ViscoElasticity Imaging using Ultrafast Ultrasonic Imaging

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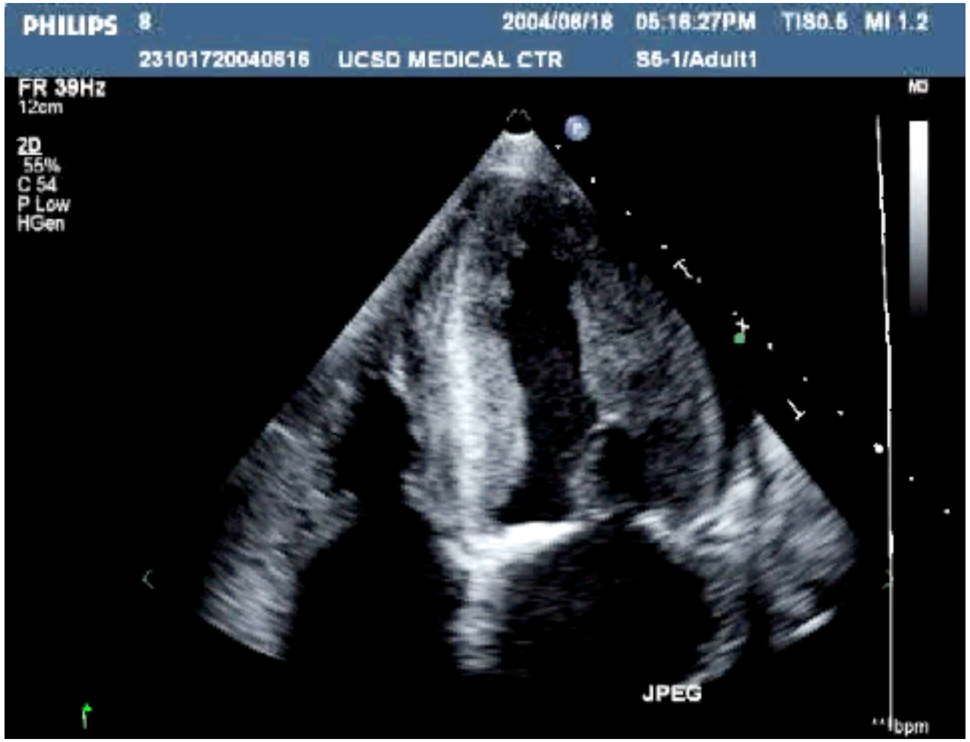
In vivo Imaging of Tissue Elasticity using Ultrasound

Basics of Ultrasound Imaging



Morphology images

- Real time $\left[20-150\right]Hz$
- Non radiative
- Cheap and portable

Ultrasound Technology improvement in the last twenty years

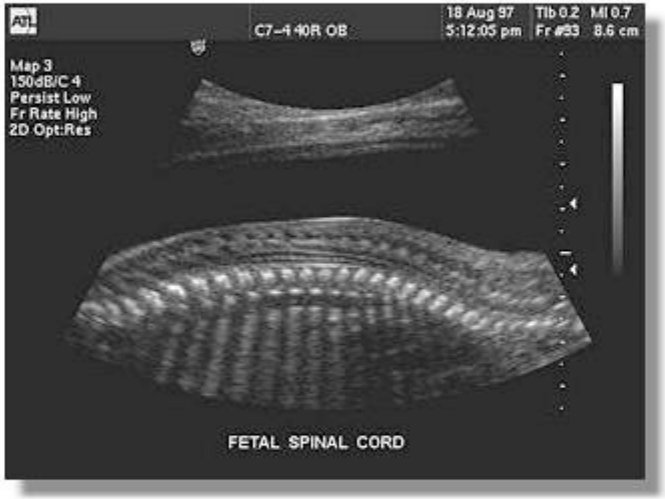
Since the advent of clinical Doppler Imaging,
the major fact is the huge improvement of sensitivity due to technology

Ultrasound Imaging

1985

1990

1995



2000

Thanks to Sensitivity improvment, the number of suspicious lesions detected is increasing

When the pathology can be described without any doubt by a morphological change
A diagnosis can be performed

A morphological Image is sometimes not enough for diagnosis …

An example of Echographic Nightmare for radiologists

Breast Cancer Diagnosis

Benign	Malignant	Benign
		
Fibrotic Lesion	Carcinoma Grade II	Viscous Cyst

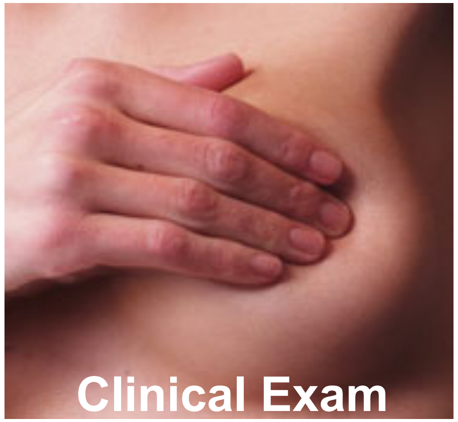
A Real Need for improving Specificity

Going from
Morphological to Physio-pathological
Imaging

Context : Case Example of Breast Cancer Diagnosis

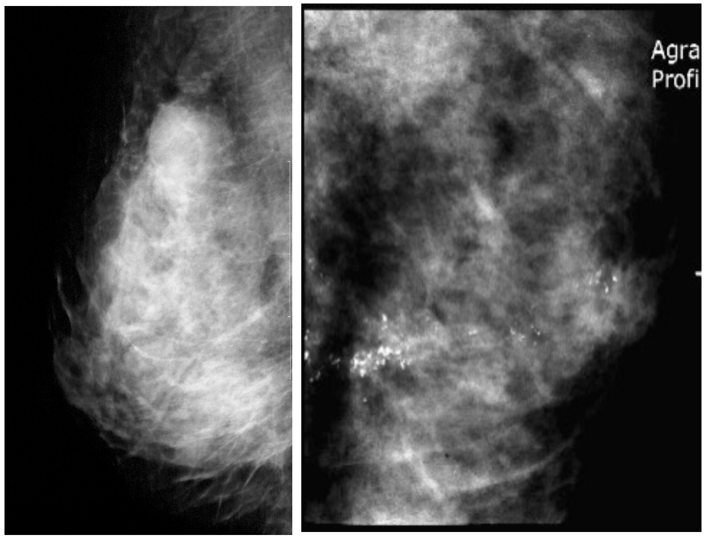
Clinical signs

- stiffness (stroma reaction)
- pain (inflammation), nipple discharge
- shape

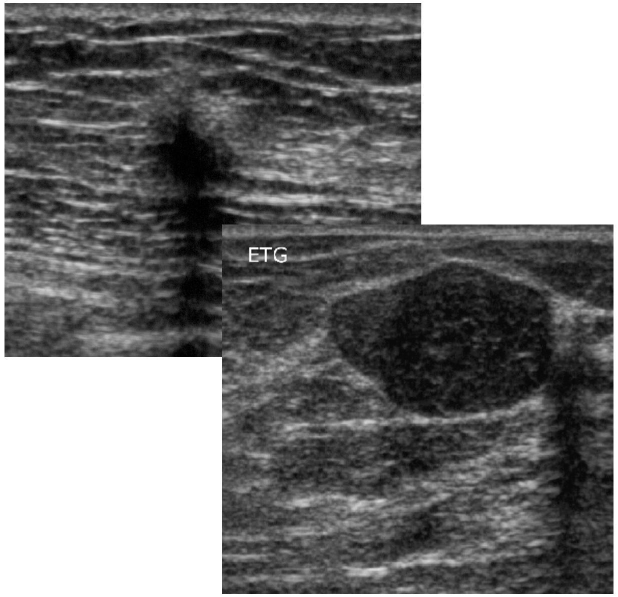


Radiological signs

X-Ray



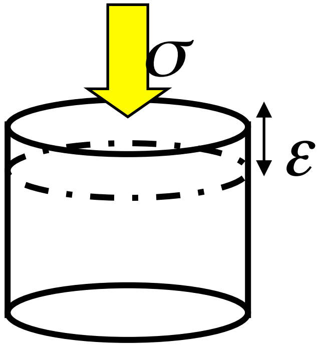
Ultrasound (US)



MRI

Palpation and Elasticity in human soft tissues

E

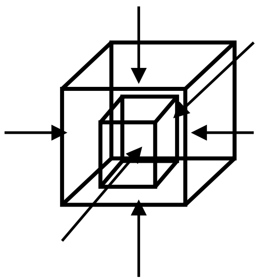


$$E = \frac{\sigma}{\varepsilon} = \mu \frac{3\lambda + 2\mu}{\lambda + \mu}$$

Young's Modulus **E**

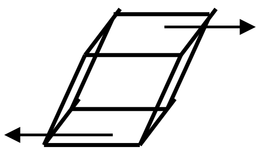
2 other mechanical coefficients are commonly used for defining the elasticity of a solid material

λ



λ ~ Bulk Compression Modulus, almost constant, of the order of **10^9 Pa,** quasi incompressible medium

μ



μ Shear Modulus, Strongly heterogeneous, varying between **10^2 and 10^7 Pa**

$\lambda \gg \mu$

$E \approx 3\mu$

Why estimating Young's Modulus (Stiffness) ?

Type of soft tissue		Young's modulus (E in kPa)	Density (kg/m^3)
Breast	Normal fat	18-24	930
	Normal glandular	28-66	1020
	Fibrous tissue	96-244	
	Carcinoma	22-560	1000 +/- 8 % ~water
Prostate	Normal anterior	55-63	
	Normal posterior	62-71	
	BPH	36-41	
	Carcinoma	96-241	
Muscle		6-7	
Liver		0.4-6	
Kidney	Fibrous tissue	10-55	

Stiffness is strongly linked to pathology… but Palpation is subjective

Elastography = imaging techniques for soft tissue stiffness assessment

Human Body Sismology : Mechanical waves in soft tissues

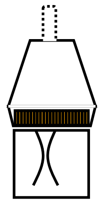
Compressional Waves propagate at $c_P \cong \sqrt{\frac{K}{\rho}}$ $(\approx 1500 \text{ m.s}^{-1})$

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

Two kind of waves propagating at totally different speeds !!

Shear waves propagate only at low frequencies < 1000 Hz (High Shear Viscosity)

Ultrasound is a compressional wave

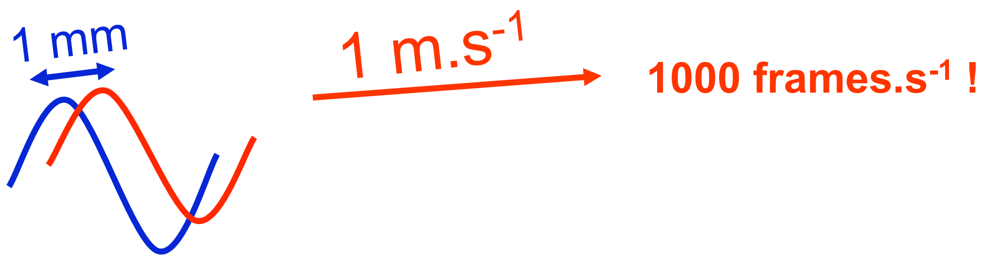


Remote Palpation

(Ultrasonic Wind)

Transient Elastography : Basic Principles

Generation of a low frequency shear wave (a few m.s^{-1})



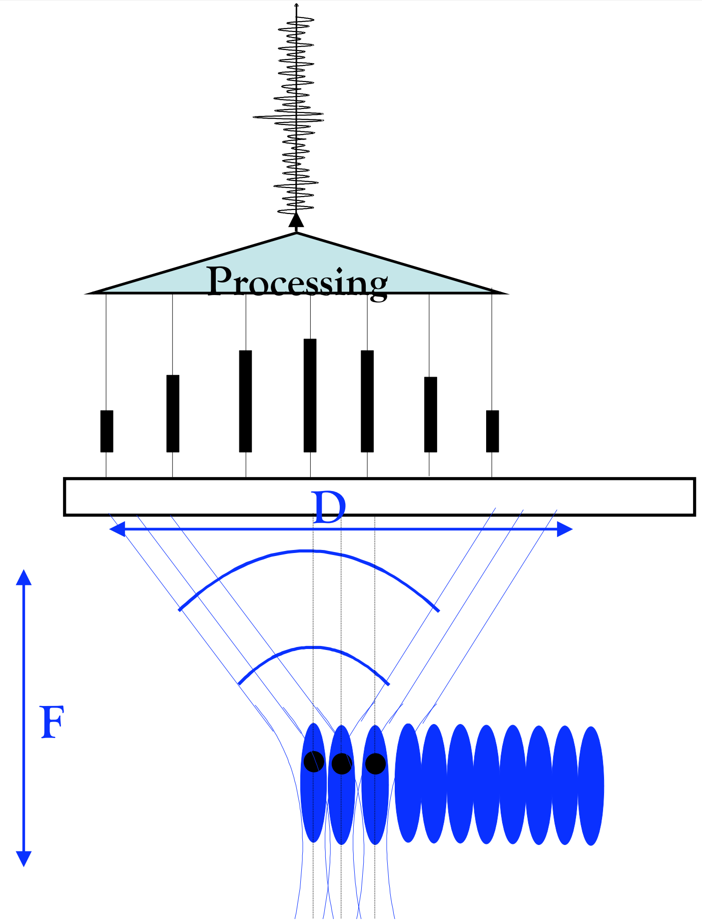
Ultrafast ultrasonic scanner !!! (up to 20000 frames.s^{-1})

First system in 1996 (128 Channels)

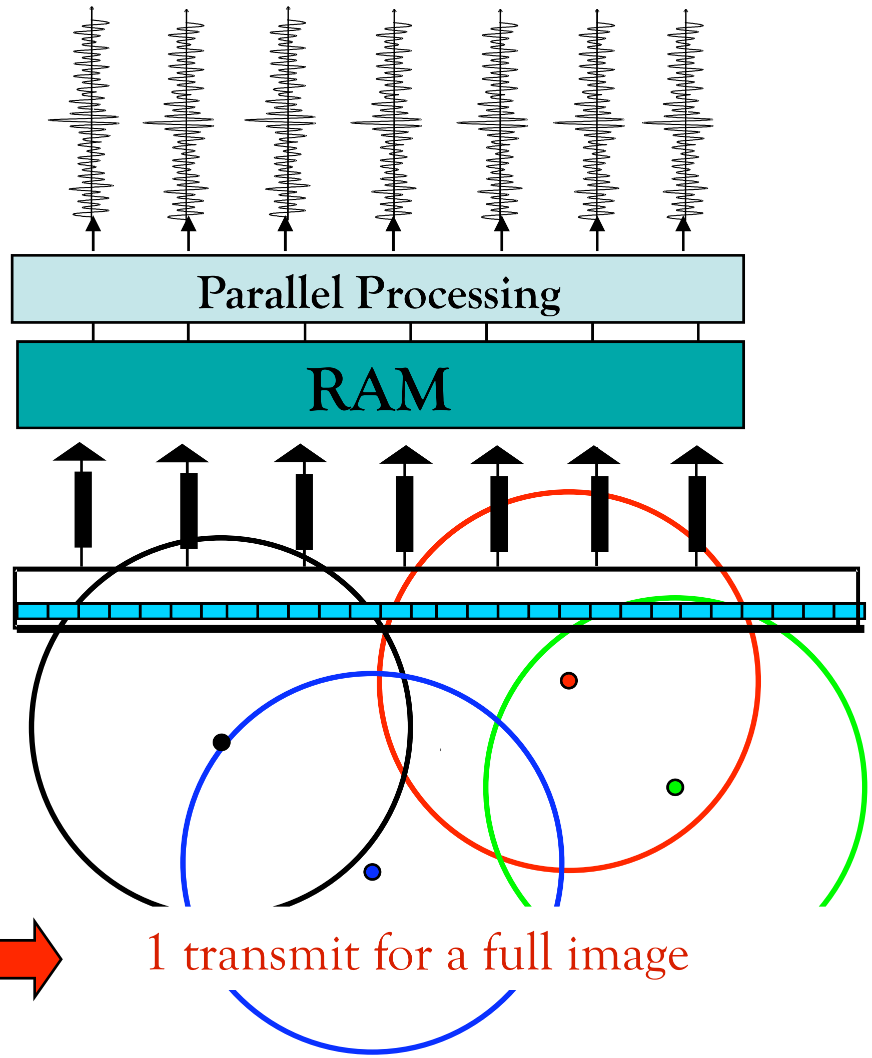
M. Fink et al

Ultrafast Ultrasonic Imaging

Conventional Imaging	Ultrafast Imaging



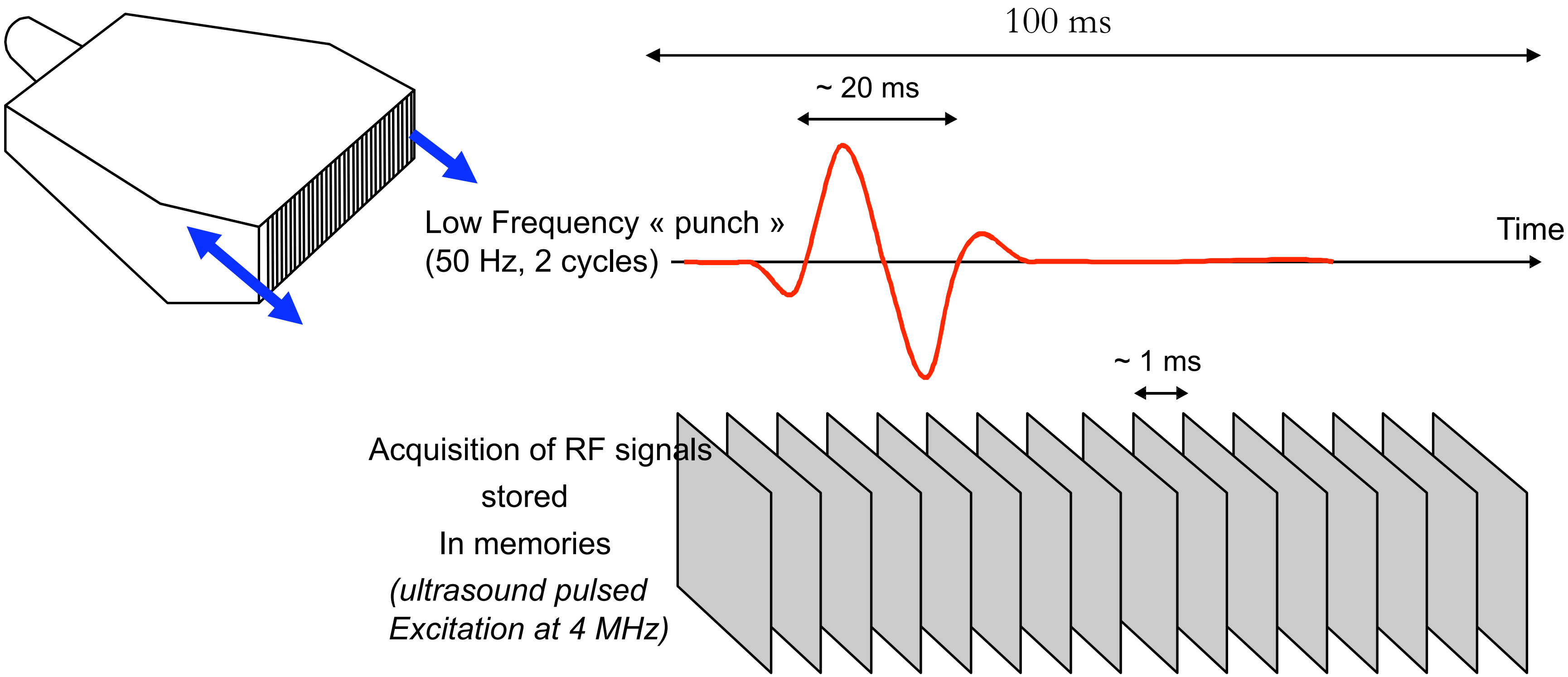
128 transmits for a full image



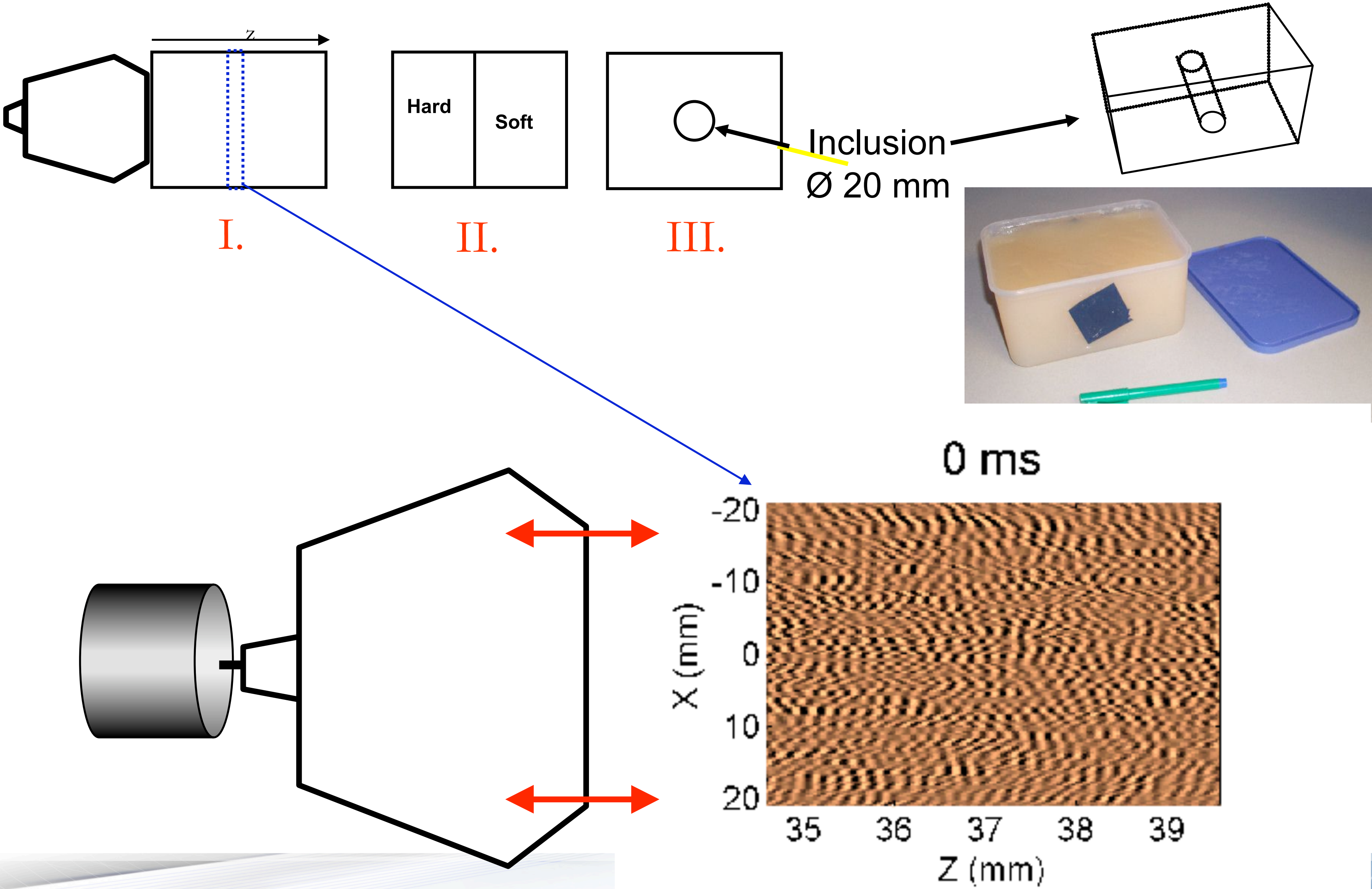
1 transmit for a full image

The Transient Elastography Technique

Shear wave generation + Ultrafast Imaging

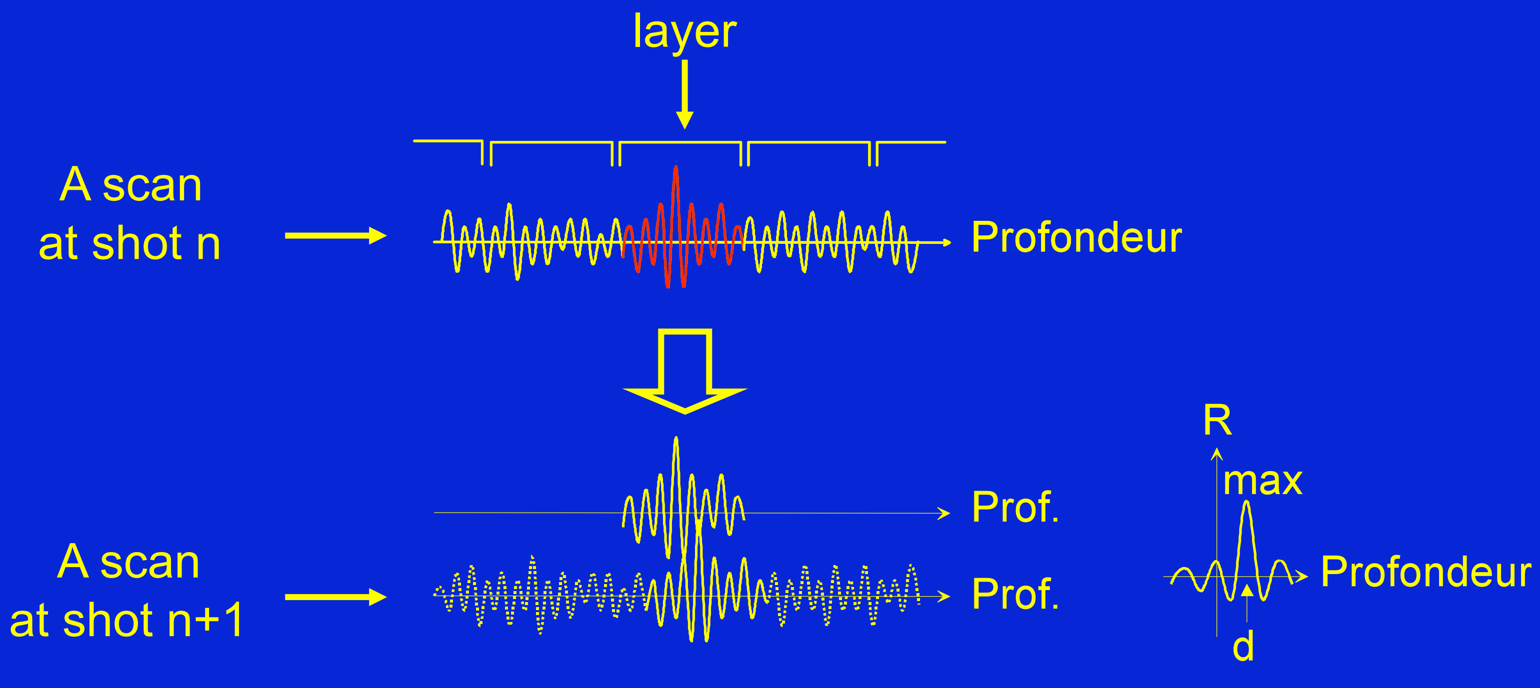


Transient Elastography in Tissue Mimicking Phantoms



Axial displacement measurement

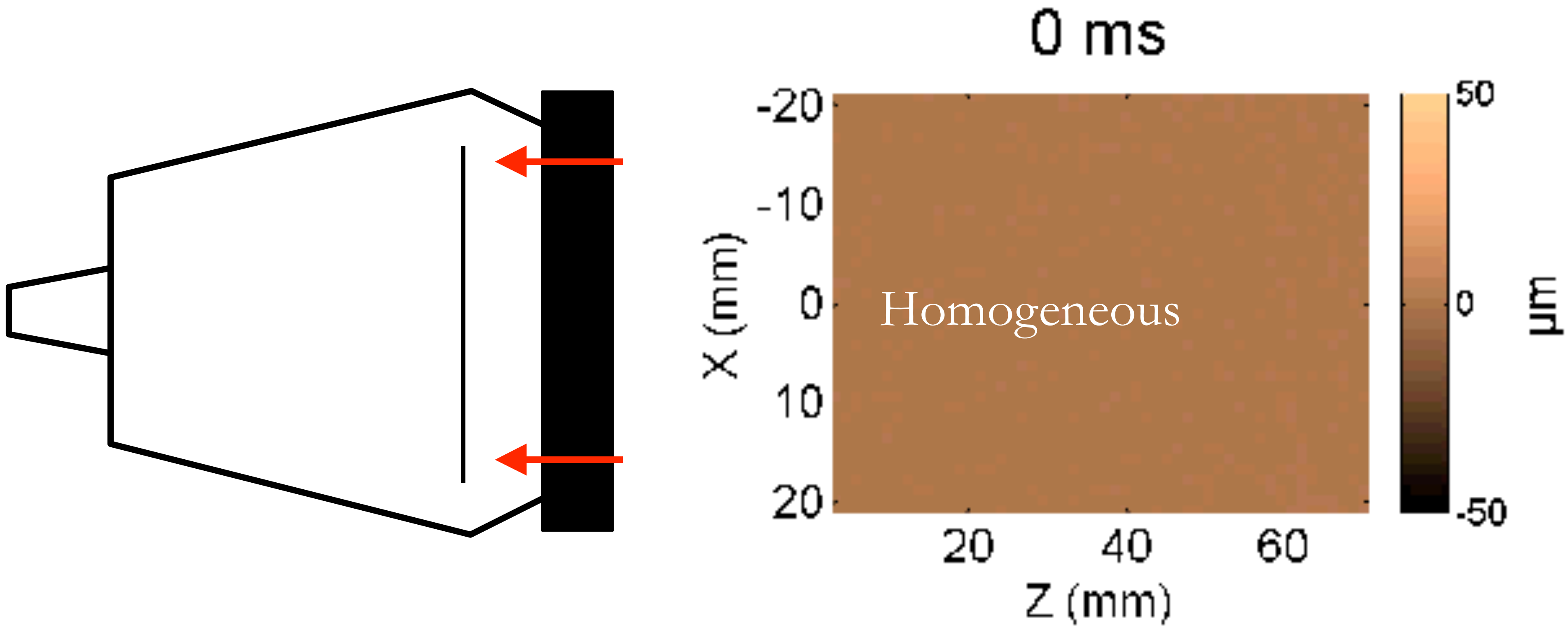
- **Cross-correlation in moving window**



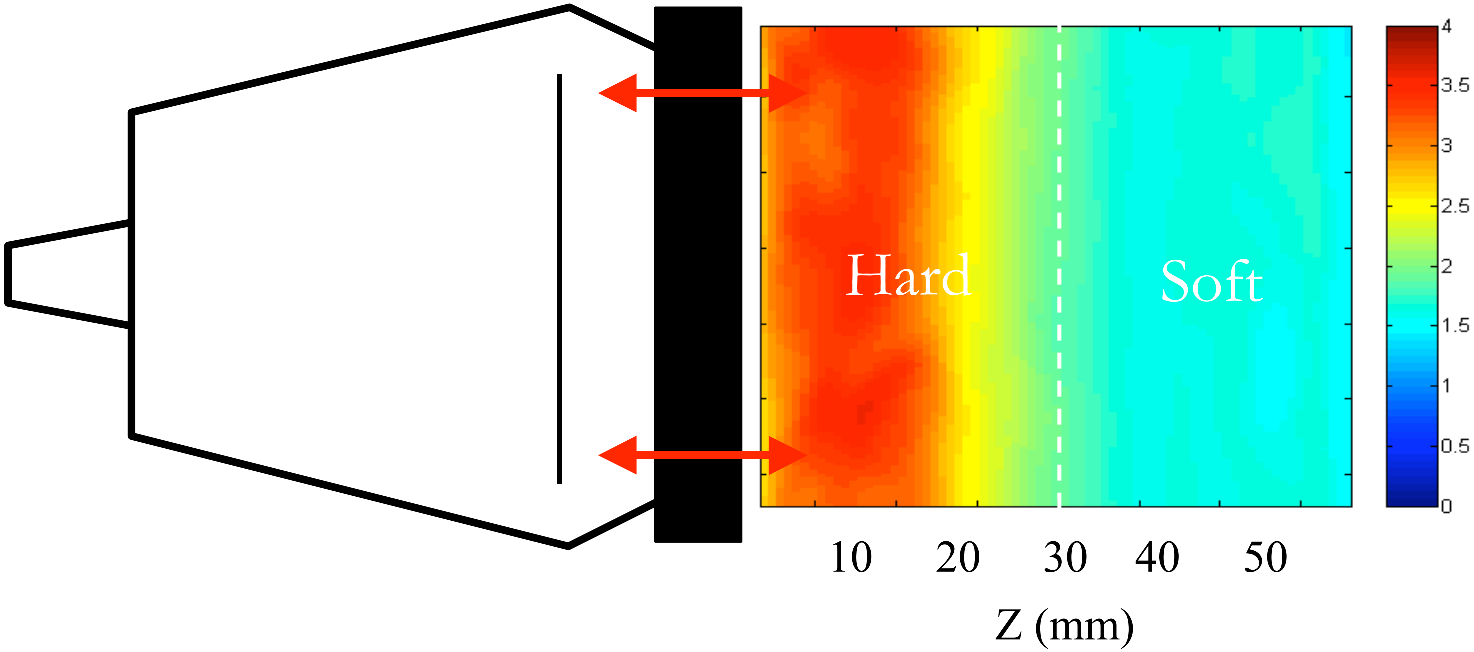
Recurence time ~ 200 µs

1 µm < d < 100 µm

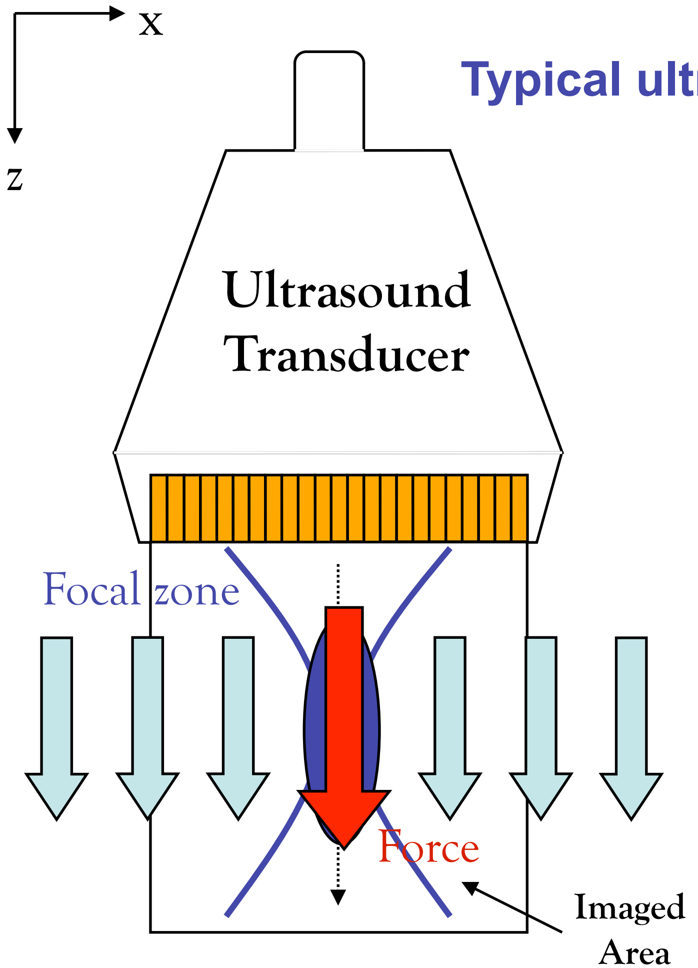
Validation in Tissue Mimicking Phantoms . I.



Validation in Tissue Mimicking Phantoms



Remote Palpation using the Ultrasonic Radiation force

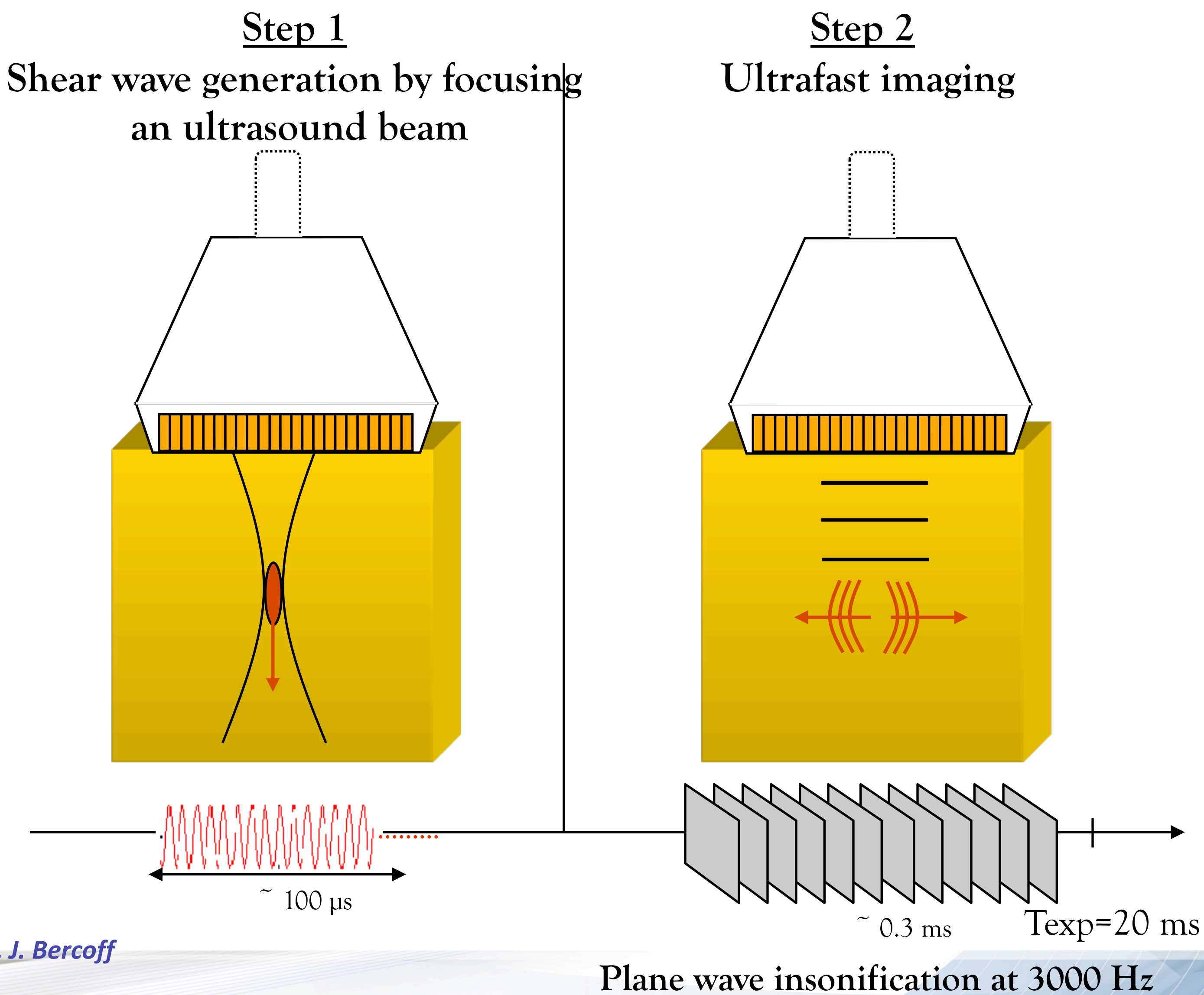


Typical ultrasonic bursts of 100 µs

$$F(\vec{r},t) = \frac{\alpha}{\rho c^2} p^2(\vec{r},t)$$

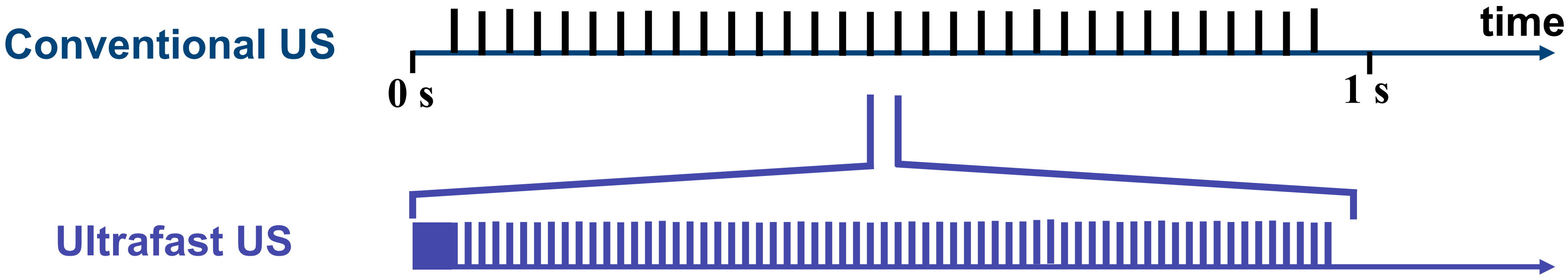
Generating low frequency (kHz range) Shear waves
Using high frequency (MHz range) Ultrasound

Ultrafast Imaging and Acoustic Radiation Force

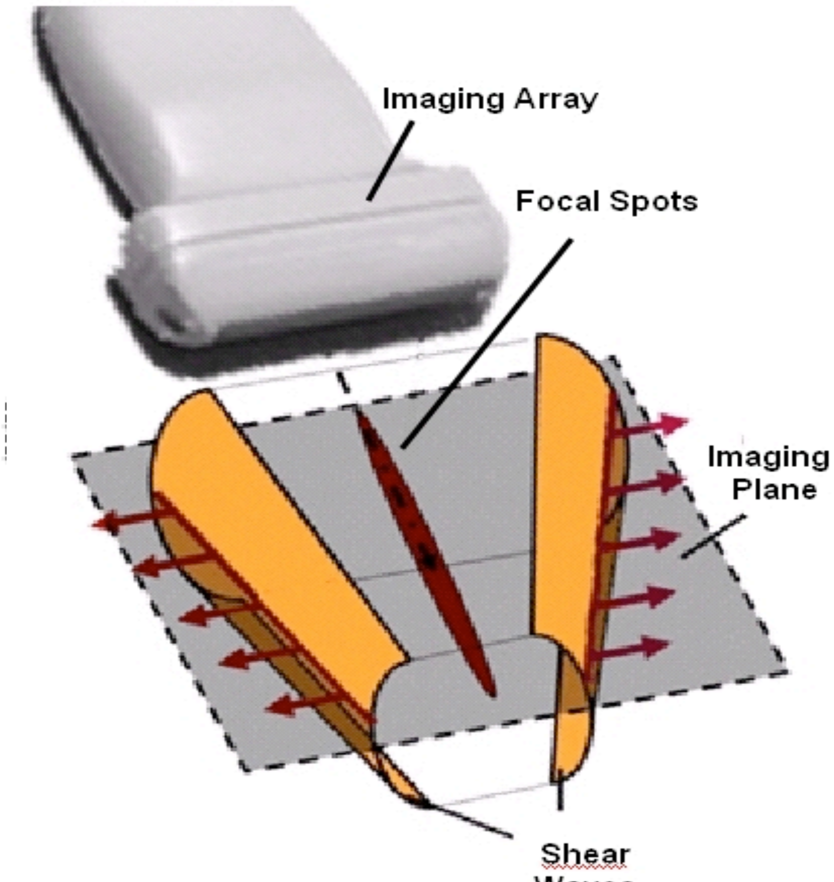


M. Fink, M Tanter, J. Bercoff

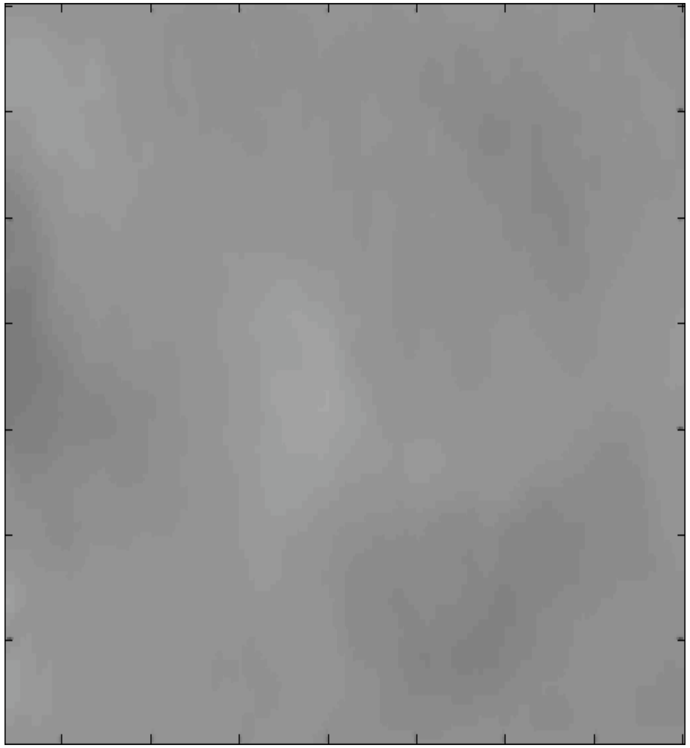
Ultrafast Imaging of the Remote Palpation

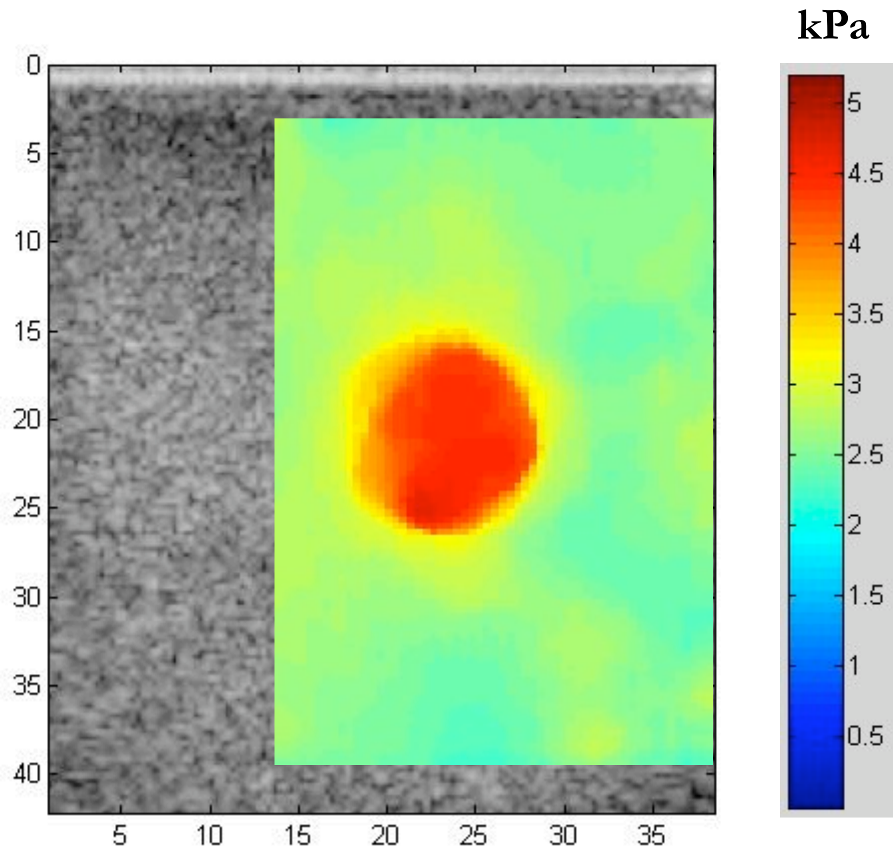


A 30 ms Experiment !!



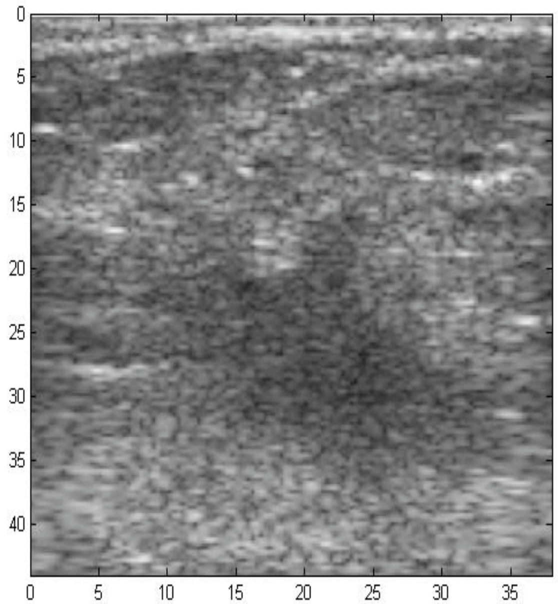
Mapping Visco-Elasticity : Inverse problem of Shear Wave Propagation

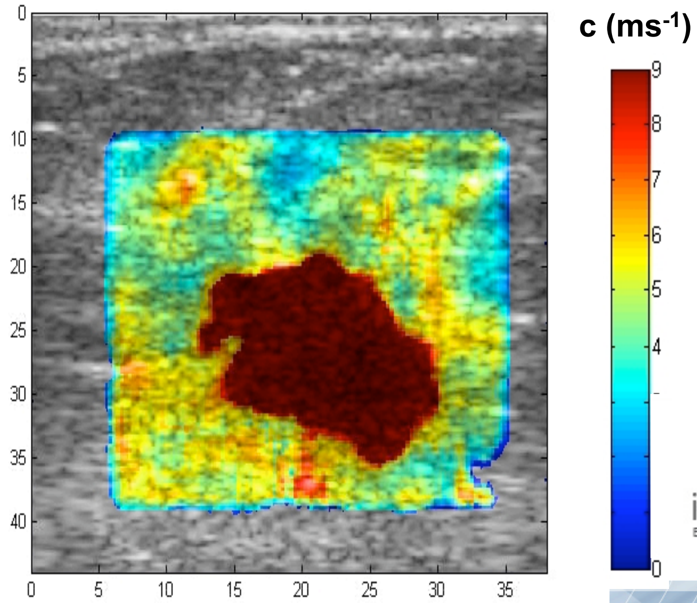




- **Freehand / does not change anything to the echographic exam**
- **Quantitative**
- **Operator independent = reproducible**
- **Ultrafast / Insensitive to motion artefacts and boundary conditions.**

Clinical Evaluation at Institute Curie : Stiff Palpable Carcinoma

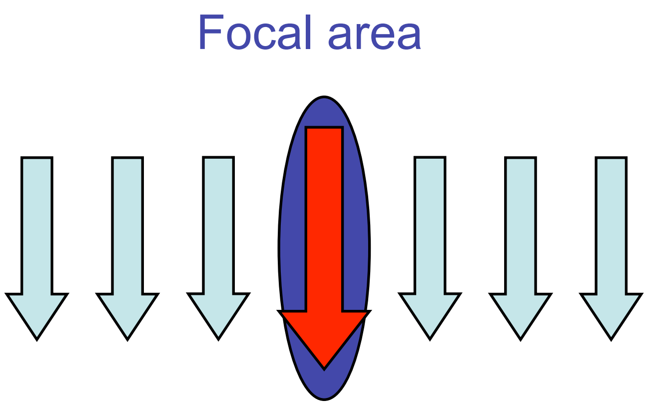




Collaboration Dpt Radiologie, Institut Curie, Dr. A. Tardivon

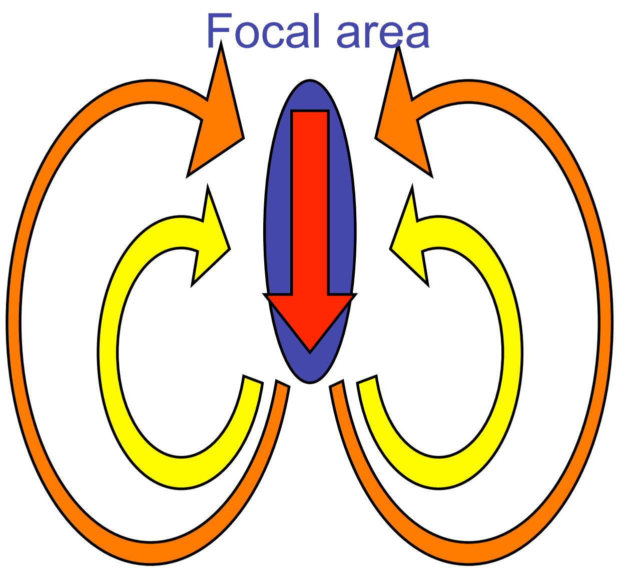
Ultrasonic Radiation force for liquid/solid differentiation

Soft solids



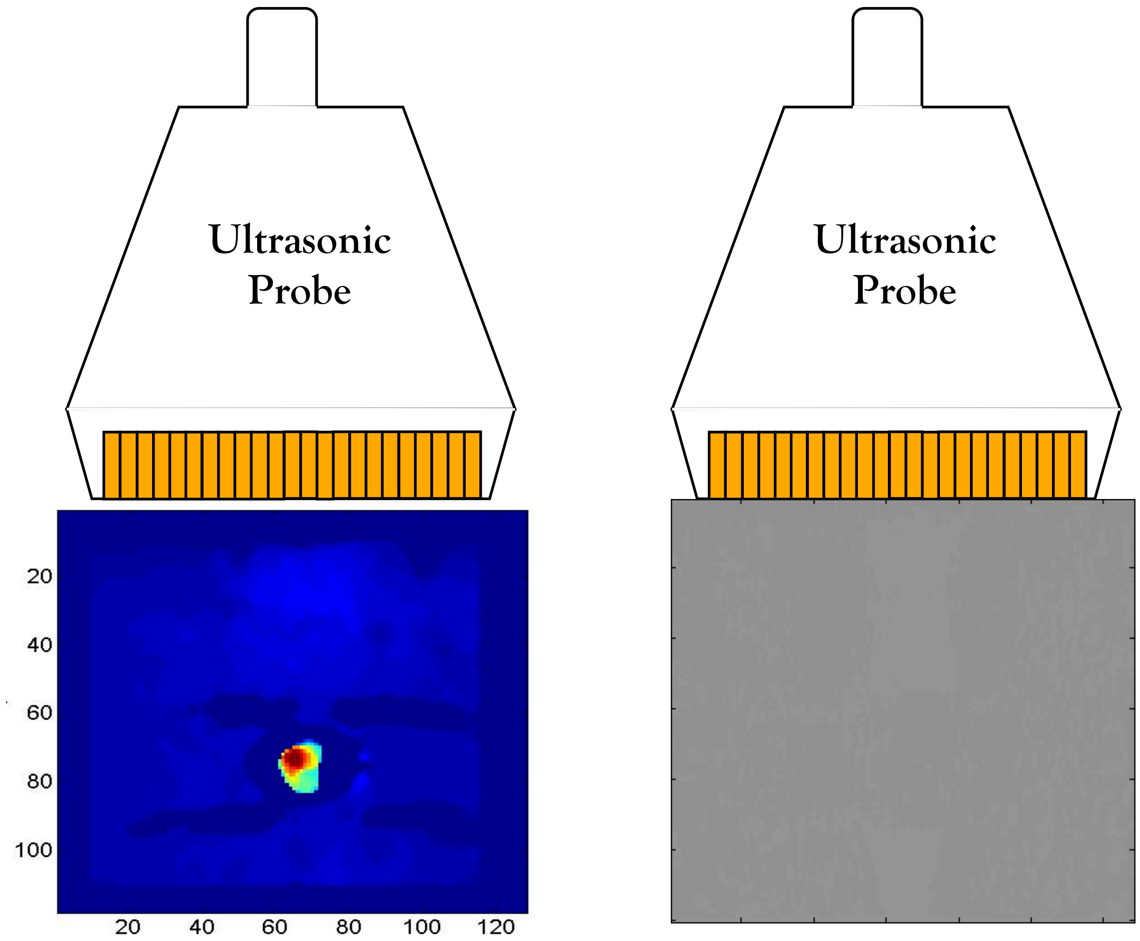
➔ **Shear wave propagation**

fluids



➔ **local flow**

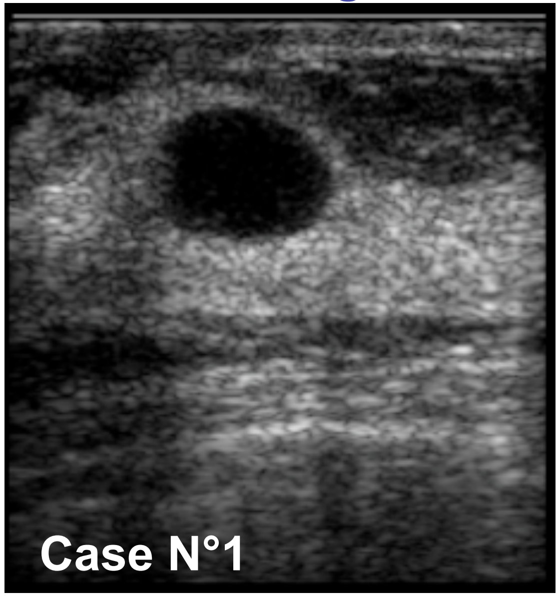
Ultrasonic Radiation force for liquid/solid differentiation

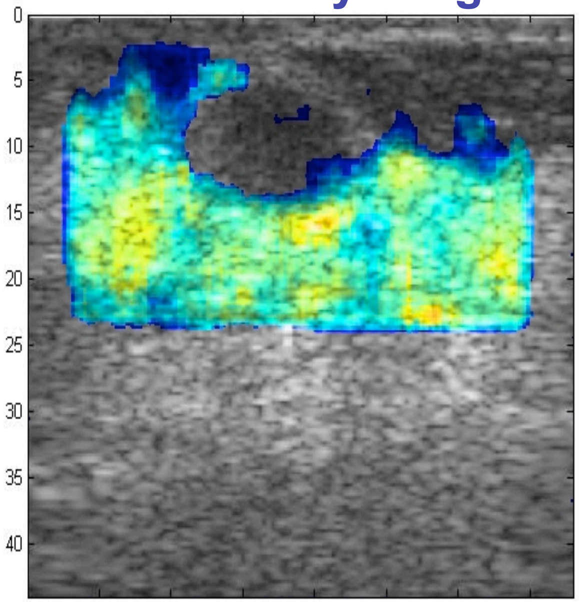


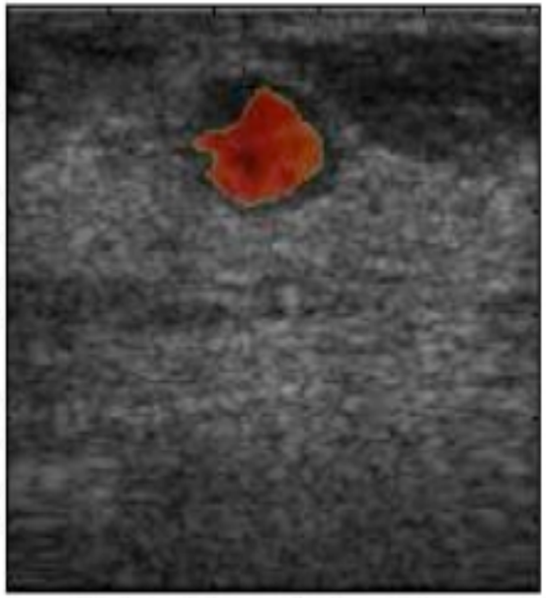
Can be done during the elasticity imaging mode

Clinical Evaluation at Institute Curie : Benign Non Viscous Cyst

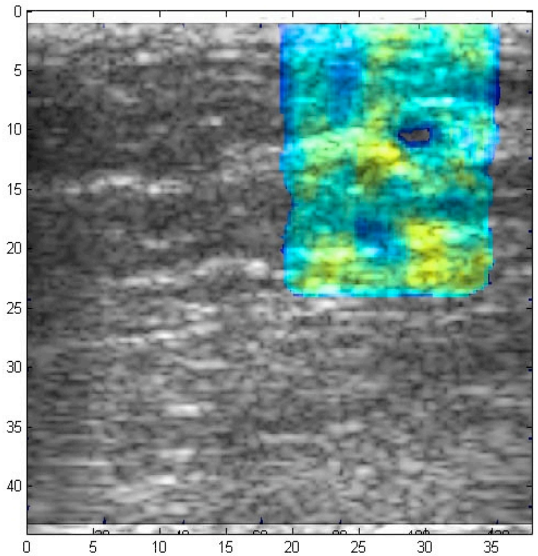
US Image | **Elasticity Image** | **Flow Detection**

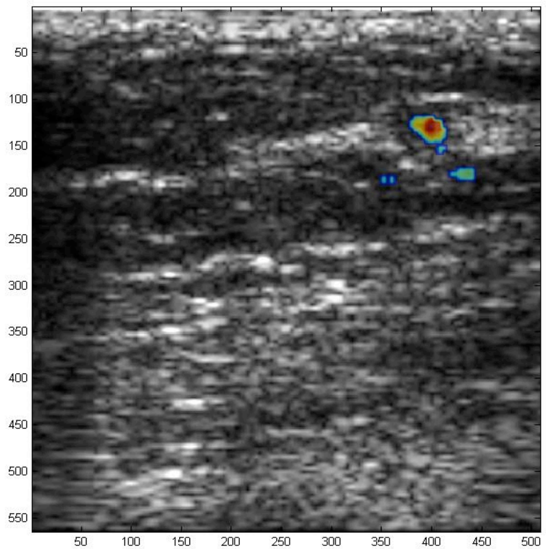




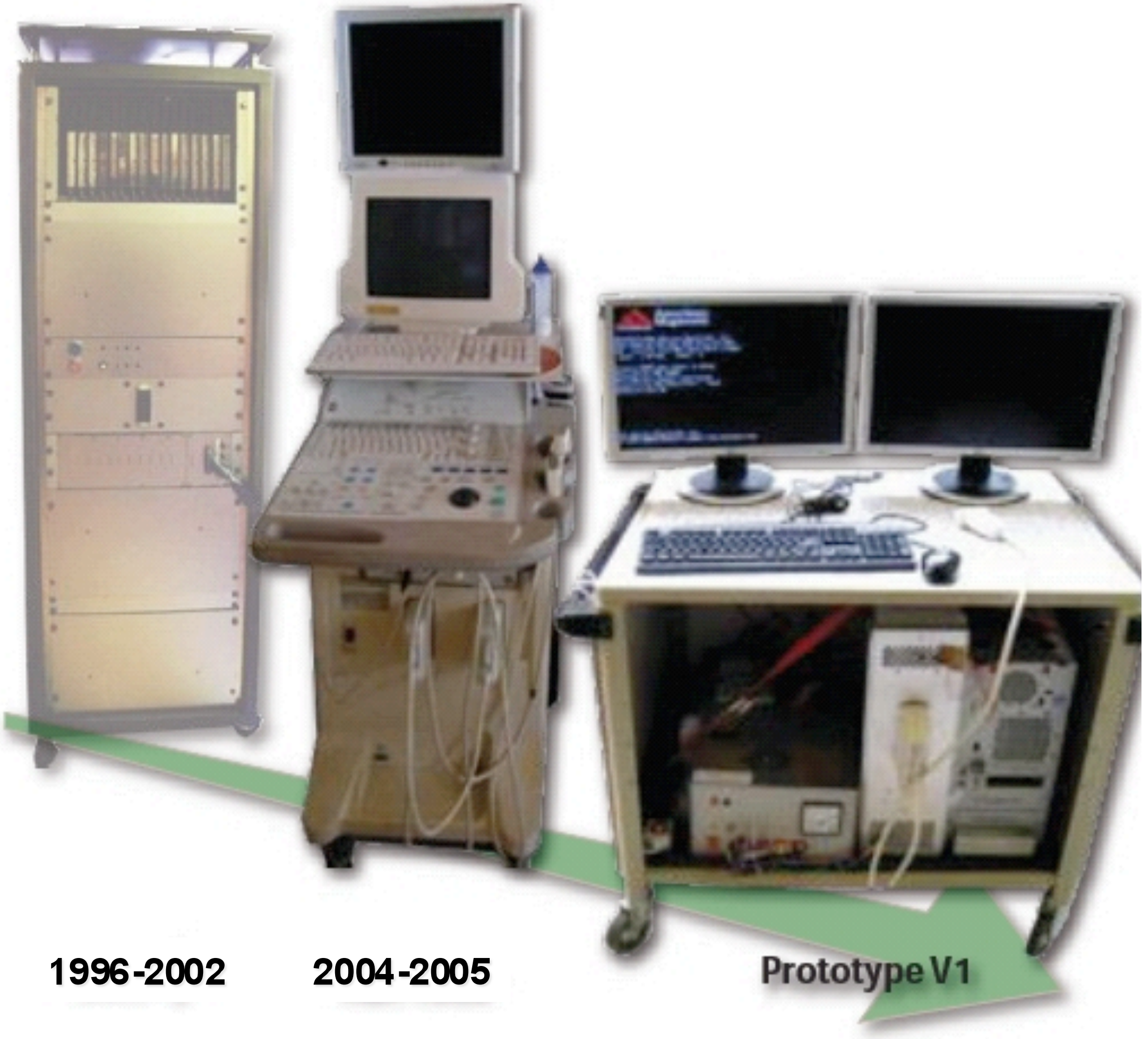


Case N°2





Leveraging this research elastography imaging modality into a product



SUPERSONIC imagine

Aixplorer ©,2008

(CE and FDA Approved)

A Theragnostic Company

SuperSonic Imagine is a Startup company in medical imaging and therapy founded end 2005

105 employees today

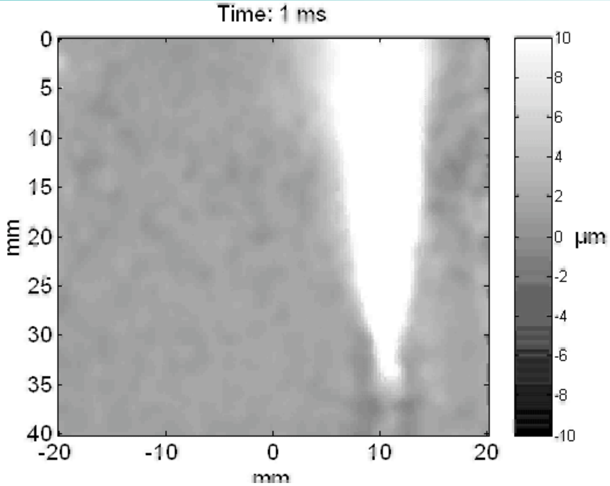
10 M€ first round (end 2005)

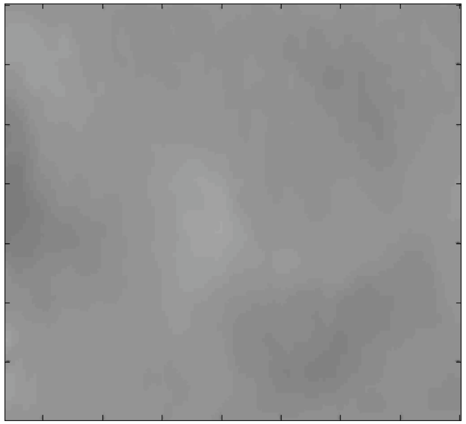
26 M€ second round (October 2008)

Biggest Venture funding in Europe in 2008

Aix en Provence & Paris

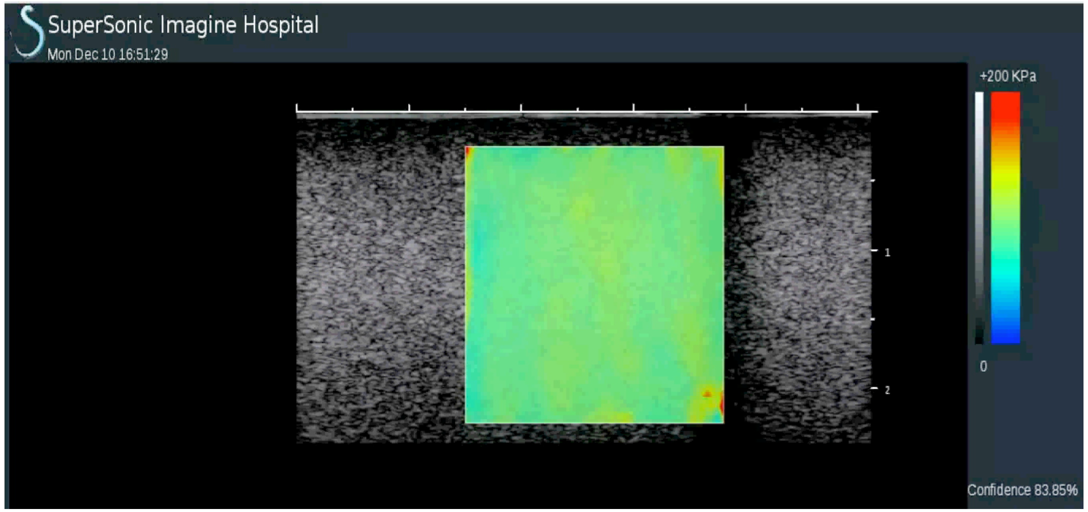
Echographic System with Real-time and Quantitative elastography





First SSI experiments : 2000-2002
45 Minutes processing

SSI Prototype 2006
some seconds processing

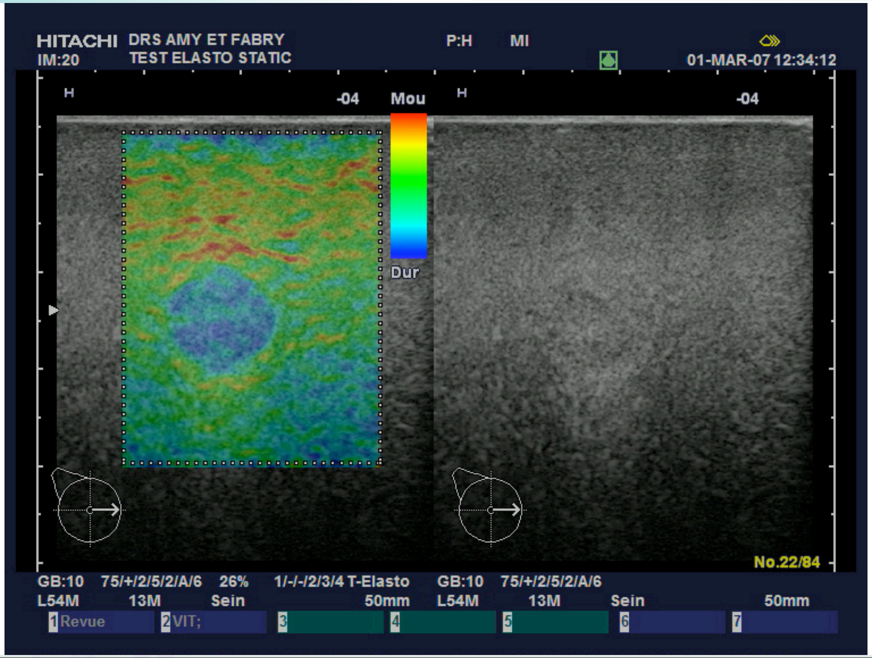


October 2007
0.2 seconds processing

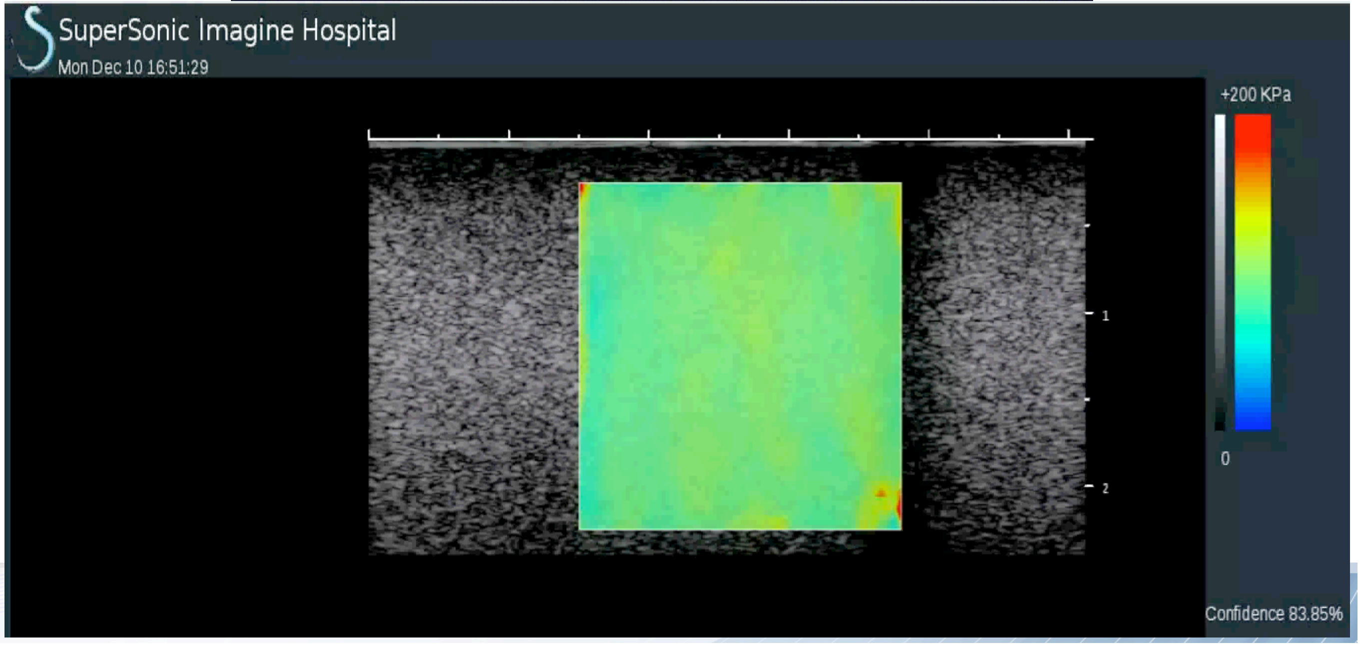
Moore's Law fastened by Video Game Industry

Comparison SSI / Static Elastography in phantoms

Static Elastography



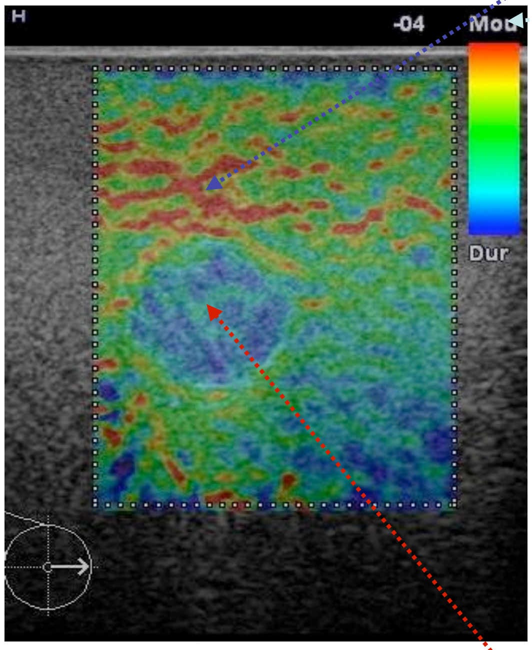
Supersonic Shear Imaging

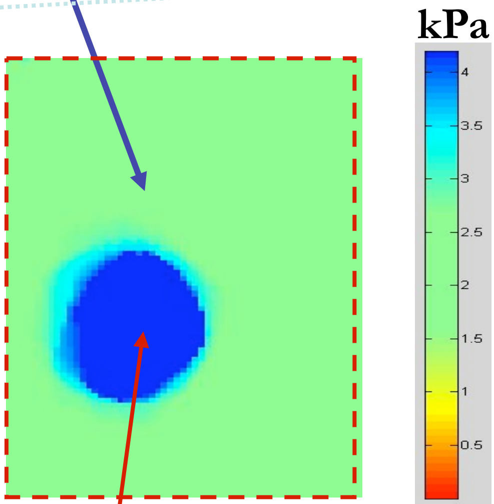


Comparison entre le mode Multi-wave (Supersonic Shear Wave) et l'élastographie statique

Pas d'artefacts

Estimation quantitaive de l'élasticité

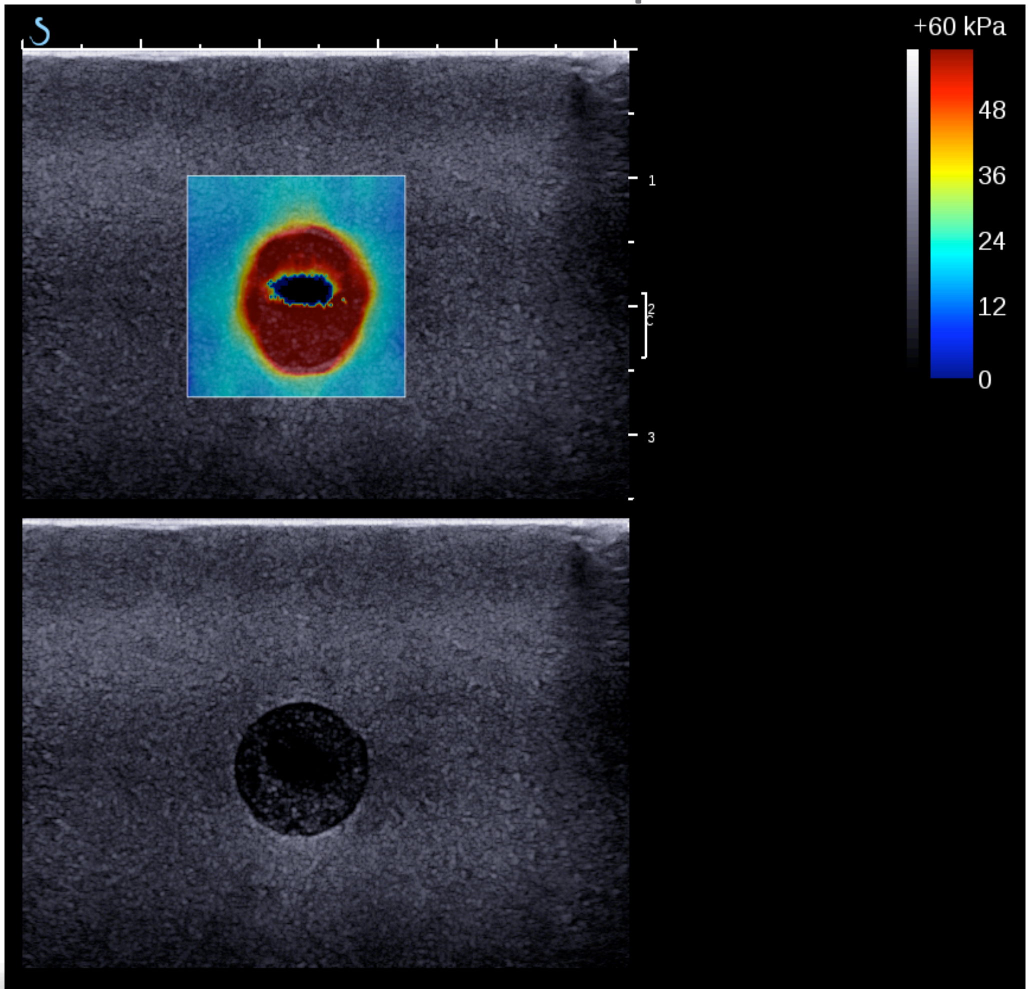


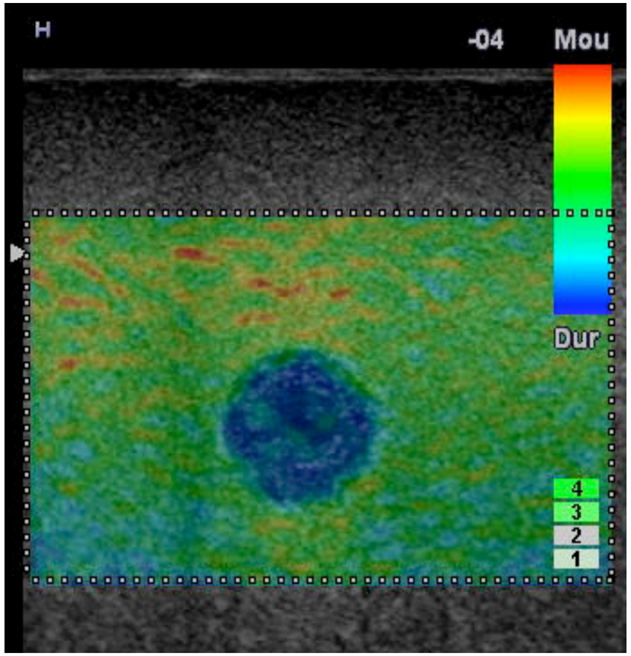


Beaucoup moins de variance dans l'inclusion et en dehors

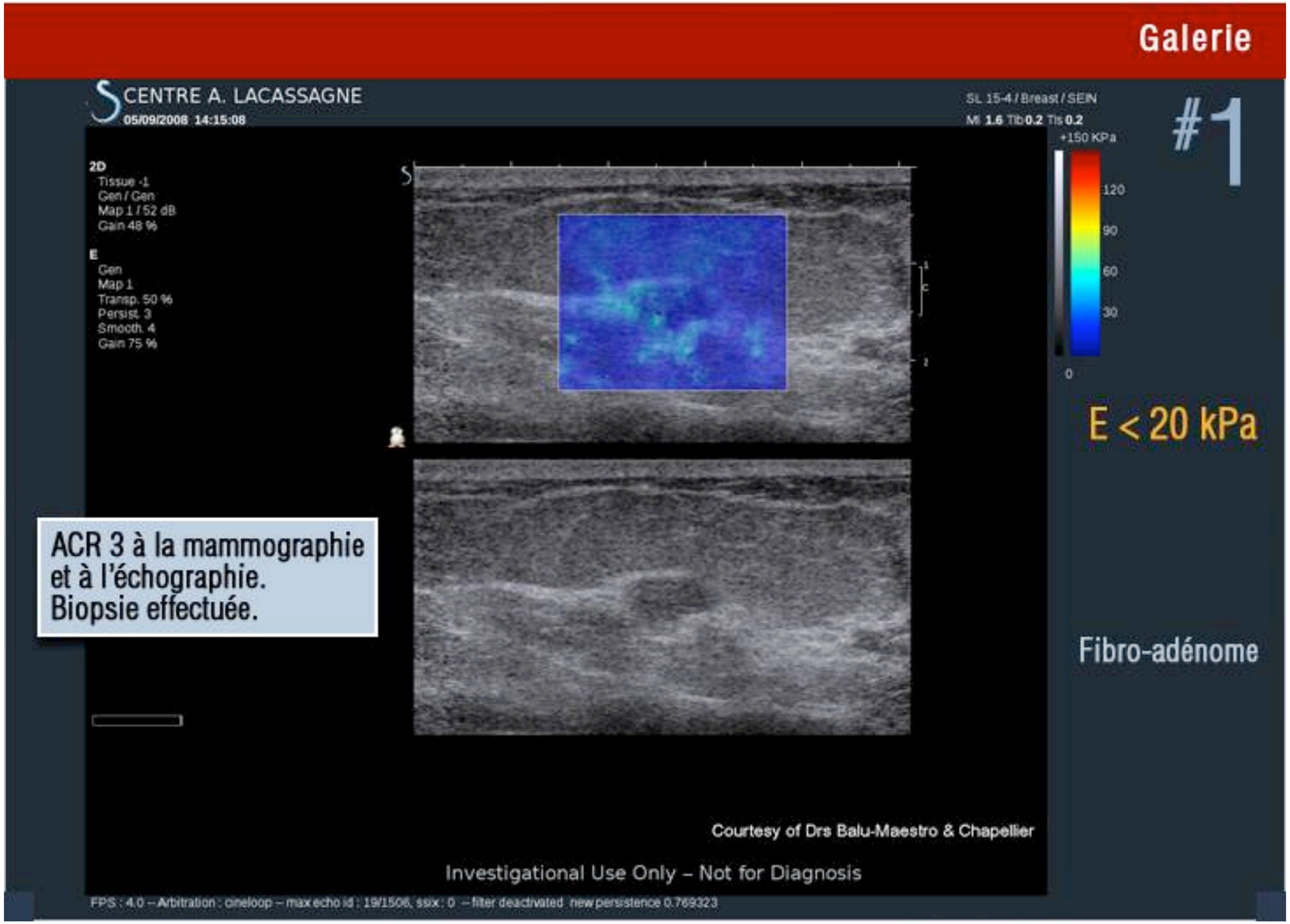
Comparison entre le mode Multi-wave (Supersonic Shear Wave) et l’élastographie statique

True assessment of tissue stiffness
Hard lesion with a liquid center

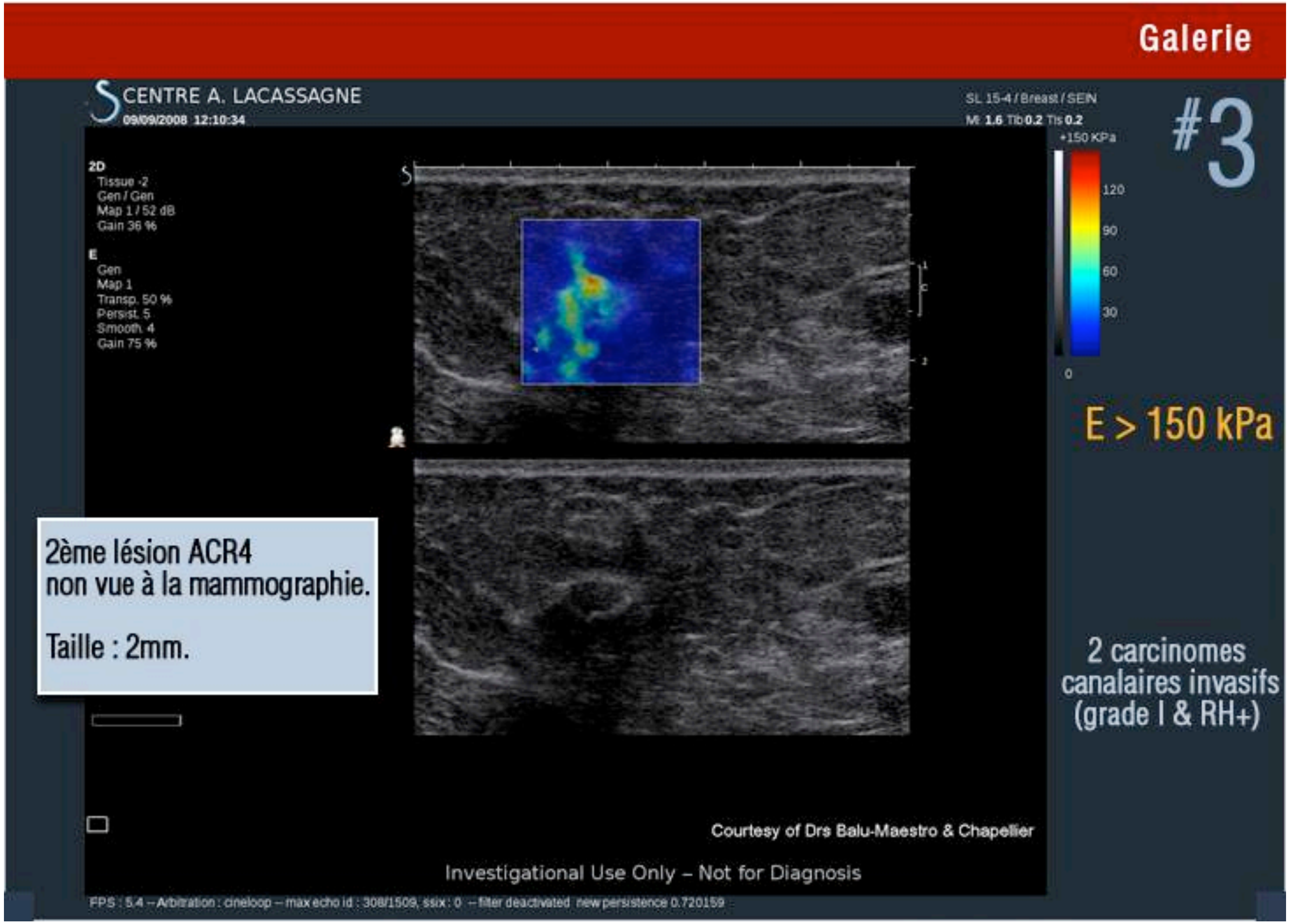




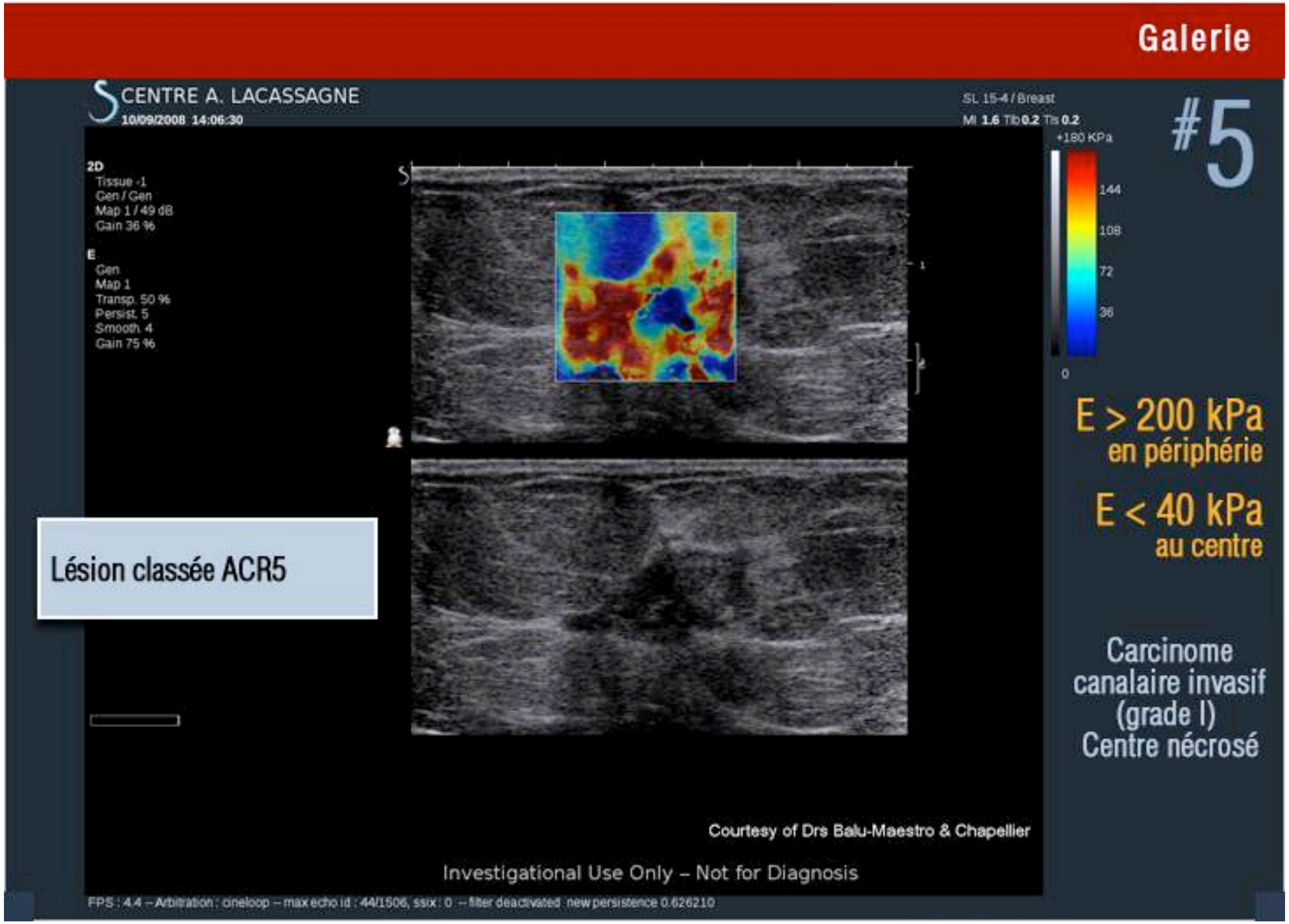
Breast Cancer Examples



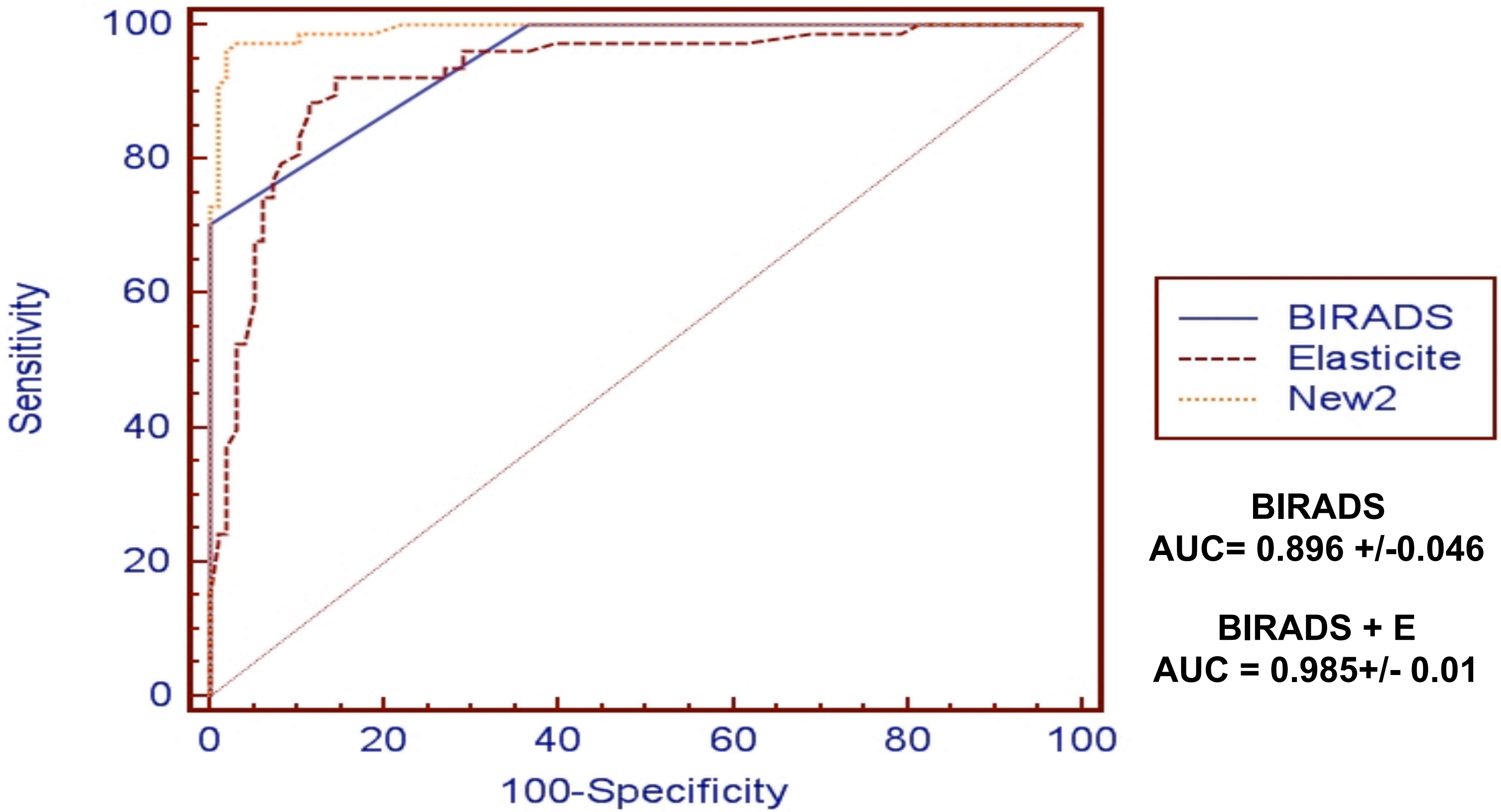
Breast Cancer Examples



Breast Cancer Examples



Specificity/Sensitivity Analysis on 175 patients



BIRADS
AUC= 0.896 +/-0.046

BIRADS + E
AUC = 0.985+/- 0.01

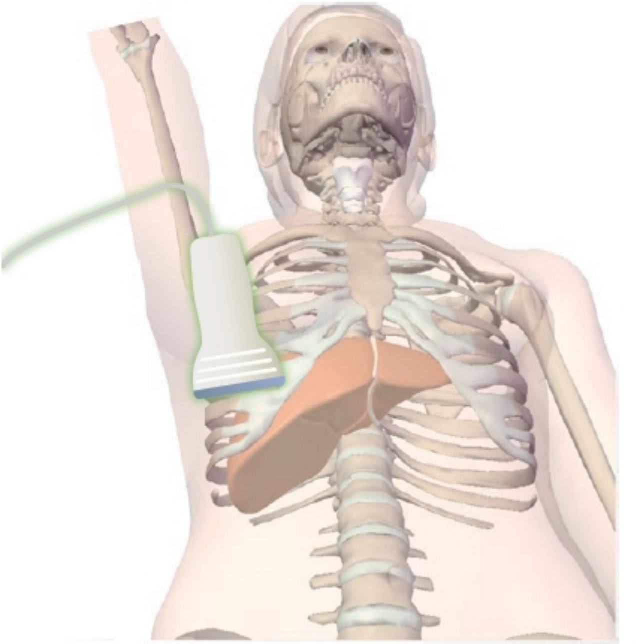
Elasticity imaging :
A strong added value to conventional Ultrasonography

~ 93 % spec. (at 95 % sens.)

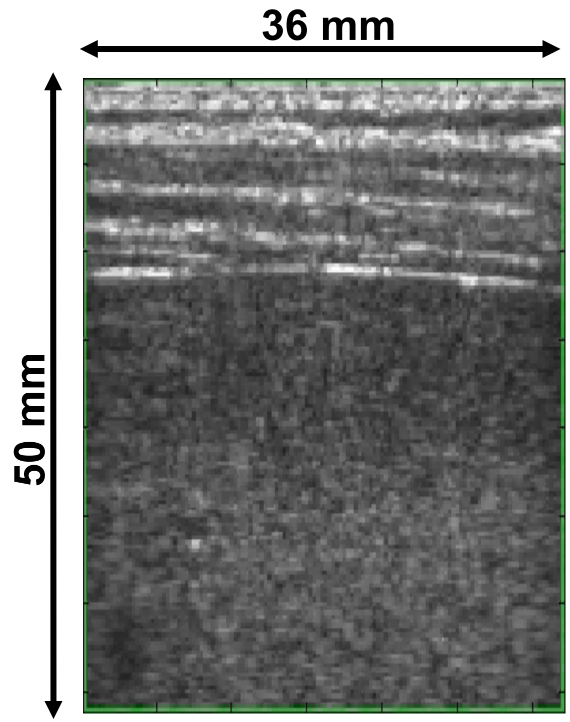
A step beyond Shear Wave Imaging

Shear Wave Spectroscopy

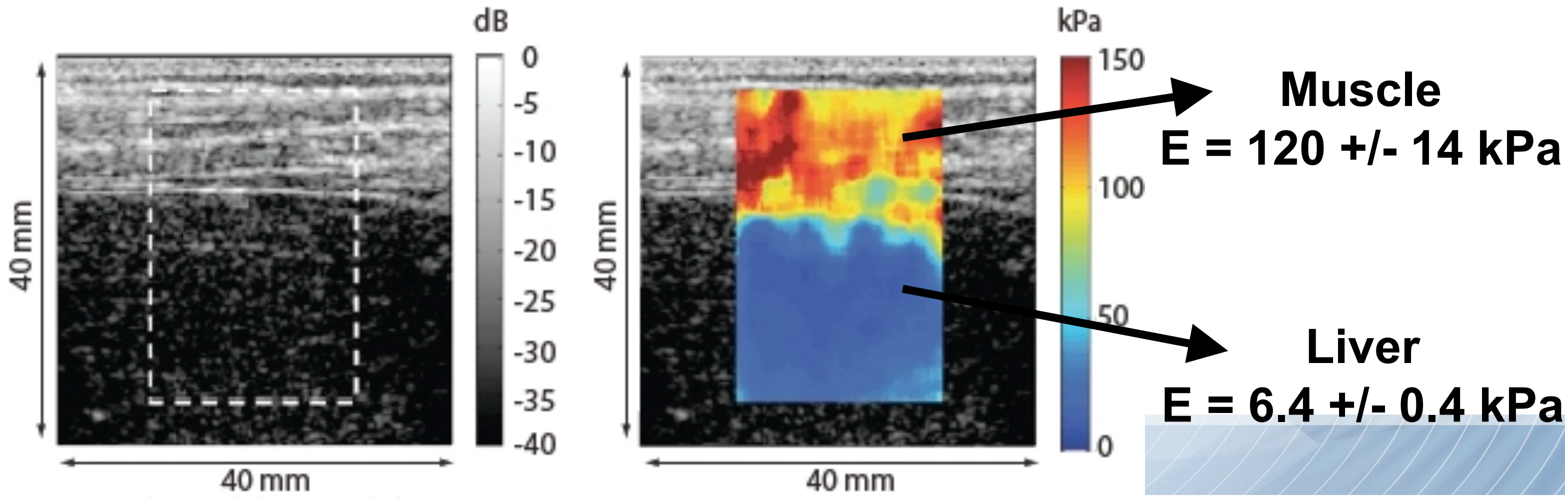
In vivo Quantitative imaging of liver elasticity for Fibrosis Staging



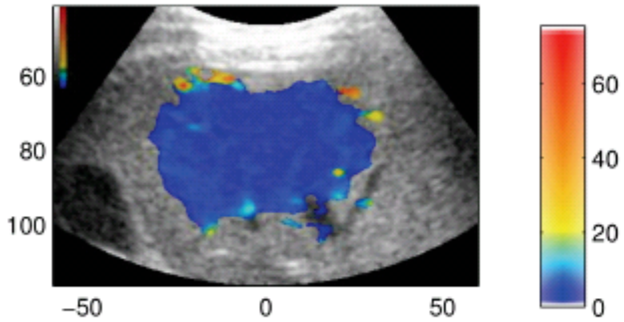
26 Years old healthy volunteer



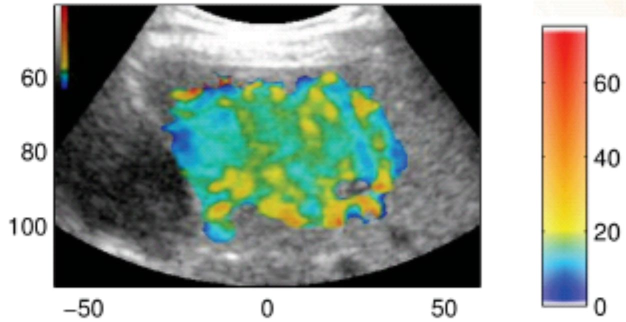
2000 frames per second



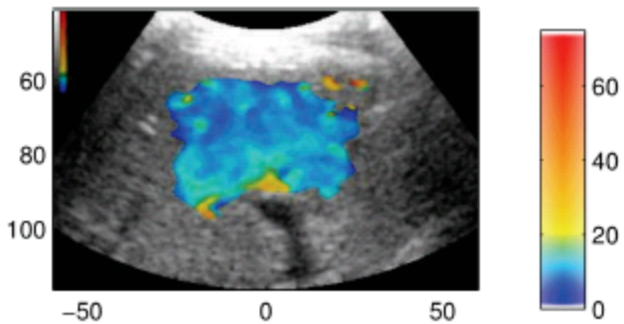
Estimation of Liver Fibrosis Degree in Hepatitis C patients



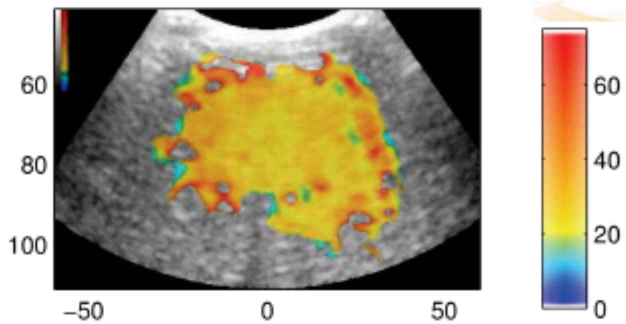
Patient F1
$E_{carte} = 4.88$ kPa
Surface 16.32 cm^2



Patient F3
$E_{carte} = 15.76$ kPa
Surface 15.54 cm^2



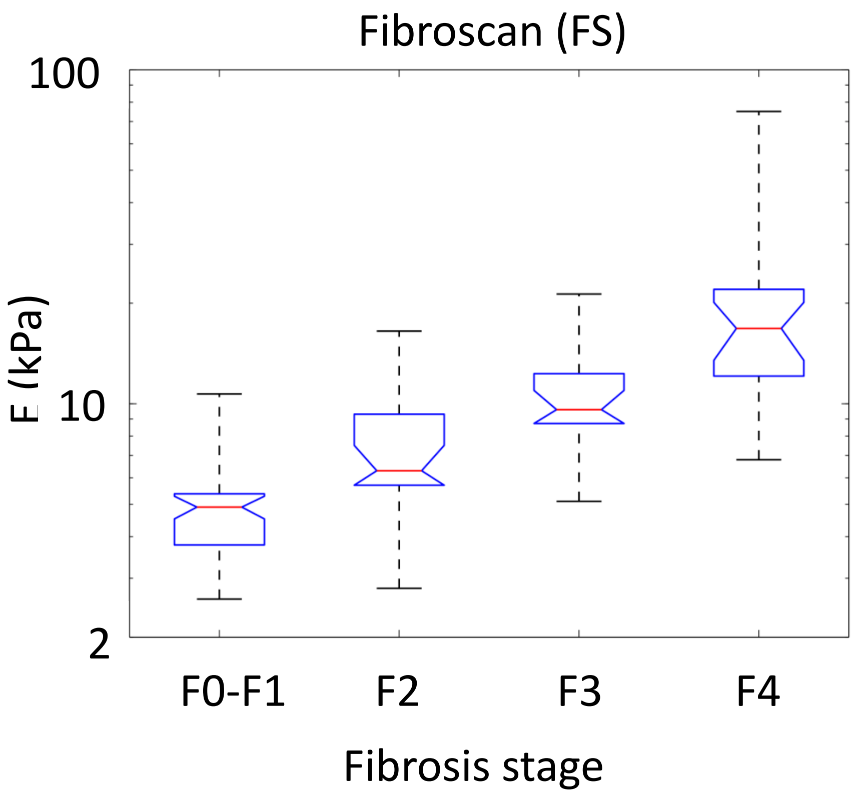
Patient F2
$E_{carte} = 10.95$ kPa
Surface 13.51 cm^2



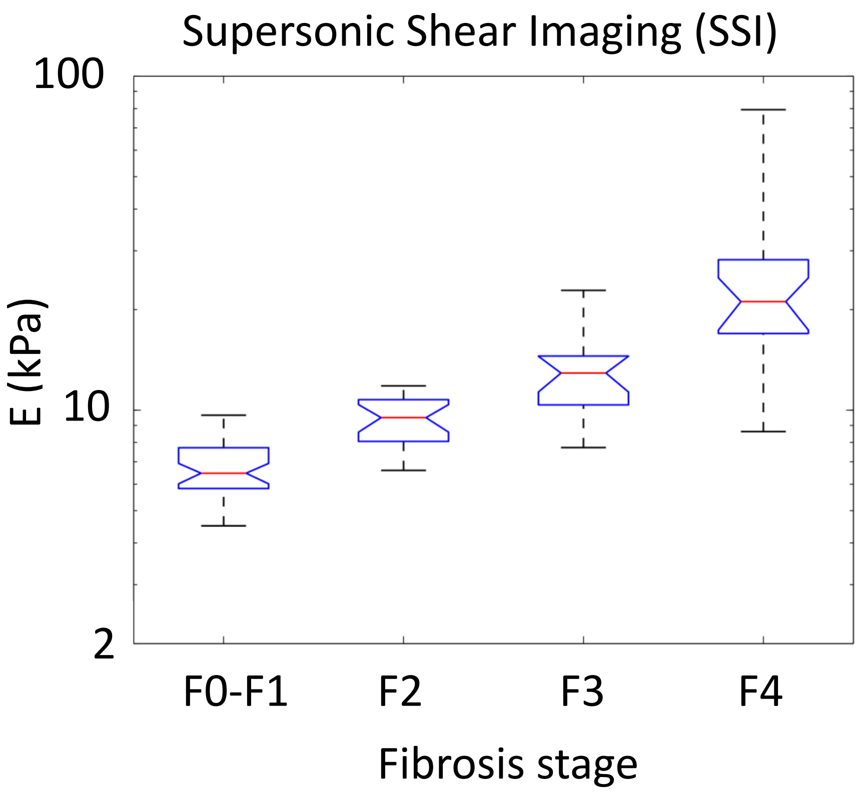
Patient F4
$E_{carte} = 31.23$ kPa
Surface 16.75 cm^2

STATISTICAL ANALYSIS

- 104 patients included in statistical analysis
- Liver staging obtained using surrogate serum markers
- 41% F0F1, 21% F2, 17% F3, 21% F4

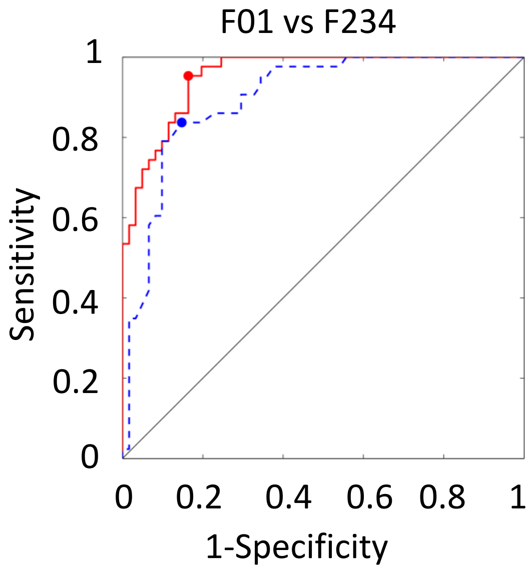


P-index: ~10^{-12}

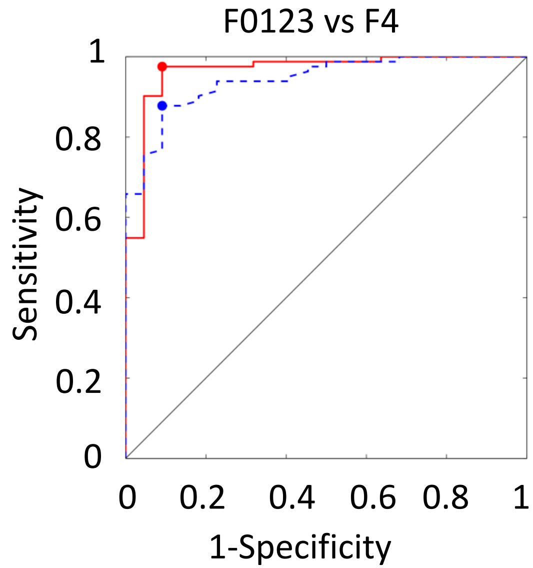


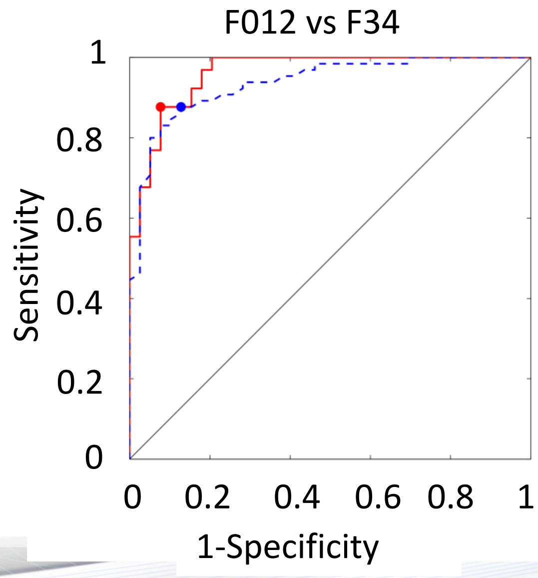
P-index: ~10^{-16}

SENSIBILITY – SPECIFICITY



AUROC
Fibroscan 0.89
*Castera FS 0.83
SSI 0.95





AUROC
Fibroscan 0.93
*Castera FS 0.90
SSI 0.96

AUROC
Fibroscan 0.95
*Castera FS 0.94
SSI 0.97

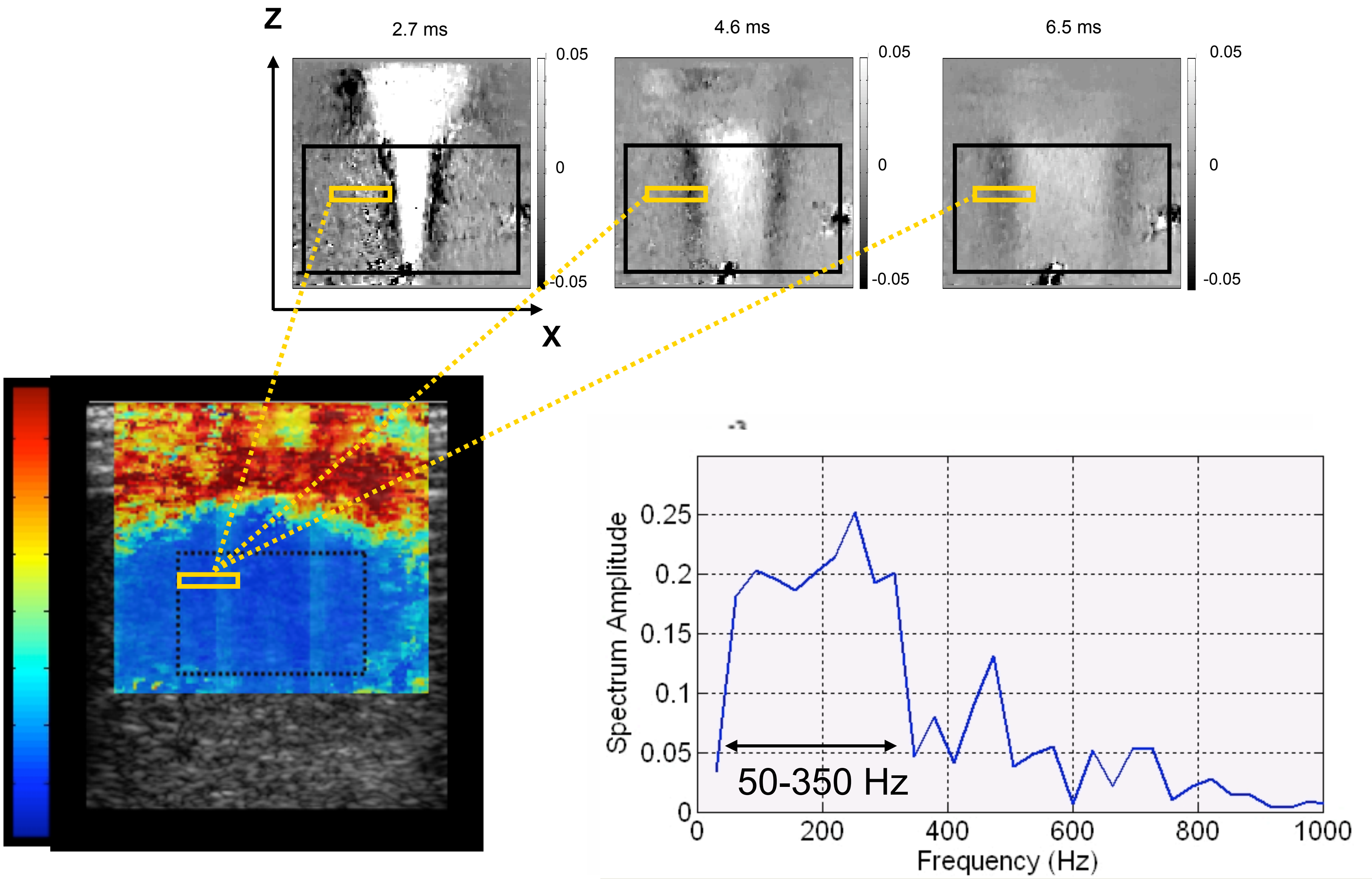
New cutoff (kPa) defined:

FS ⇨ F≥2 5.80; F≥3 8.70; F=4 10.30

SSI ⇨ F≥2 8.94; F≥3 10.98; F=4 16.81

*Castera *et al.*, Gastroenterology, 2005

Can we assess viscoelastic properties of liver using SSI ? I.

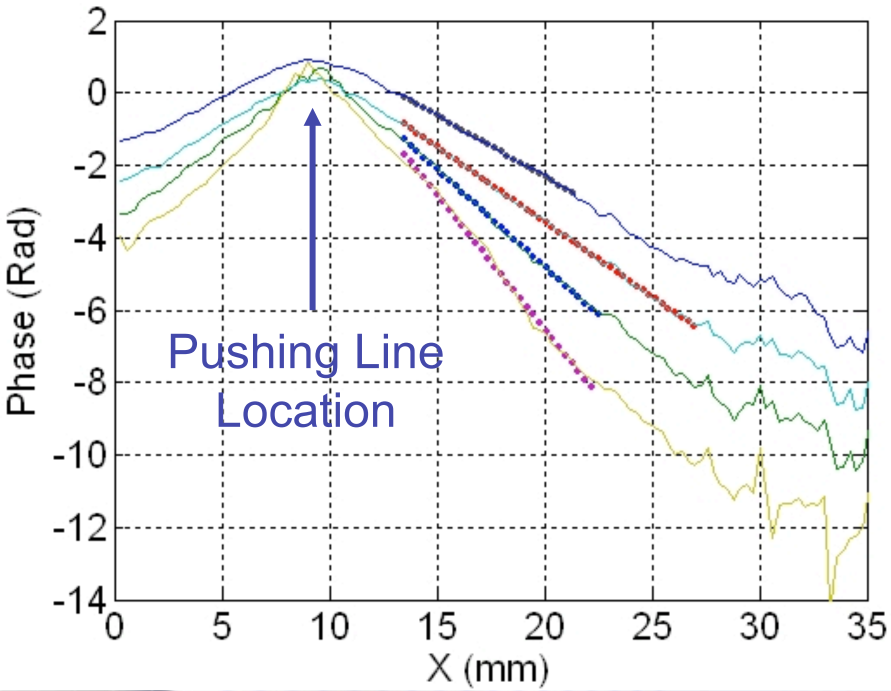


Can we assess viscoelastic properties of liver using SSI ? II.

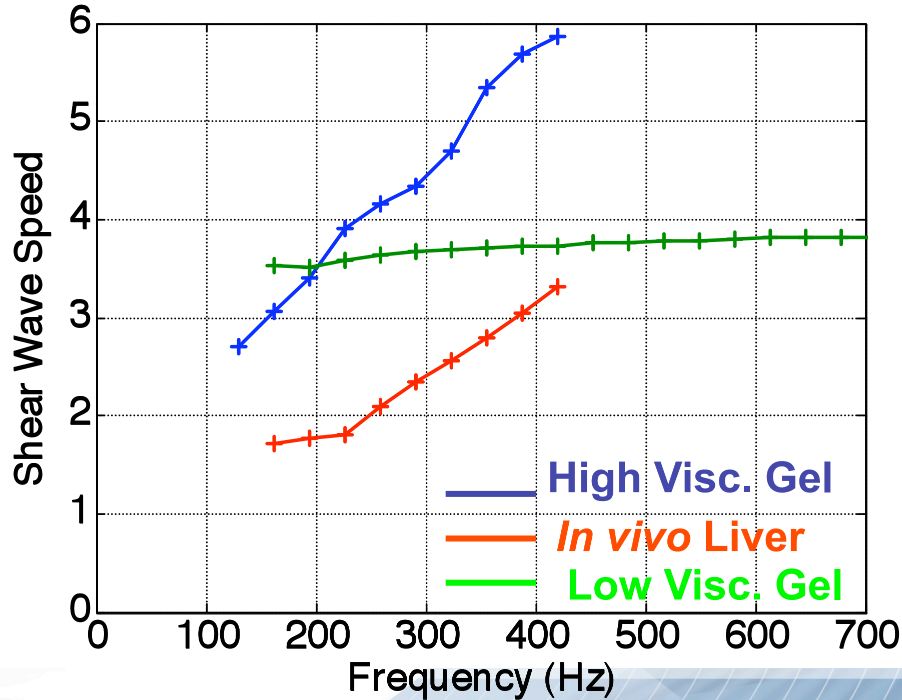
SuperSonic Wave Generation → Plane Wave Approximation is valid !!!

$$e^{j(kr-\omega t)} \approx e^{j(kx-\omega t)} \approx e^{-L_a x} . e^{-j\phi(x)}$$

$$\phi(x) = \frac{2\pi f}{c_s} x$$

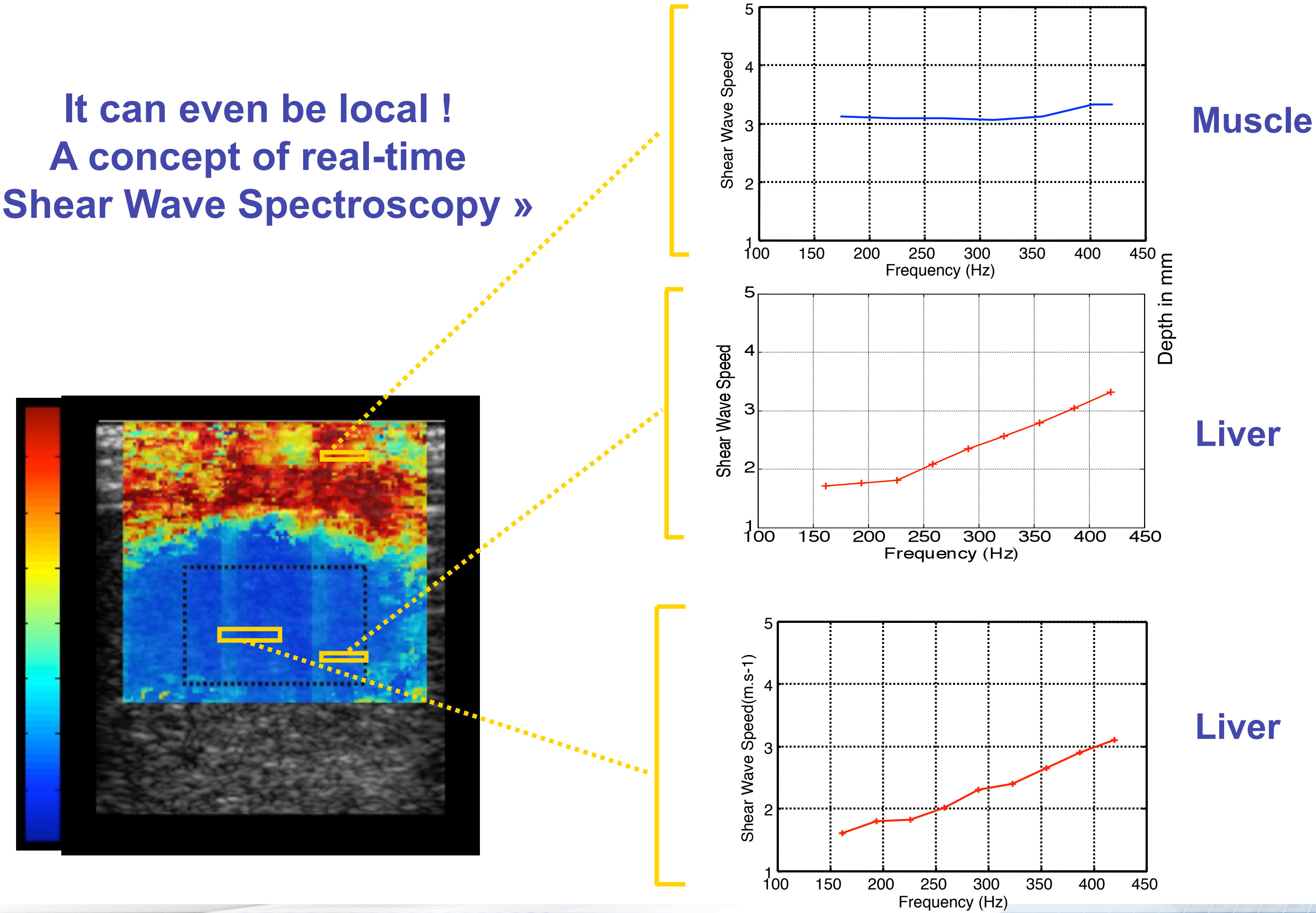


Shear Wave Phase Speed ($m.s^{-1}$)
Versus Frequency

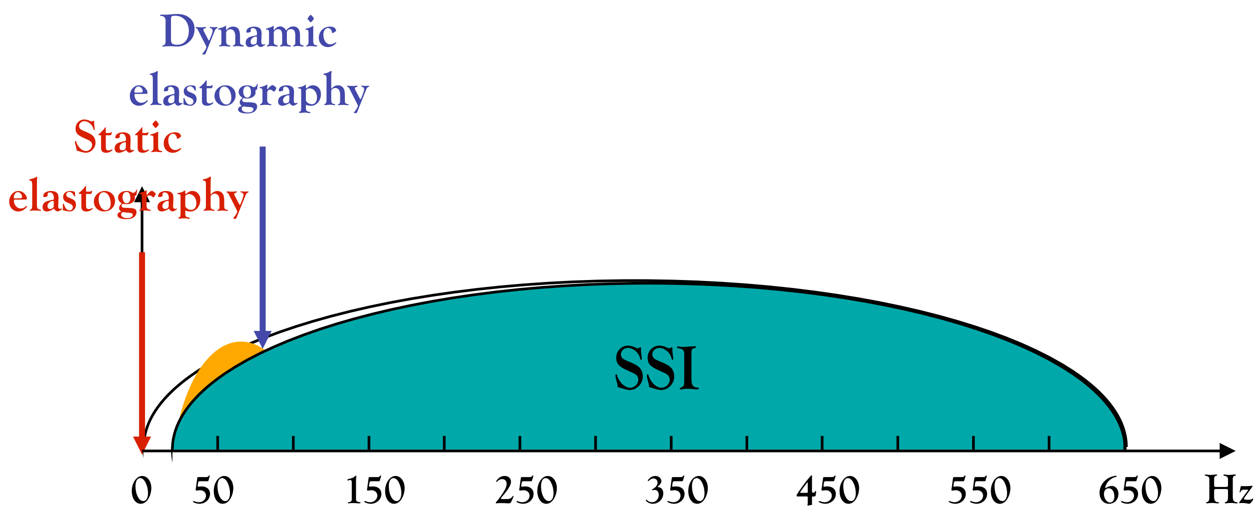


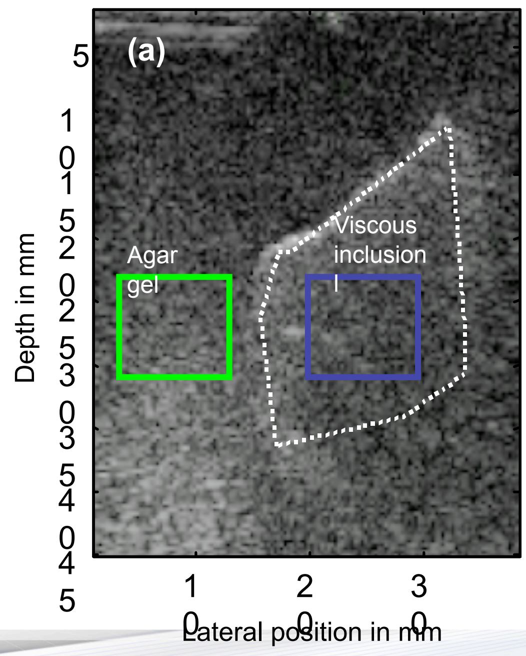
Can we assess viscoelastic properties of liver using SSI ? III.

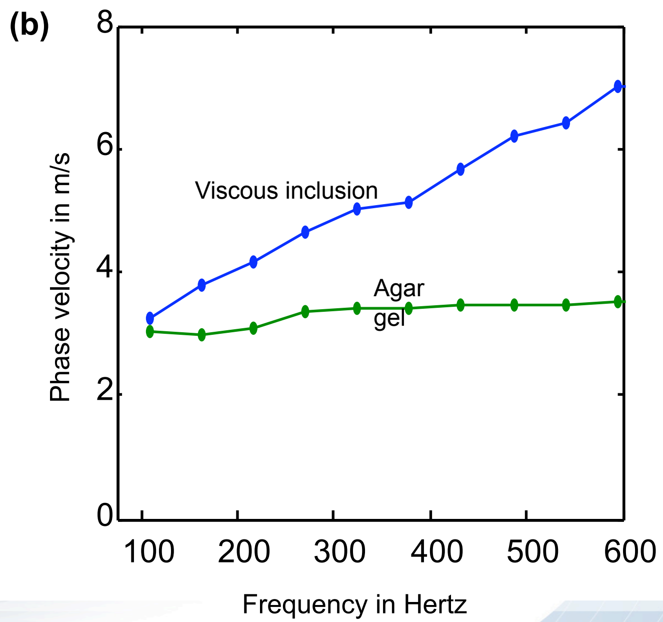
It can even be local !
A concept of real-time
«Shear Wave Spectroscopy »



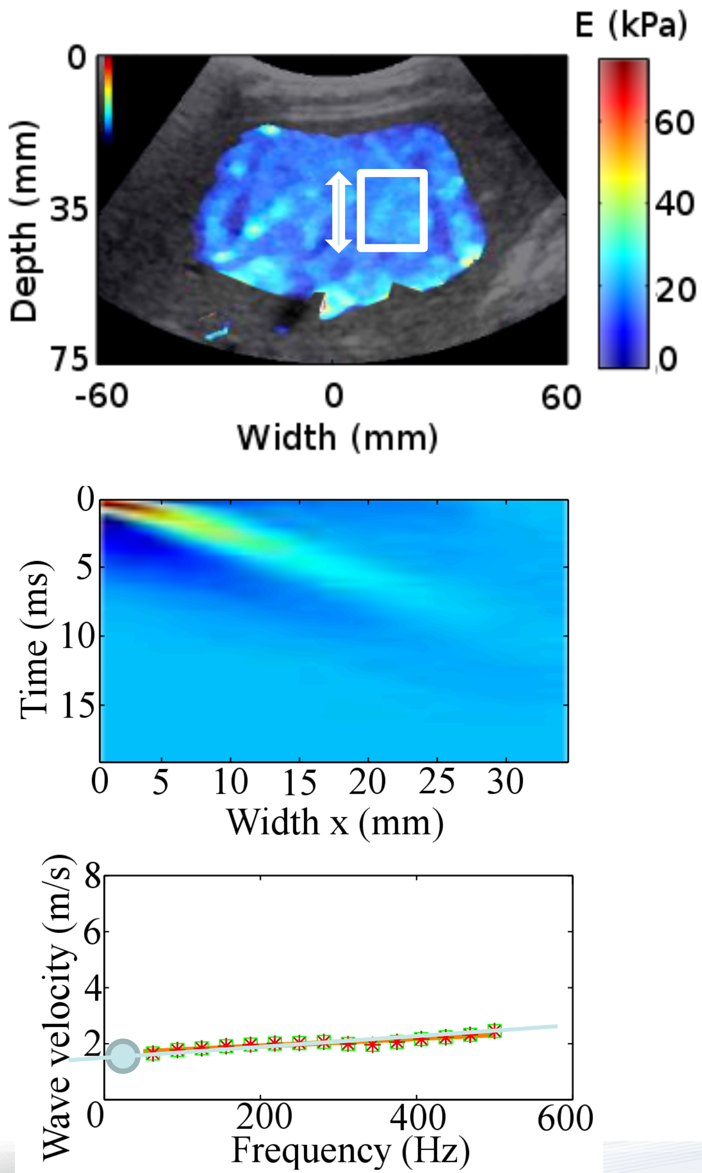
Shear Wave Spectroscopy : a Broadband approach for Elasticity



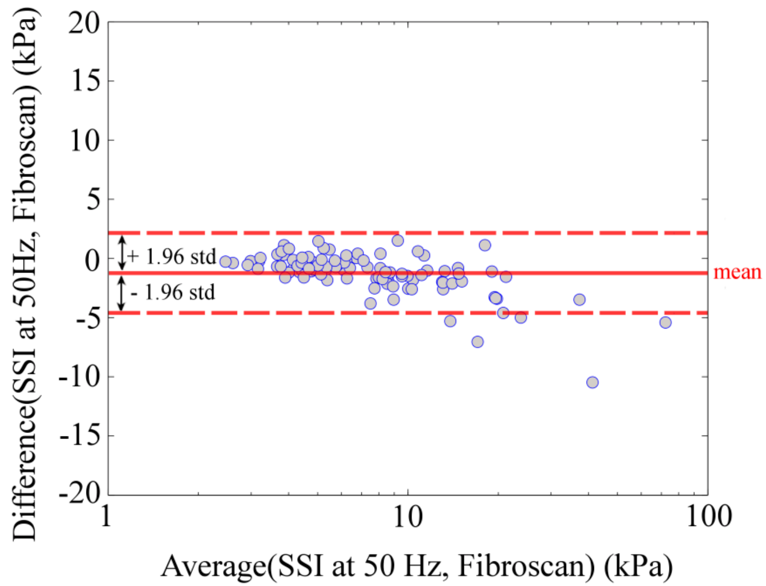




SHEAR WAVE DISPERSION

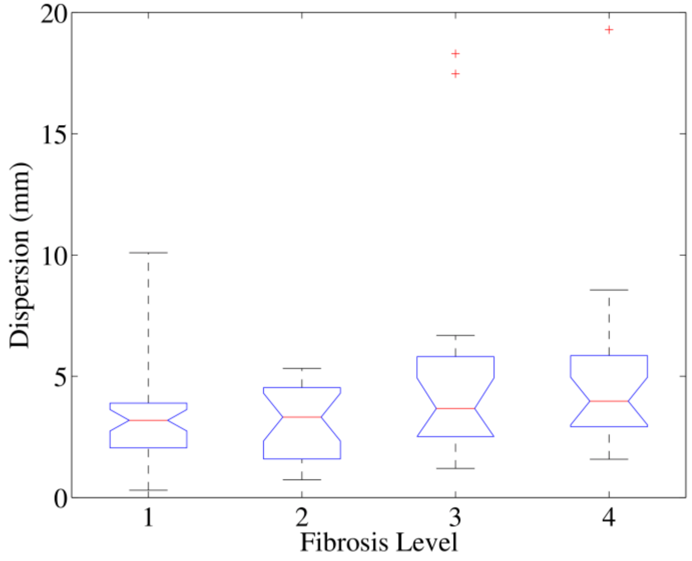


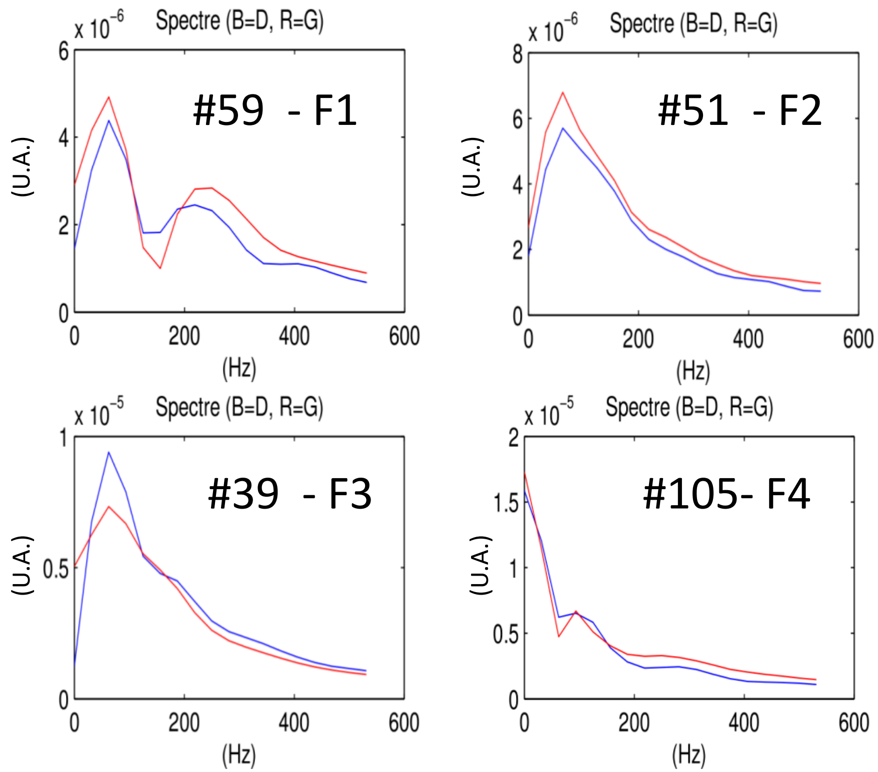
Good correlation between SSI at 50 Hz and FS (χ=0.96)



SHEAR WAVE DISPERSION

P-index: ~10^{-2}





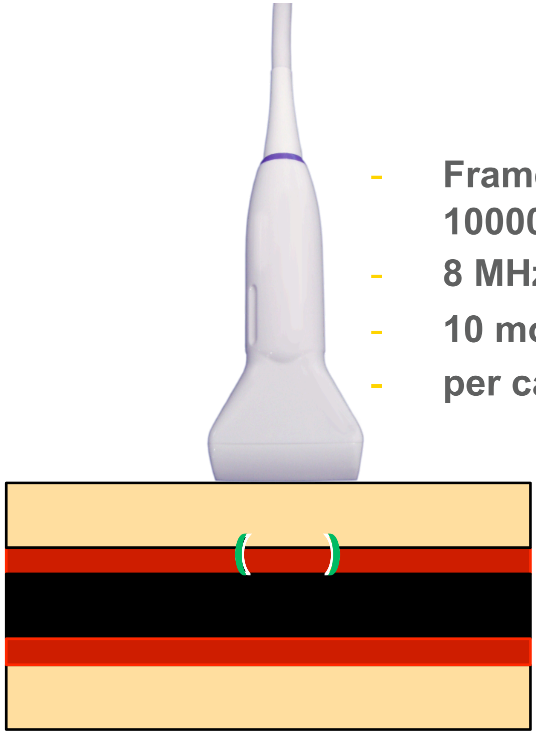
The slope of the dispersion curve is not related to the fibrosis level

Future works: Is there a relationship between spectral properties and liver pathologies?

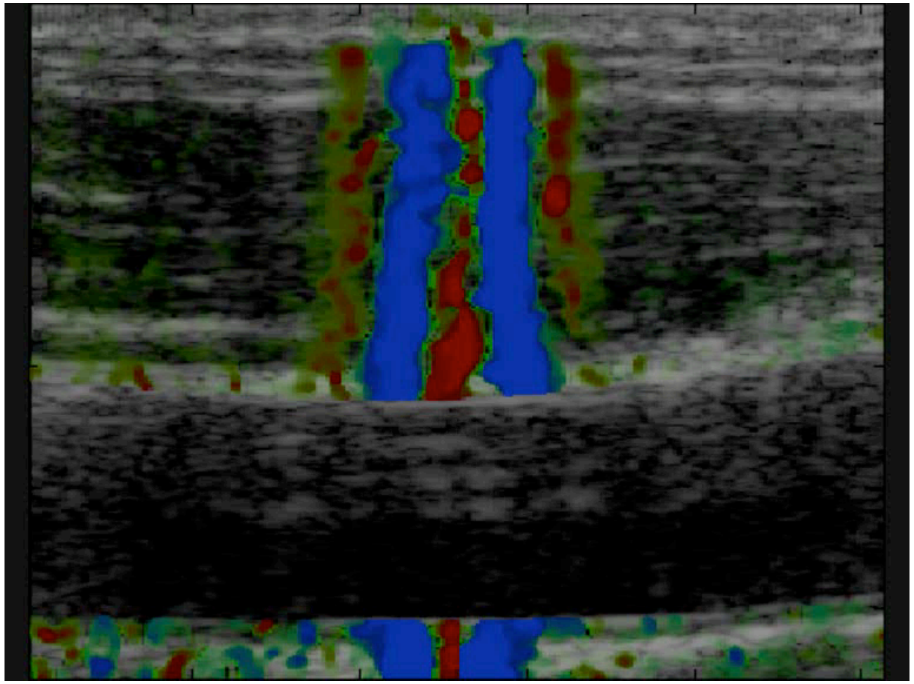
Real Time Dynamics of Elasticity Changes

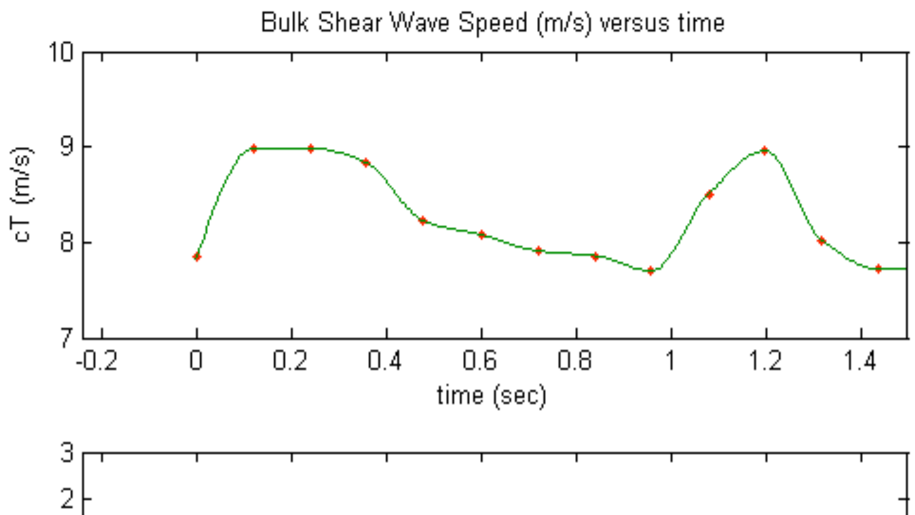
Real Time Elasticity Imaging of the carotid during one single cardiac cycle

Generating a « pushing beam » at the surface of the arterial wall enables the precise estimation of local visco-elastic properties of arterial wall



- Frame rate ~ 5000 to 10000 Hz
- 8 MHz central frequency
- 10 movies acquired
- per cardiac cycle

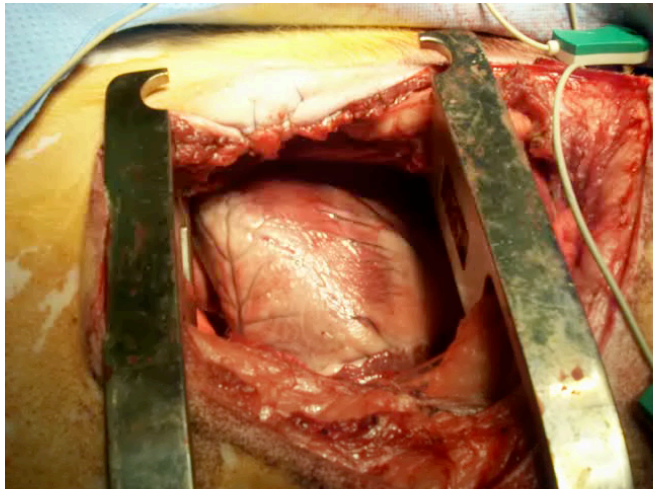


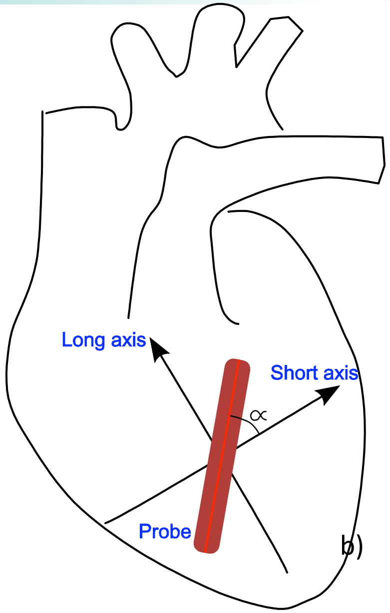


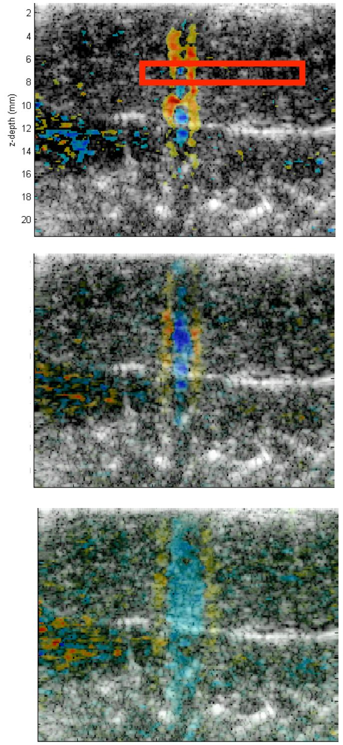
Athérosclérosis, fibrodysplasia, myocardial fibrosis…

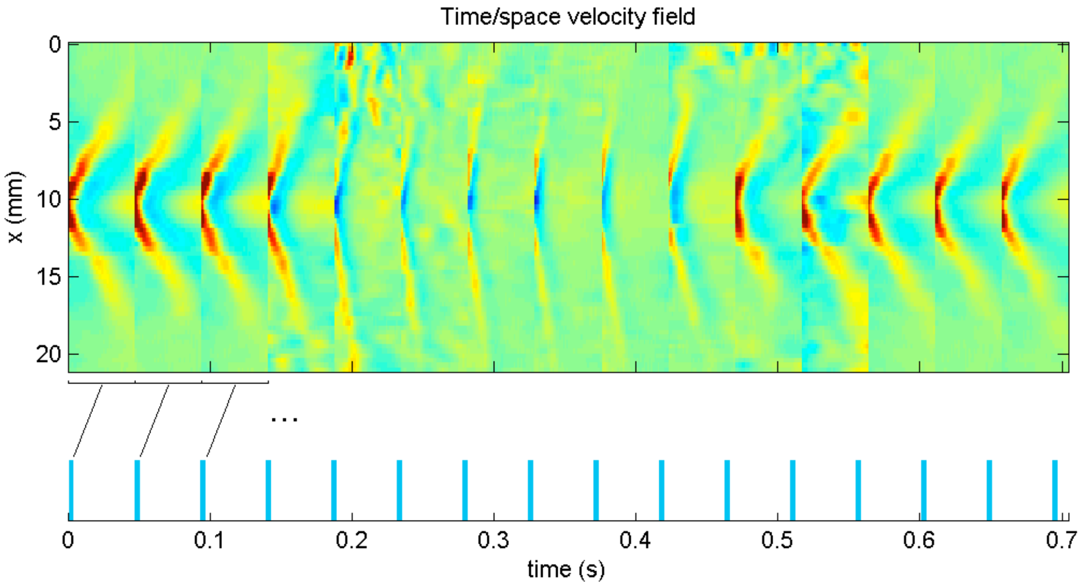
Coll. Hospital Pompidou, Paris

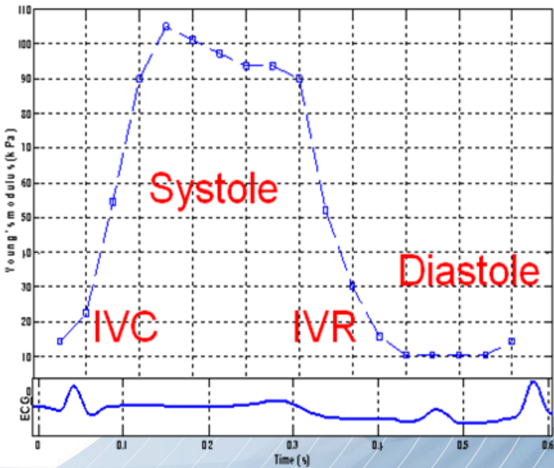
Real Time Elasticity Changes of *in vivo* Cardiac Muscle (Sheep Model)



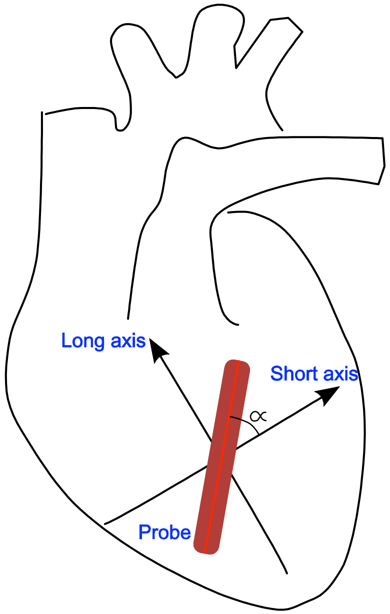


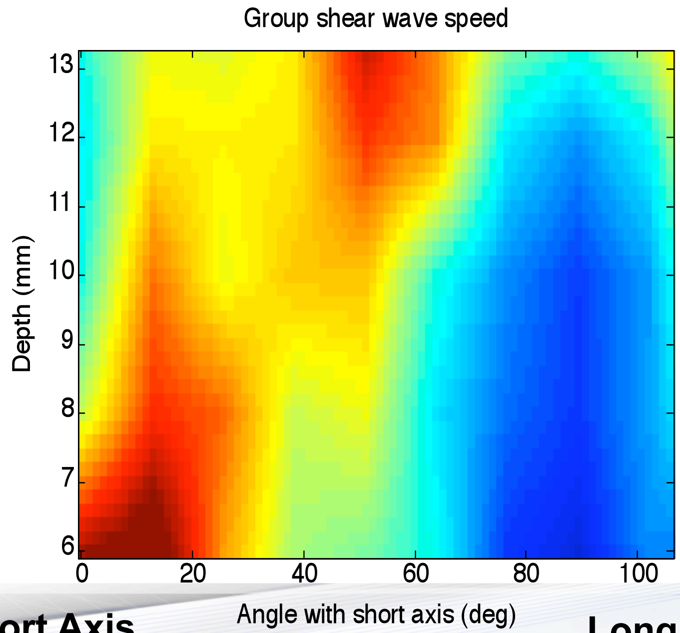






Real Time Elasticity Changes of *in vivo* Cardiac Muscle (Sheep Model)

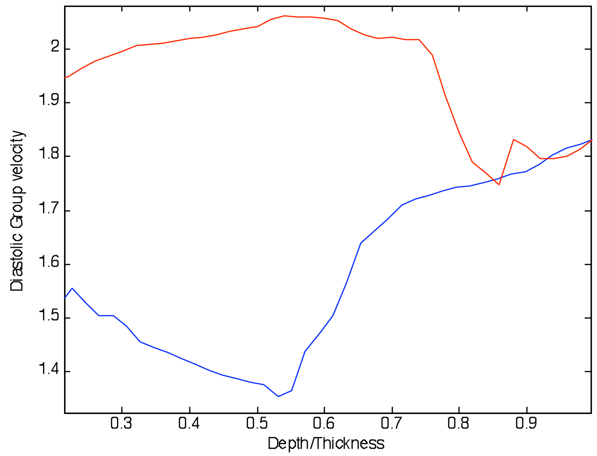




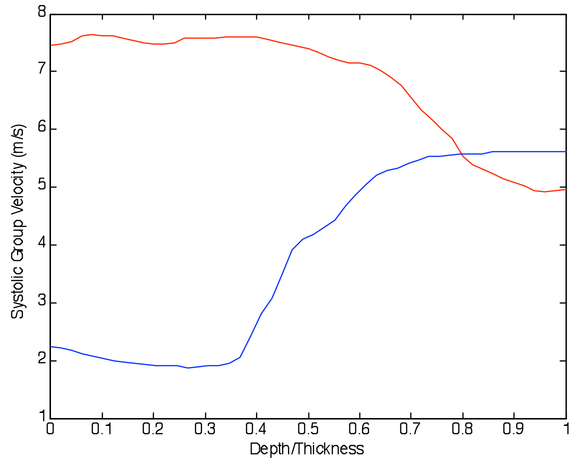
Short Axis **Long Axis**

Anisotropy Dynamic Changes

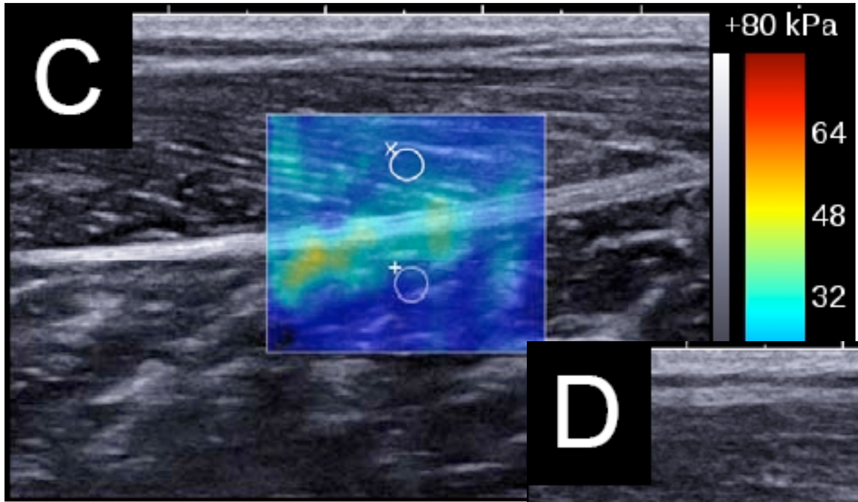
Diastolic Event

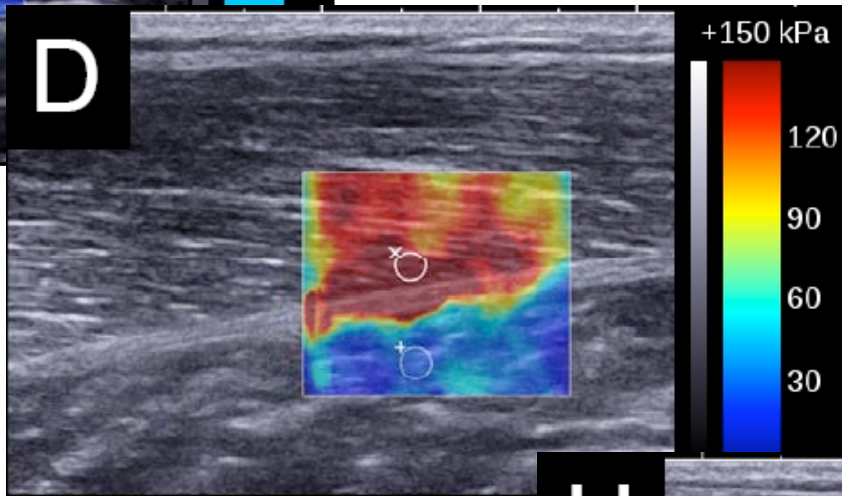


Systolic Event

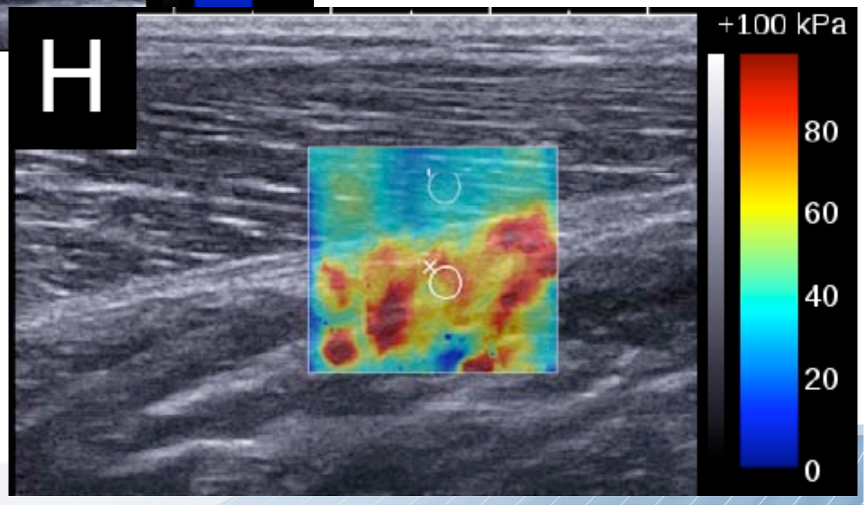


Dynamics of Muscle Contraction





Gastrocnemius Contraction

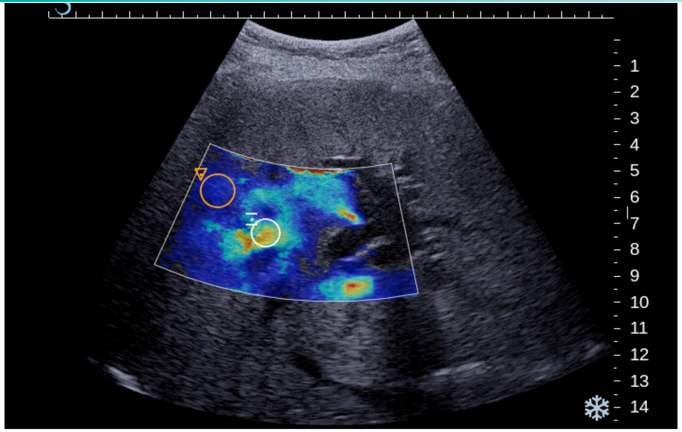


Soleus Contraction

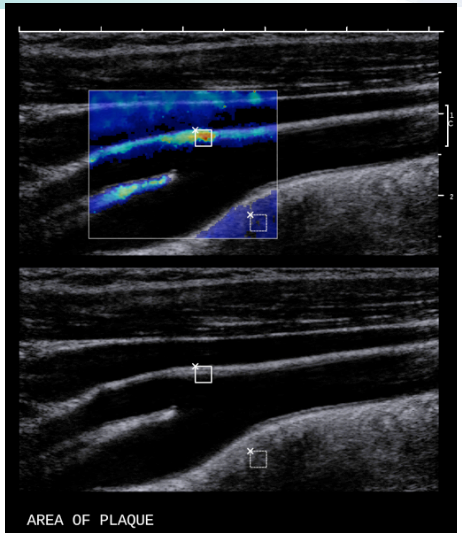
Quel Futur pour l’Elastographie ultrasonore ?

Vers une réelle et large maturité clinique

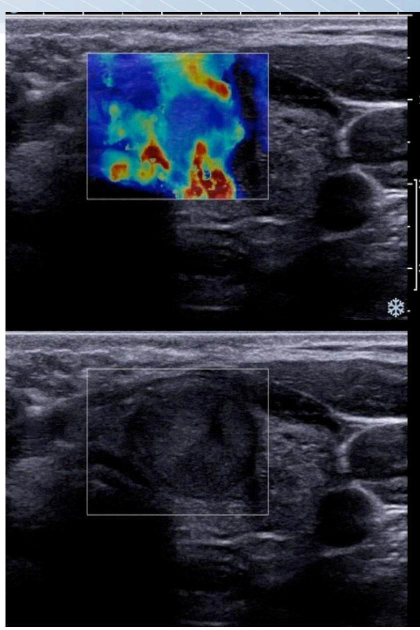
Supersonic Shear Wave Imaging : Other Applications



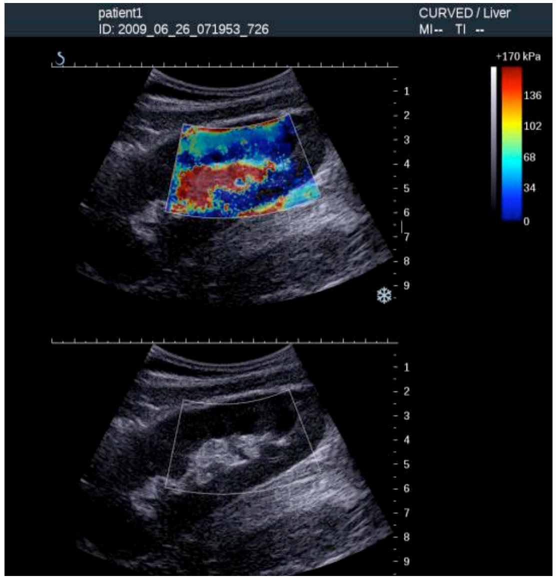
Liver Cholangitis carcinoma



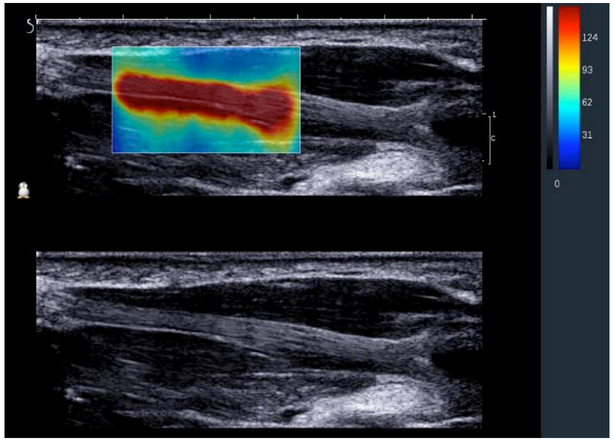
Carotid Plaque



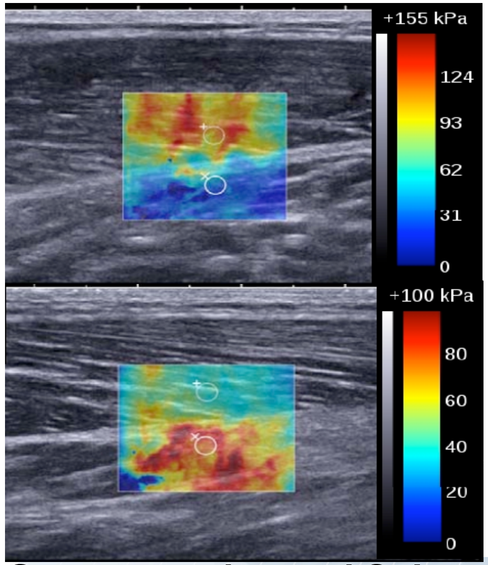
Thyroid Nodule



Transplanted Kidney



Tendon Elasticity



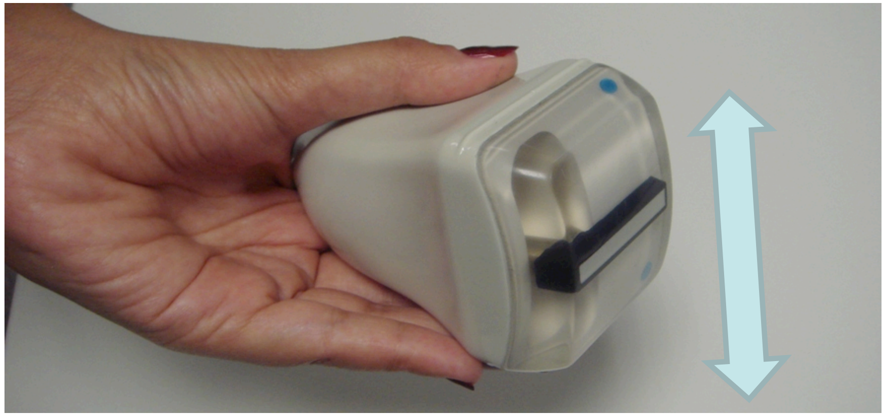
Gastrocnemius and Soleus Contraction

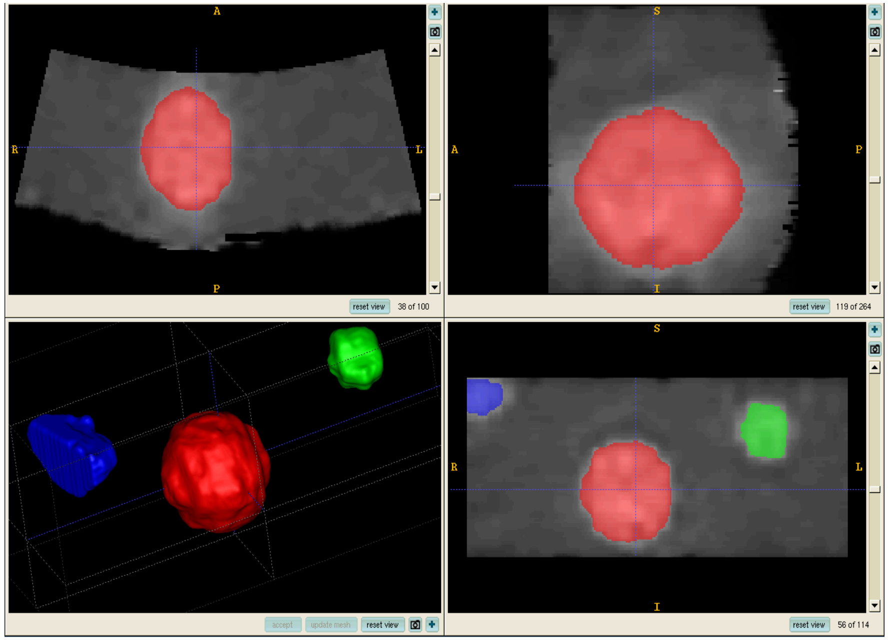
Quel Futur pour l'Elastographie ultrasonore ?

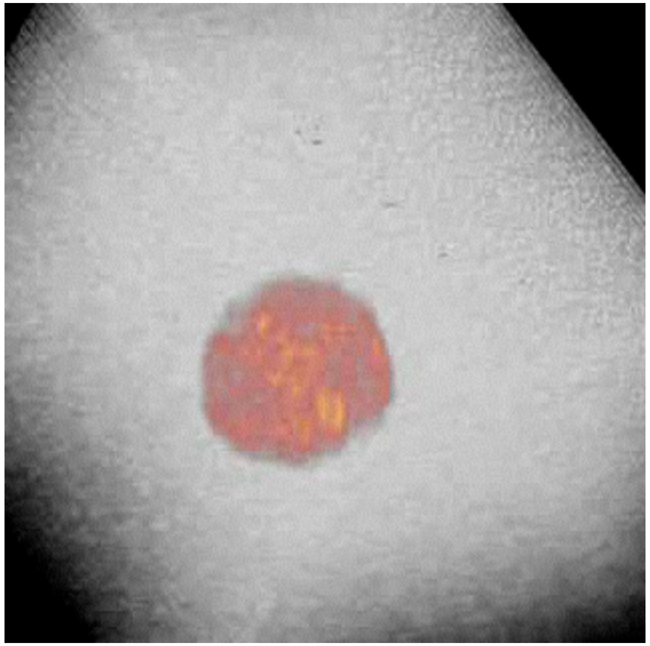
Vers une réelle et large maturité clinique

Vers l'élastographie 3D

3D Ultrasonic Wobbler Probe

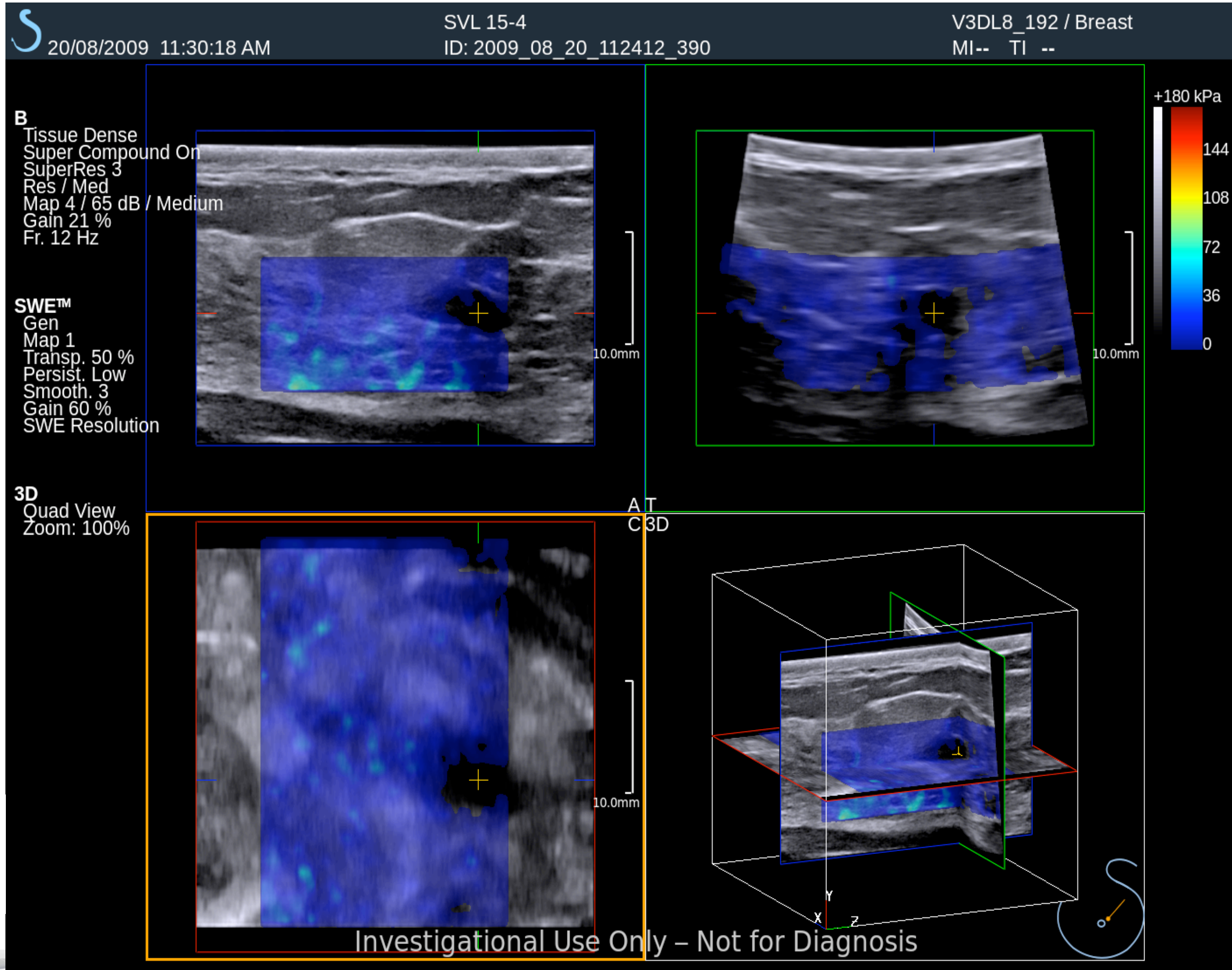






N . Felix, JL Gennisson

3D Shear Wave Elastography : Preliminary *in vivo* results



Quel Futur pour l’Elastographie ultrasonore ?

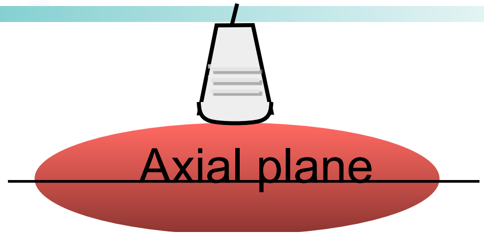
Vers une réelle et large maturité clinique

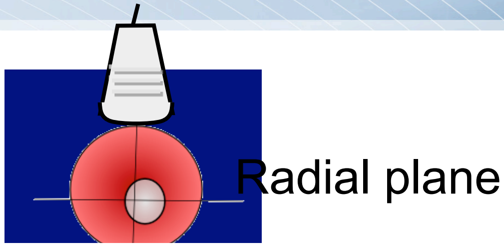
Vers l’élastographie 3D

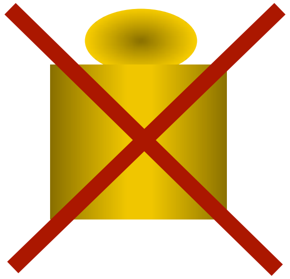
Vers une caractérisation plus performante

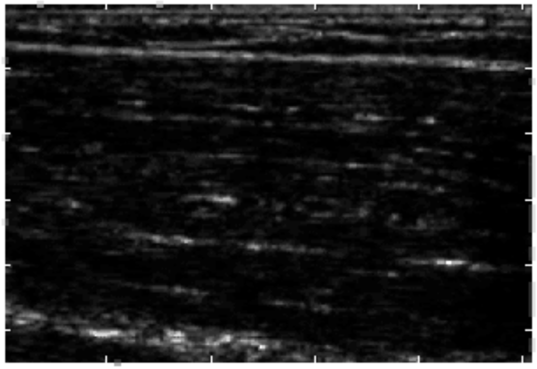
Quantitative viscoelasticity imaging of muscles using SSI

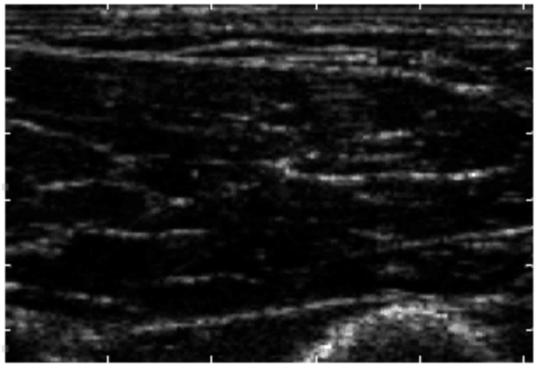
Biceps Brachii

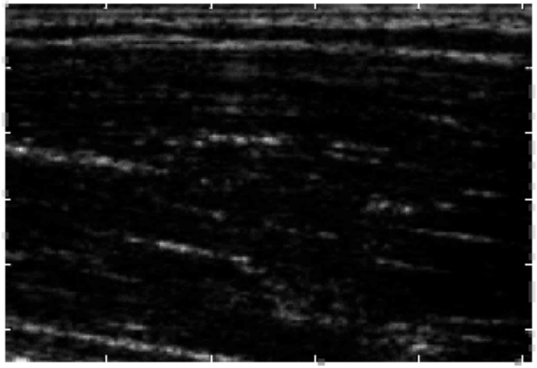


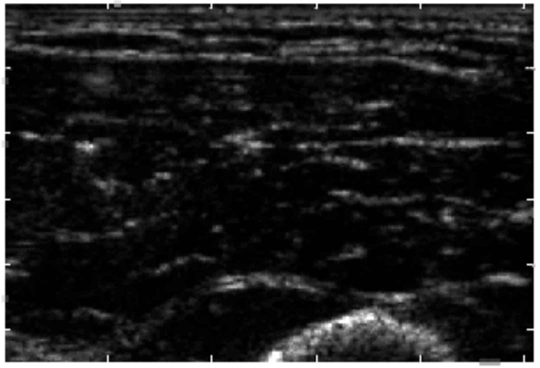




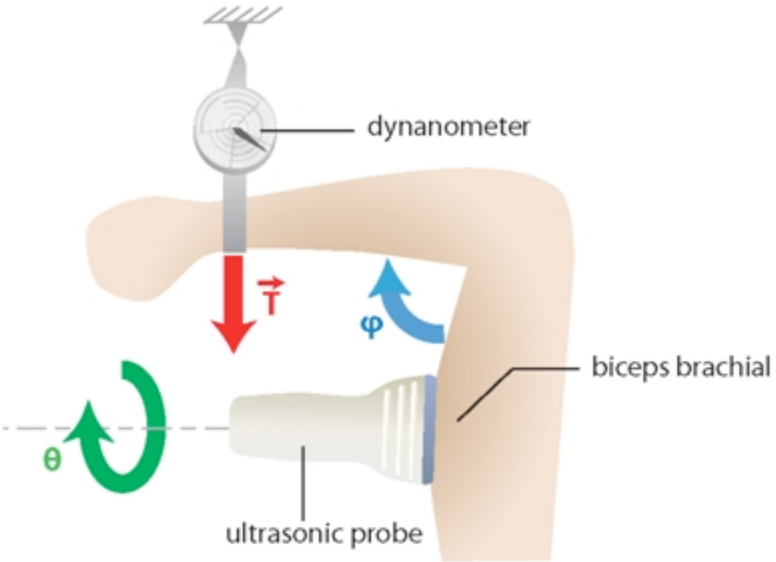




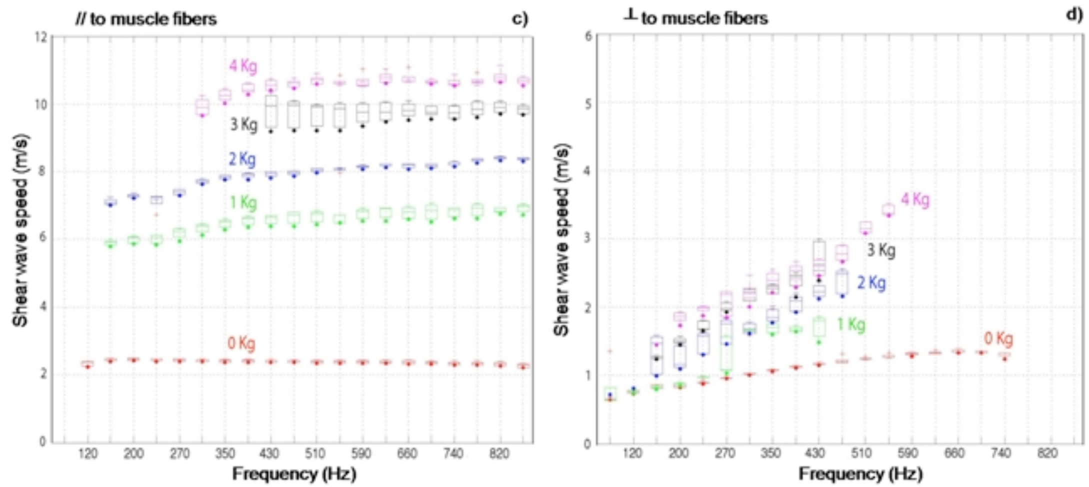




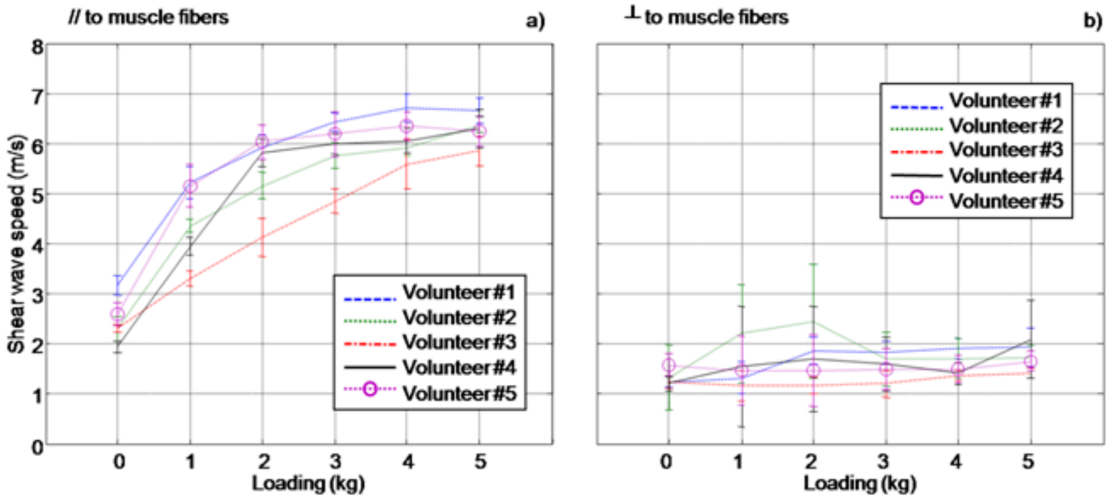
Shear Anisotropy, Shear Viscosity, Shear Nonlinearity …

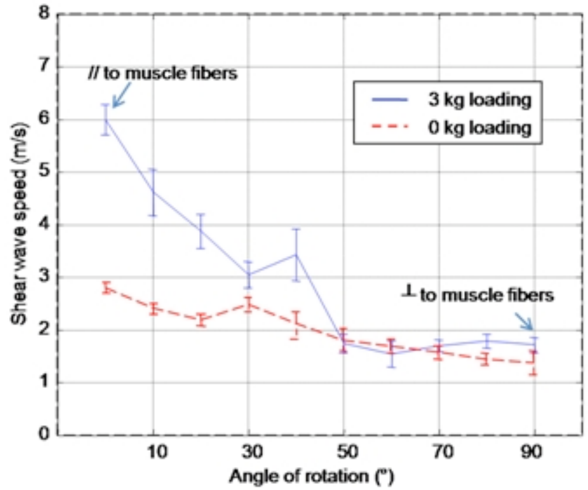


Viscosity & Contraction



Anisotropy & Contraction





Quel Futur pour l’Elastographie ultrasonore ?

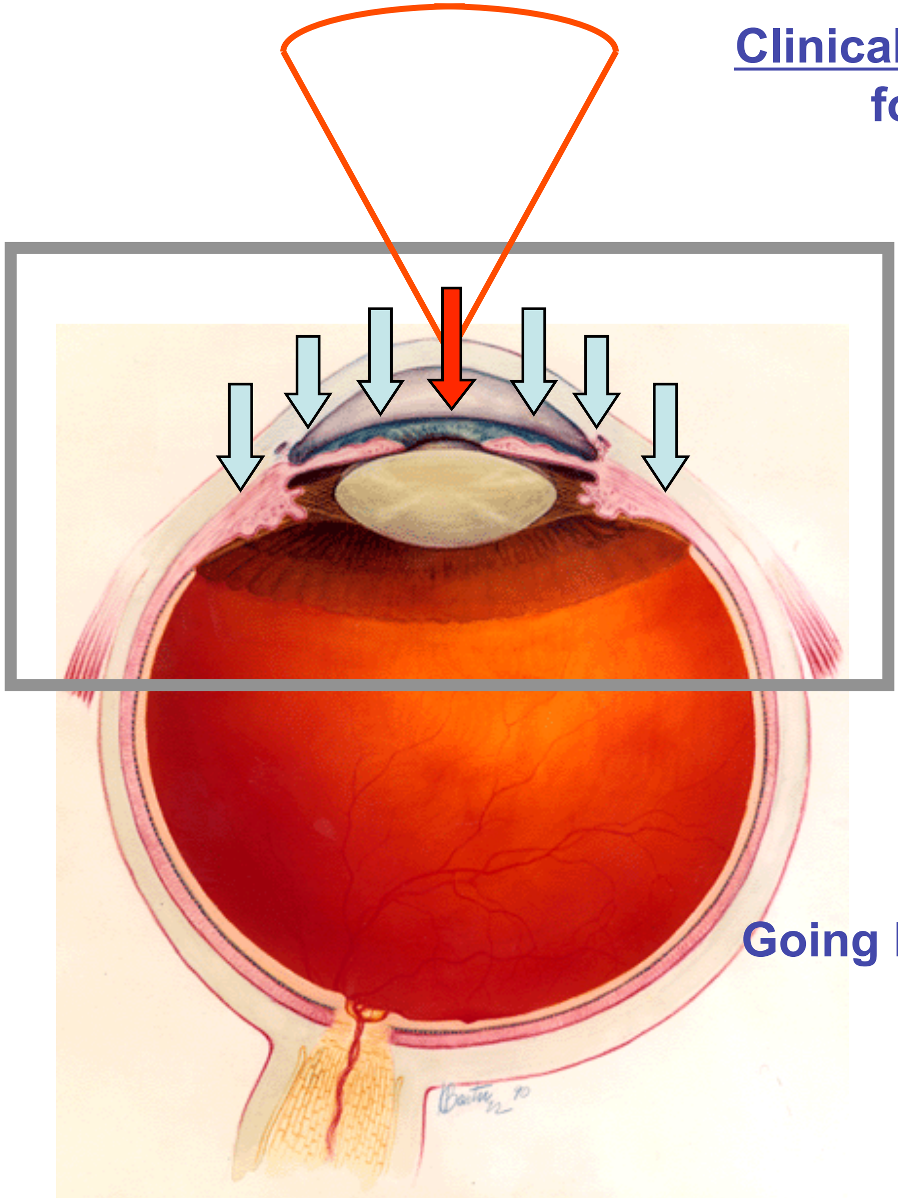
Vers une réelle et large maturité clinique

Vers l’élastographie 3D

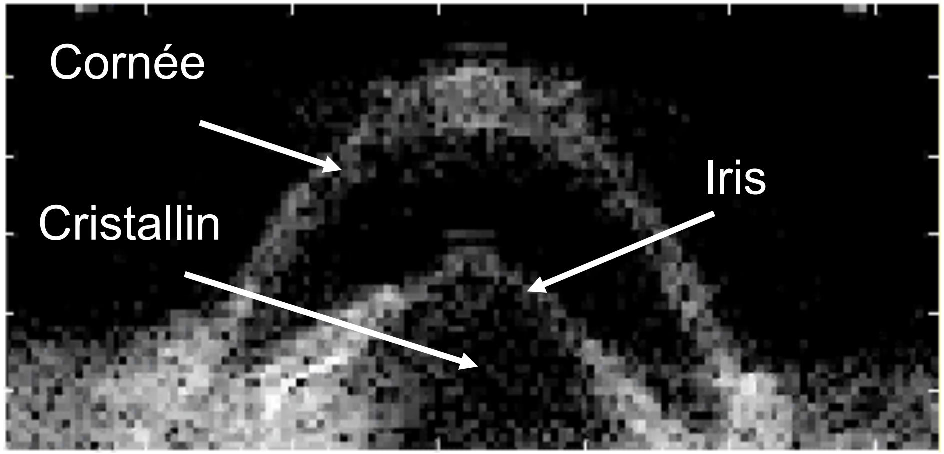
Vers une caractérisation plus performante

Vers une MicroElastographie

Corneal Visco-Elasticity mapping Supersonic Shear Imaging



Clinical Rational : Estimate Corneal Viscoelasticity for the diagnosis of Keratocone before Laser adaptive correction of cornea

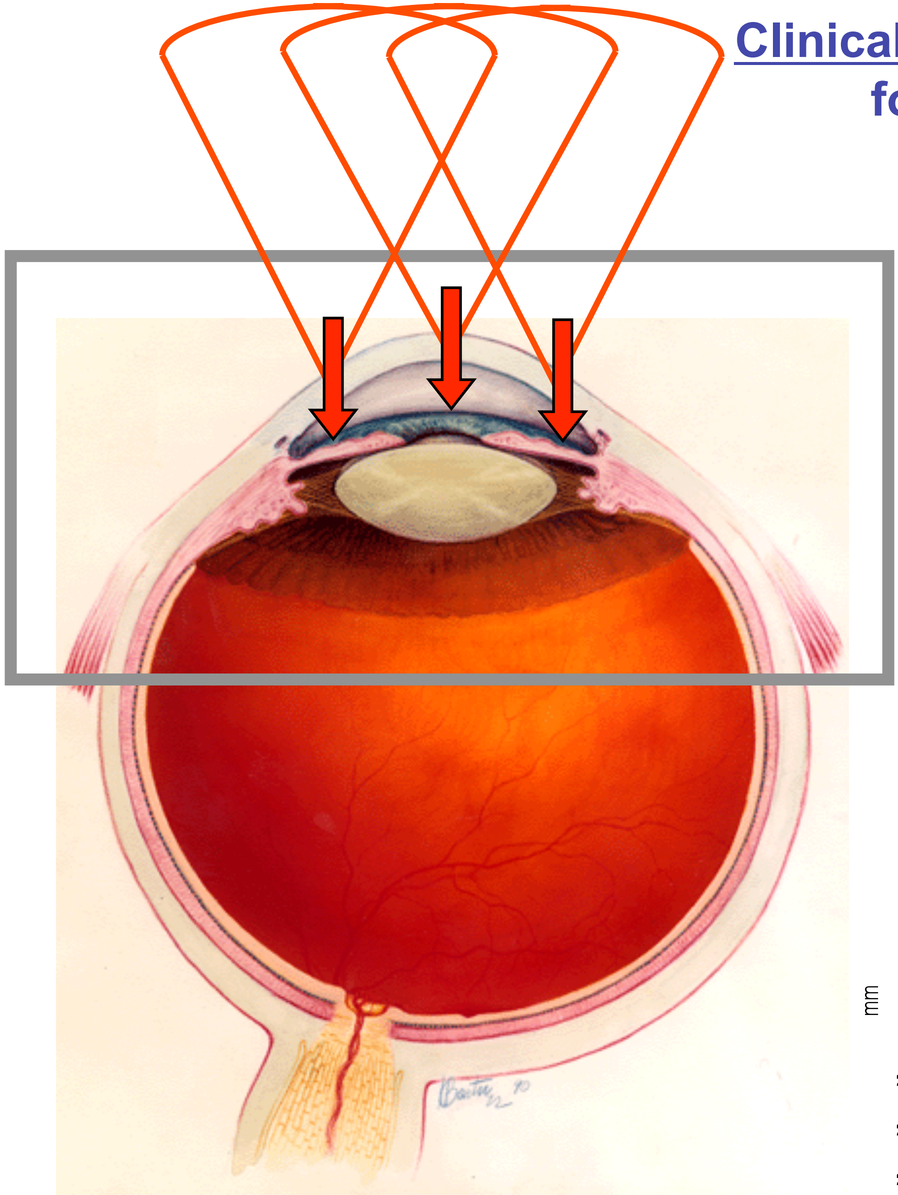


***In vitro* Pork Eye**

Going Much higher in Frequency and Frame rates :

- **16 MHz linear array**
- **20.000 frames per second**
- **Less than 1 µm displacement estimation**

Corneal Visco-Elasticity mapping Supersonic Shear Imaging



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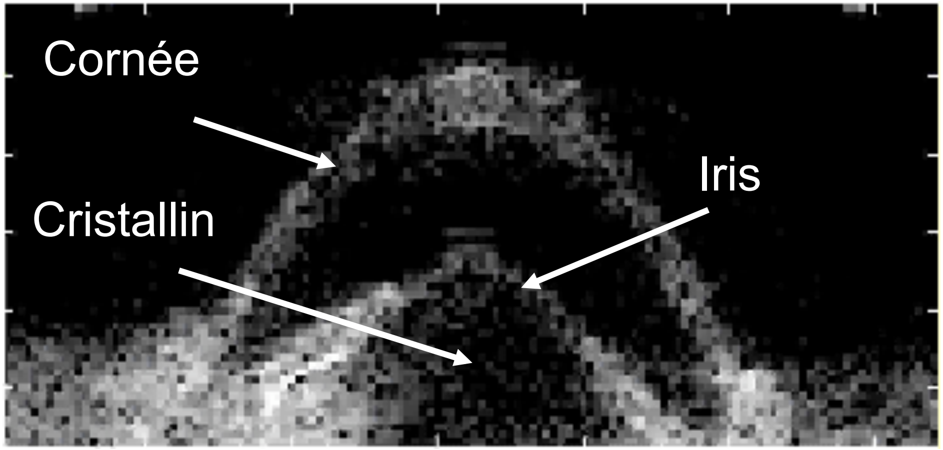
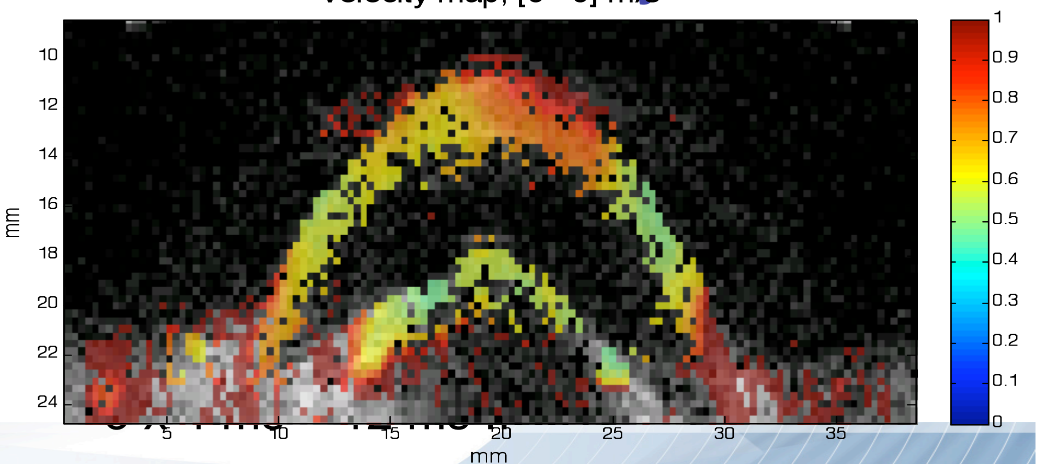


In vitro Pork Eye



Quel Futur pour l'Elastographie ultrasonore ?

Vers une réelle et large maturité clinique

Vers l'élastographie 3D

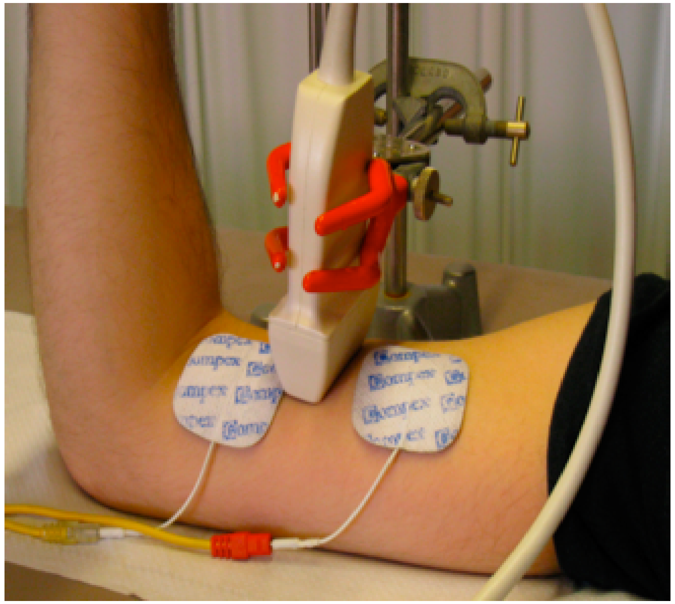
Vers une caractérisation plus performante

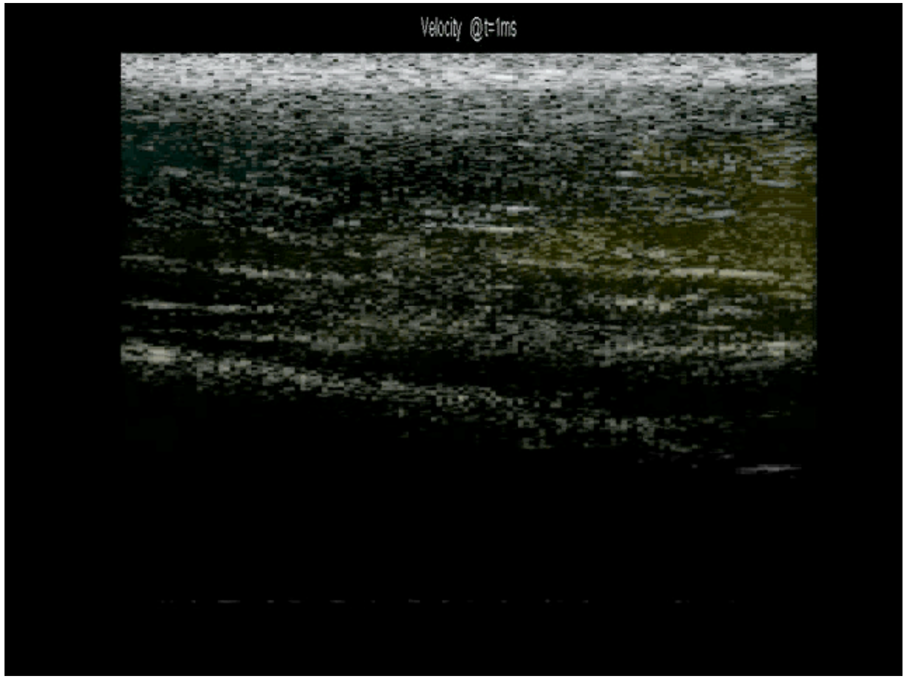
Vers une MicroElastographie

Vers une imagerie électromécanique du corps humain

Ultrafast Ultrasonic Imaging of Action Potentials

Our body is the ground of many transient phenomena at time scales of the order of milliseconds that were up today impossible to image



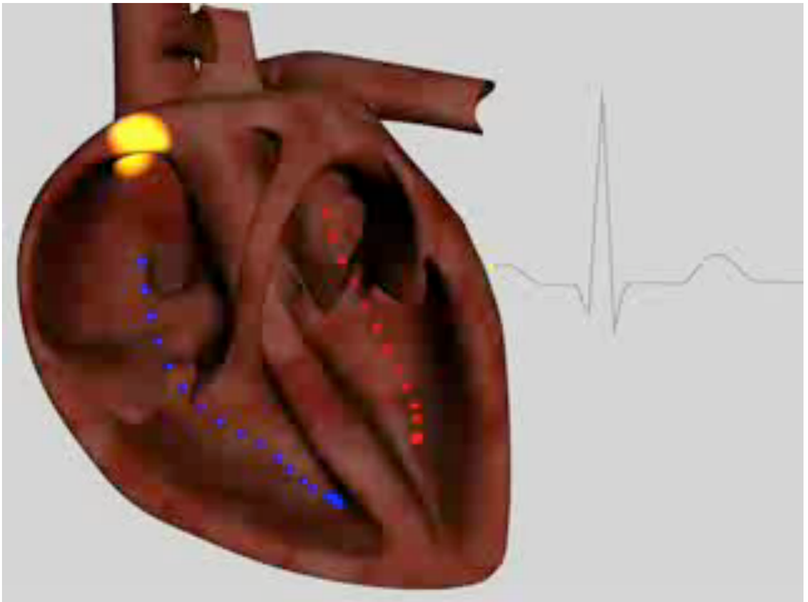


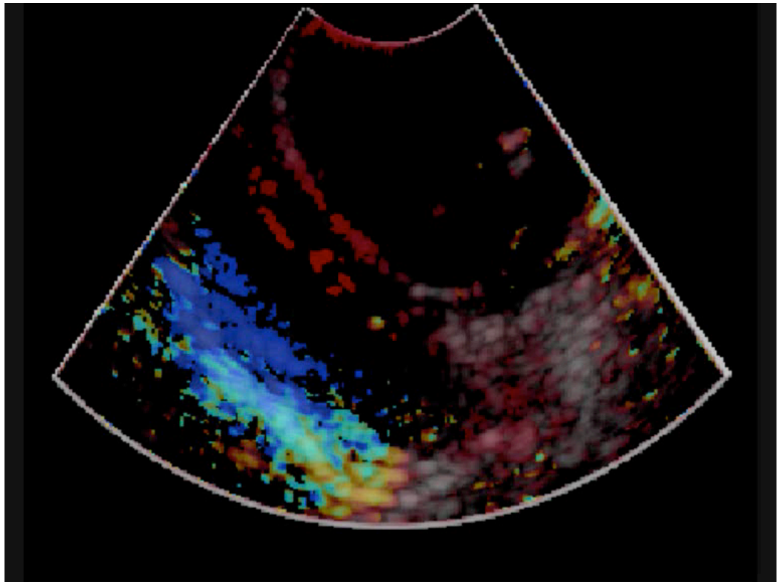
2000 images/s

What link between Shear waves and Action Potential ?

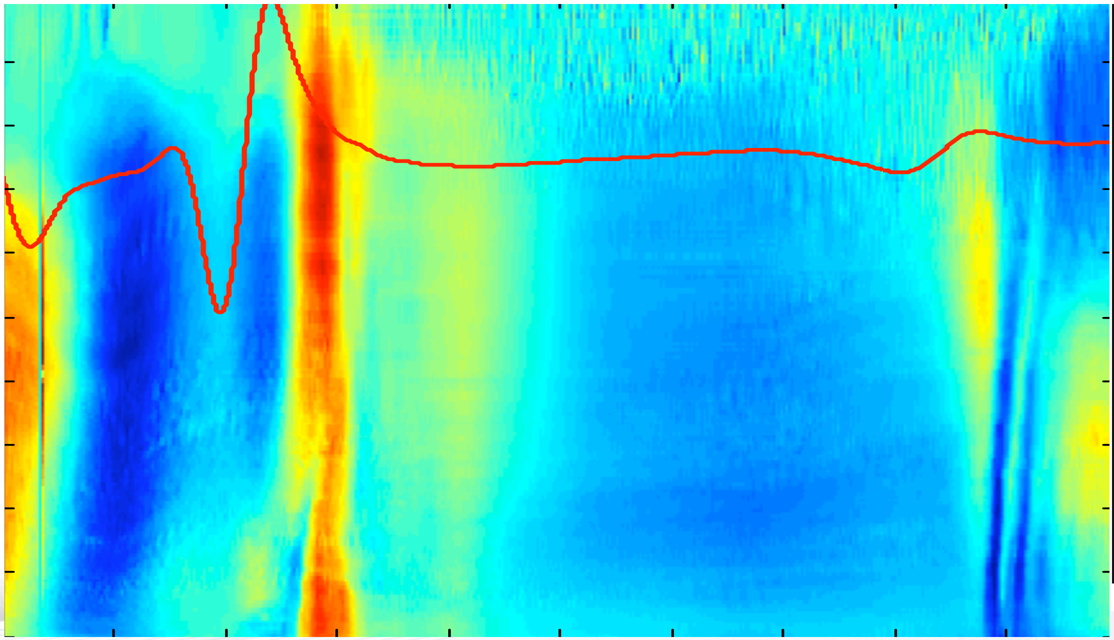
Can we use mechanical vibrations where electromagnetic waves are limited due to large wavelengths (cardiology, epilepsy,…) ?

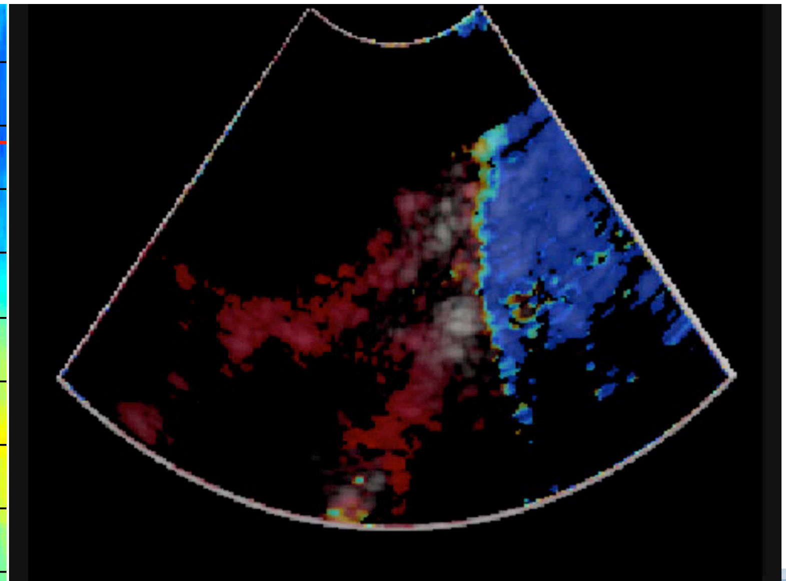
Ultrafast Imaging of Heart Electric Potentials





Short Axis





Long Axis

Thank you for your attention !

A great team of young and passionate scientists…

Inserm U979 « Physique des Ondes Pour la Médecine »

http://www.institut-langevin.espci.fr/EPOM

Nouvelles techniques d'imagerie et de thérapie basées sur l'utilisation innovante de tout type d'ondes (ultrasons, optiques, électromag.,…)

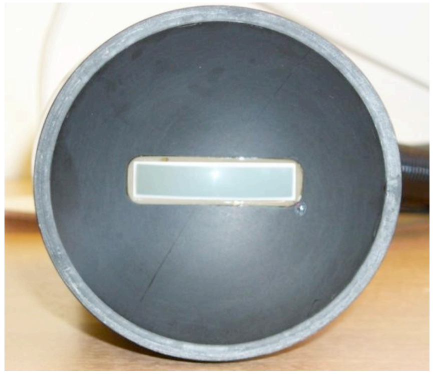
« Du concept physique jusqu'à l'expérimentation clinique et le transfert technologique »

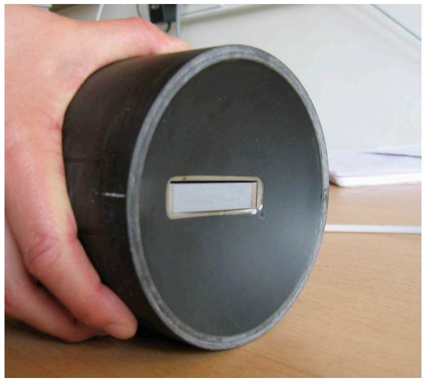
30 personnes (13 chercheurs permanents, 17 Thésards&Postdocs)

12 Echographes ultrarapides entièrement programmables
2 systèmes de thérapie ultrasonore 512 voies
1 IRM 7T Petit Animal
4 Systèmes OCT
2 Systèmes acousto-optiques,…

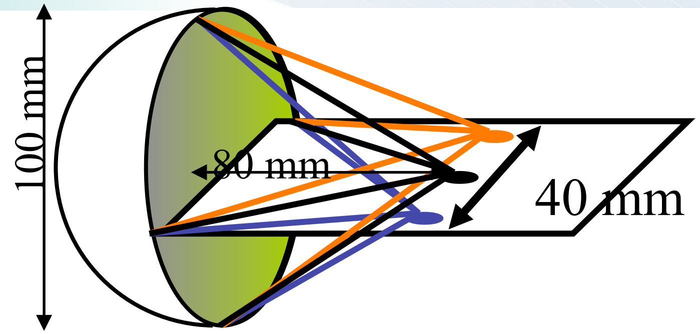
Monitoring Elasticity changes during H.I.F.U. treatments

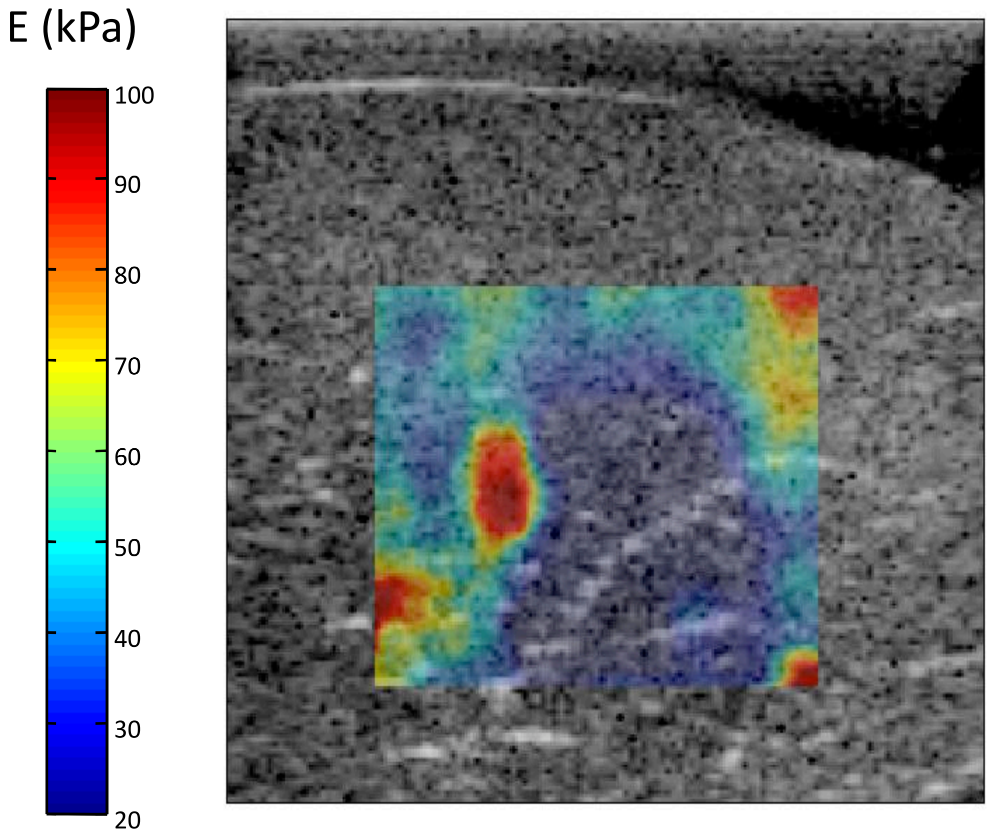
Vermon Imaging probe
(128 elements, 5 MHz)



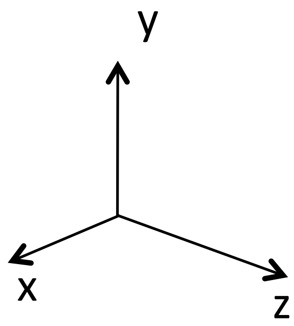


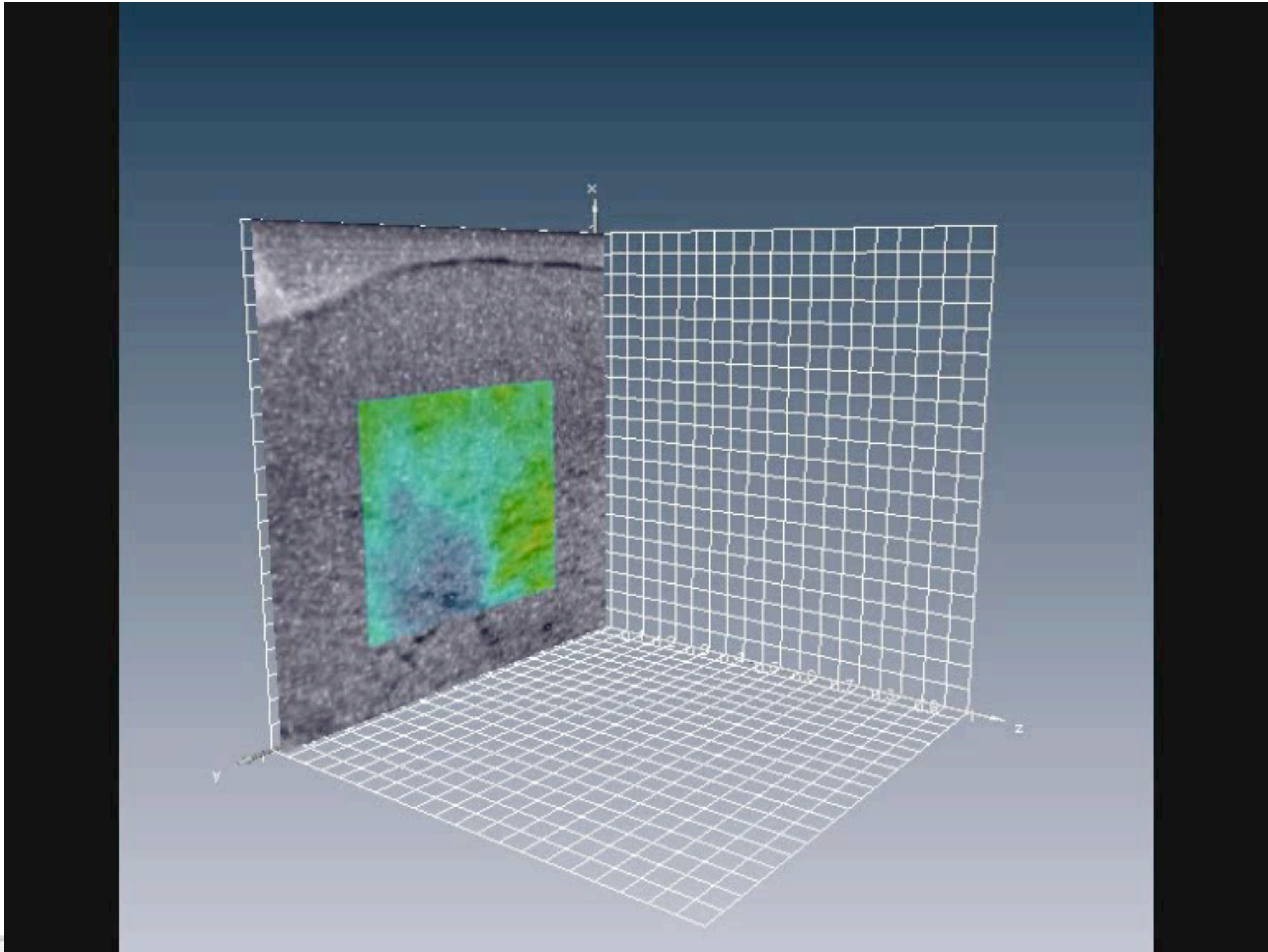
IMASONIC HIFU Array
(200 elements,1 MHz, 5 W_{el} per element)



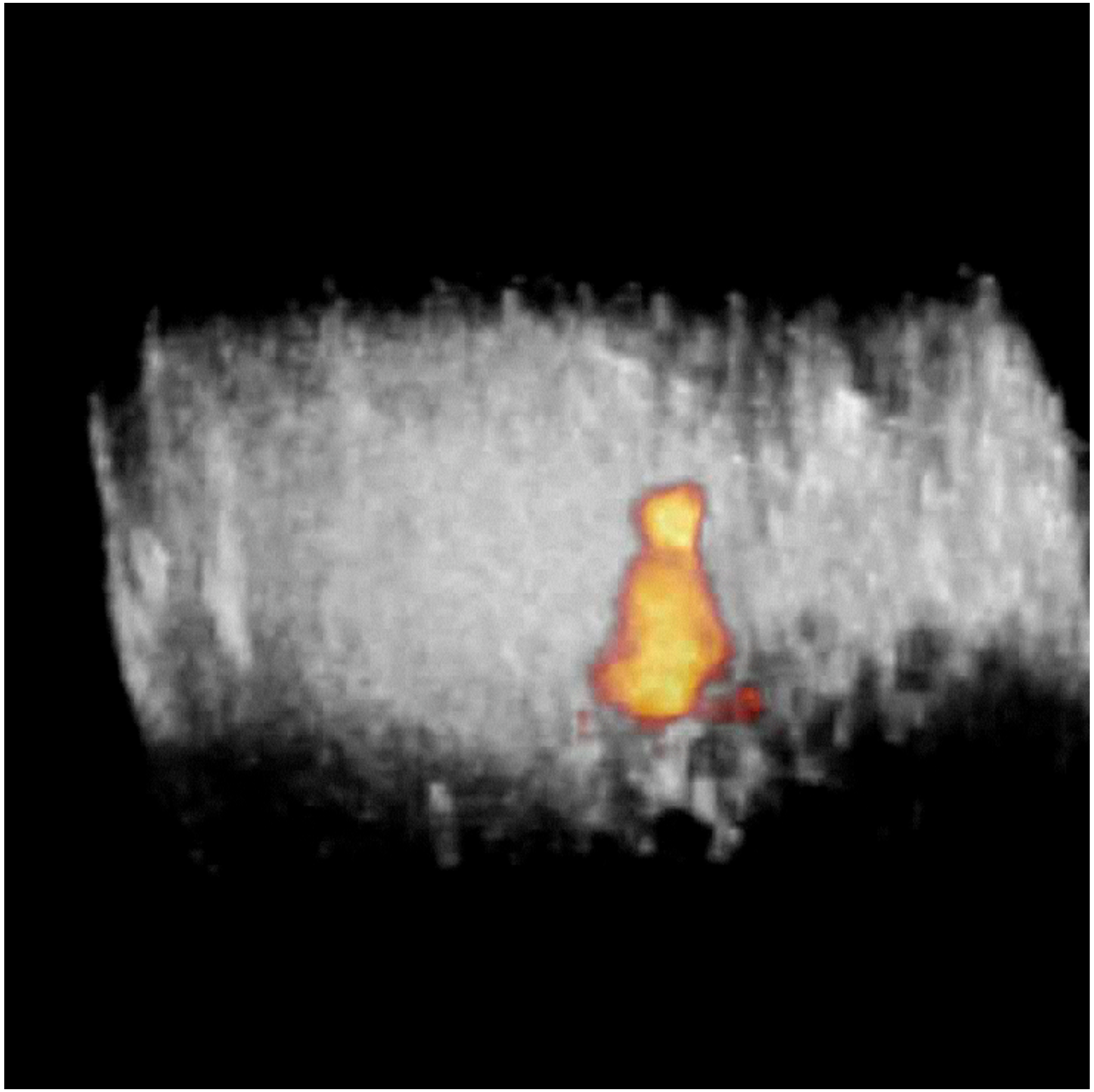


3D acquisition after HIFU lesion (multiple 2D scans)

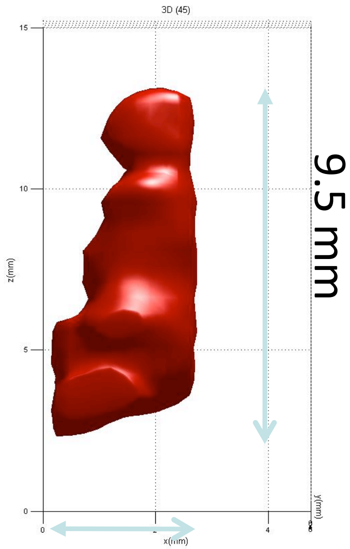




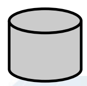
3D reconstruction of the Thermal Lesion



Irregular shape of the lesion
Bubbly lesion ?
(Crum et al., Roy et al.)



2.2 mm



Le retour des cliniciens sur la technologie issue du laboratoire

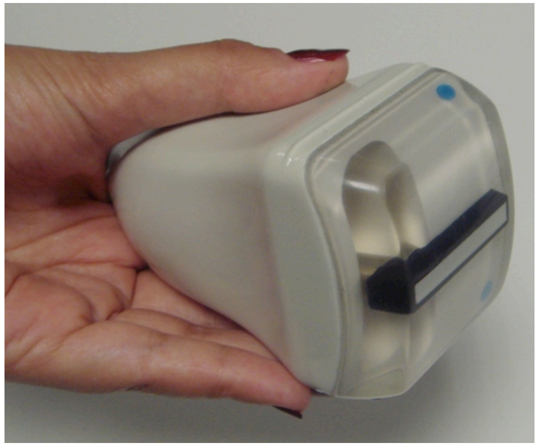
***« La qualité de l'image en mode B d'Aixplorer® est superbe. Nous avons eu l'occasion de la comparer avec plusieurs systèmes de référence de l'imagerie du sein : à maintes reprises, les résultats d'Aixplorer® nous sont apparus plus significatifs, offrant des images plus propres avec un bruit de fond des images sonores réduit, ainsi que des limites plus claires par rapport aux structures et lésions ordinaires* », Dr David Cosgrove, Emeritus Pr., Imperial College, London**

***« Au cours des derniers mois, nous nous sommes entretenus avec des centaines de docteurs et d'échographistes dans de nombreux pays et je ne saurais dire combien ont affirmé que cet élastographie ShearWave™ offrait la meilleure qualité d'image qu'ils n'avaient jamais vue.* » Edward McClenny, General Manager de SuperSonic Imagine en Amérique**

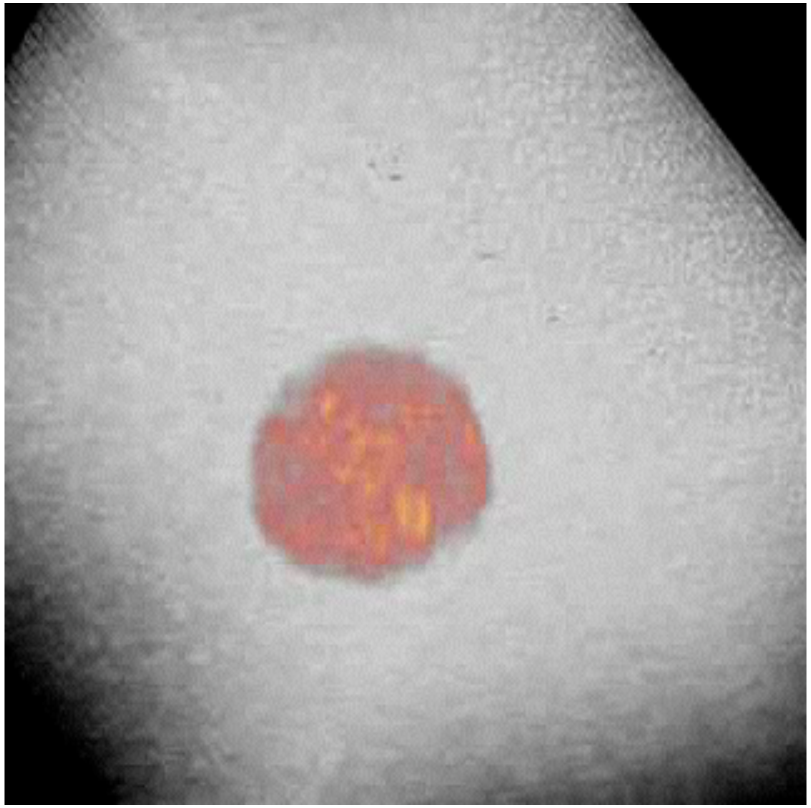
***« Des experts cliniciens américains et mondiaux ont mis en exergue que le système offrait une efficacité clinique exceptionnelle, car il permet une meilleure caractérisation des lésions. En se basant sur leurs constats, bon nombre d'entre eux considèrent que les fonctionnalités en mode B et le principe de l'élastographie ShearWave™ d'Aixplorer® sont la prochaine étape et le futur des ultrasons »*
Jacques Souquet, CEO Supersonic Imagine**

1D Linear Probes

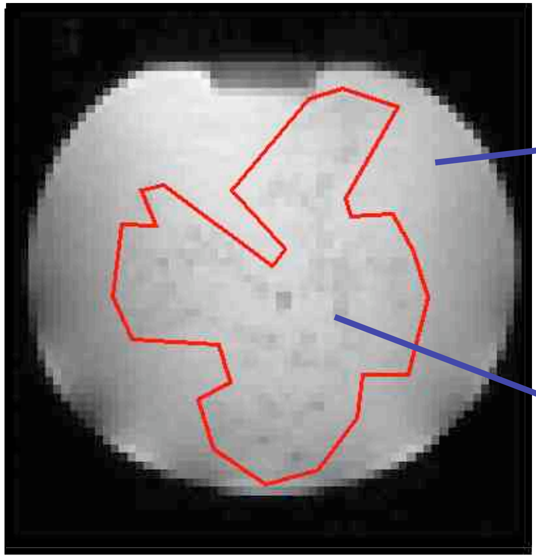
Wooble Probes (Mechanical)



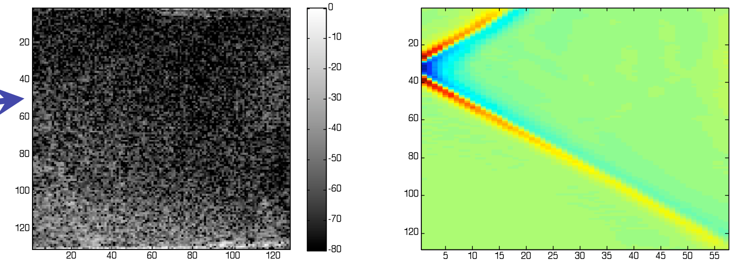
10 mm Stiff Inclusion



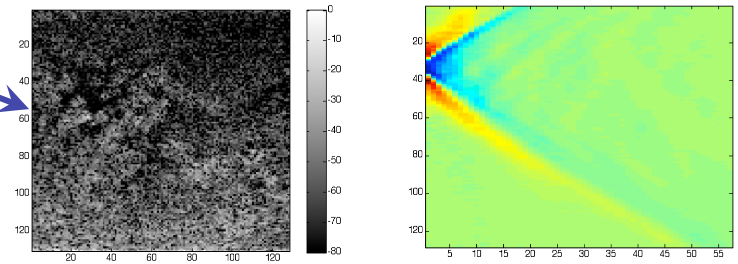
Where does macroscopic shear viscosity comes from ?

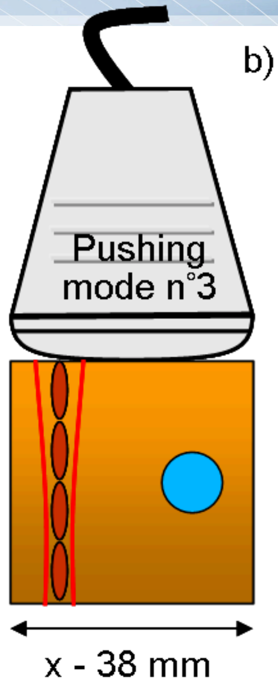


Without MicroStructure

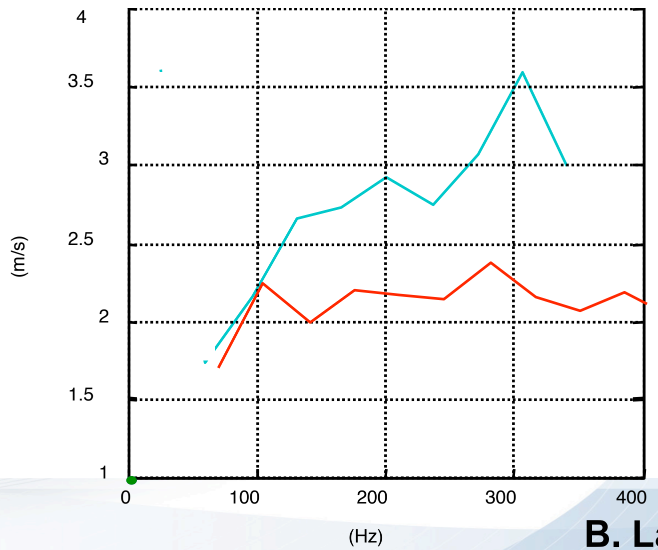


With MicroStructure





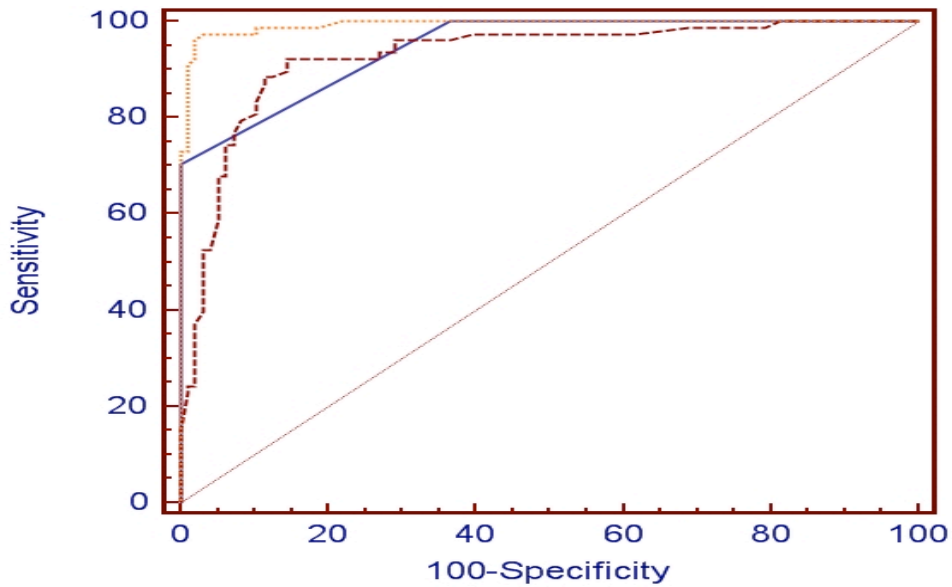
$v_\phi(\omega)$



B. Larrat, J.L. Gennisson et al

MR-Elastography vs SSI Elastography : Specificity/Sensitivity

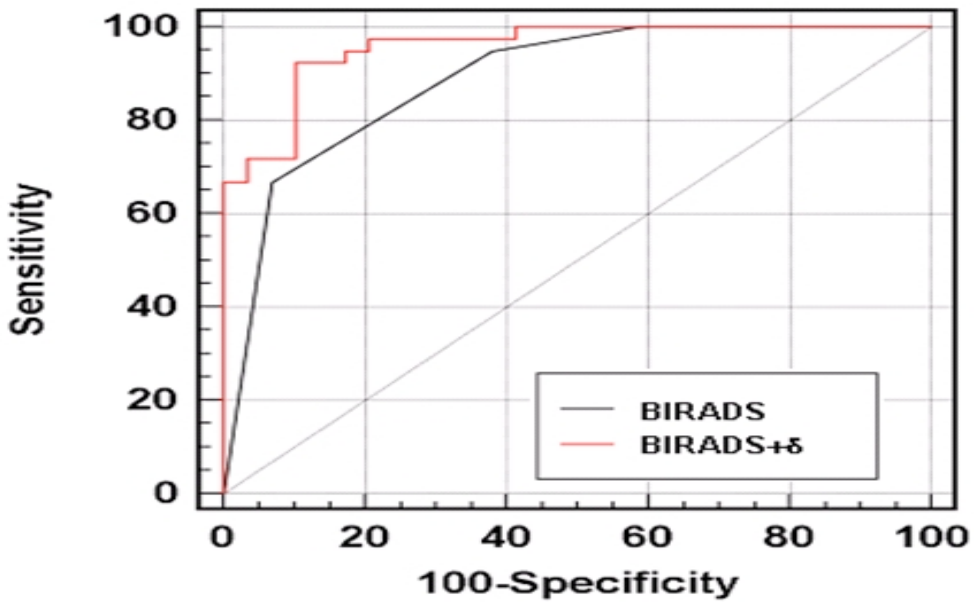
Breast Cancer Diagnosis



ROC Analysis of SSI mode

(175 patients)

~ 80% spec. (at 100% sens.)
~ 93 % spec. (at 95 % sens.)

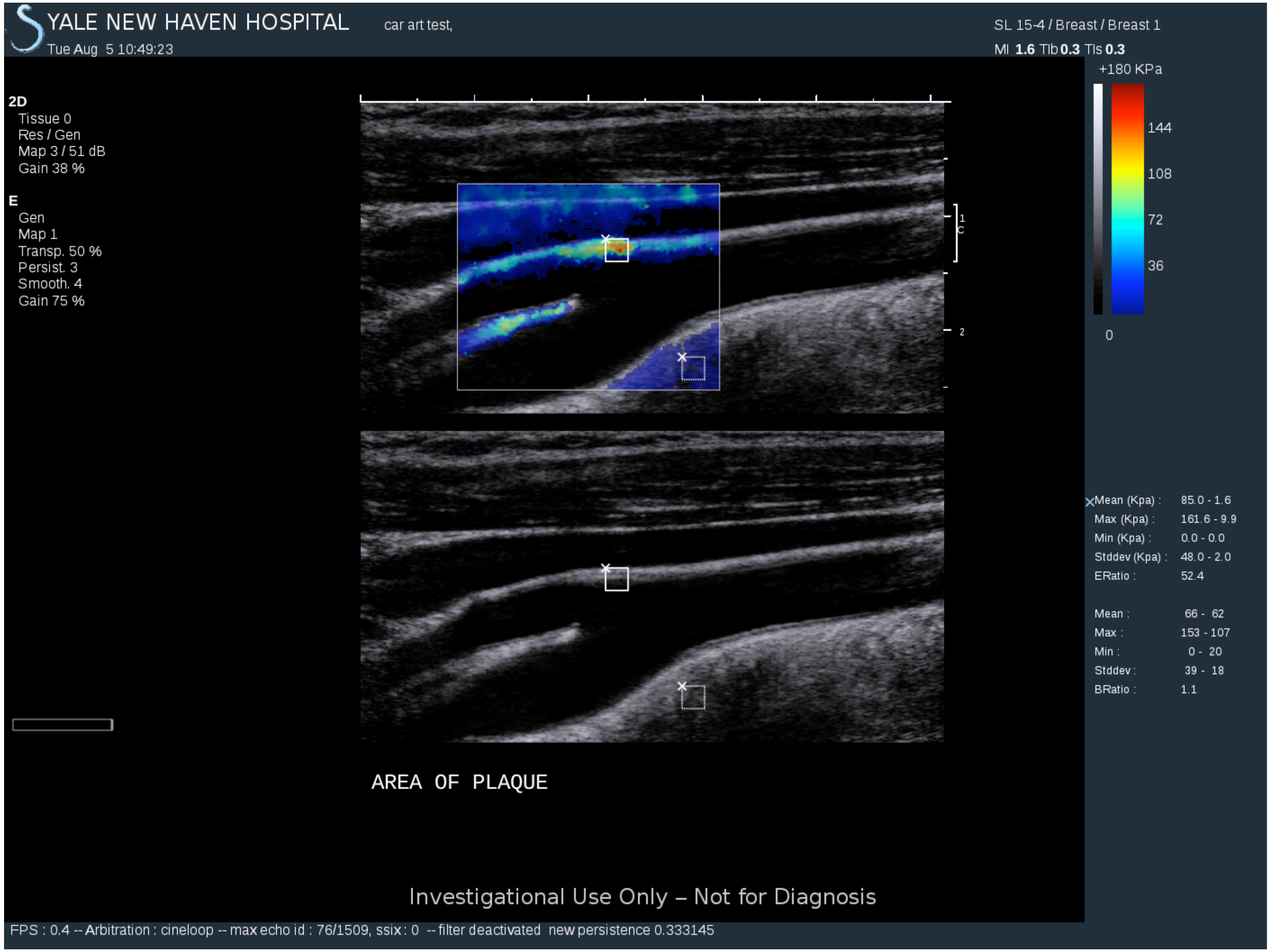


ROC Analysis of MR Elastography

(68 patients)

~60% spec. at (100% sens.)
~ 75 % spec. at (95 % sens.)

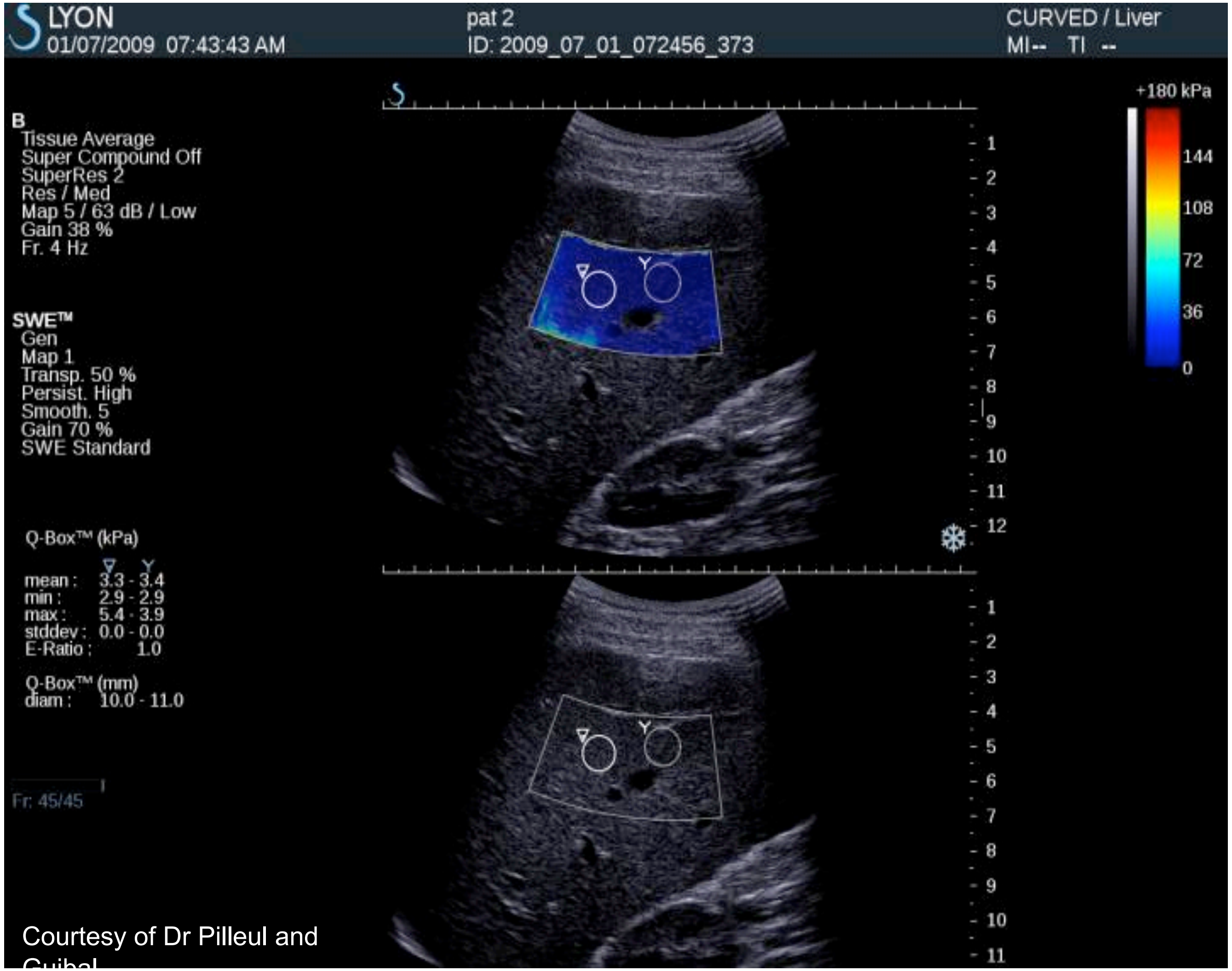
In vivo assessment of carotid plaque elasticity



150 µm resolution in the elasticity image

Clinical Case: Healthy Liver

- Curved probe:
  - 192 elements
  - 3.5 MHz
  - 60 mm radius
- Pathology:
  - intestinal scan
  - Healthy Liver
- Elasto:
  - Soft: 3.4 kPa
  - Vein is clear

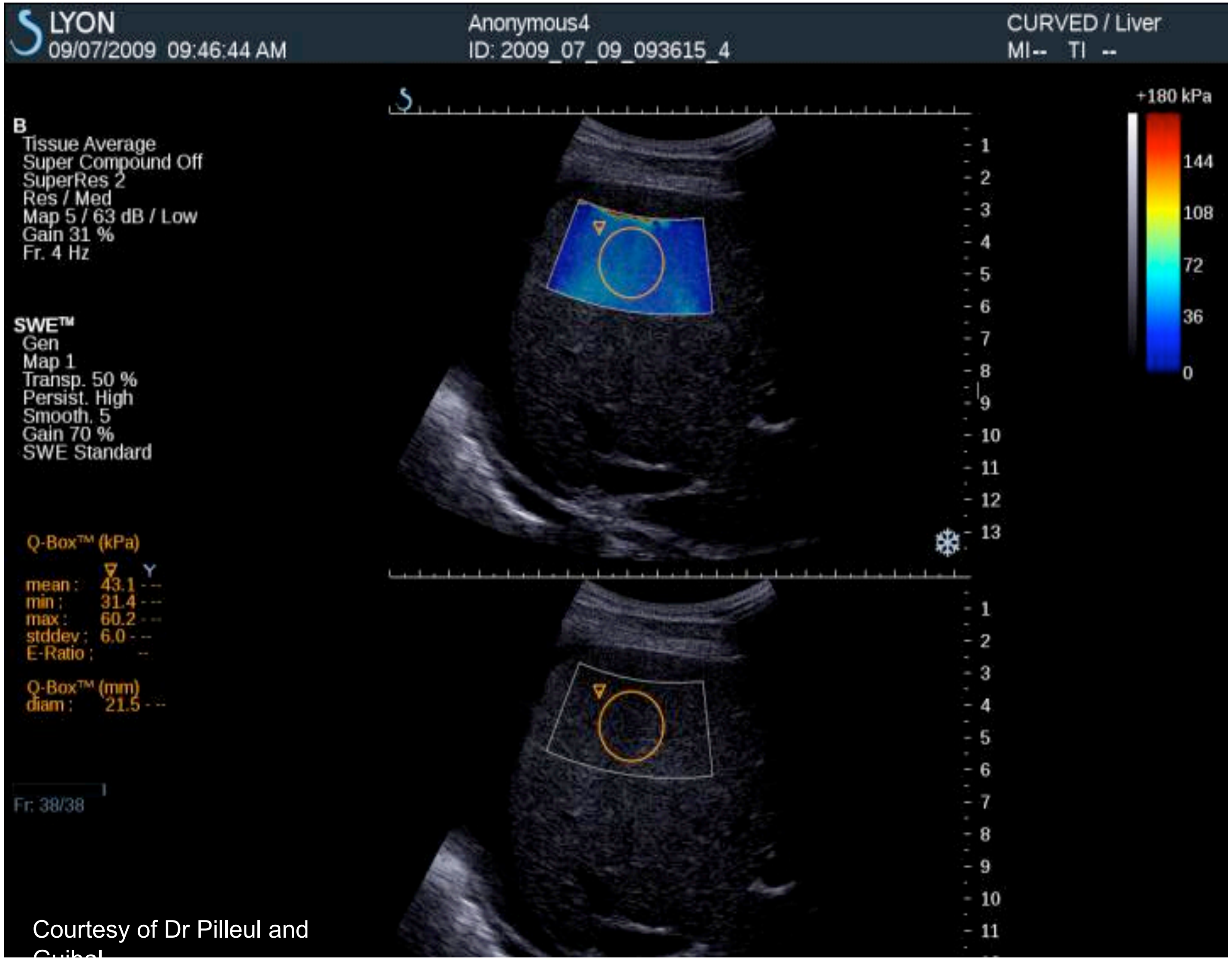


Courtesy of Dr Pilleul and Guibal

Clinical Case: Cirrhosis

- Pathology:
  - Tips
  - Cirrhosis

- Elasto:
  - Liver is hard: 43 kPa

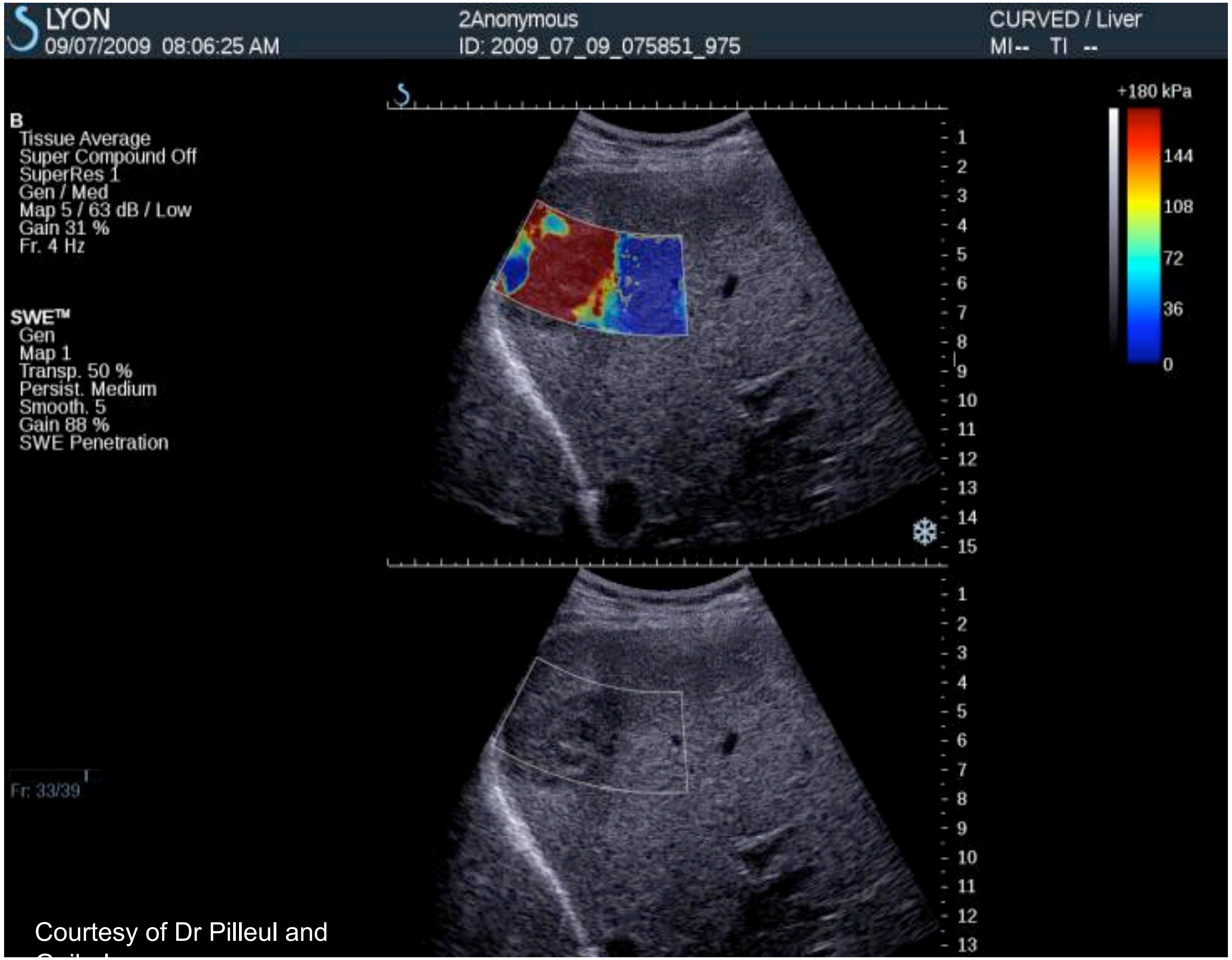


Courtesy of Dr Pilleul and Guibal

Clinical Case: very hard lesion

- <u>Pathology:</u>
  - Turberculosis
  - Hepatic lesion what kind ?

- <u>Elasto:</u>
  - Lesion is very hard.

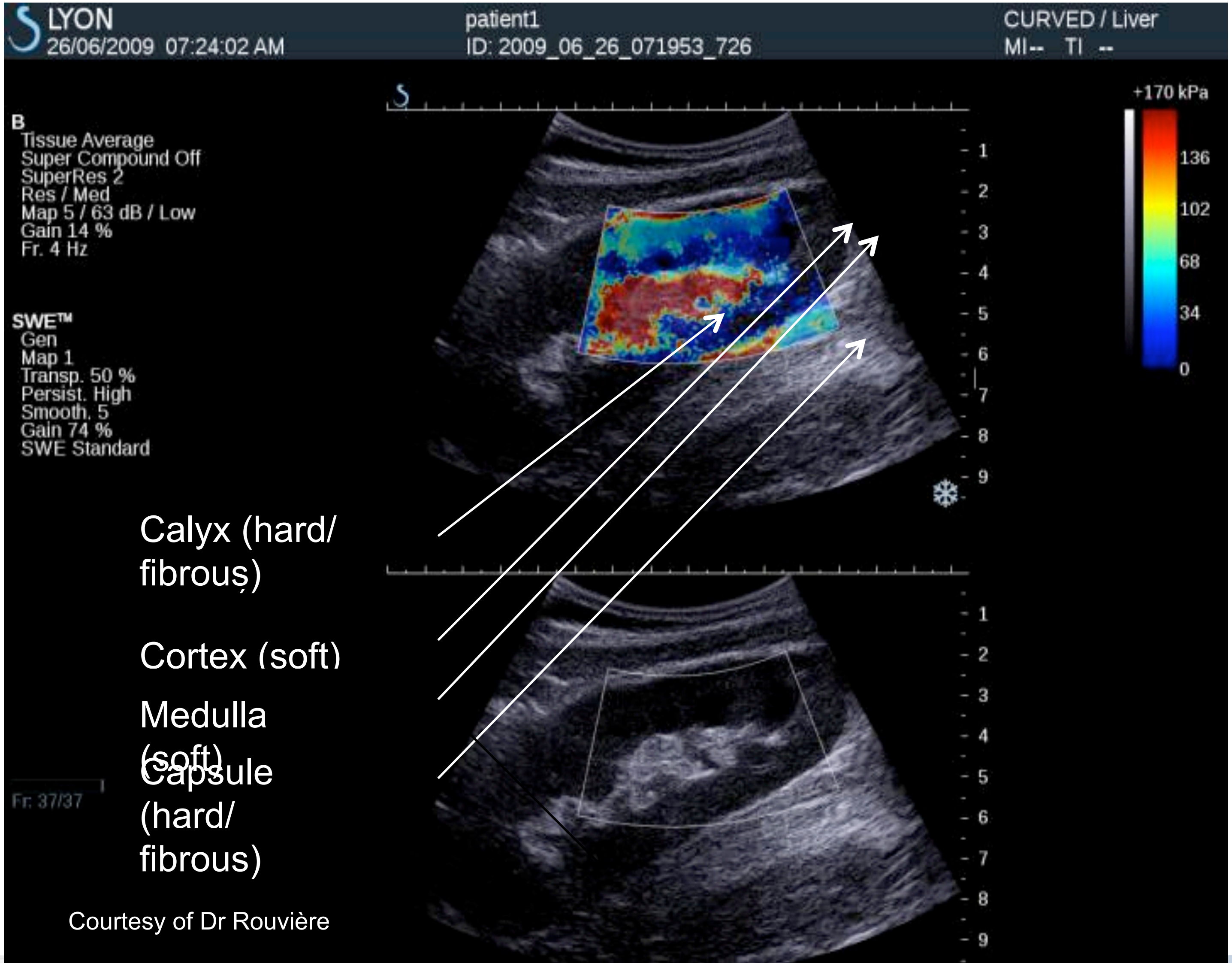


Courtesy of Dr Pilleul and

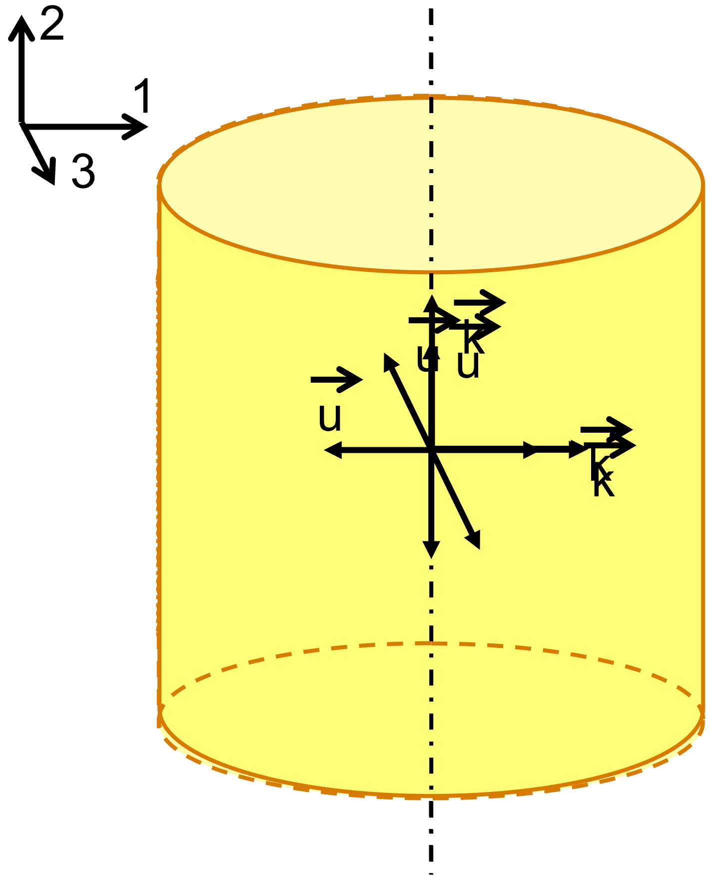
Clinical Case: Transplanted kidney

- Pathology:
  - Transplanted kidney

- Elasto:
  - Nice correlation with anatomy



Acoustoelasticity Theory



Murnaghan 1951
Hugues and Kelly, 1953

Isotropic media + uniaxial stress → Three plane shear waves

Isotropic media → One plane shear wave

$$\rho_0 c_S^2 = \mu$$

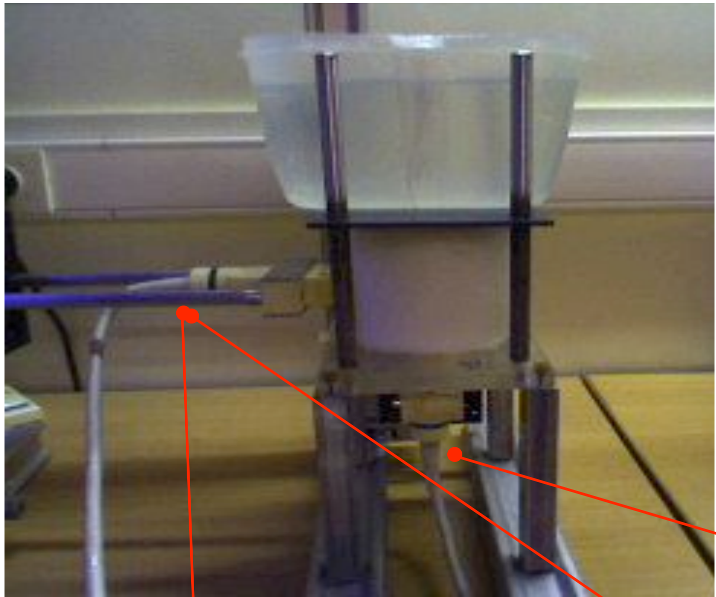
$$\rho_0 V_{S13}^2 = \mu + \sigma_{22}\left(1 + \frac{A}{6\mu}\right)$$

$$\rho_0 V_{S21}^2 = \mu - \sigma_{22}\left(\frac{A}{12\mu}\right)$$

$$\rho_0 V_{S12}^2 = \mu - \sigma_{22}\left(1 + \frac{A}{12\mu}\right)$$

A : Landau coefficient
(coming from the third order development
of the strain energy tensor)

Experimental setup



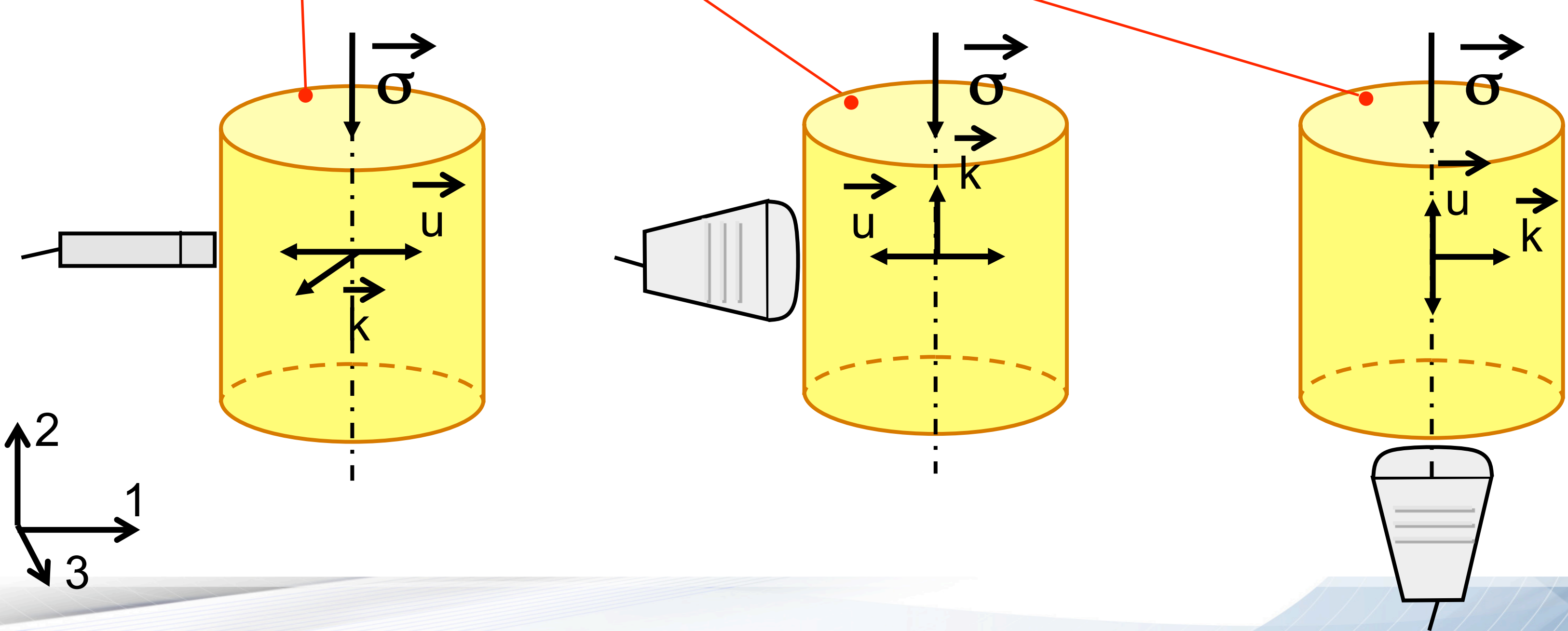
8 phantoms with different elasticities:

3 PVA phantoms:

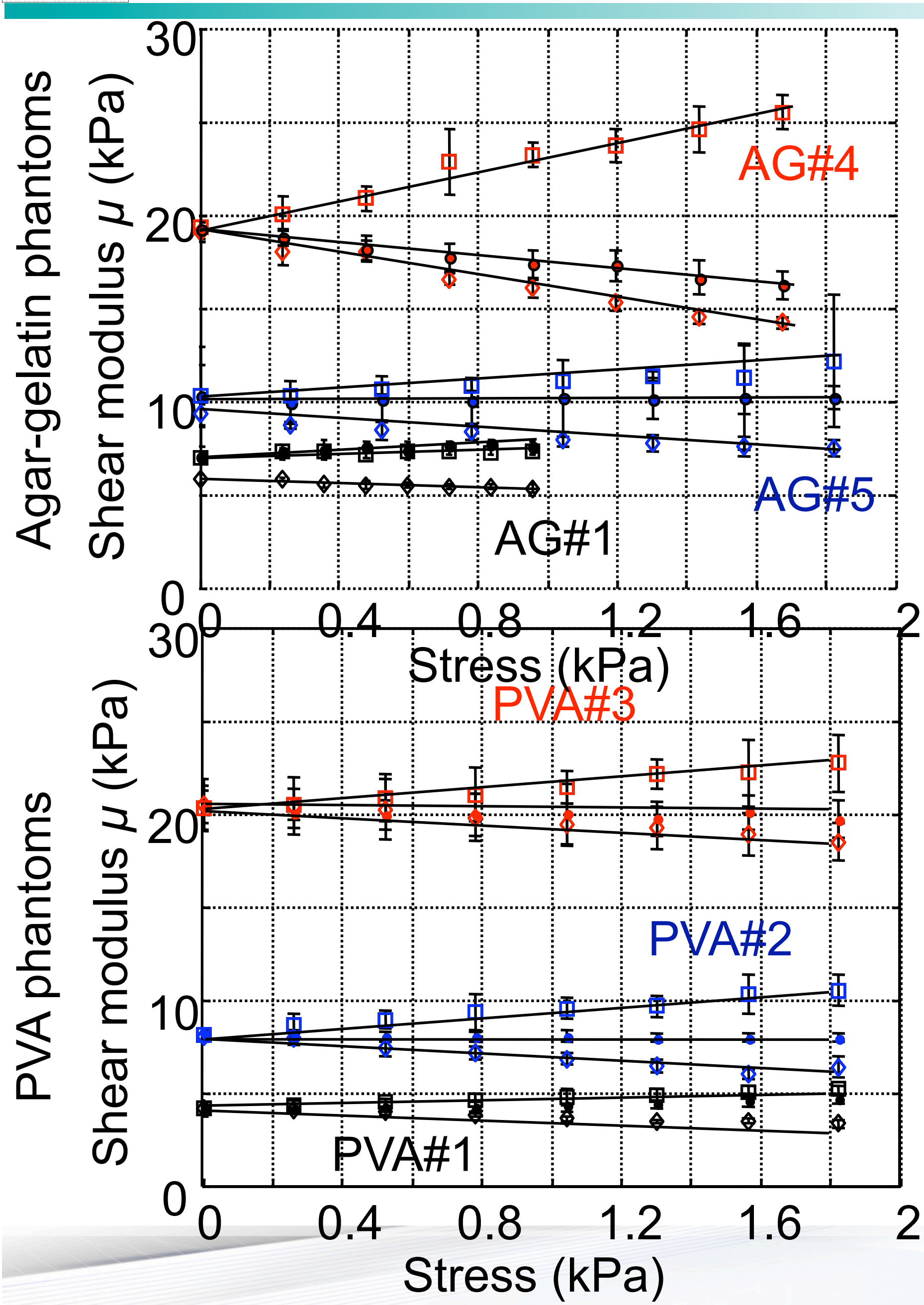
(2, 3 and 5 freezing-thawing cycles)

5 Agar-gelatin phantoms

(3% per volume of agar, 5%, 7%, 8.5%, 10% and 13% per volume of gelatin)



In vitro results



	Shear modulus μ	Nonlinear shear modulus A
AG#1	6.6 ± 0.6	-37.7 ± 9.8
AG#2	8.5 ± 0.8	-22.7 ± 2.5
AG#5	9.9 ± 0.5	-5.9 ± 1.2
AG#3	16.6 ± 0.1	101.4 ± 9.0
AG#4	19.2 ± 0.1	394.4 ± 77.2
PVA#1	4.1 ± 0.1	-17.5 ± 7.5
PVA#2	8.1 ± 0.1	11.0 ± 1.4
PVA#3	20.4 ± 0.1	43.6 ± 12.2

J.-L. Gennisson et al.