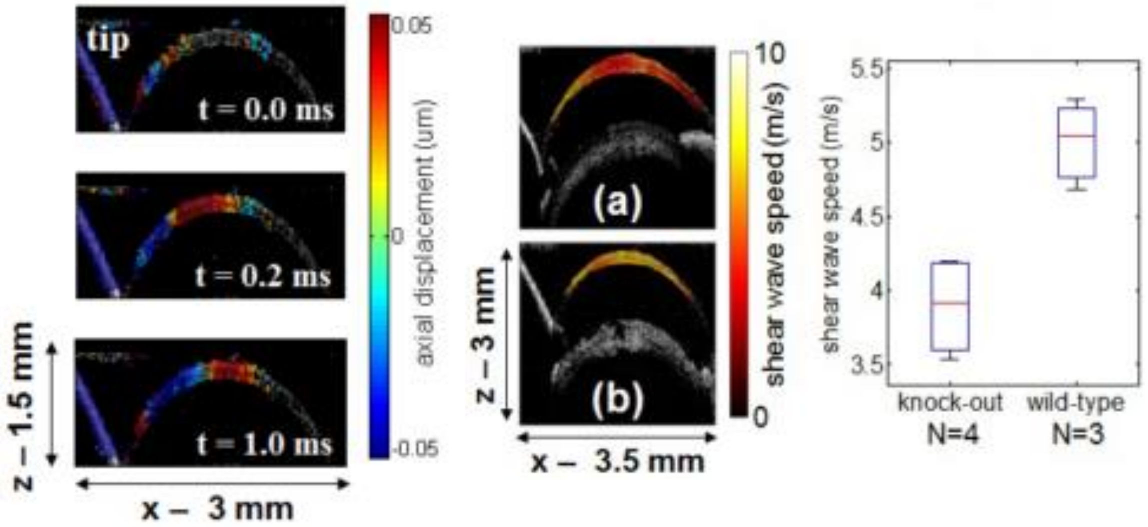
- Ultrasound elastography – 84% accuracy
- MR elastography – 94% accuracy

Features of MR elastography

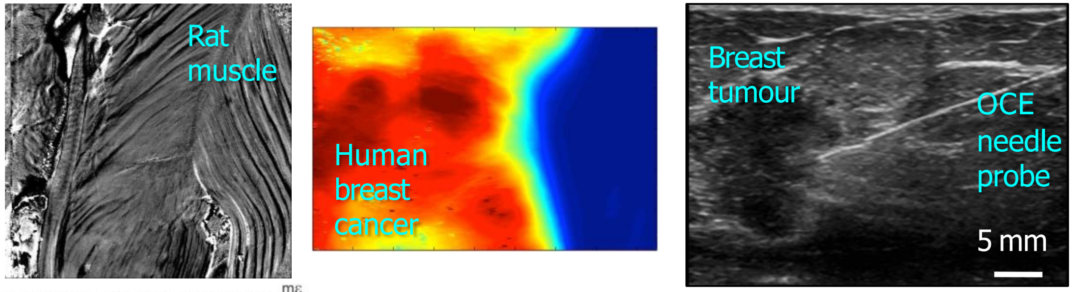
- Deeper penetration
- High resolution
- Commercially available

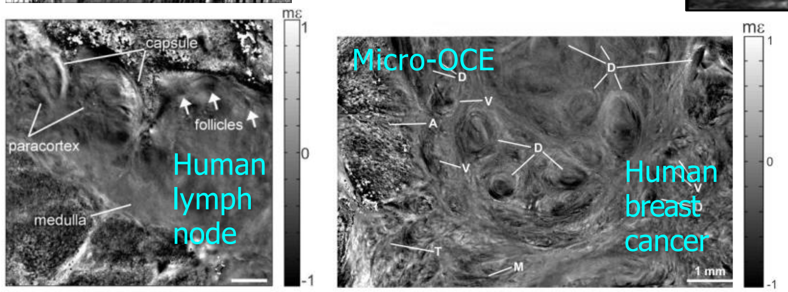
OCT elastography – emerging applications

Cornea - RK Wang group



Breast tumour, lymph nodes, skeletal muscle

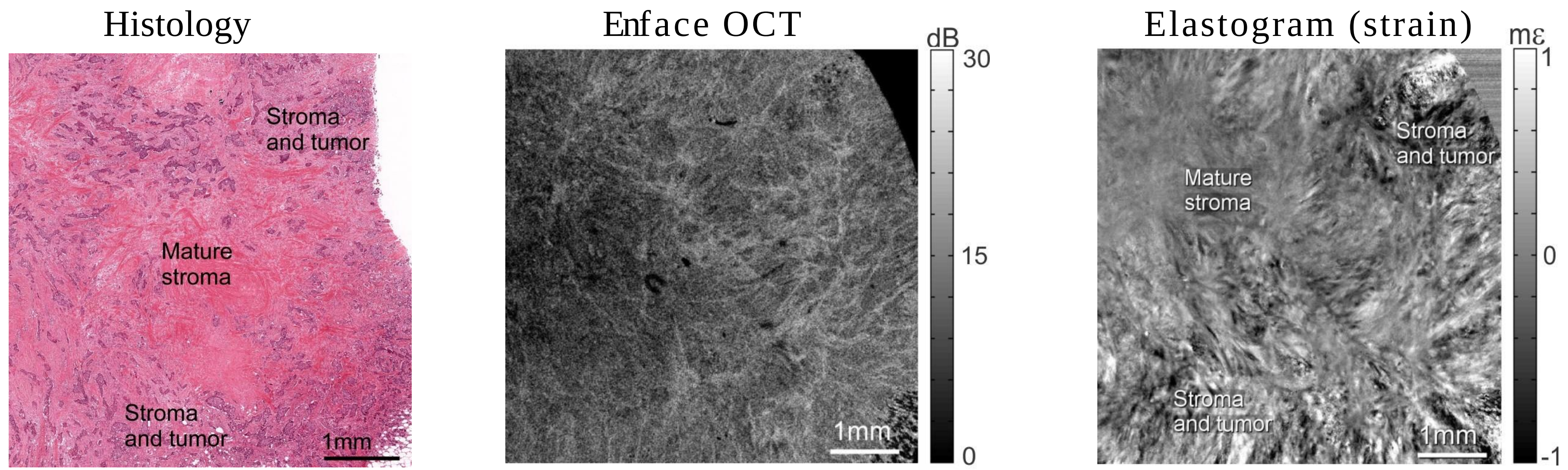


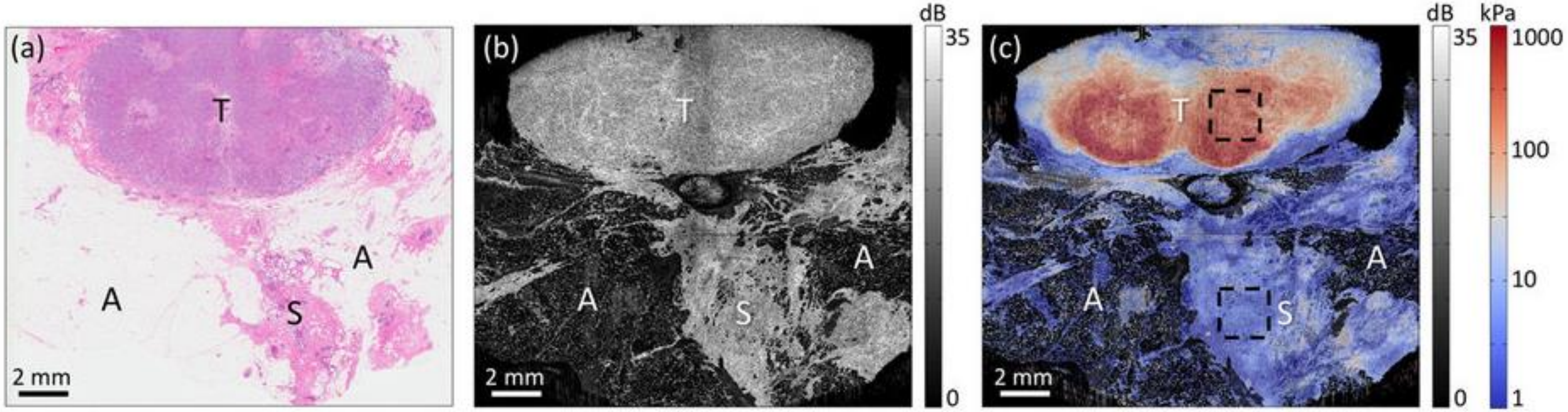


Kennedy *et al.*, Sampson group, *J Biomed Opt*, Dec 2013; *Opt Lett* May 2014; *Biomed Opt Express* June 2014

Features of OCT elastography

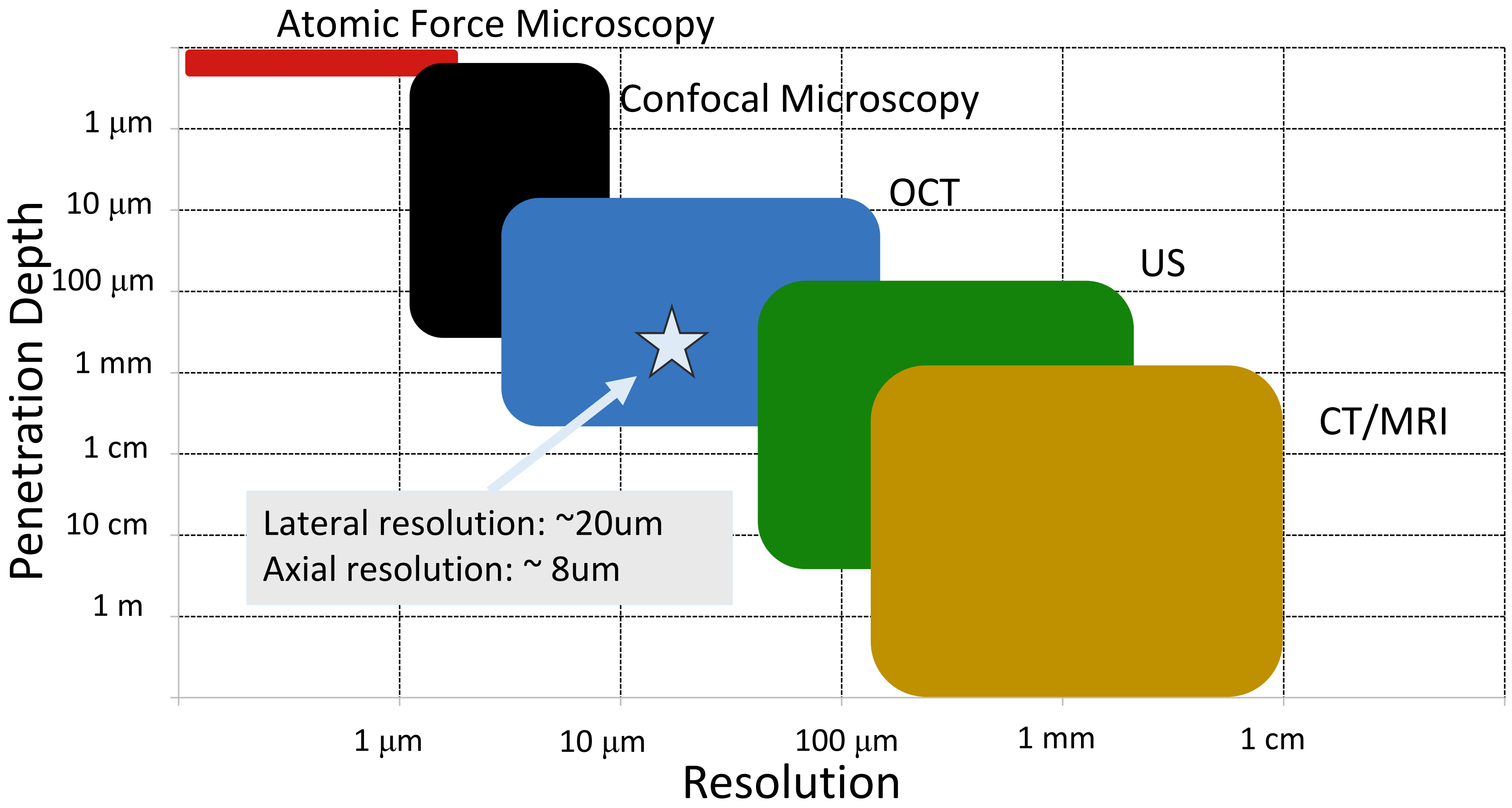
- Higher resolution (1 ~ 50 um)
- Higher sensitive (sub nm disp.)
- Higher acquisition speed (>1kHz)
- **Very low penetration (0.5 ~ 3 mm)**
- Clinical applications NOT available





(**a**) H&E histology. (**b**) *En face* OCT image. (**c**) Fused *en face* OCT and quantitative micro-elastogram. Elasticity is plotted on a logarithmic scale. Dashed boxes indicate regions over which mean elasticity values were calculated. A = adipose, S = stroma, T = tumour.

Medical Imaging Techniques

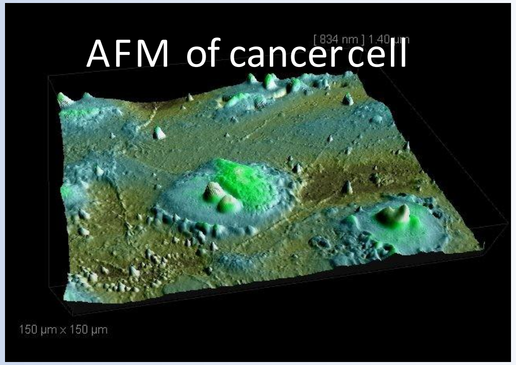


Scale of measurement

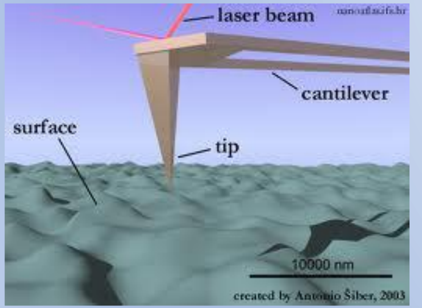
Elasticity depends on tissue material and structure *at the scale being probed*

Example: cancer cells versus cancerous tissue

On the microscopic scale –
Cancer cells are 10 times softer than healthy cells



On the macroscopic scale –
Cancerous tissue >10 times stiffer than healthy tissue



Force sensor with piconewton resolution
Tip on cantilever senses sample surface

Lateral resolution: 1 nm
Axial resolution: 1 Å

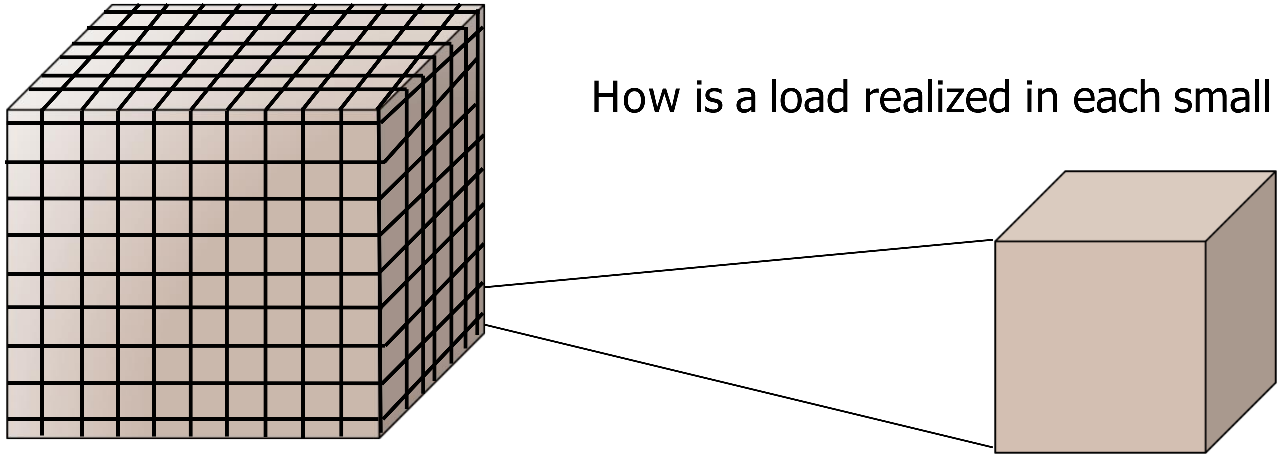
So, how do we measure mechanical properties in elastography?

Imaging tissue deformation

- We need to make some assumptions:

Assumption 1:
Mechanically homogeneous over a resolution element

- Take a complex block of tissue and break it up into homogeneous, small volumes



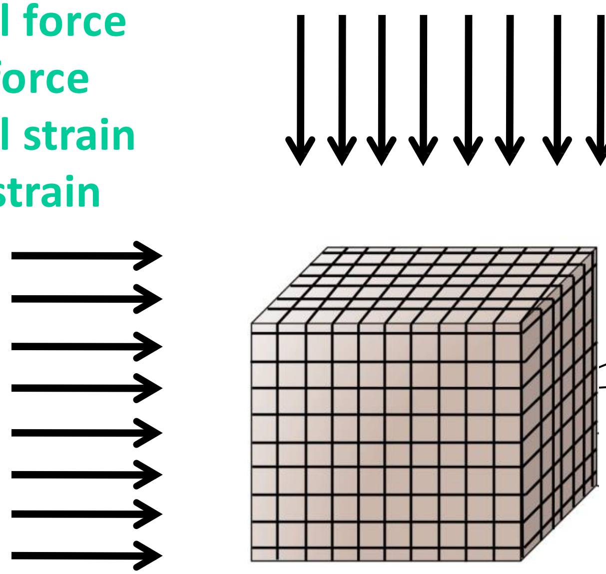
How is a load realized in each small volume?

Describe behaviour using continuum mechanics

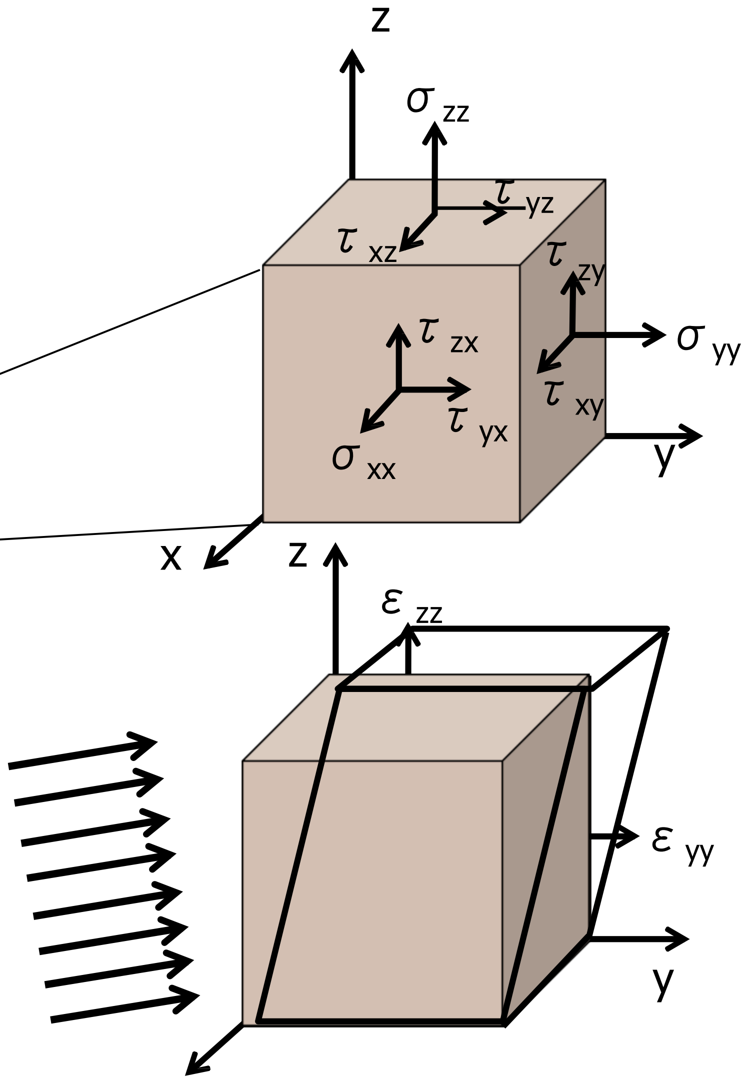
Stress and Strain

- When any load (force) is applied, a **stress** results on each surface of each volume

σ : normal force
τ : shear force
ε : normal strain
γ : shear strain



- Stress causes a shape change



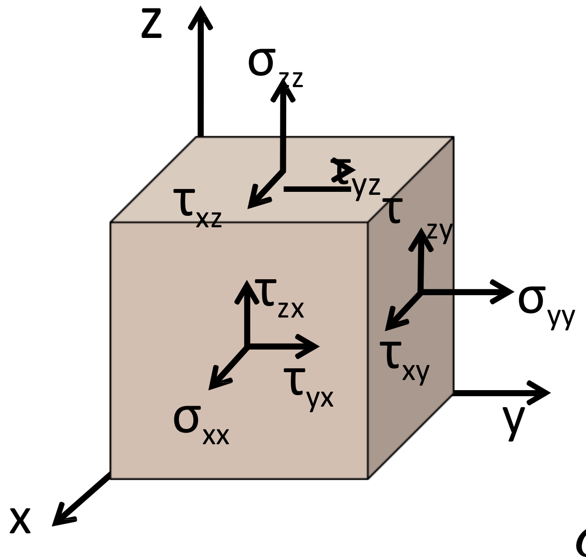
$$\varepsilon_{xx} = \frac{\partial u}{\partial x}$$

$$\varepsilon_{yy} = \frac{\partial v}{\partial y}$$

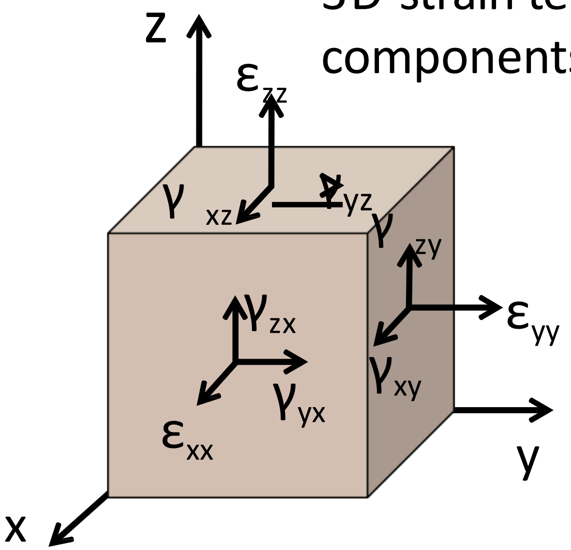
$$\varepsilon_{zz} = \frac{\partial w}{\partial z}$$

Relating stress and strain

3D stress tensor – 9 stress components



3D strain tensor – 9 strain components



$$\sigma_{ij} = C_{ijkl}\varepsilon_{ij}$$

- Relate stress and strain through an elastic constant
- **9 stress x 9 strain = 81 elastic constants to describe behaviour!**

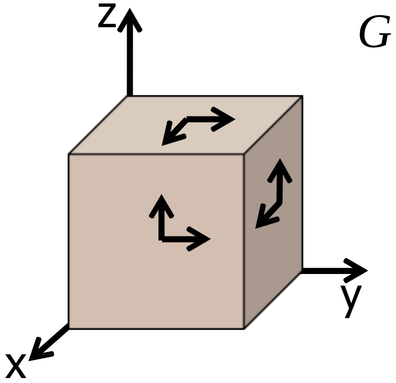
Assumption 2:
Isotropic (direction independent) properties

→

Reduces to two elastic constants
- shear modulus, **G**
- bulk modulus, **K**

Elastic moduli

Shear Modulus, G – shear stress and strain Describes tendency to change in shape



$$G = \frac{\tau}{\gamma}$$

Relate E and K through geometry:

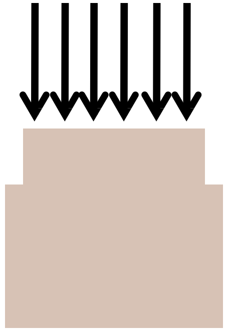
$$K = \frac{E}{3(1-2\upsilon)}$$

Relate E and G through geometry:

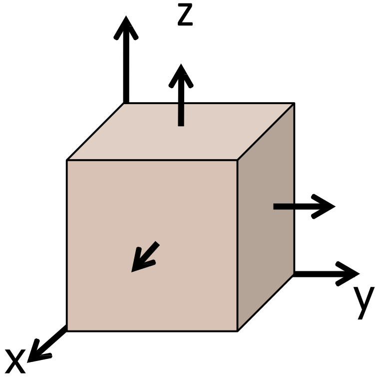
$$E = 2G(1+\upsilon)$$

$$E \approx 3G$$

Bulk Modulus, K – compressibility Describes tendency to change in volume



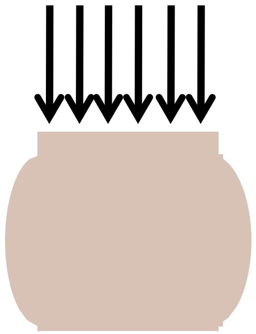
Young's Modulus, E – special case: longitudinal stress and strain, most commonly used to quantify stiffness



$$E = \frac{\sigma}{\varepsilon}$$

Assumption 3:
Tissue is incompressible
(Volume is conserved)

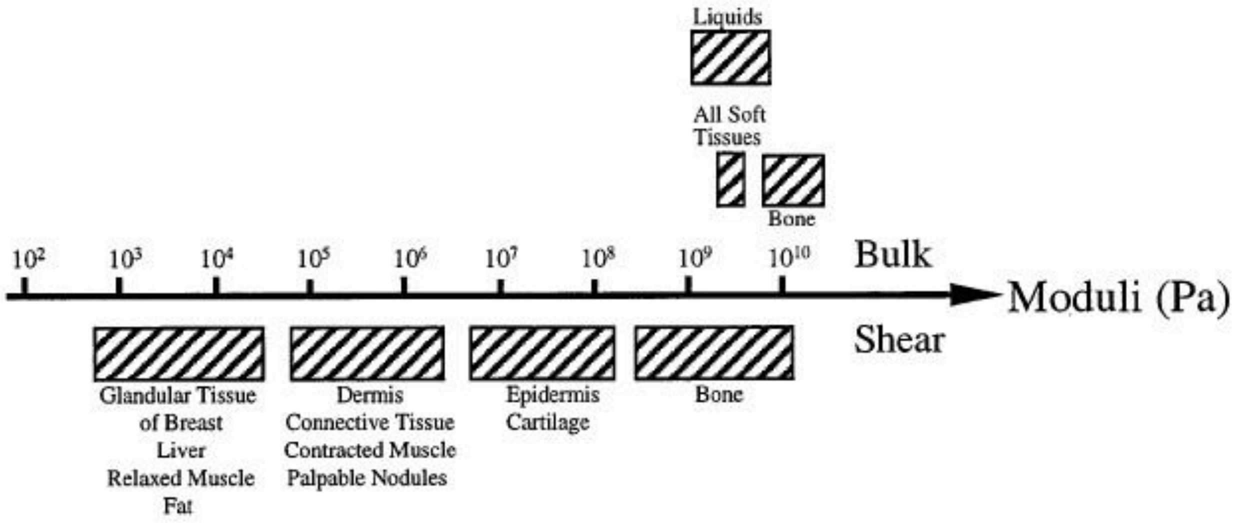
Poisson's ratio, υ – relates change in shape to change in volume



$$\upsilon = \frac{\varepsilon_{xx}}{\varepsilon_{zz}}$$

= 0.5 for tissue

So, which moduli for Tissue?



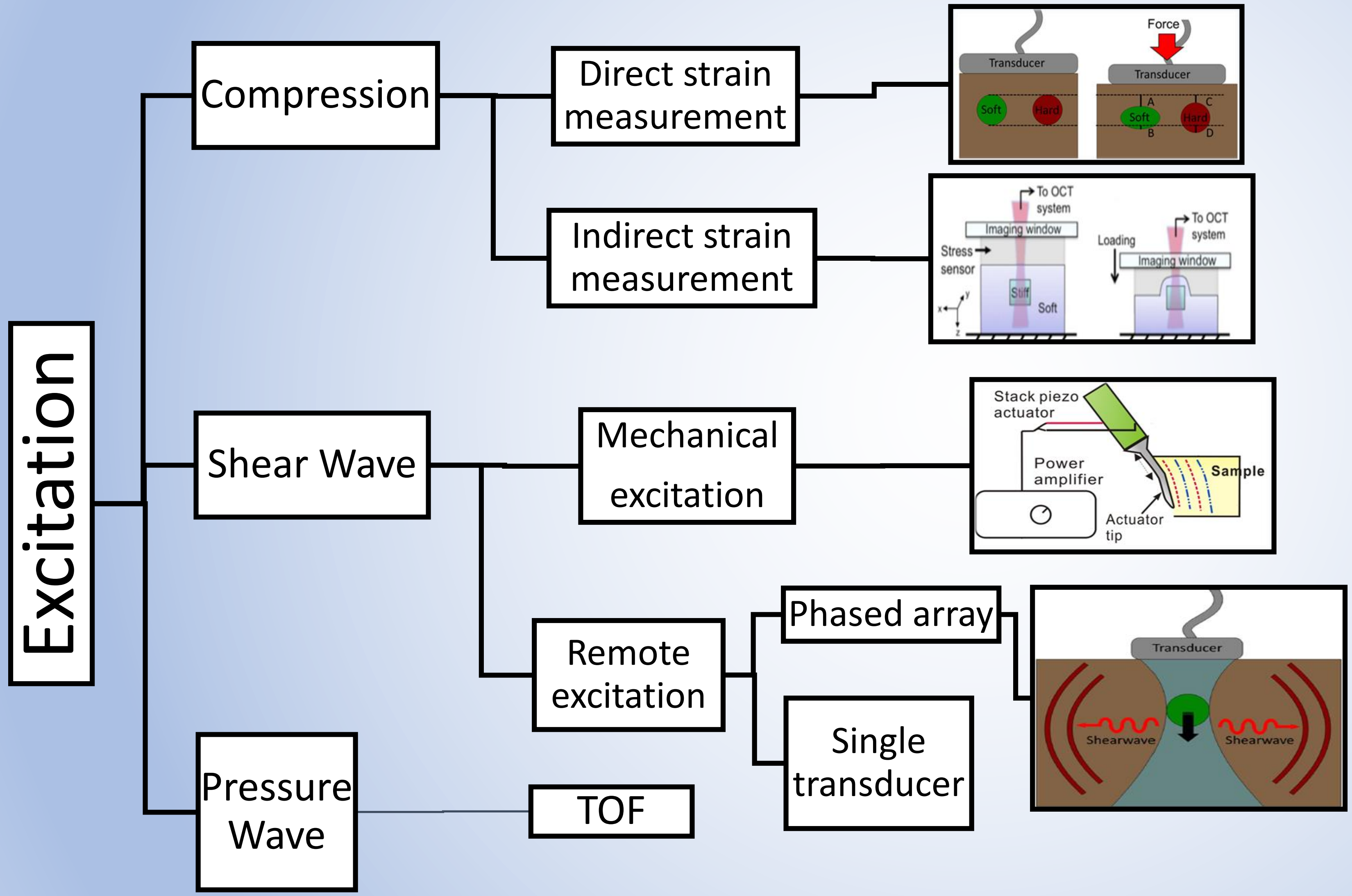
Shear modulus (G) or Young's modulus (E=3G) has largest dynamic range in tissue

How do we get to a modulus in elastography?

Tissue motion → Imaging system → Displacement → Algorithm → Modulus → Elastogram

Assumption 4: Displacement can be related to modulus

Deformation types (inducing strain)



For homogeneous isotropic linear elastic materials

$$E = \frac{\sigma}{\varepsilon}$$

$$G = \rho {v_s}^2$$

$$K = \rho {v_c}^2$$

Newton-Laplace equation

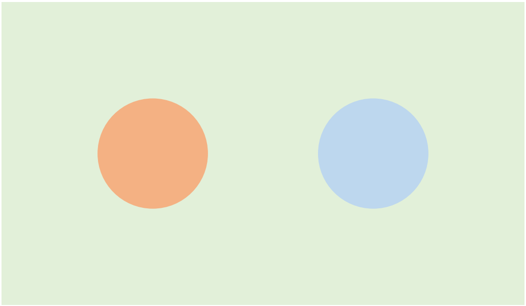
$$E = 2G(1+\nu) = 3K(1-2\nu)$$

(Poisson's ratio ~ 0.499)

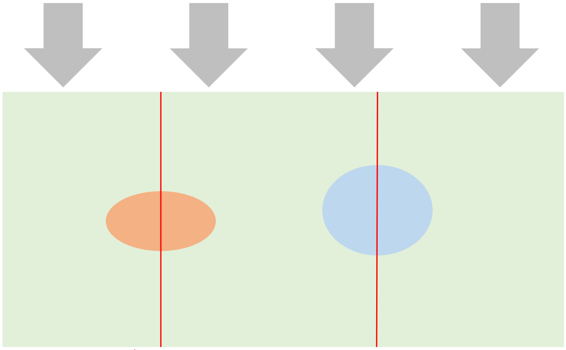
How it works? - **compression**

Mechanical Load

Pre-compression



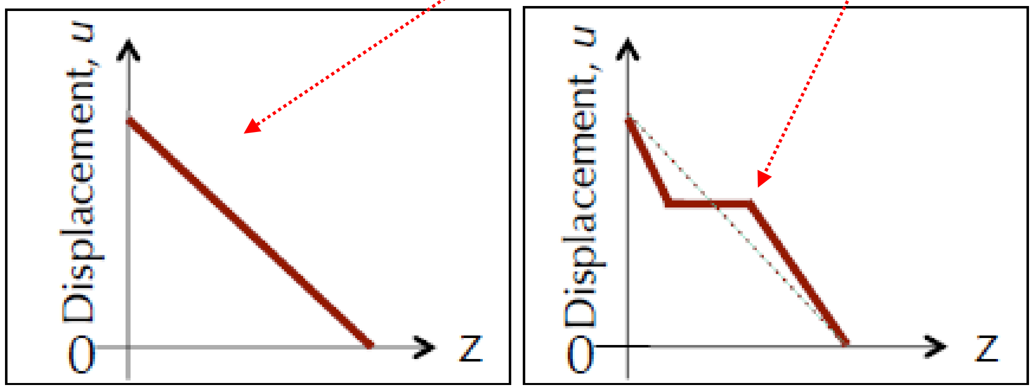
Post-compression

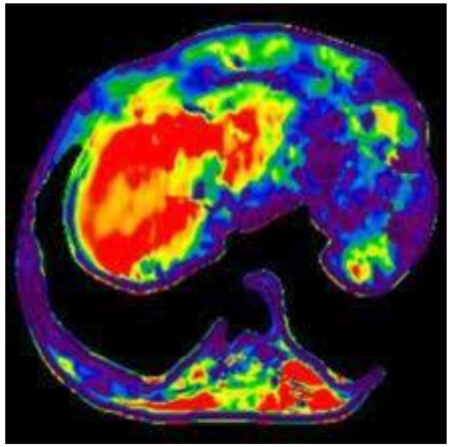


- Press at low frequency (<10 Hz)
- Displacement -> strain ~ modulus

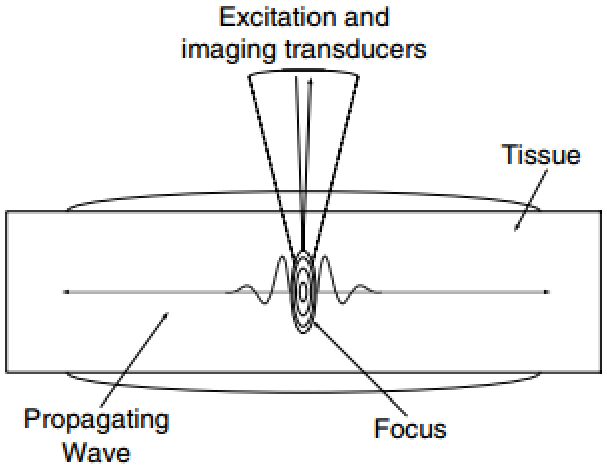
$$\varepsilon = \frac{du}{dz} = \frac{\sigma}{E}$$

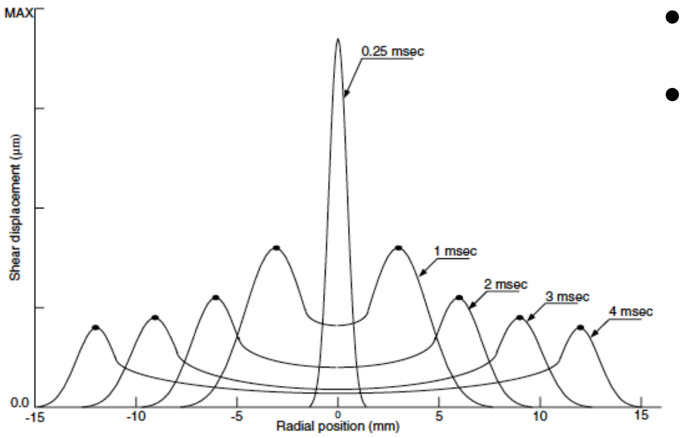
Mechanical property estimation





How it works - **transient (SW)**



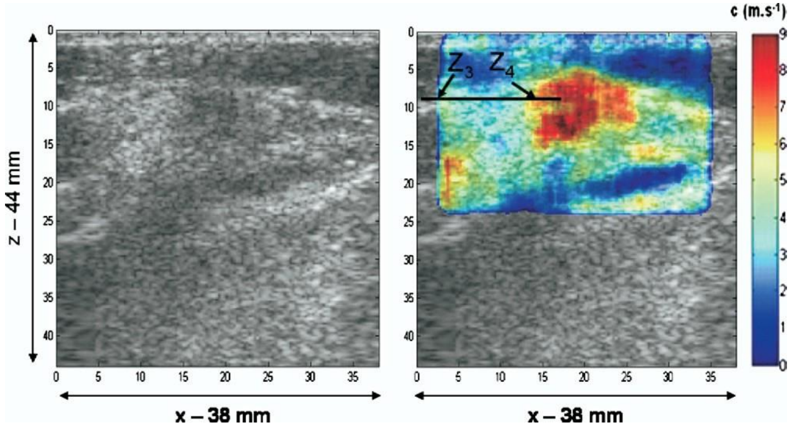


- Acoustic radiation force impulse
- Generates shear waves
- Displacement -> shear wave speed ~ modulus

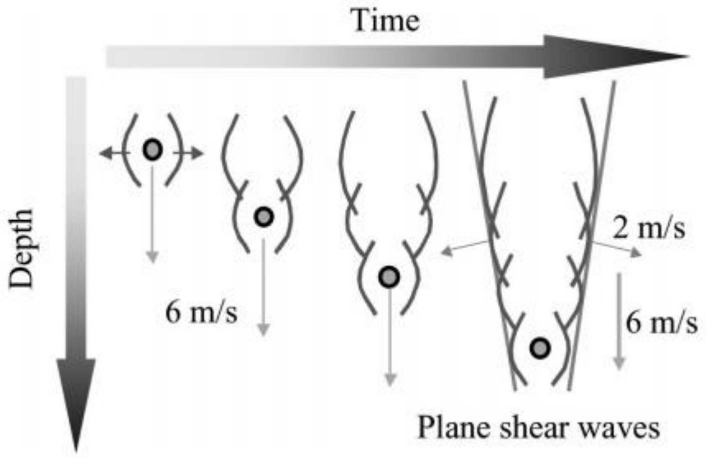
Shear wave speed to modulus:

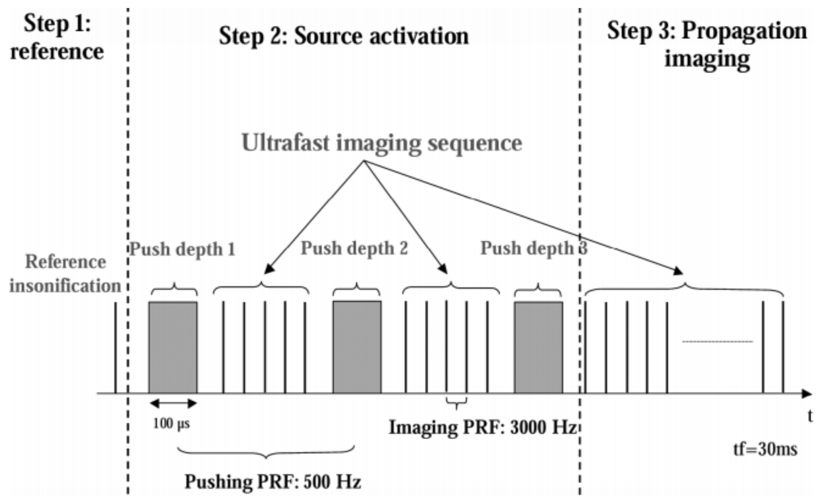
$$c_s = \sqrt{\frac{E}{3\rho}}$$

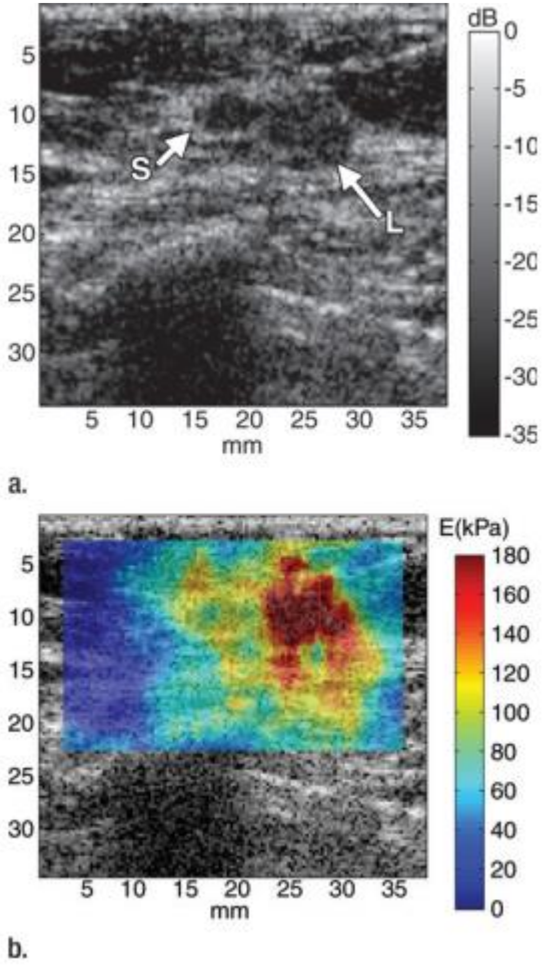
Ultrasound image and shear wave speed image of invasive ductal carcinoma in human breast
(M. Tanter *et al.*, *Ultrasound Med. Biol.*, 2008)

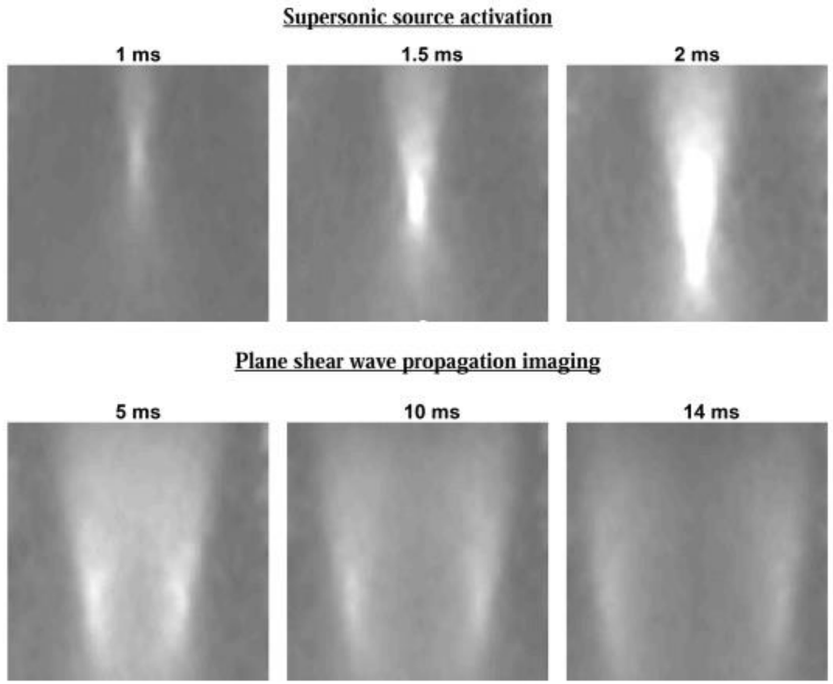


How it works - **supersonic SW**



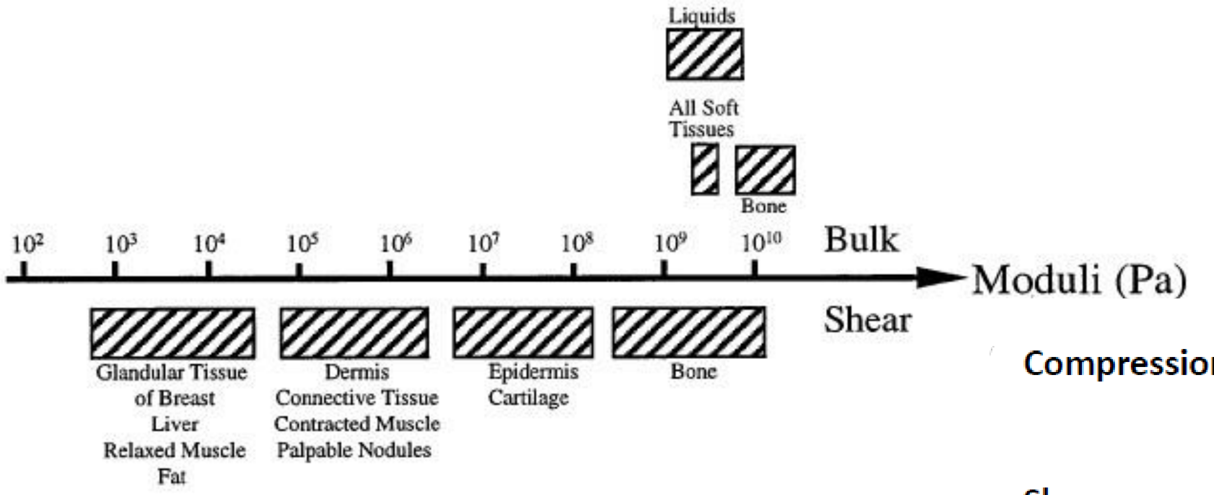






Mach 3 supersonic regime in an elastic phantom

- Higher SNR
- Wider spatial extent of shear wave
- Lower frame rates
- Displacement -> shear wave speed ~modulus



Compressionnal waves propagate at $c_P \cong \sqrt{\frac{K}{\rho}}$ $(\approx 1500 \text{ m.s}^{-1})$

Shear waves propagate at $c_s = \sqrt{\frac{\mu}{\rho}}$ $(\approx 1\text{-}10 \text{ m.s}^{-1})$

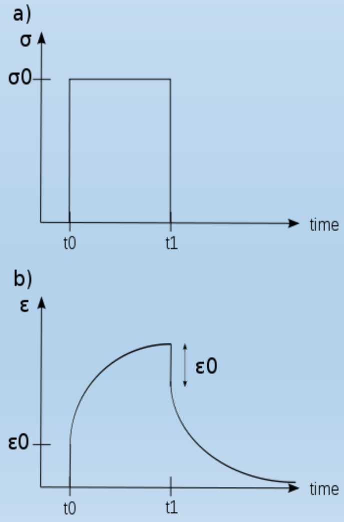
Two kind of waves propagating at totally different speeds !!

Type	E(kPa)	G(kPa)	K(GPa)	c_t (m/s)	c_s (m/s)
Fat	-1	-0.3	2-2.5	-0.5	1490-1540
Liver	1-24	0.3-8	2-2.5	0.5-2.8	1490-1540
Muscle	3-30	1-10	2-2.5	1-3.2	1490-1540
Prostate	6-45	2-15	2-2.5	1.4-3.9	1490-1540
Myocardium	20-150	6.7-50	2-2.5	2.6-7.1	1490-1540
Fibrotic Liver	30-300	10-100	2-2.5	3.2-10	1490-1540

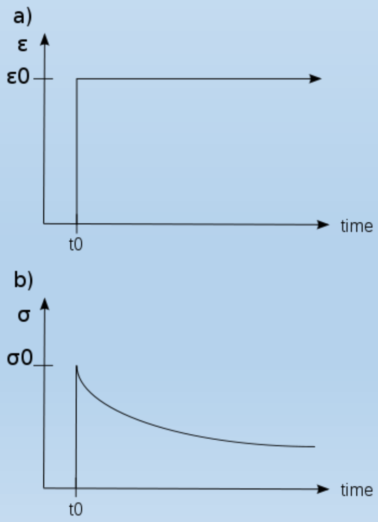
Is tissue purely elastic?

- Young's modulus defines elastic (linear, instantaneous) material behaviour
- But more commonly tissue is viscoelastic
- Viscosity is resistance to flow
- Viscoelastic behaviour is non-linear and time-dependent

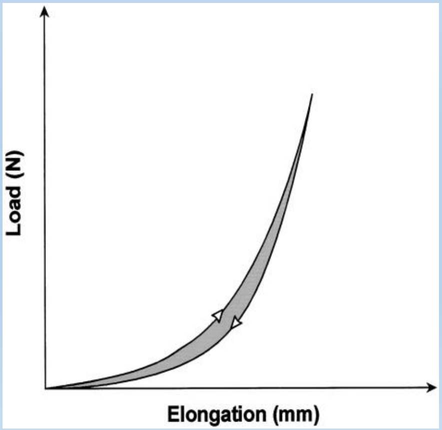
Creep – time-dependent strain



Relaxation – time-dependent stress



Hysteresis



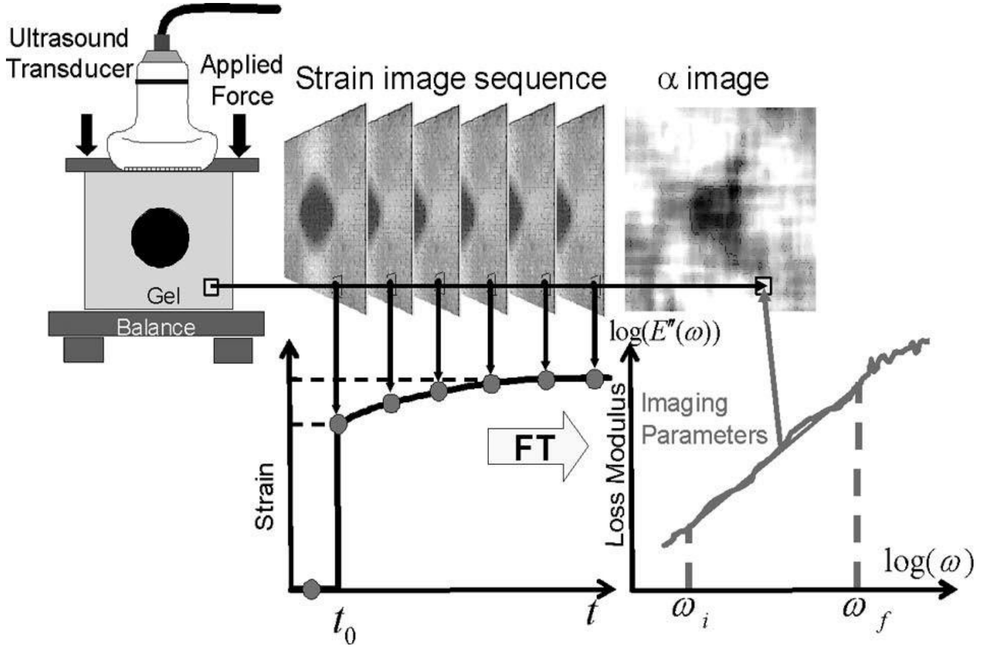
In elastography,

- small
- wait for stress relaxation before acquiring, OR
- use acquisition speed >> tissue flow

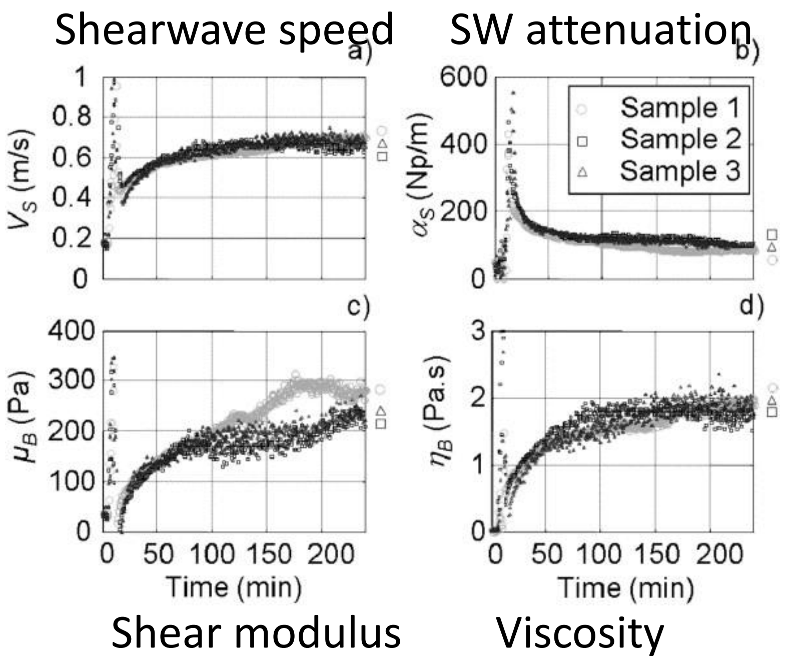
Viscoelasticity in elastography

Assumption 5: Tissue is linear elastic

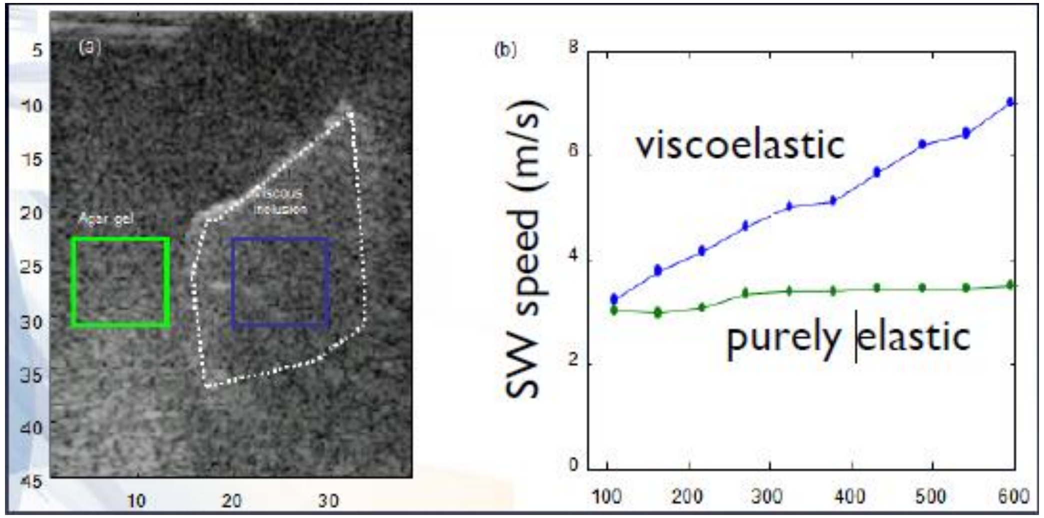
- Assumed in most elastography techniques to simply quantify stiffness
- But disease alters tissue viscoelasticity as well as stiffness
- Possibility for viscoelastic contrast in elastography – changes in time-dependent properties
- Study of viscous or viscoelastic properties is called rheology



Creep response of breast tissue in compression elastography



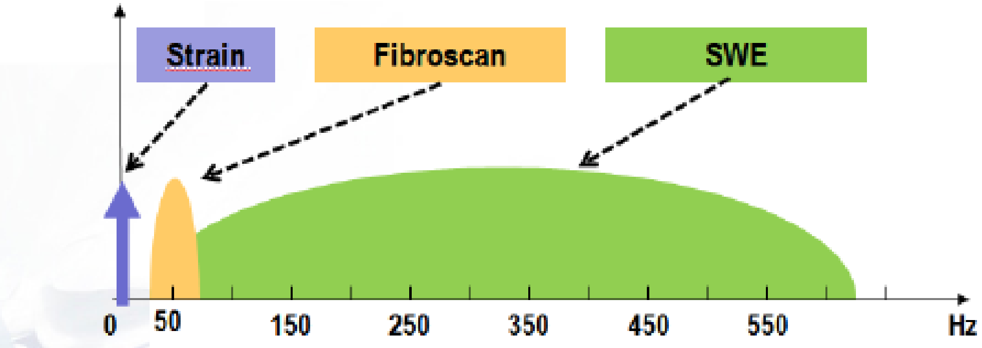
Viscoelastic measurement

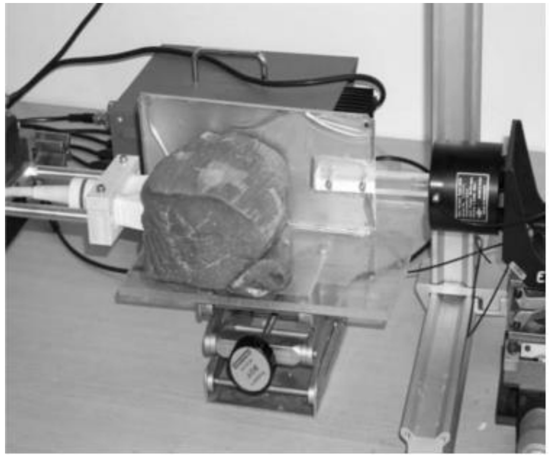


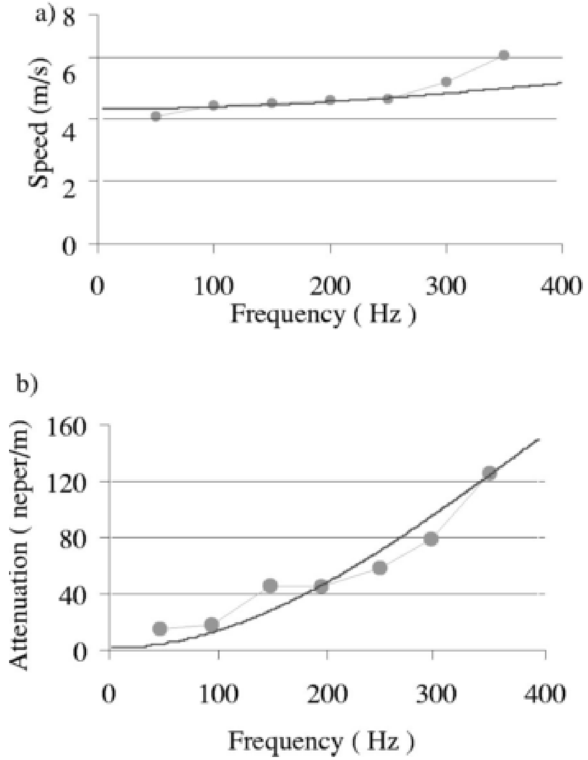
$$C_T^V = \sqrt{\frac{2(\mu_1^2 + \omega^2 \mu_2^2)}{\rho(\mu_1 + \sqrt{\mu_1^2 + \omega^2 \mu_2^2})}}$$

Shearwave speed equation derived from the Voigt model

If viscosity,μ_2 is zero, ??

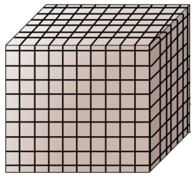


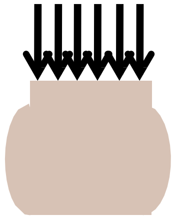


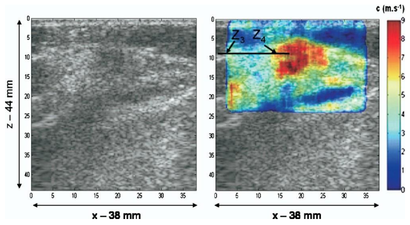


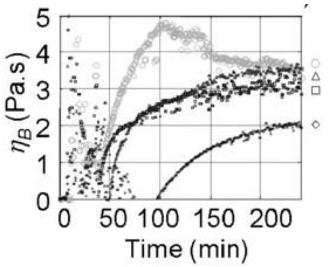
Mechanical properties of tissue – Summary

- Tissue mechanical properties determined by content, structure, and scale
- To form an image of these properties, make **some assumptions**:
  1. Mechanical homogeneity within a resolution element
     – Enables use of continuum mechanics to describe behaviour
  2. Isotropic (direction-independent) properties
     – Reduces 3D elasticity tensor to shear and bulk moduli
  3. Incompressible (volume is conserved)
     – Allows simple relation of shear and Young's modulus (E = 3G)
  4. Local displacement is related to elastic modulus
     – Modulus is estimated from displacement in compression, vibration, and transient techniques
  5. Linear elastic
     – Simple model facilitates estimation of Young's modulus (stiffness)
- More complex models of tissue behaviour (e.g., viscoelasticity) can provide further diagnostic information









Feasibility of a hybrid elastographic-microfluidic device to rapidly process and assess pancreatic cancer biopsies for pathologists

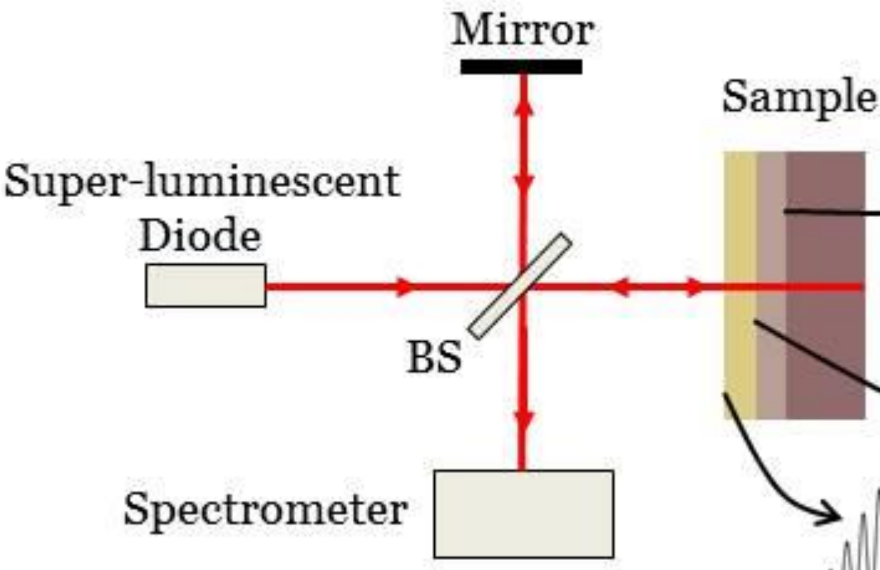
- Ronnie Das, Thu-Mai Nguyen, Saniel D. Lim, Matt O'Donnell, Ruikang K. Wang and Eric J. Seibel
- IEEE EMBS Special Topic Conference on Healthcare Innovations & Point-of-Care Technologies, Oct 8-10, 2014, Seattle WA

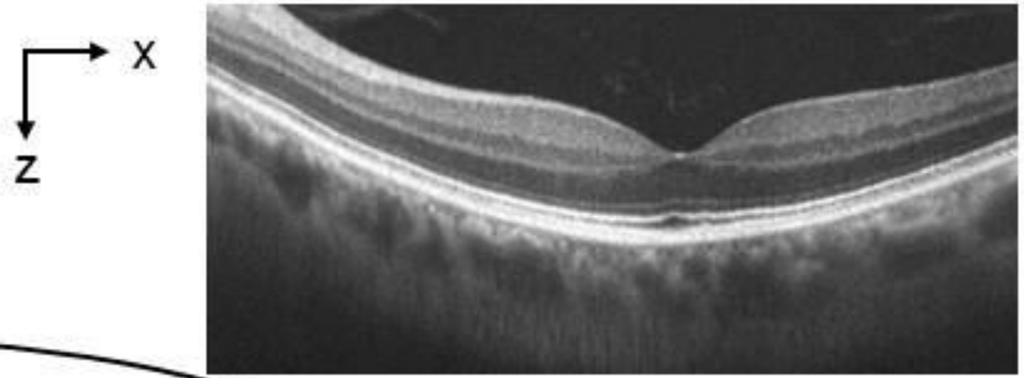
- Objectives:

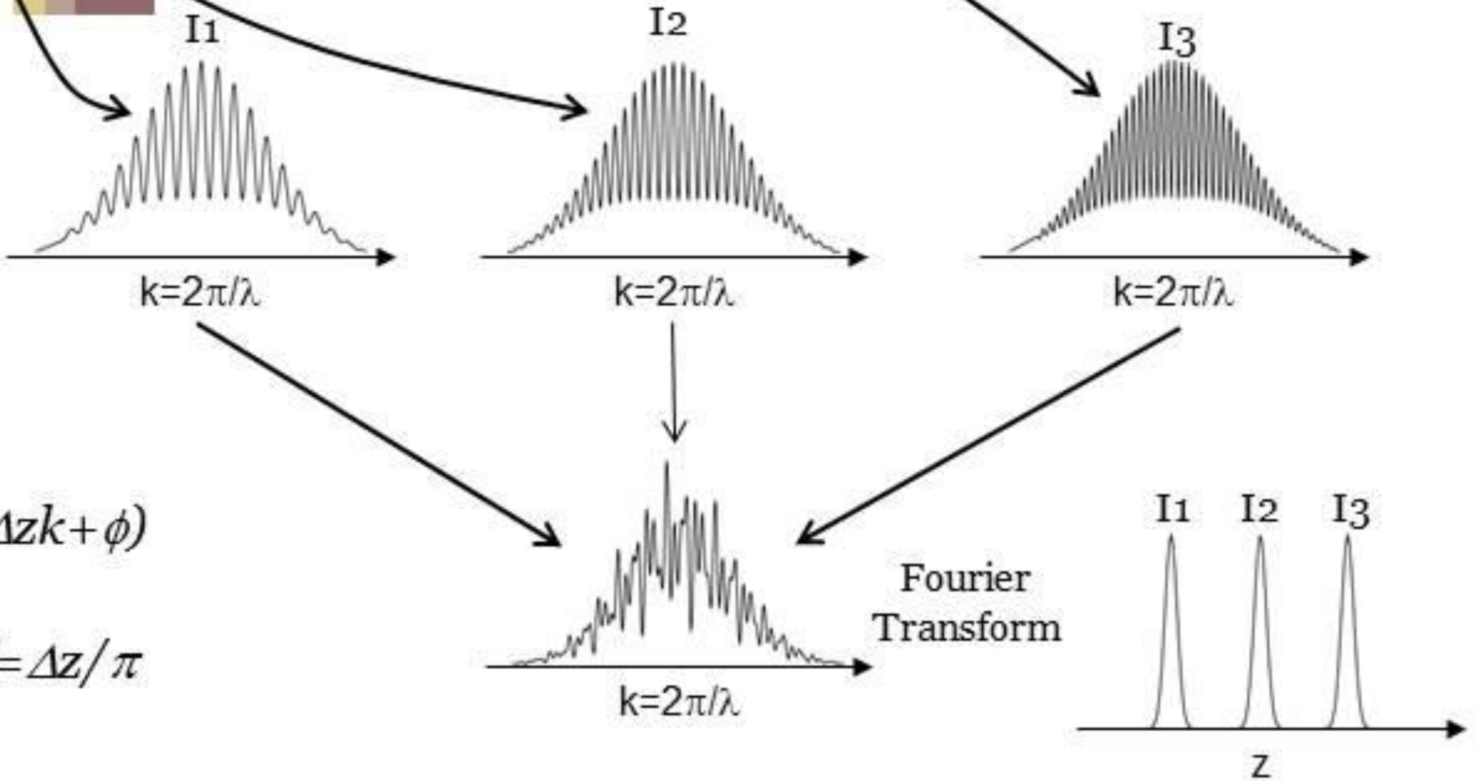
1) To measure the elasticity of pancreatic tissue specimens using optical coherence tomography shear wave elastography (OCT-SWE)

2) To determine feasibility of OCT-SWE to identify distinct structures in the specimens

Optical Coherence Tomography



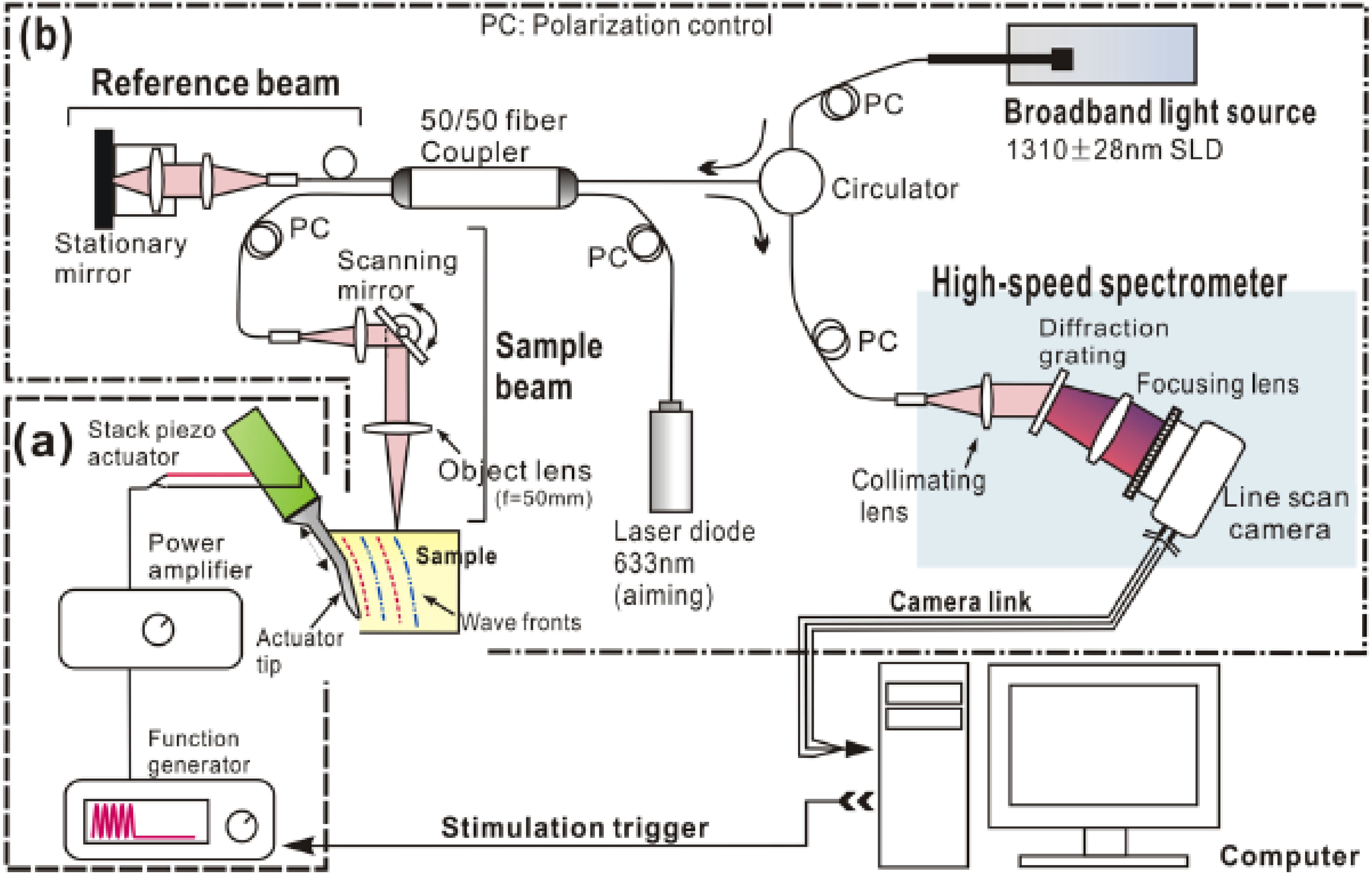




$$I = E_S^2 + E_R^2 + 2Re[E_S E_R^*]\cos(2\Delta zk + \phi)$$

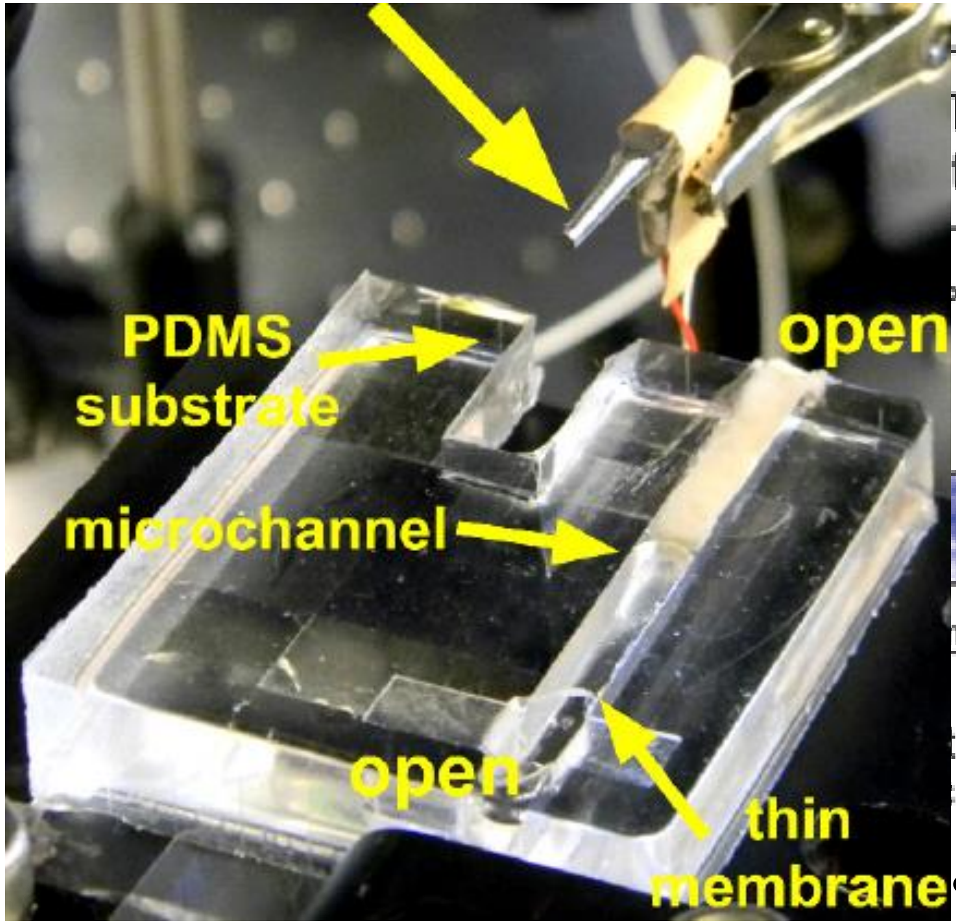
$$f = \Delta z / \pi$$

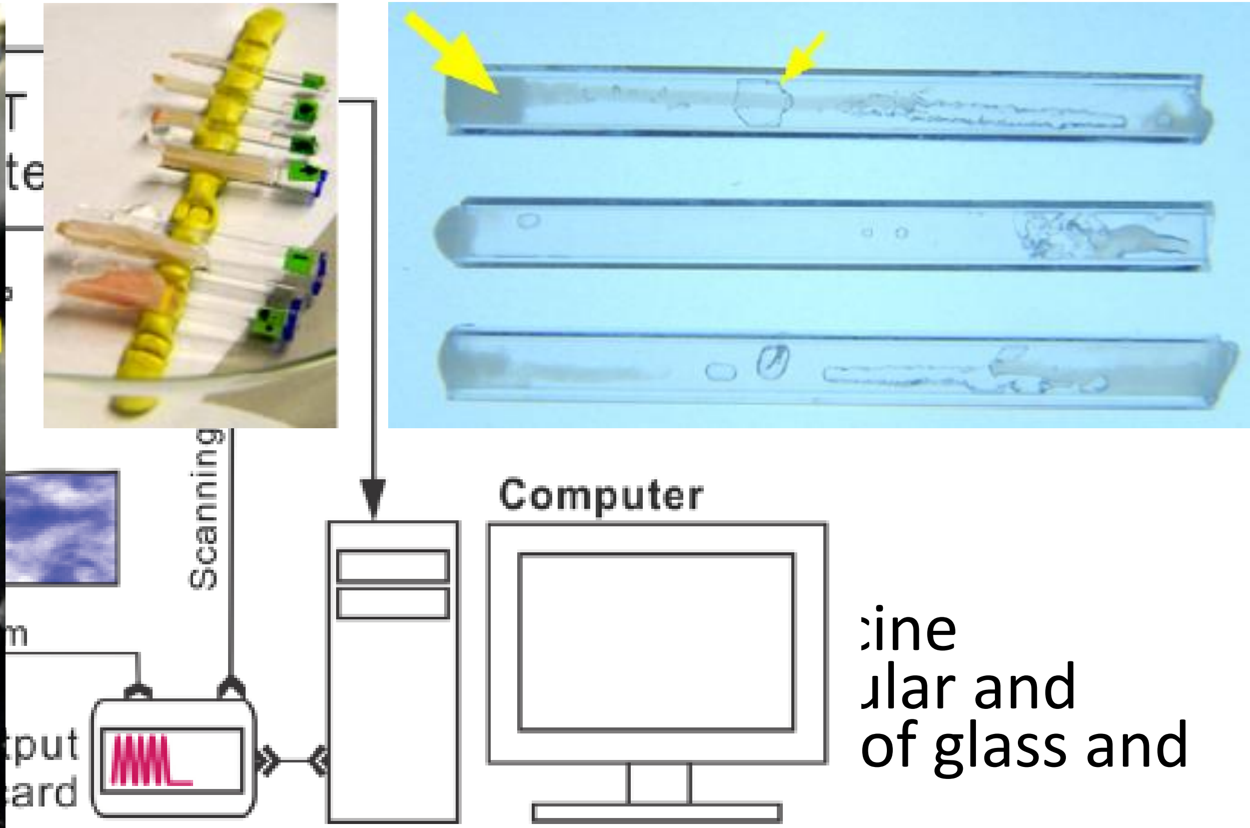
Courtesy R. Nick Graf



(b)
PC: Polarization control
Reference beam
50/50 fiber
Coupler
PC
Broadband light source
1310±28nm SLD
Circulator
Stationary
mirror
PC
Scanning
mirror
PC
Sample
beam
High-speed spectrometer
Diffraction
grating
Focusing lens
PC
(a)
Stack piezo
actuator
Object lens
(f=50mm)
Collimating
lens
Line scan
camera
Power
amplifier
Sample
Wave fronts
Laser diode
633nm
(aiming)
Actuator
tip
Camera link
Function
generator
Stimulation trigger
Computer

Methods

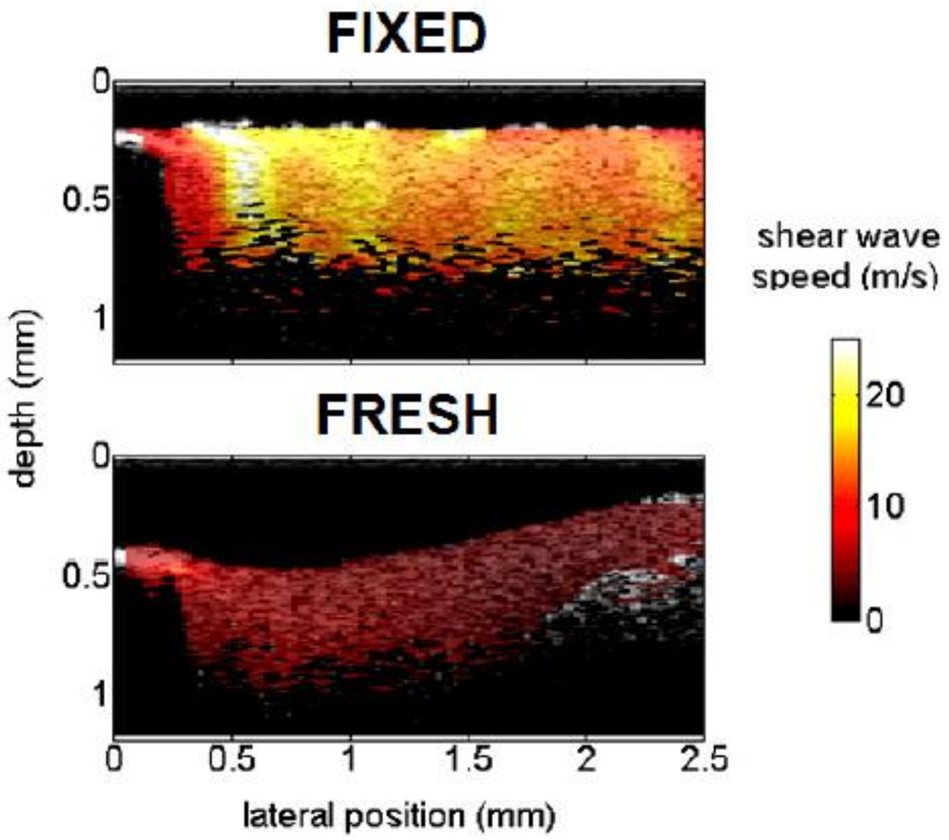




ine
lar and
of glass and

- 1% agarose hydrogel phantom with 4% agarose inclusion

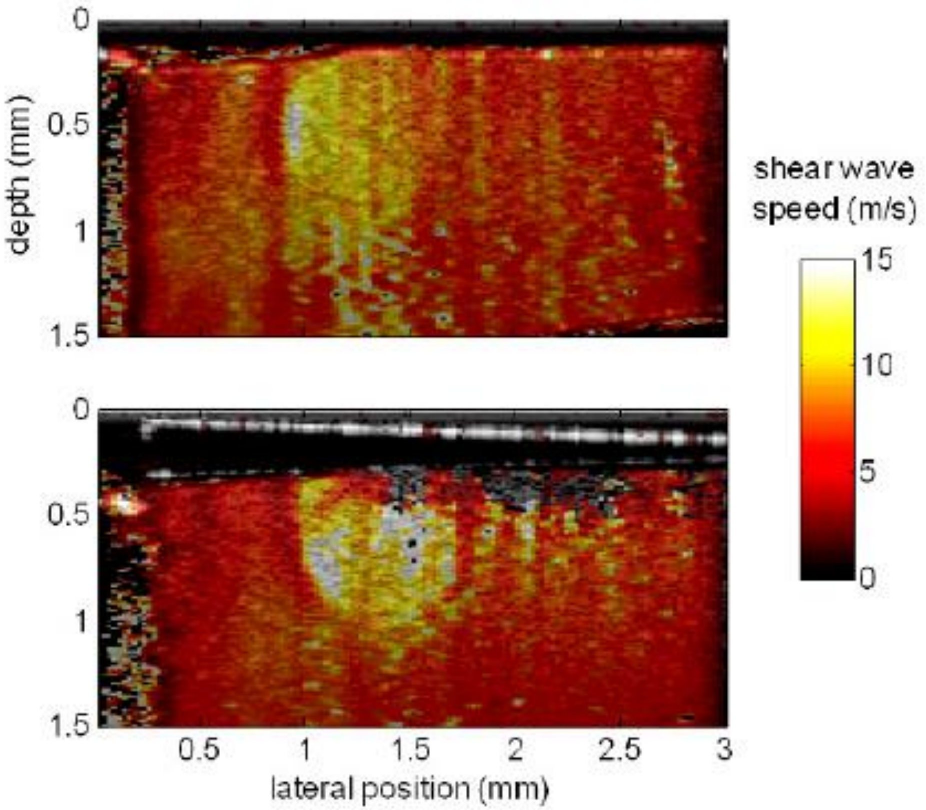
Results



Remarks

- No significant difference by channels
  - Glass substrate/ enclosed glass / PDMS channels
- Measured shear wave speed distribution
  - Flesh vs Fixed: **3.5 m/s vs 14.5 m/s**
- Estimated shear modulus
  - Flesh vs Fixed: **18 kPa vs 227 kPa**

Results

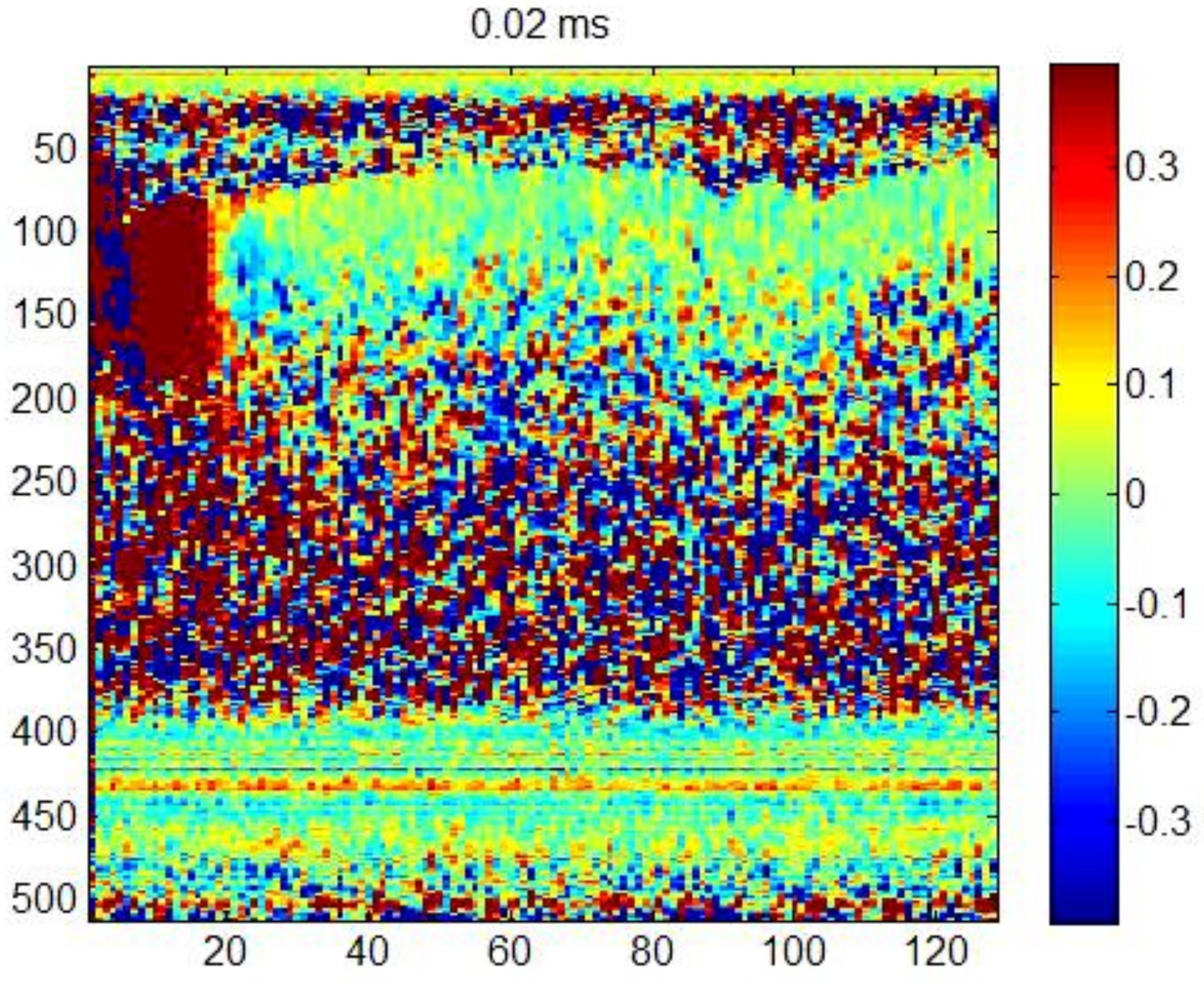


free space (upper), microchannel (lower)

Remarks

- Differenciated 4% agarose from 1% agarose hydrogel phantom
  - Shear wave : **11.18±1.48 m/s vs 6.62±2.65 m/s**

Fixed pancreatic tissue, placed on a glass plate



Comparisons of Loading Schemes

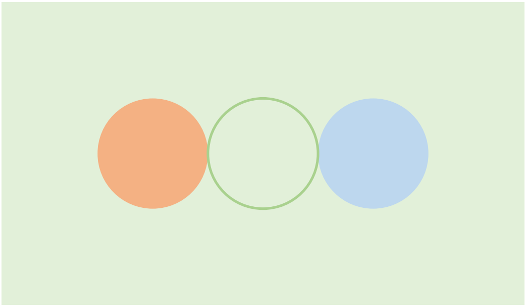
Loading Method	Measured Parameter	Axial Resolution*	Lateral Resolution*	Assumptions **		Quantitative?	Non-contact?
				Strain Contrast	**Elasticity**		
Quasi-static Compression	Local Strain	50 ~ 200 µm	10 ~ 30 µm	Uniform Stress Field	Required Local Stress Distribution	No	No
Dynamic Compression						No	No
Dynamic Compression /w stress sensor	Local Strain Local Stress	n/a	10 µm			Yes	No
				Shear Wave Variation	**Elasticity**		
Shear Wave by Piezo	Phase Velocity, Cs	~ 10 µm	~ 10 µm	N/A	Uniform Density	Yes	No
Shear Wave by ARF						Yes	Yes

**** Incompressible, linear, elastic and isotropic medium**

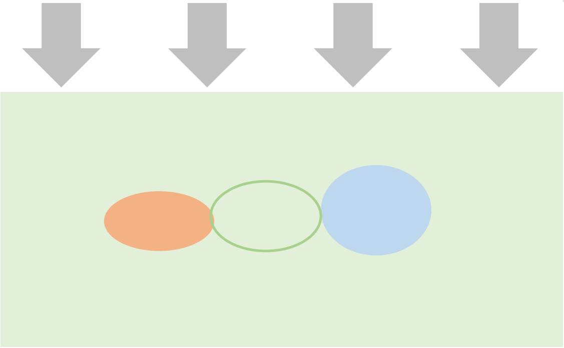
From displacement to modulus

Mechanical Load

Pre-compression



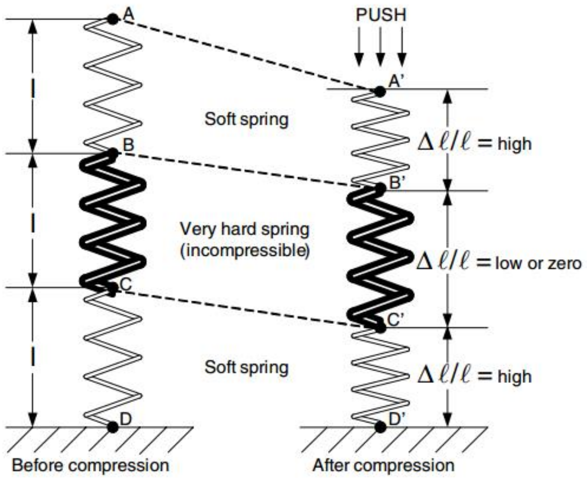
Post-compression

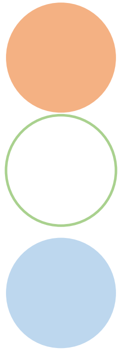


Imaging

Ultrasound MRI OCT

Mechanical property estimation

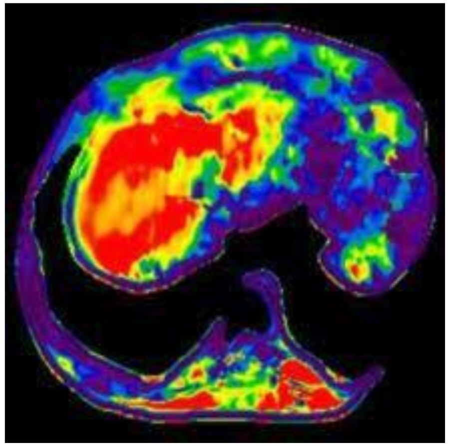




Stiffness1

Stiffness2

Stiffness3



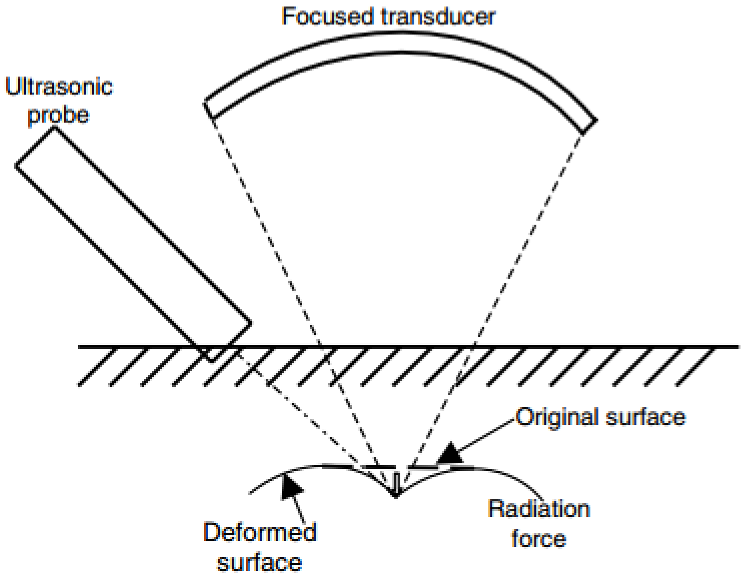
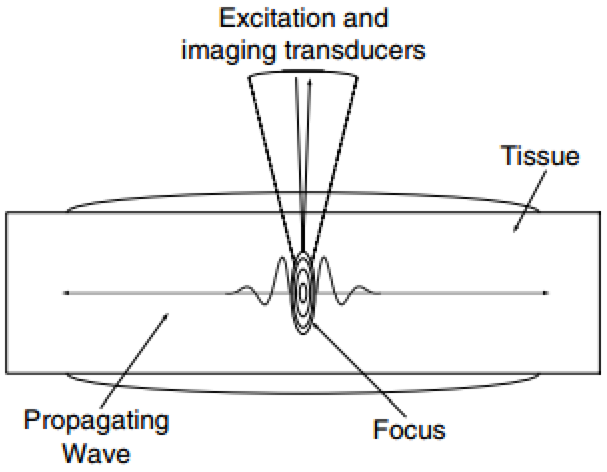
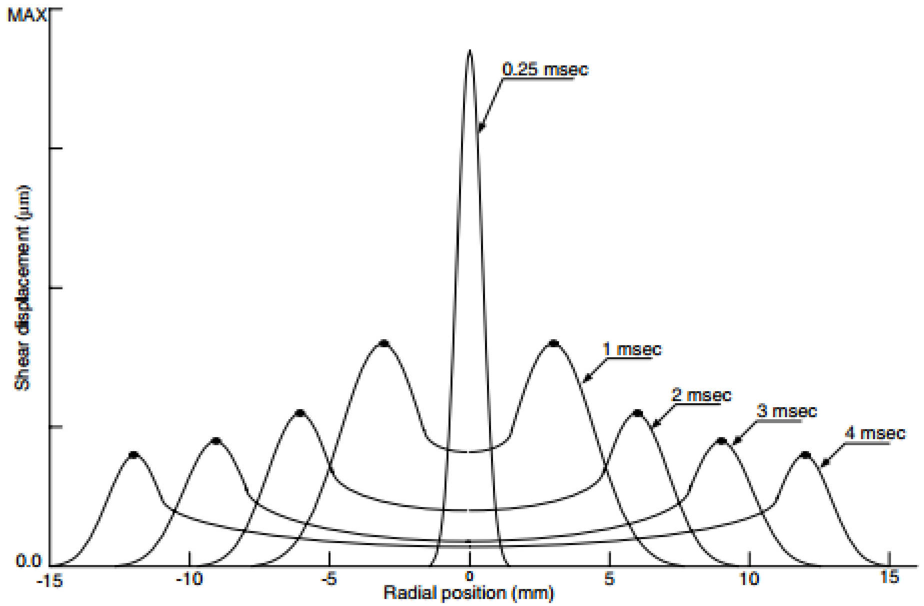


Figure 11. Schematic representation of the early work by Sugimoto to measure the displacement of a specimen's surface under radiation force.





Excitation Methods

- Mechanical excitation
  - **Compression loading (quasi-static / dynamic)**
  - **Vibration by piezoelectric actuator (dynamic)**

- Acoustic radiation force (ultrasound)
  - **Internal**
  - **Internal shear wave**

- Internal endogenous force
  - **Respiratory, heart**