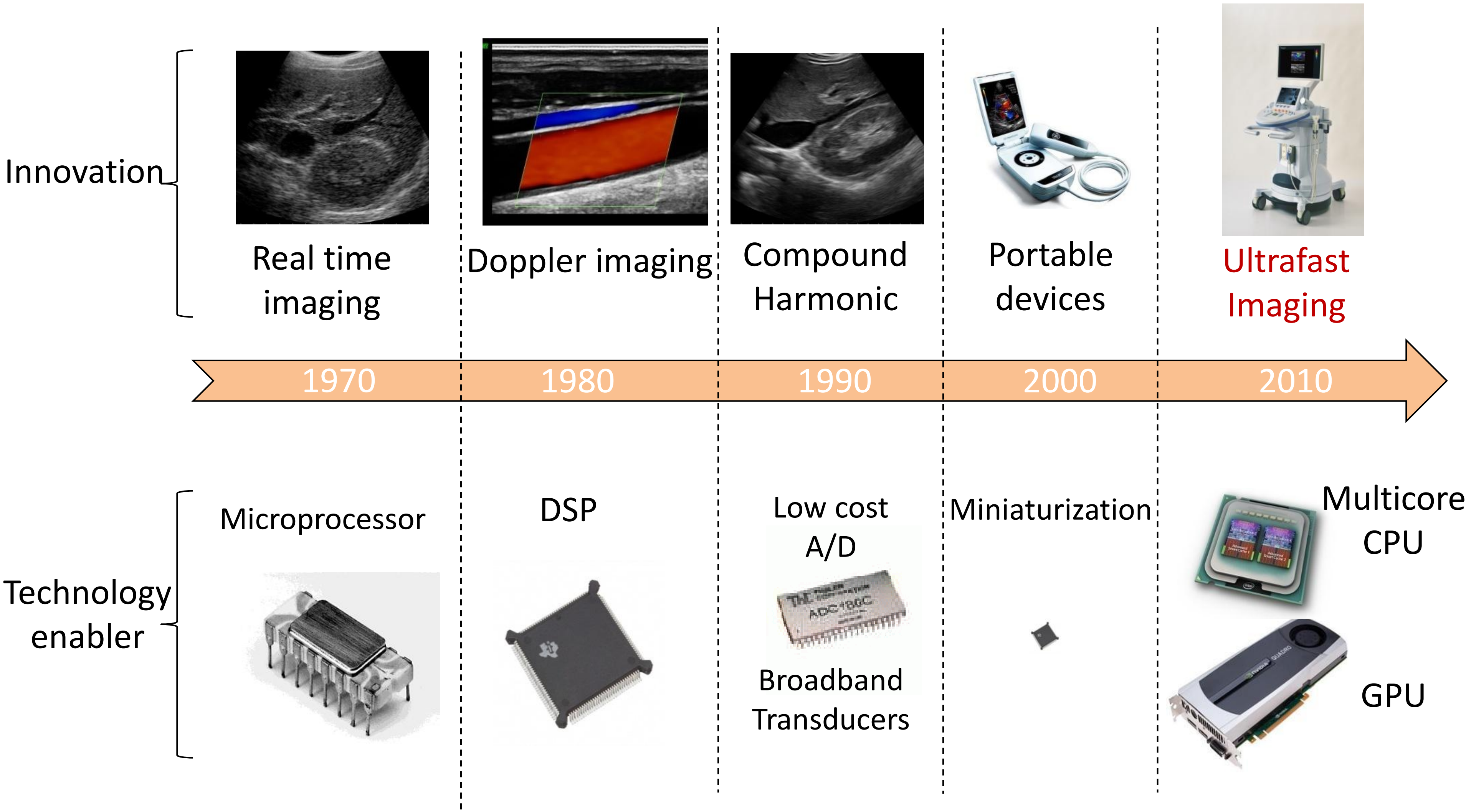
# Plane Wave Imaging and Applications for Ultrafast Doppler, Elastography, and Contrast

**Mathias Fink & Mickael Tanter**

**Short Course IEEE IUS, Dresden 2012**

# Ultrasound Technology Evolution



# How to obtain an ultrasonic image ?

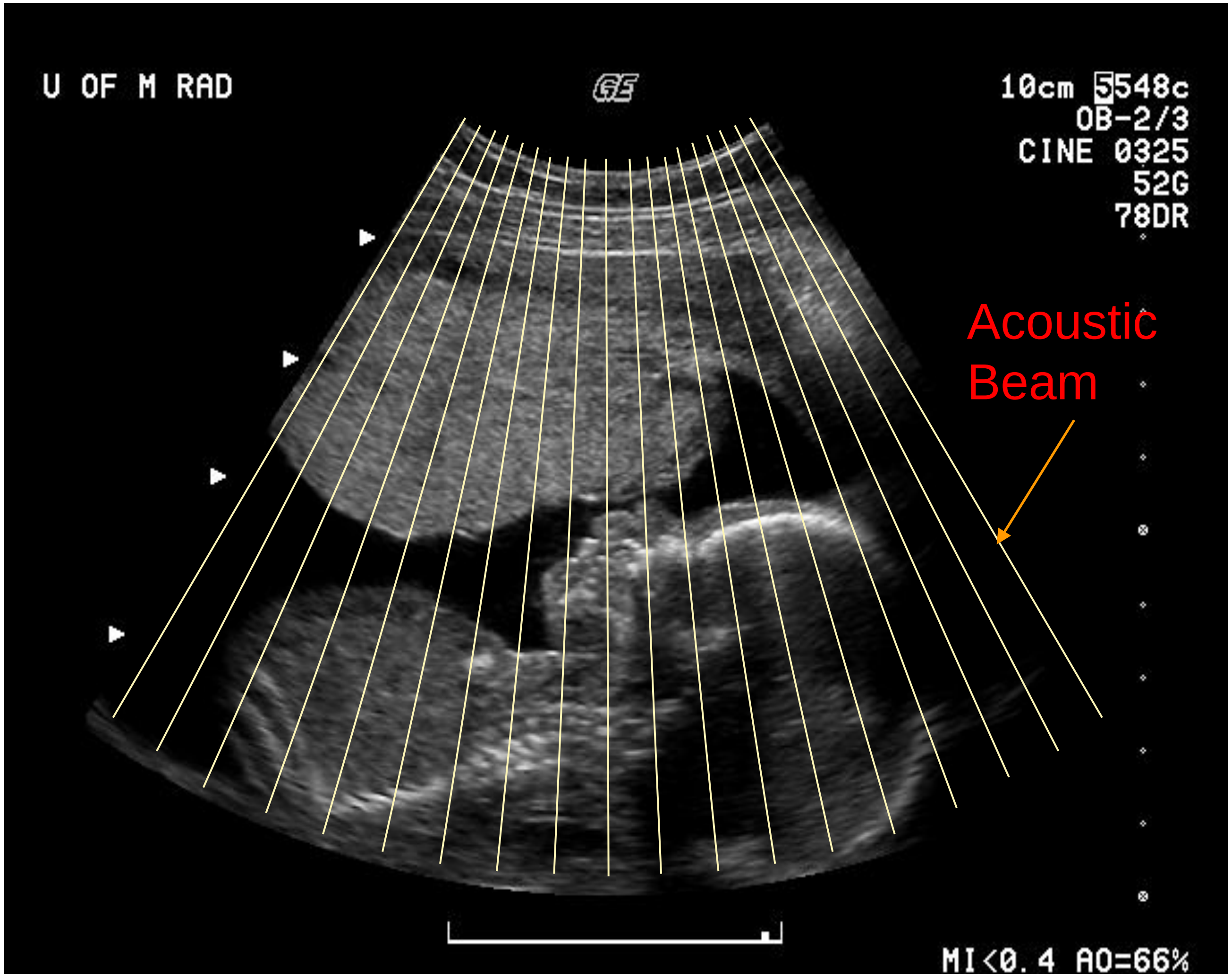
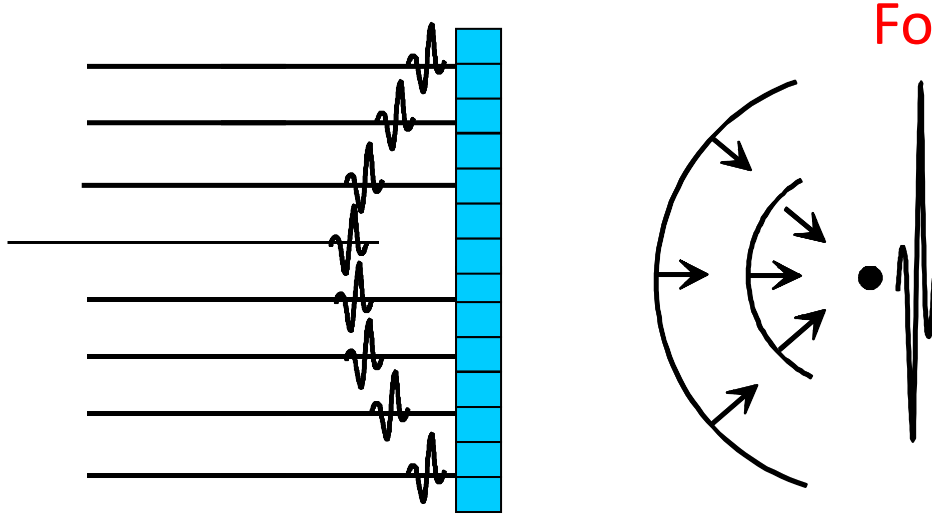


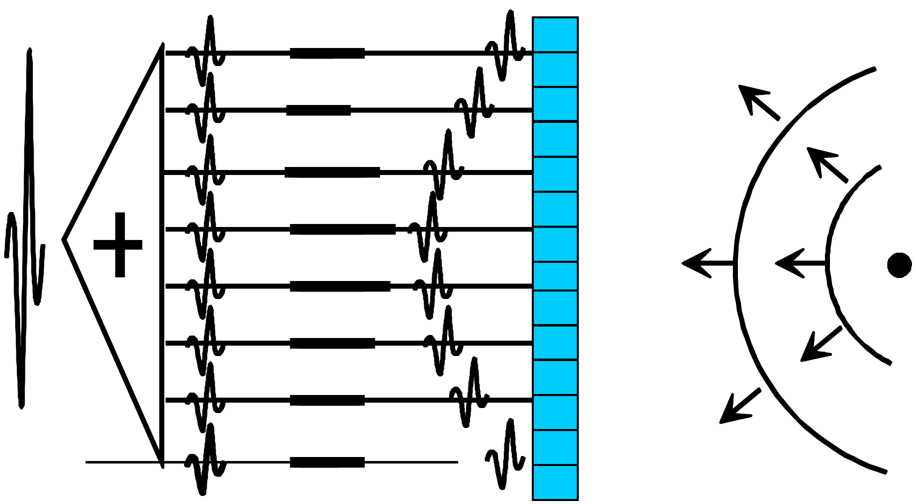

**Image formation using <u>sequential</u> transmit beams**

# Focusing in transmit/receive mode



Focusing in transmit

Ultrasonic speed uniform *c*

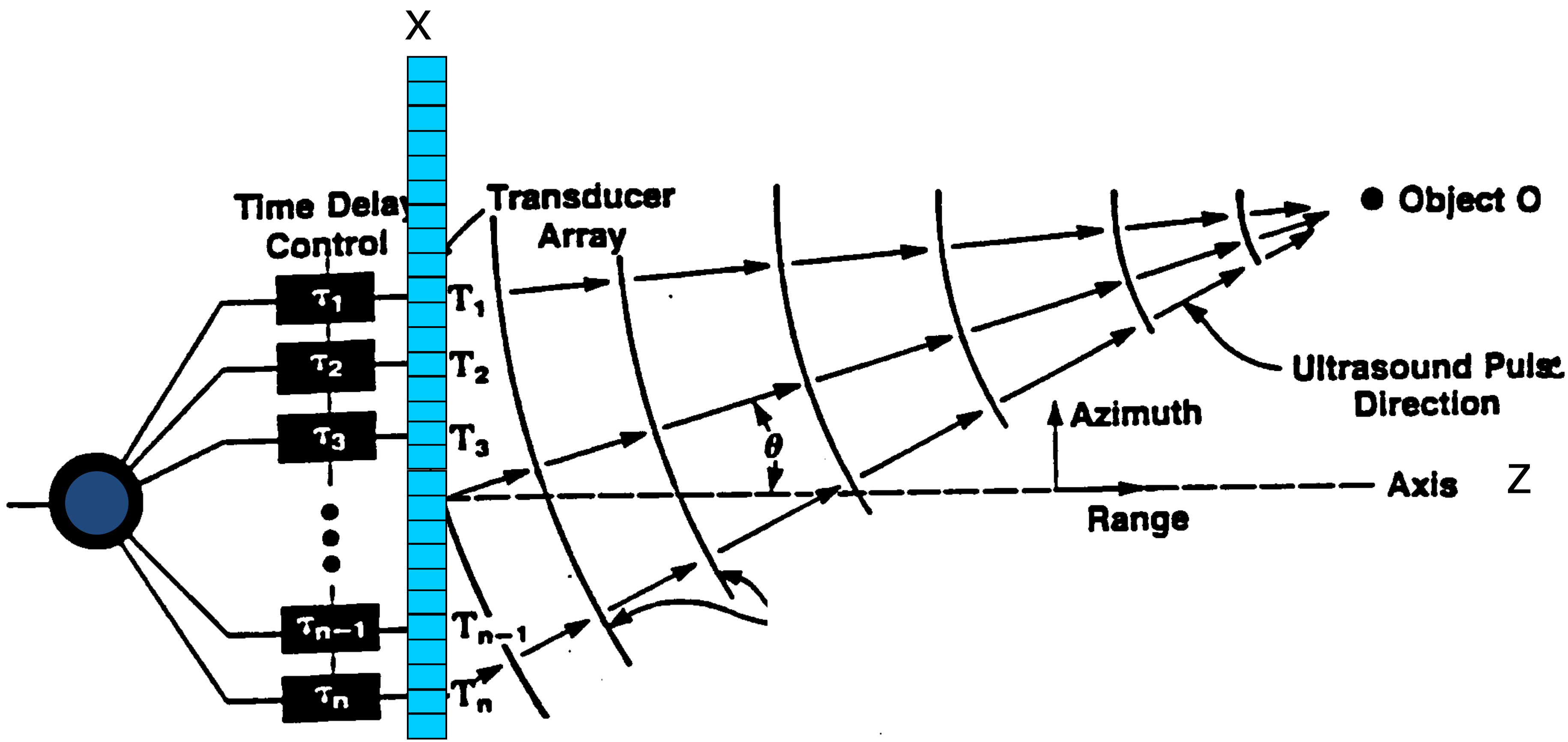


Focusing in receive

*Beamforming*

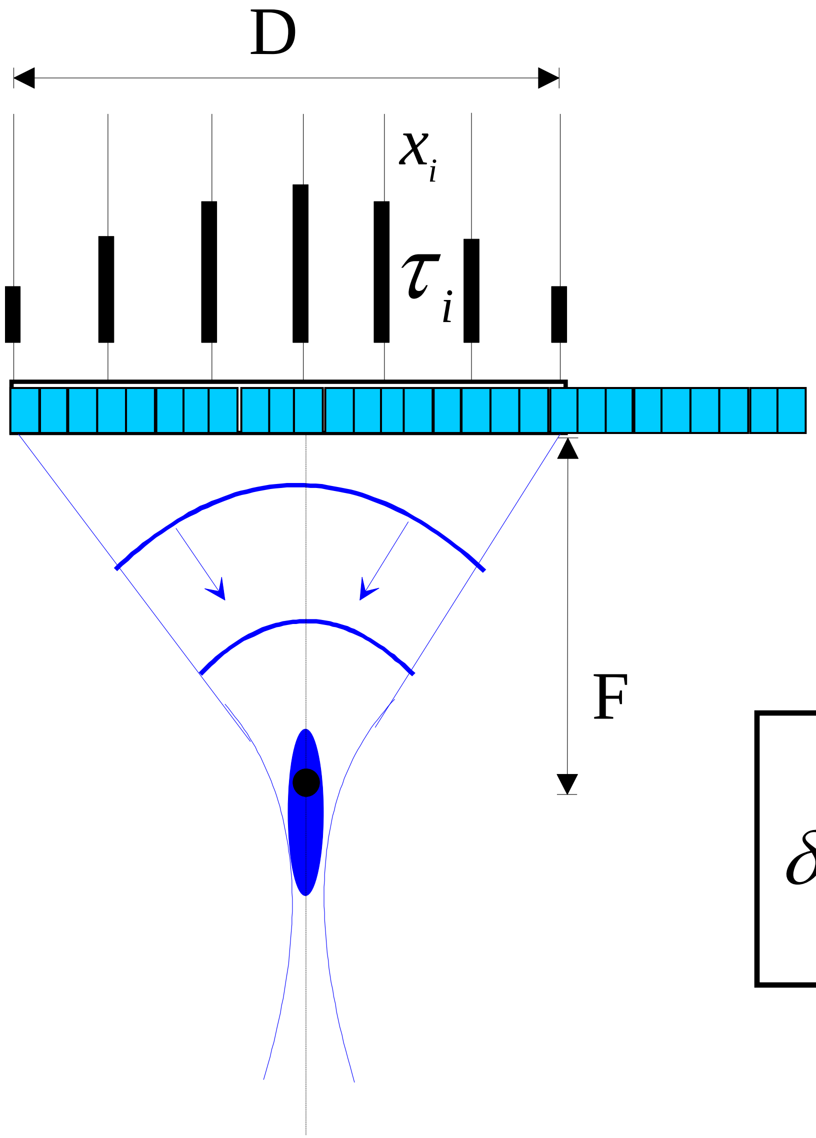
Double focusing

# Steering and Focusing




$$\tau\left(x_i, \sin\theta_m, z_n\right) = \frac{-x_i \sin\theta_m}{c} + \frac{x_i^{\,2}\cos^2\theta_m}{2 z_n c}$$

# Focal spot dimension in transmit mode



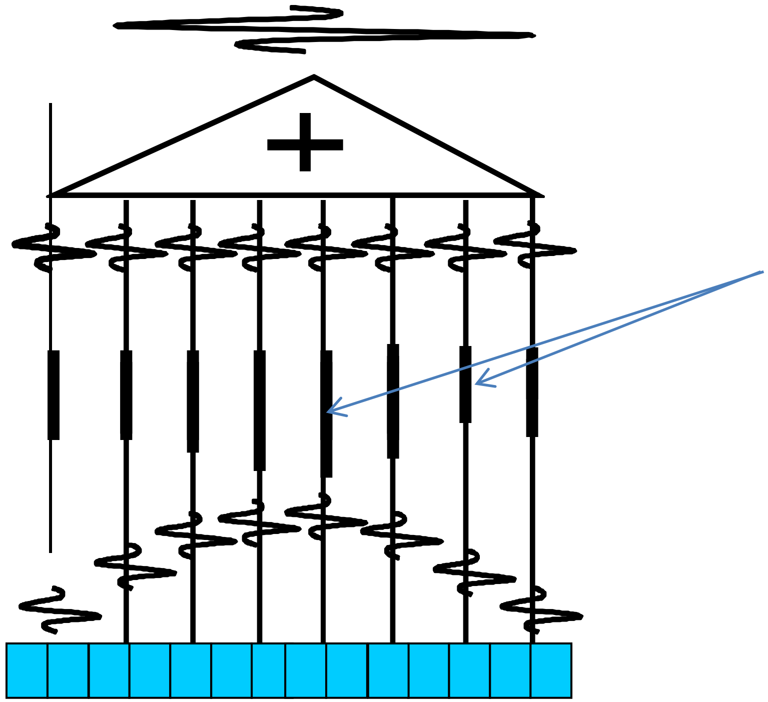

$$\tau_i = \frac{\sqrt{F^2 + (x_i - x)^2}}{c_0}$$

$$\delta_l = \frac{\lambda F}{D} \qquad \delta_a = 7\lambda\left(\frac{F}{D}\right)^2$$

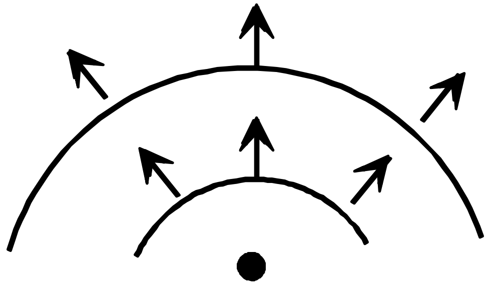
# Transmit Beam Forming

- Time Delay Accuracy – typically $\lambda/32$
- Aperture Control – determined by format
- Apodization – primarily for depth of field
- Fixed focus – multiple zone / frame rate

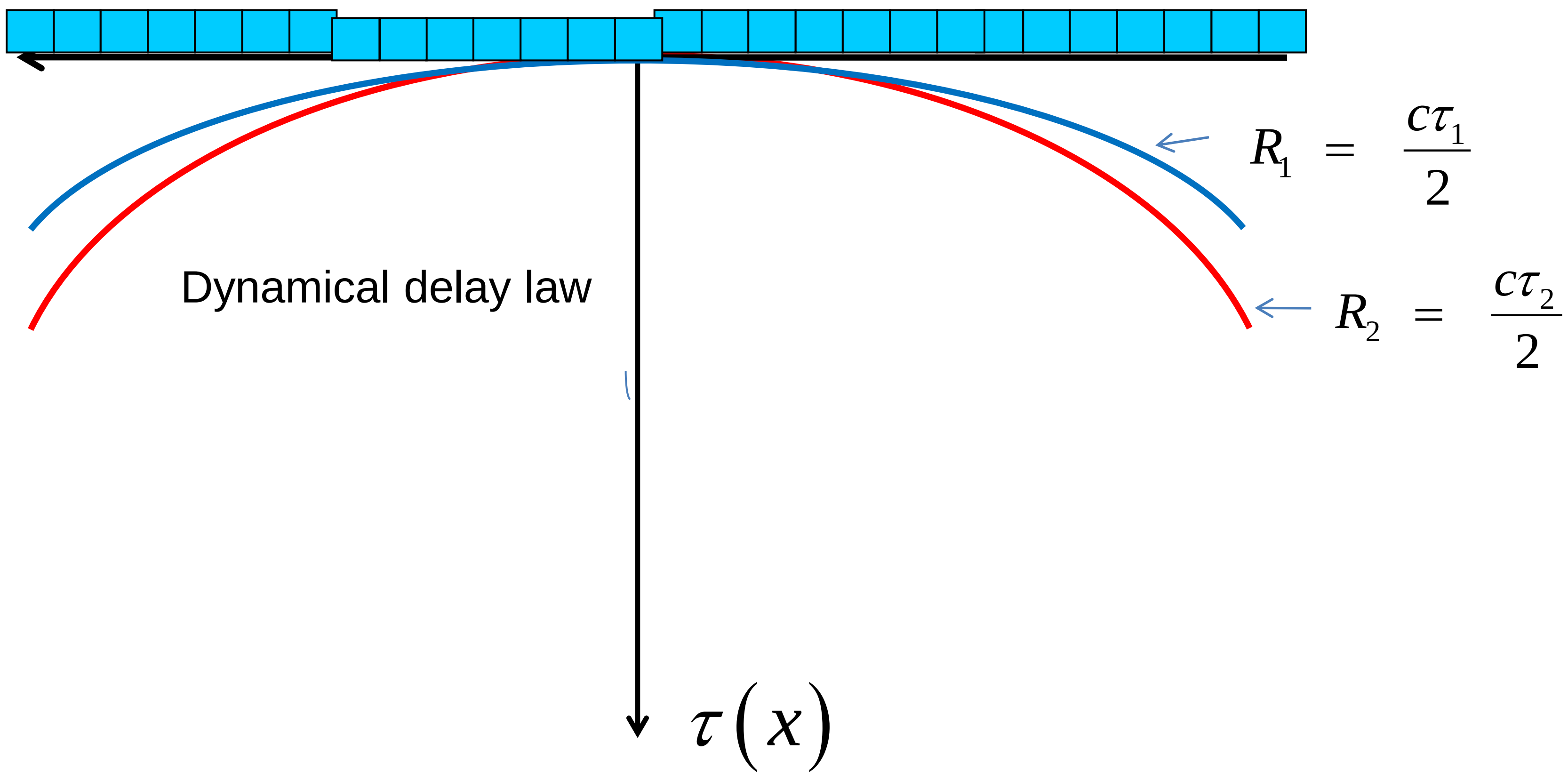
# Beam Forming in Receive Mode




$$\tau_i = \frac{\sqrt{F^2 + (x_i - x)^2}}{c_0}$$

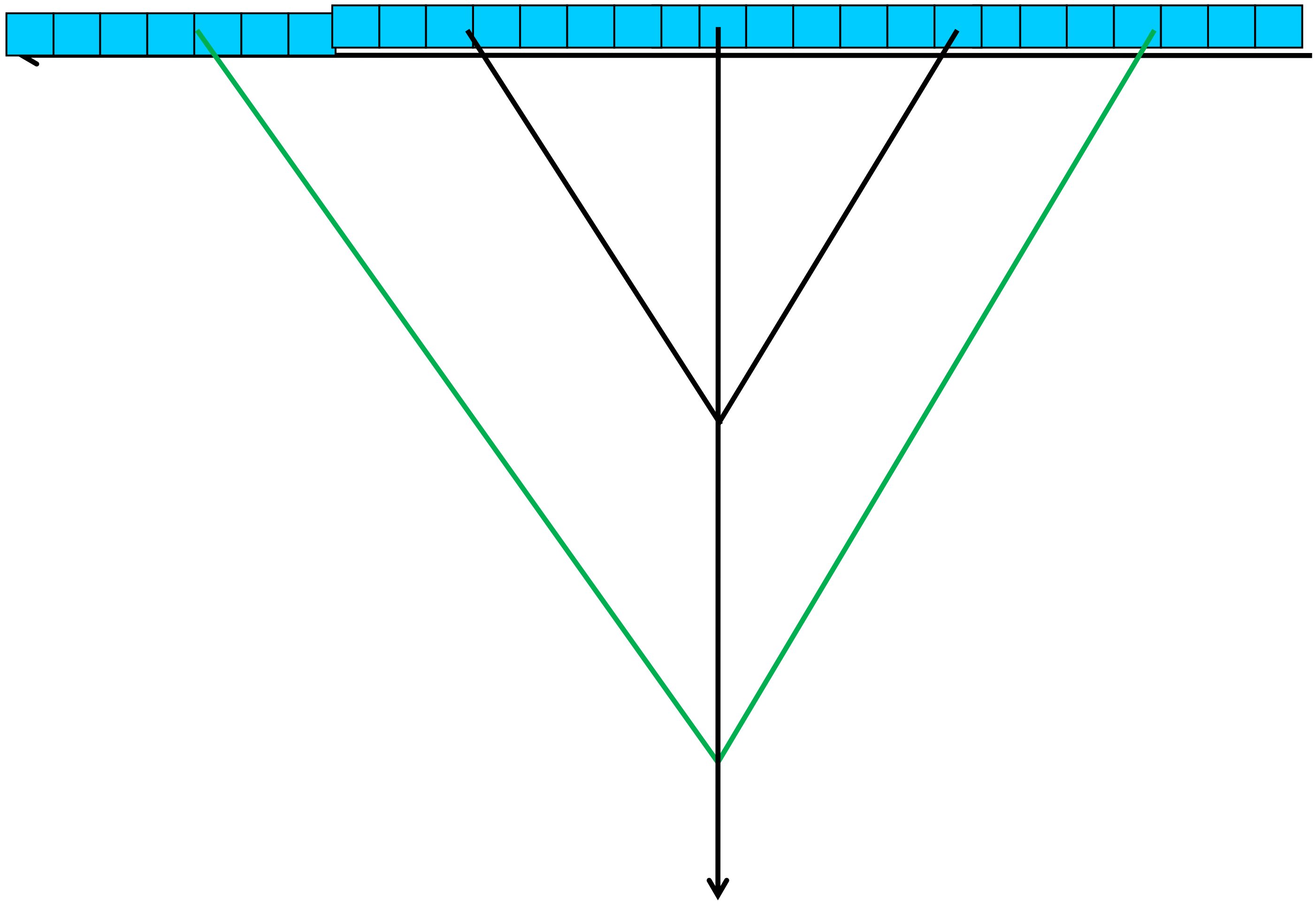


# In receive mode, Dynamical Focusing with variable focal depth



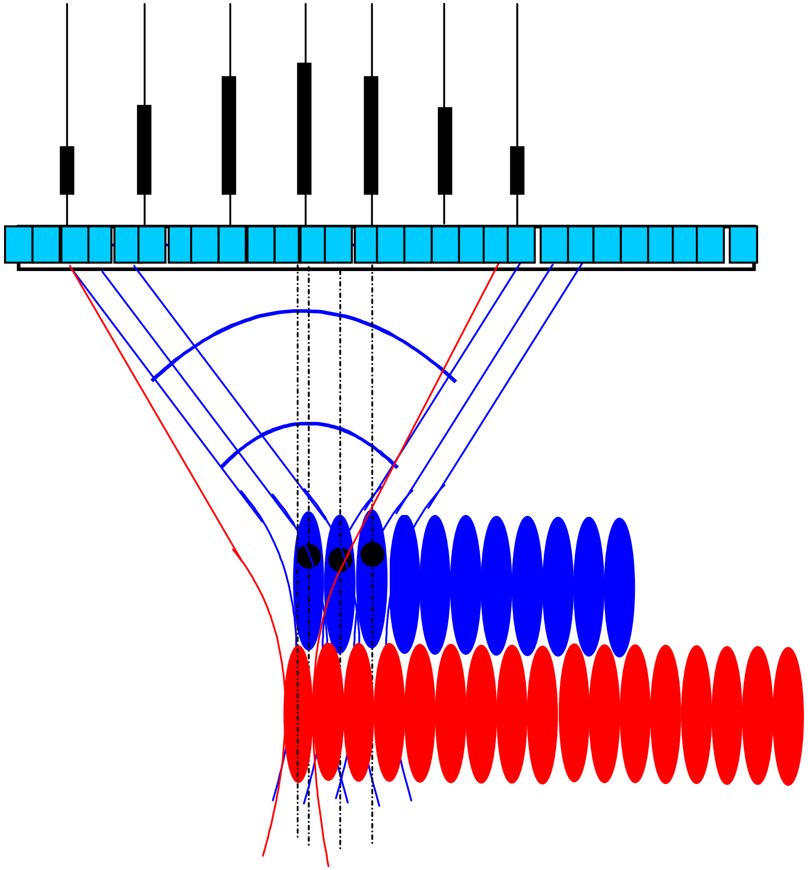

The focal depth is varying continuously with the time of arrival of the echoes

# Dynamical Apodization



To get the same spatial resolution at all the depths
F/D must stay constant  on the whole depth of exploration

# Frame Rate with Sequential Imaging



**Typically, to get an image :**
128 shots x 4 focal depths
= 512 ultrasonic shots

**Time of flight – two ways:**
60 µs for 5 cm

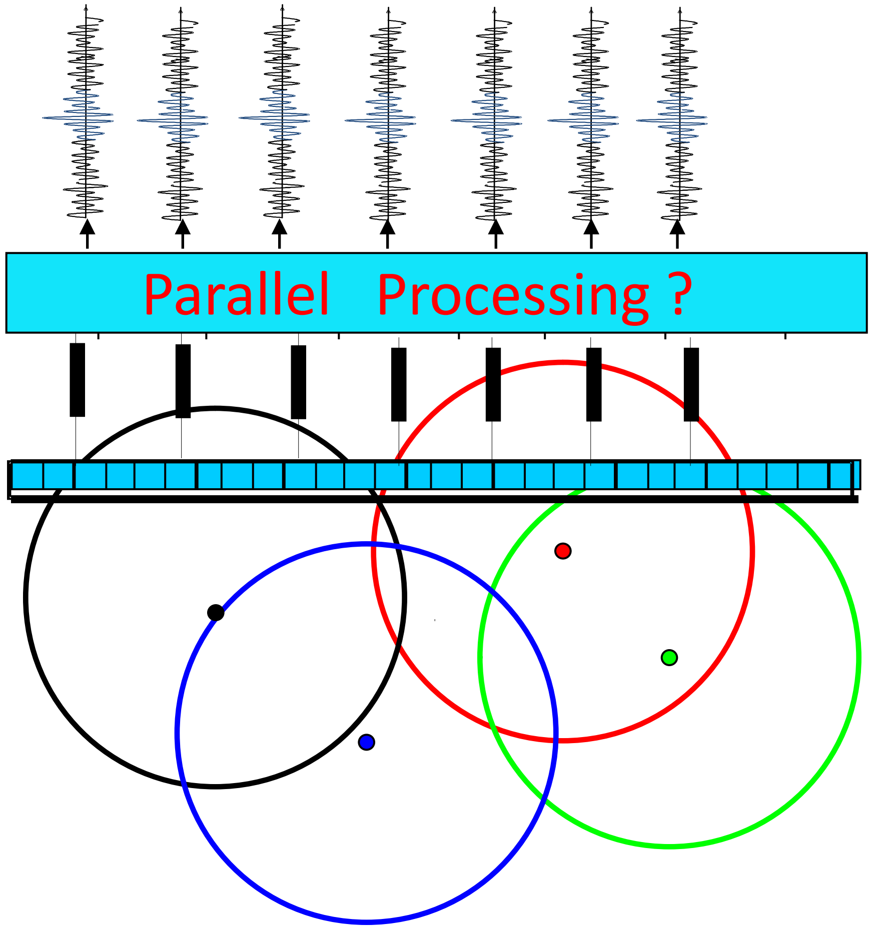
**Time to get a full image:**
512 x 60 µs = 0,032 s
**Frame rate:**
1/0,032 = 35 frames/ second

**25 to 50 frames/sec**

# How to go faster ?

Replace the focused transmit beams by one unfocused transmited beam that illuminated the whole field of view

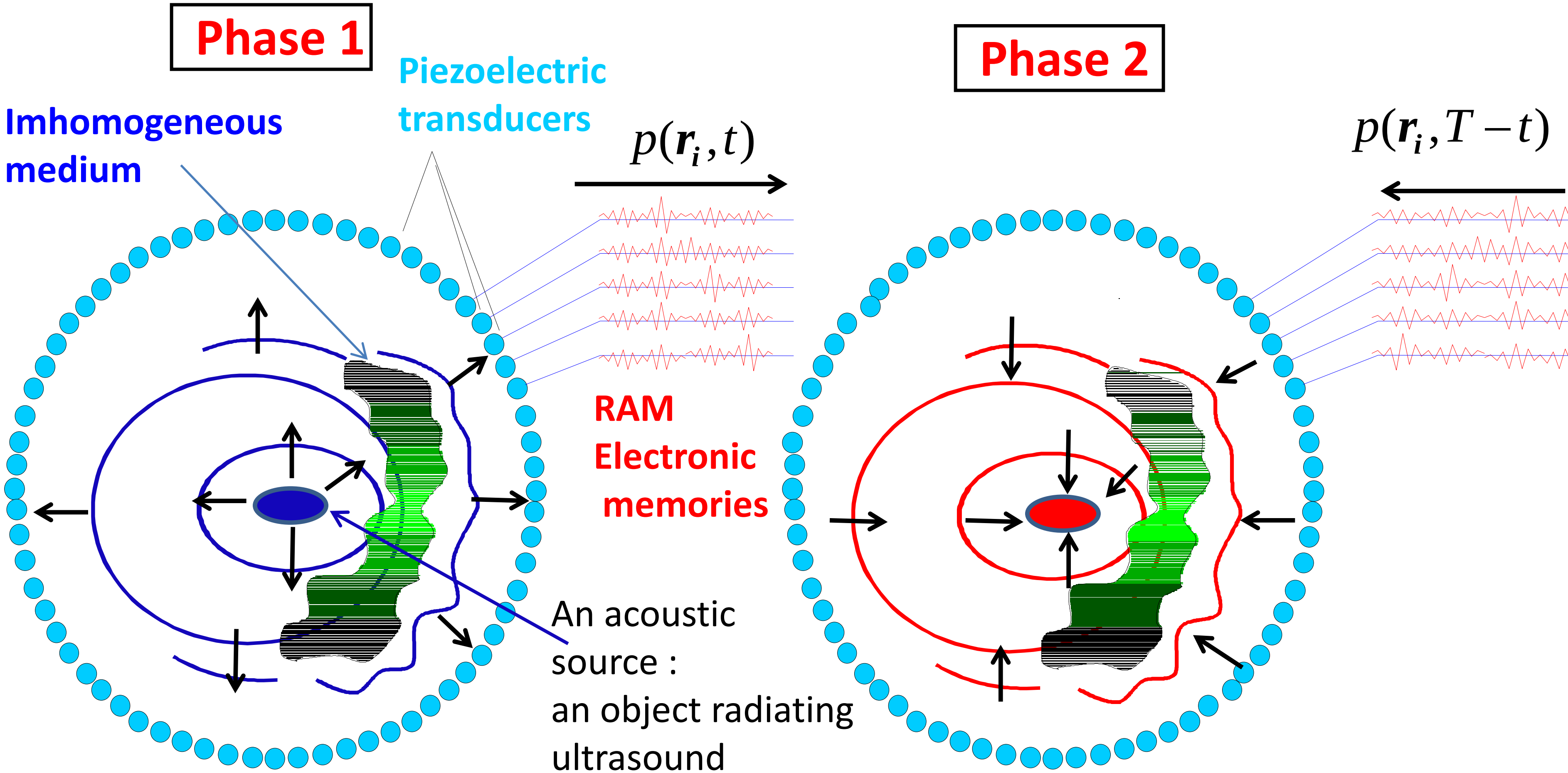
# Ultrafast Imaging



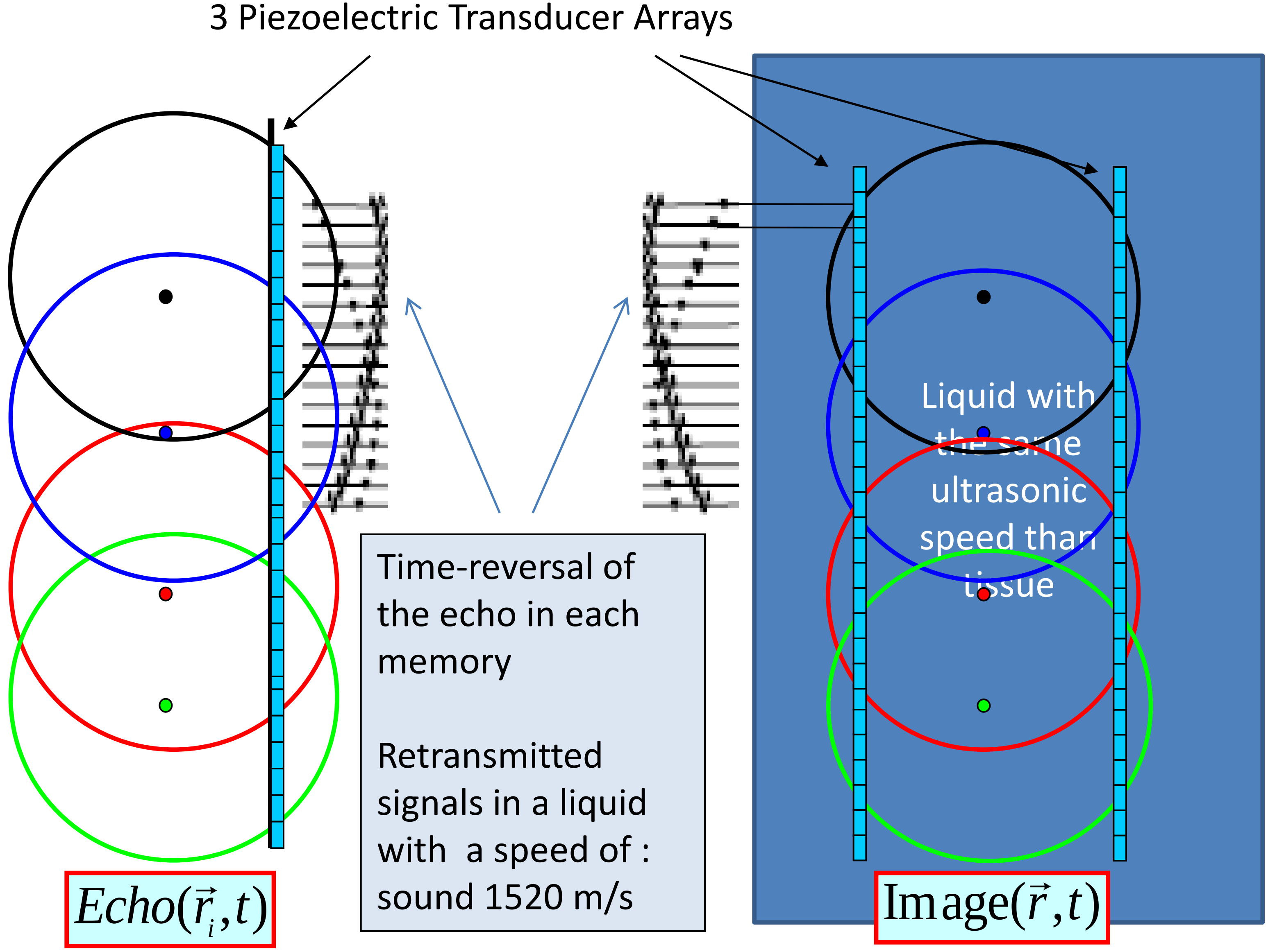

Plane Wave Insonification

One shot : One image

# The Time-Reversal approach : An elegant way to build the Acoustic Image of any source radiating ultrasound



# Ultrafast Imaging with Time-Reversal




Time-reversal of the echo in each memory

Retransmitted signals in a liquid with a speed of : sound 1520 m/s

*M. Fink,* "L'imagerie ultrasonore« , *Revue de Physique Appliquée*, **18**, **1983**, p.527-556

# The Dynamic Electronic Lens Approach

446

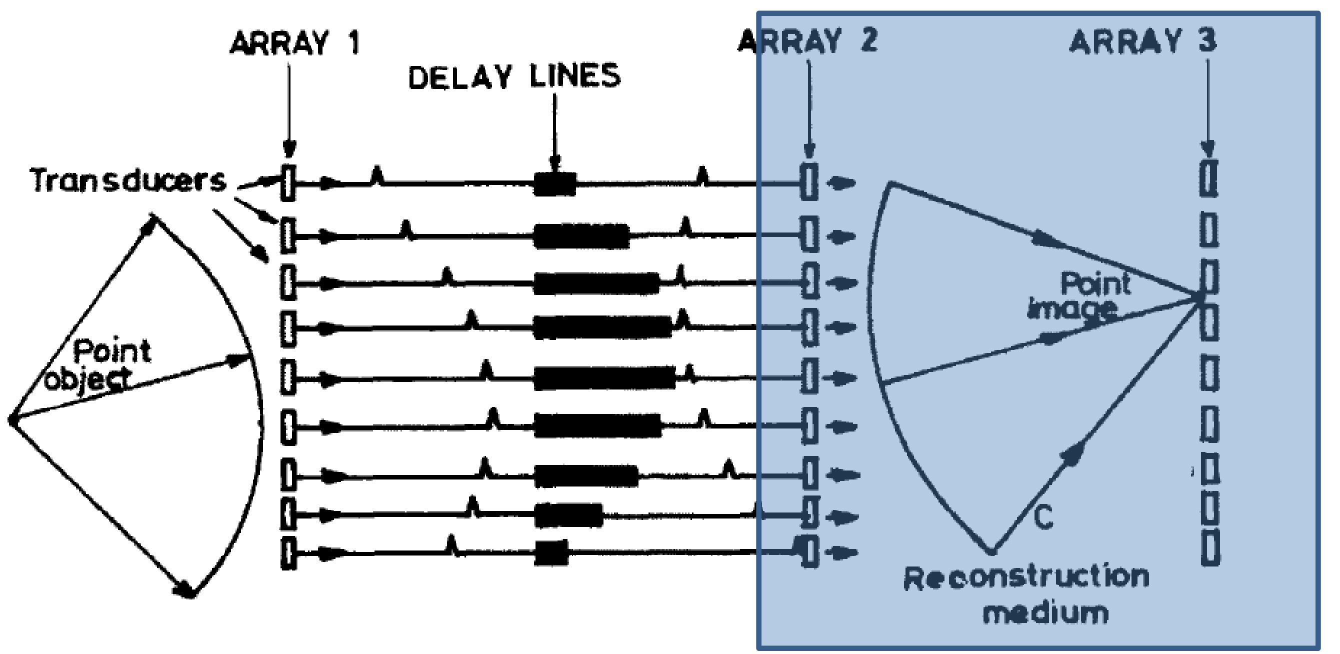


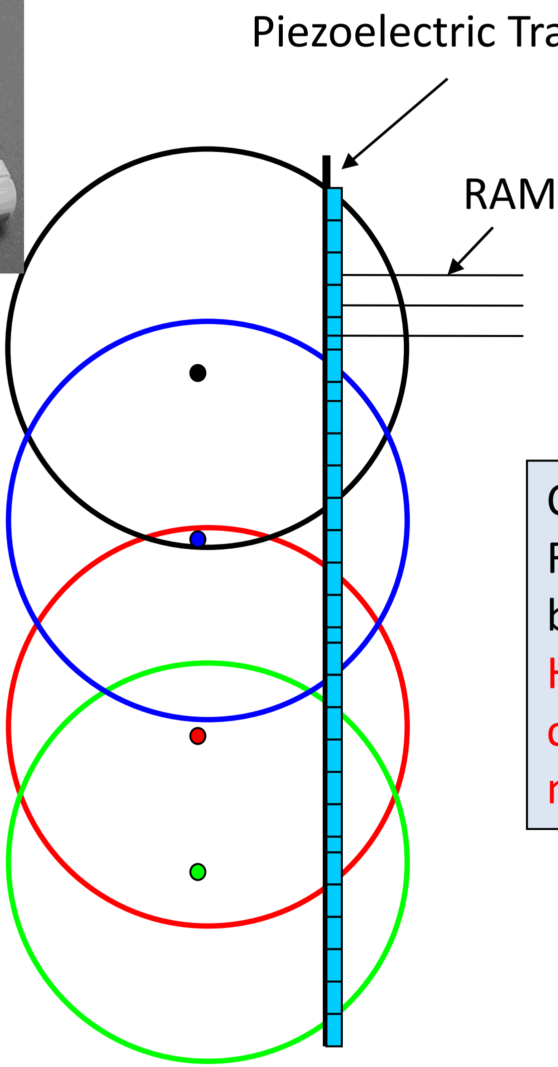

Fig. 3 - Electronic lens with delay lines and 2 transducers arrays,

$$\frac{1}{f} = \frac{1}{z} - \frac{1}{z'} = \frac{2\,z' - ct}{ctz'} . \qquad (4)$$

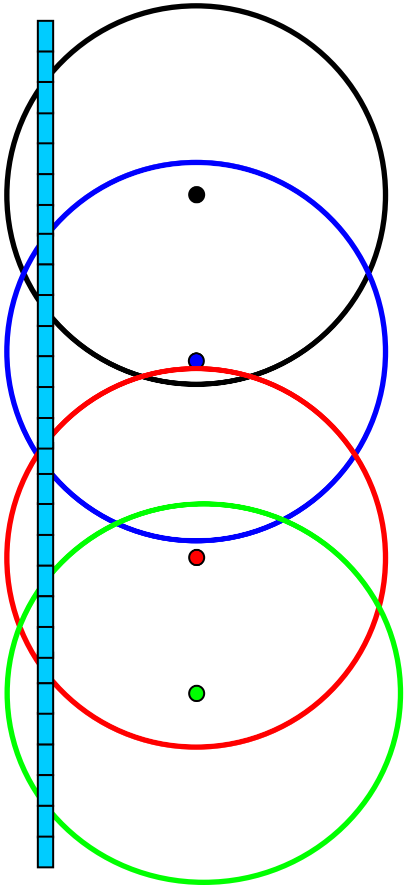
$$\Delta\tau(x_n, t) = \frac{-\,x_n^2}{2\,cf} = \frac{-\,x_n^2}{c^2}\left(\frac{1}{t}\right) + \frac{x_n^2}{2\,cz'} \qquad (5)$$

*M. Fink "Principles and techniques of acoustical imaging" , Imaging processes and coherence in physics"Springer, Lecture Notes in Physics,* ***1979****, p 438-452*

# The Computed Time-Reversal Approach




Computed Time Reversal and backpropagation
Hypothesis:
c uniform: 1520 m/s

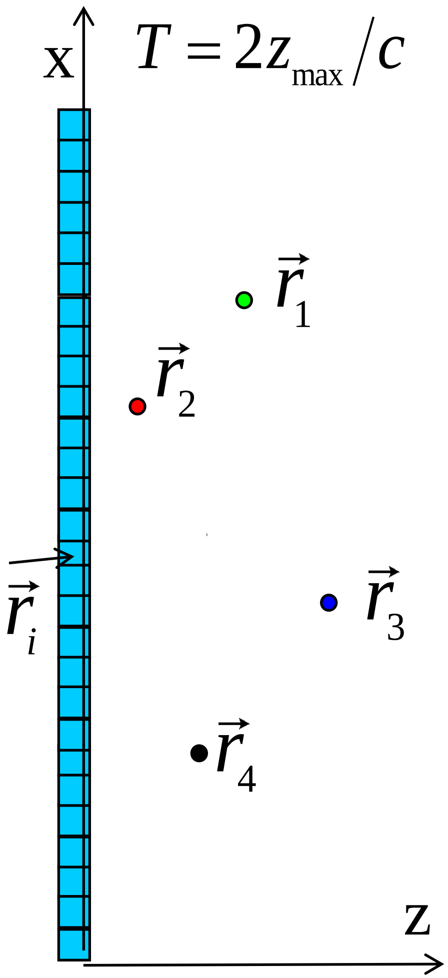


$Echo(\vec{r}_i, t)$

$\mathrm{Image}(\vec{r}, t)$

# Echoes and Images

$$Echo_i(t) = \begin{cases} \sum_n \alpha_n e(\vec{r}_i - \vec{r}_n; t - \tau_{ni}) & t \geq 0 \\ 0 & t < 0 \end{cases}$$




with $\tau_{ni} = \left\{ z_n + \sqrt{z_n^2 + (x_i - x_n)^2} \right\} / c$

## Time-reversal Imaging

$$\mathrm{Image}(\vec{r},t) = \sum_i Echo_i(T-t) \otimes G_0(\vec{r} - \vec{r}_i; t) \qquad \vec{r} = \{x, z\}$$

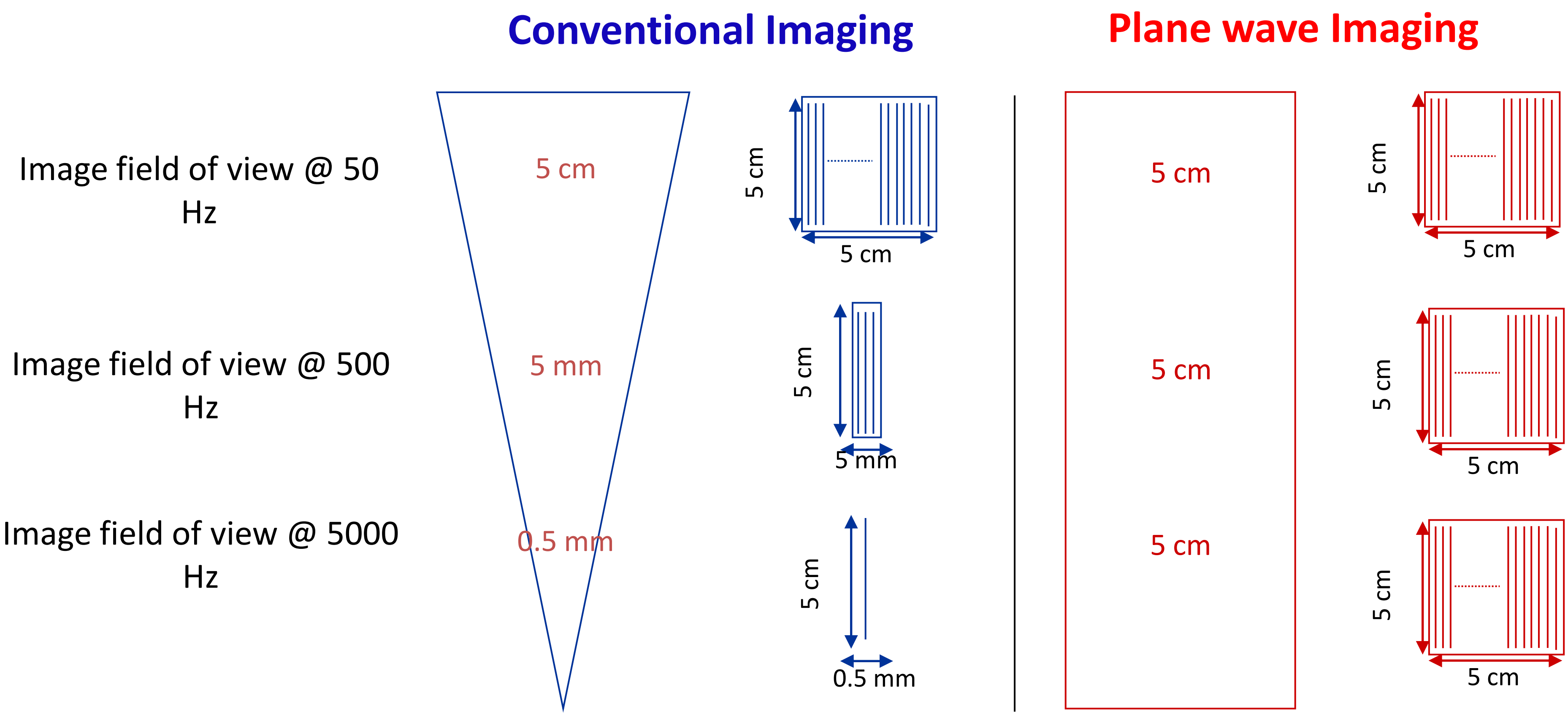
with $G_0(\vec{r};t) = \delta(t - |\vec{r}|/c) / 4\pi|\vec{r}|$ the Green's function

$$IMAGE(\vec{r}) = \mathrm{Image}(\vec{r}, t = z/c)$$

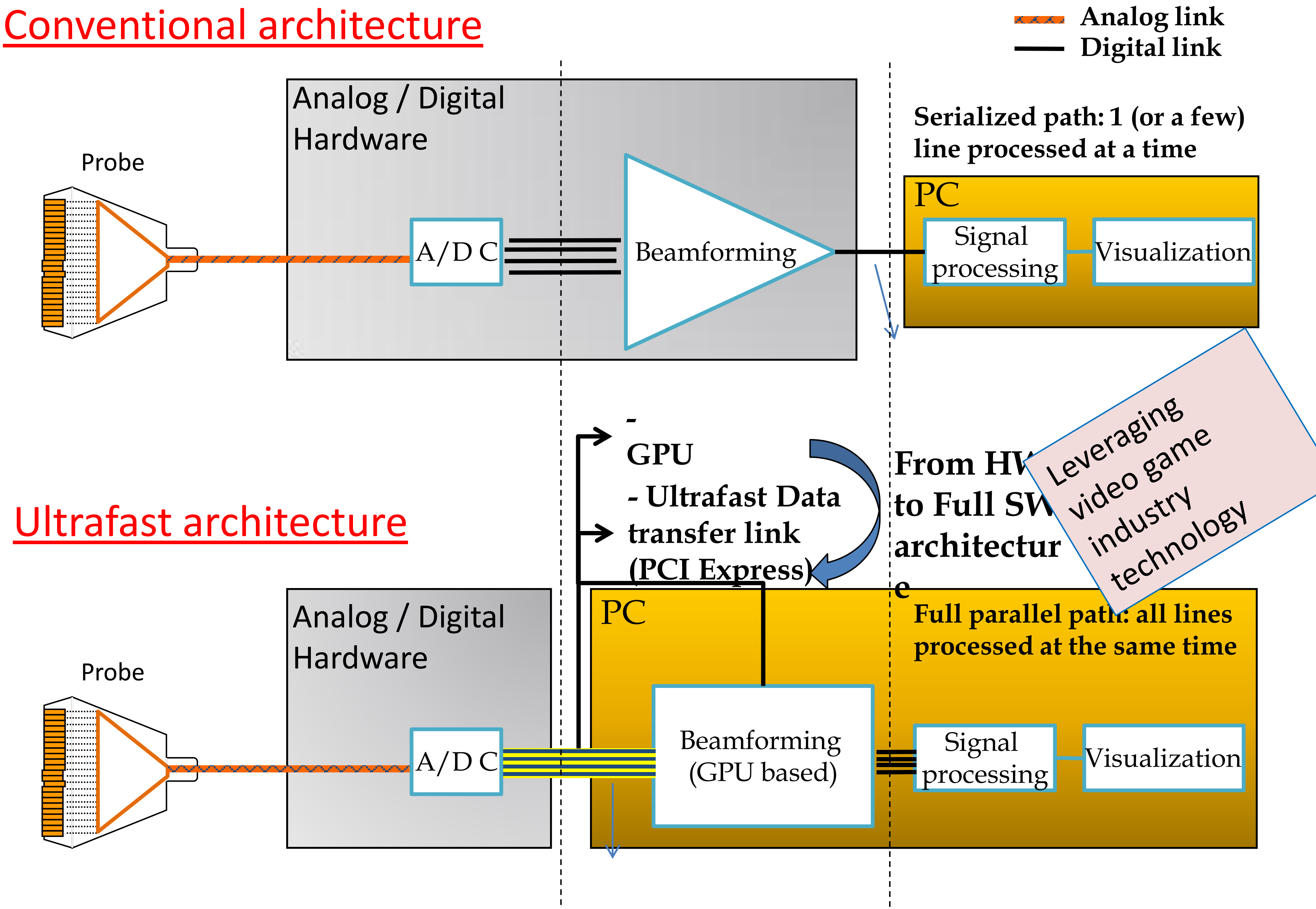
## Parallel beam forming

$$\mathrm{Image}(\vec{r}, T-t) = \sum_i Echo_i(t) \otimes \delta(T - t - |\vec{r} - \vec{r}_i|/c)$$

# Conventional Imaging / Ultrafast Imaging



# System Architecture



# The Ancestors: A 20 transducers array For Ultrafast Imaging

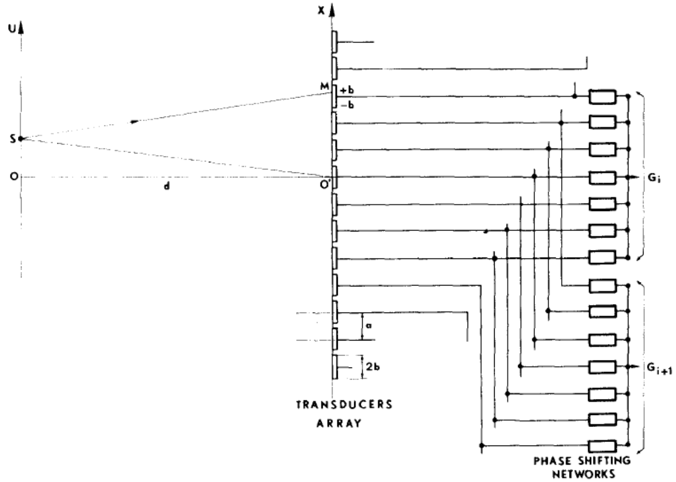



FIG. 1. Receiving array and transducers groups connections.

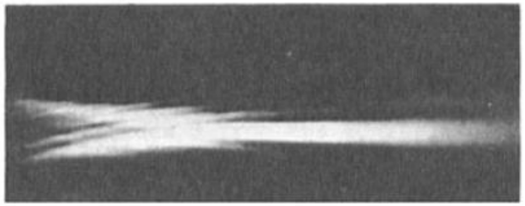


Fig. 3 : Reconstructed acoustical field distribution

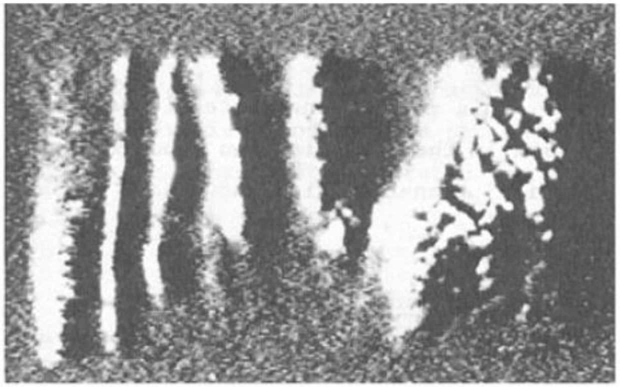


Fig. 4 : Image of the heart


*B. Delannoy, R. Torguet, C. Bruneel, E: Bridoux, J. M. Rouvaen, and H. Lasotaa Acoustical image reconstruction in parallel-processing analog electronic systems, J, Appl, Phys, 50(5), May 1979, 3153*

*B. Delannoy, R. Torguet, C. Bruneel, and E. Bridoux, **Ultrafast** electronical image reconstruction device, in Echocardiography, edited by C.T. Lancee (Nijhoff, The Hague, 1979), Vol.1, Chap. 3, pp. 447–450. 1273–1282 (1984).*

# The Explososcan

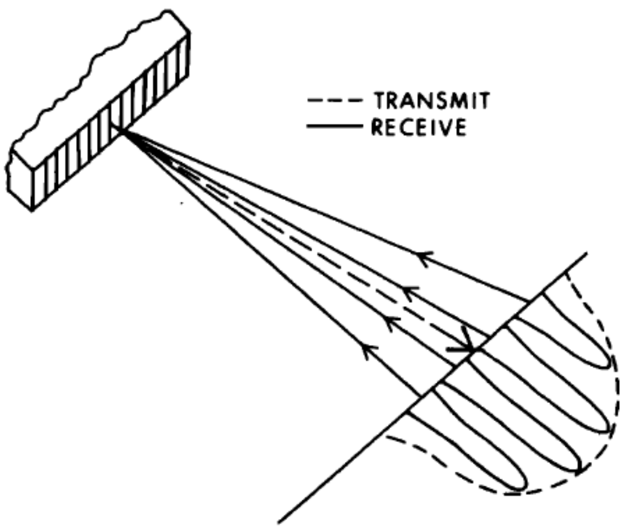



FIG. 1. The Explososcan concept. For each oriented acoustic transmit burst, dashed line, information in four individual receive directions, solid lines, about the transmit direction is acquired simultaneously. Transmit beam response, dashed curve, extends beyond the four receive beam responses, solid curves.

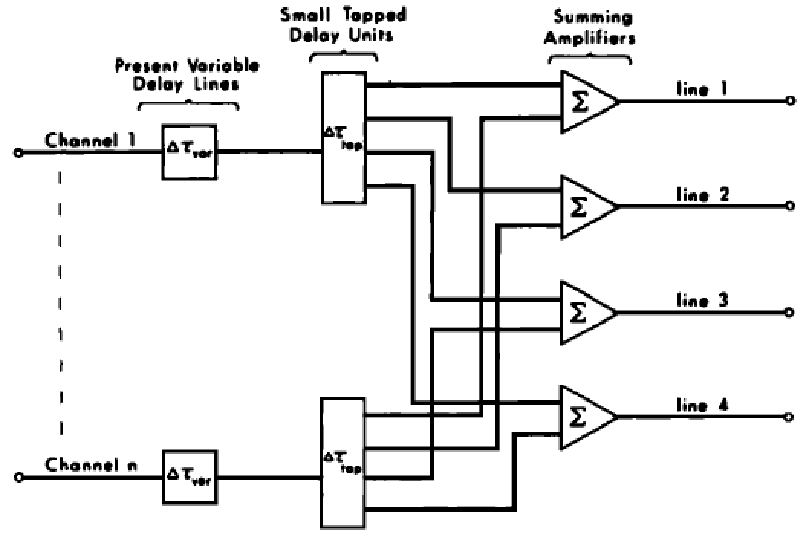



FIG. 6. Schematic of receiver delay processing to achieve four to one parallelism in receive. Note that $\Delta\tau_{tap}$ and the four summing amplifiers are the additional processing circuitry which was connected to the conventional phased array system.

1274 J. Acoust. Soc. Am., Vol. 75, No. 4, April 1984

*D. Shattuck, M. Weinshenker, S. Smith, O. von Ramm, 1984*

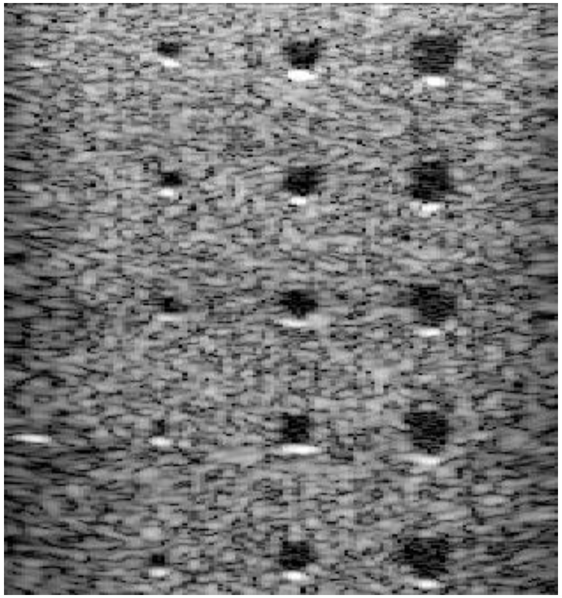
# Image Comparison

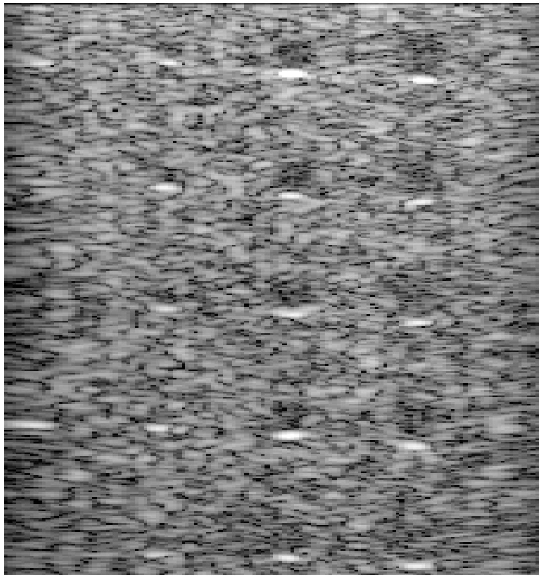
Conventional
4 focal depths
512 beams

25 Frames/s

Ultrafast Imaging
1 unfocused beam : 1 Plane Wave

18 000 F/s





- Very High Frame Rate is reached by using plane wave transmissions and Time-reversal processing  or parallel receive beamforming

- **Loss of Transmit Focusing degrades image quality**

  **Slightly Lower Resolution**
  **Much Lower Contrast**

- How to reach High Frame Rate without compromising Image Quality ?

- Synthetic recombination of multiple angles plane wave transmissions – **Coherent compounding**

# Coherent Plane Wave Compounding

The coherent addition of plane waves with different incident angles allows to synthetize any focused wave

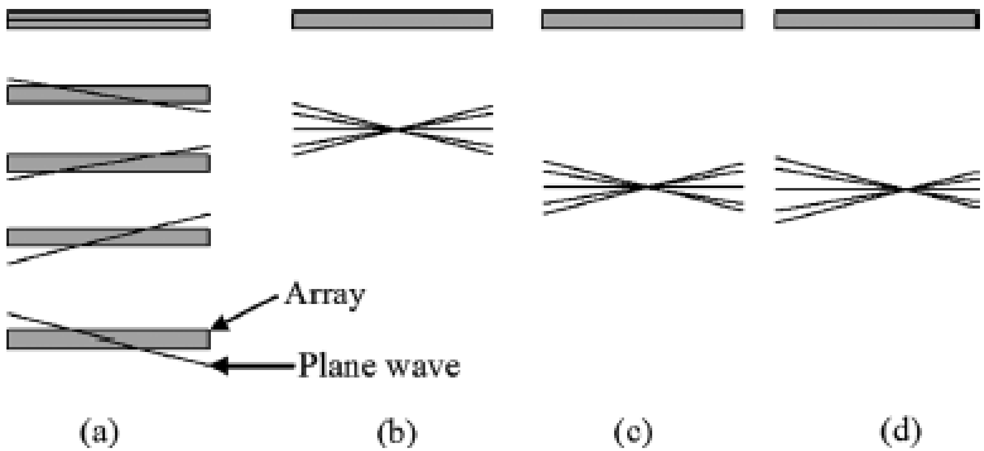



Fig. 4. (a) Individual plane waves send with the compound method. (b), (c), (d) The addition of the plane waves with the adequate delays enables focus at different depths and laterally. This focusing is performed synthetically. If this synthetic focusing is the same as in the standard focusing method, the final image must have the same quality in both methods.

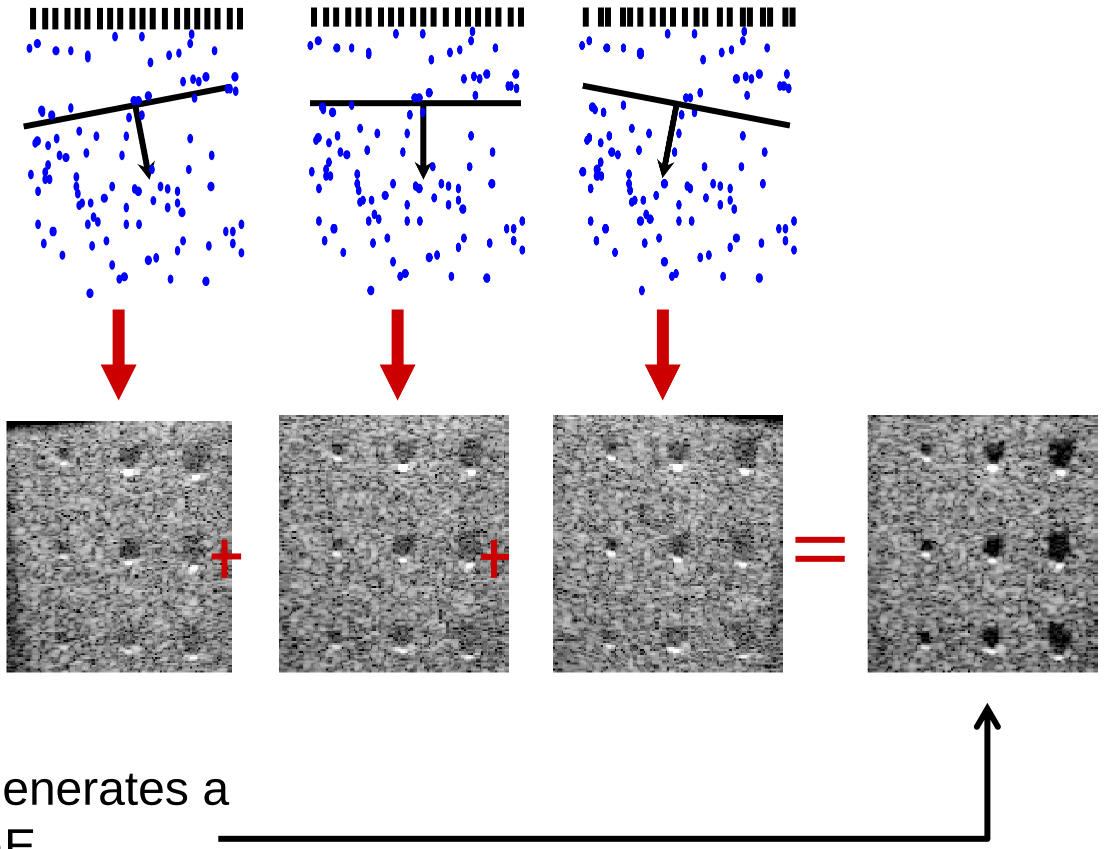
*Coherent plane-wave compounding for very high frame rate ultrasonography and transient Elastography.*
*G. Montaldo, M. Tanter, J. Bercoff, N. Benech, M. Fink IEEE Trans.UFFC, March 2009*

# Ultrafast Imaging with coherent plane wave compounding

Illumination with a set of
Plane Waves
with DIFFERENT ANGLES

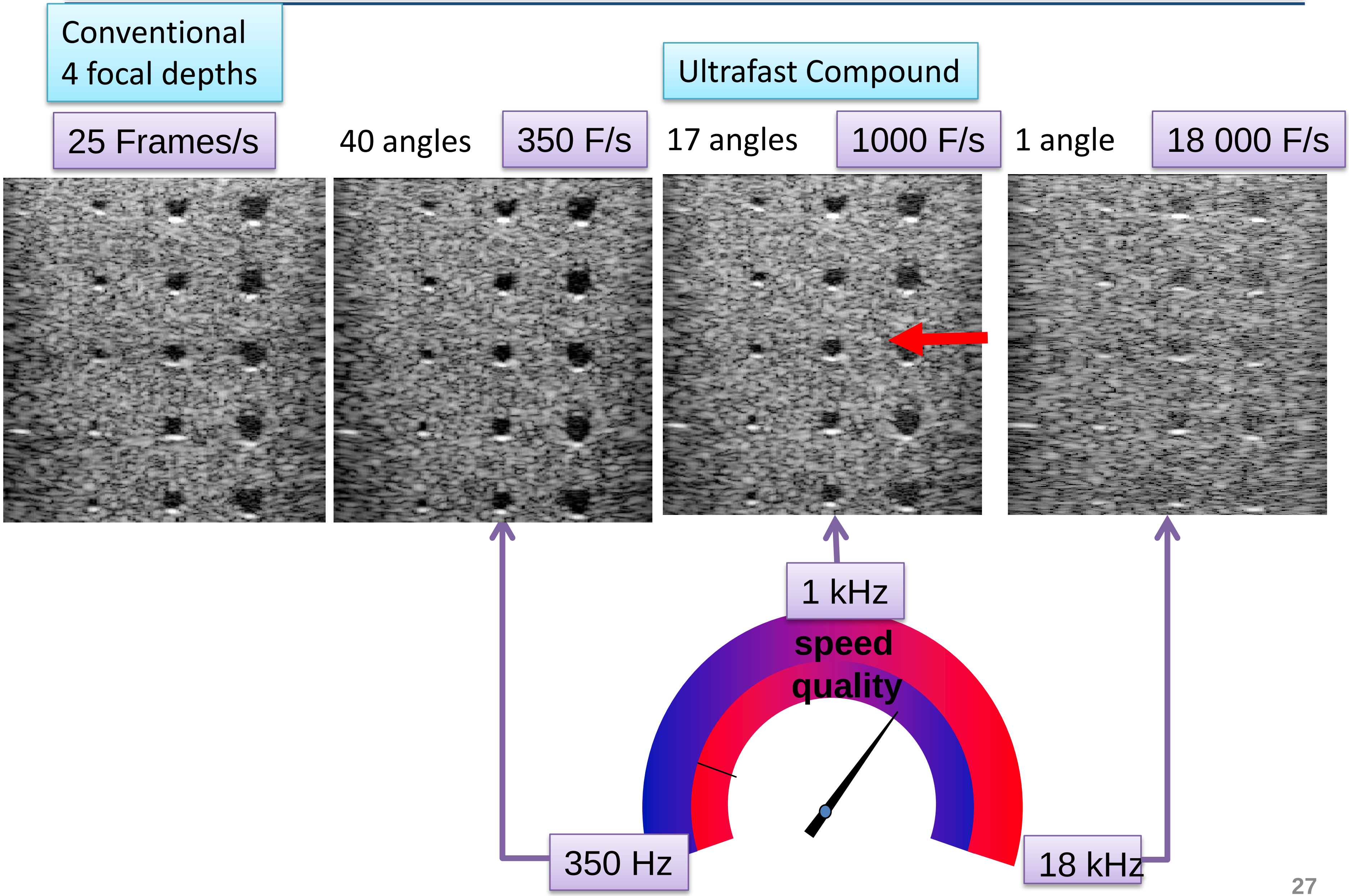
Each plane wave gets
a LOW QUALITY IMAGE

The coherent addition generates a
HIGER QUALITY IMAGE



*Coherent plane-wave compounding for very high frame rate ultrasonography and transient Elastography.*
*G. Montaldo, M. Tanter, J. Bercoff, N. Benech, M. Fink IEEE Trans.UFFC, March 2009*

# Trade-off between speed and quality

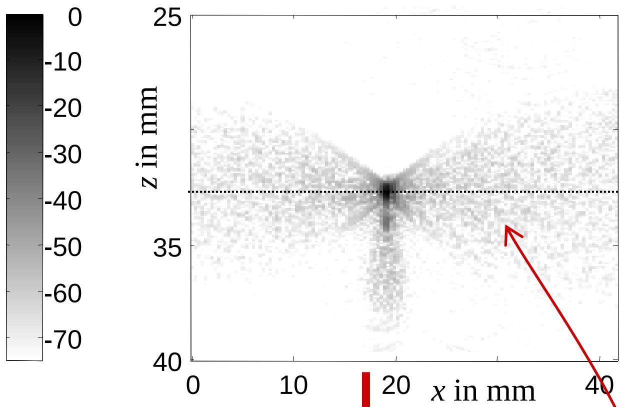


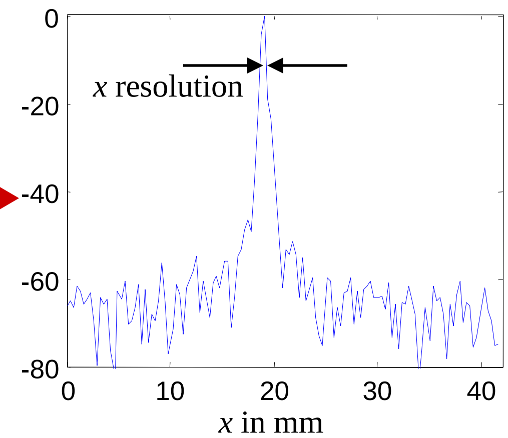
# Quantitative Comparison: The PSF function

The Point–Spread–Function is the image of a point-like object

We can measure: **RESOLUTION** and **CONTRAST**

Measured PSF

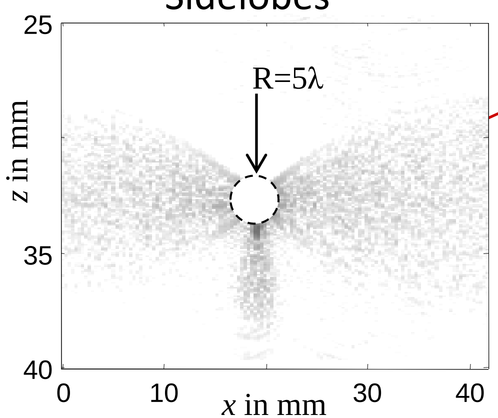



Resolution:

Size of the spot
At -6dB

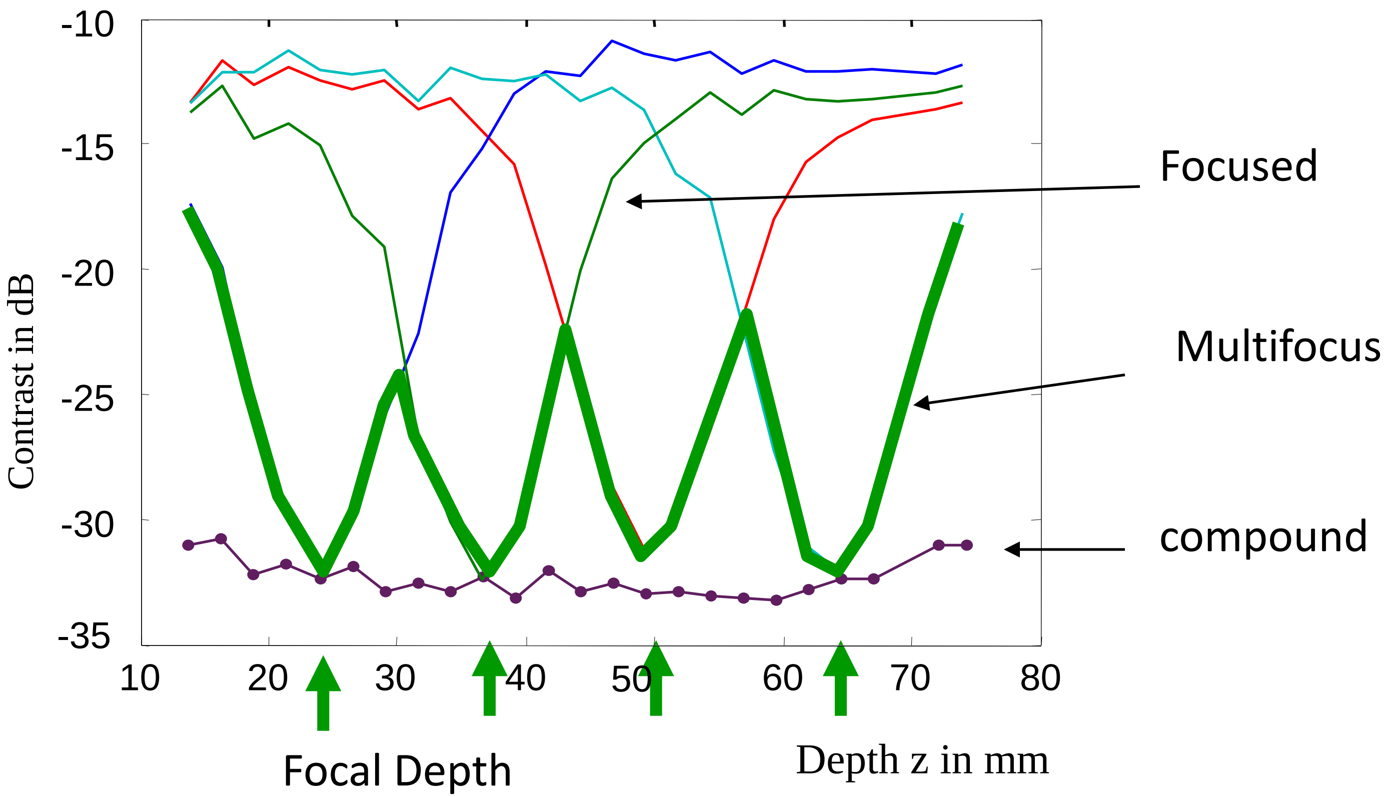
Sidelobes




$$Contrast = 10Log_{10} \frac{Sidelobes\_Energy}{Total\_Energy}$$

# Quantitative Comparison: CONTRAST

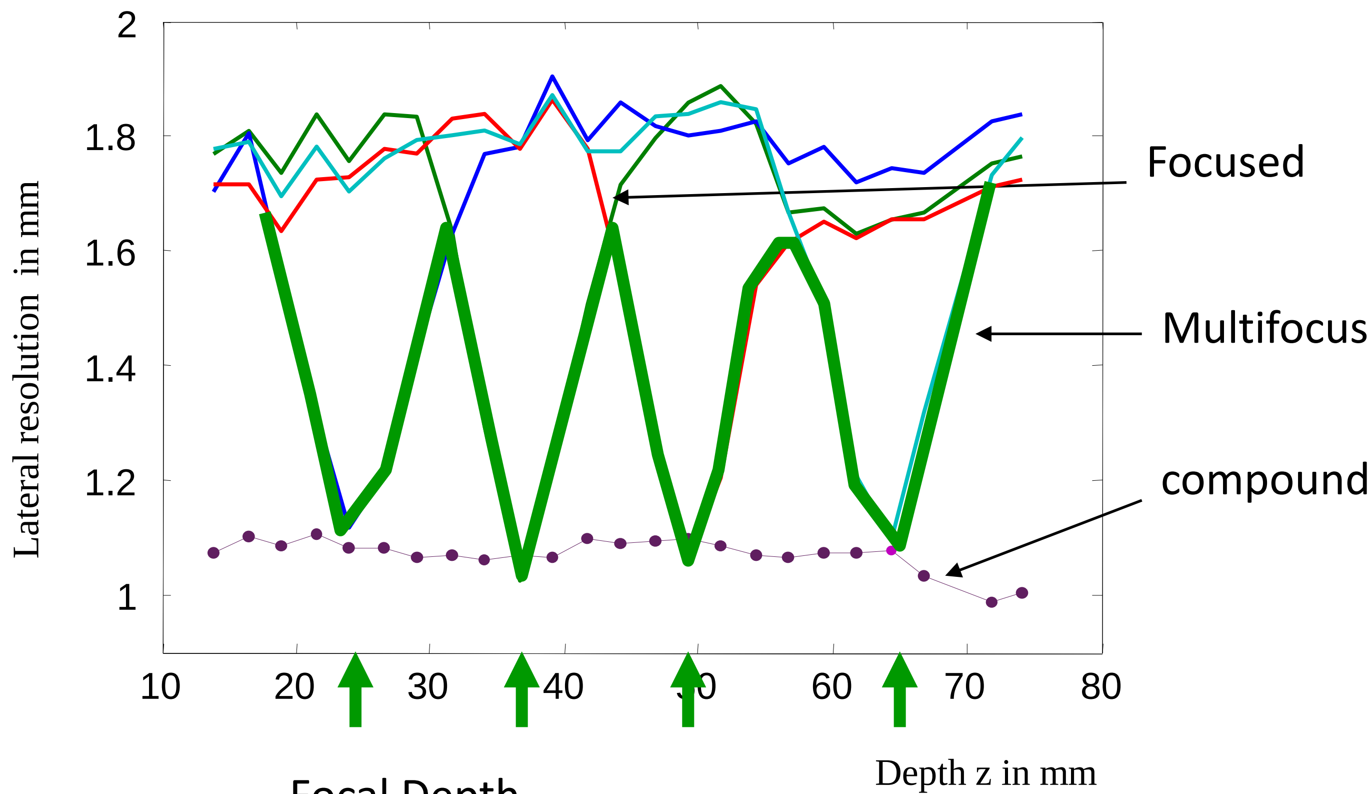
4 Mhz probe (linear Array 128 elements)




Better CONTRAST using Plane Wave Coherent Compounding !

# Quantitative Comparison: RESOLUTION

4 Mhz probe (linear Array 128 elements)




Focal Depth

Better RESOLUTION using Plane Wave Coherent Compounding !

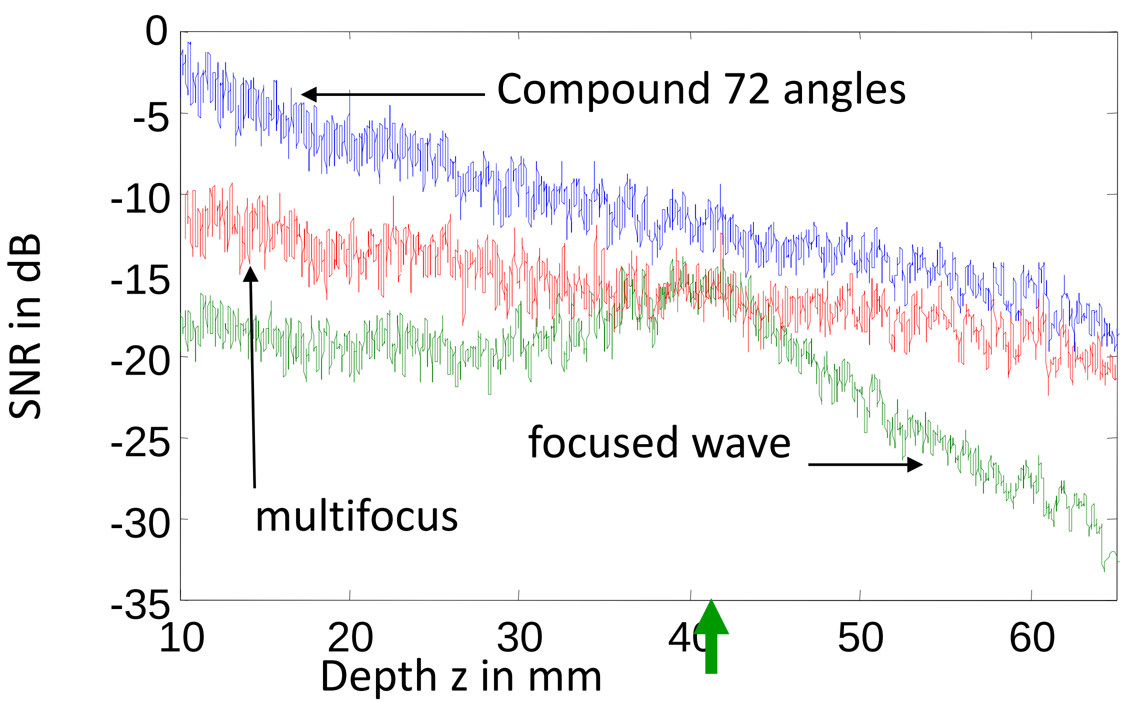
# Quantitative Comparison: SNR

SNR estimation:

1) acquisition of 10 images
2) for each pixel in the image

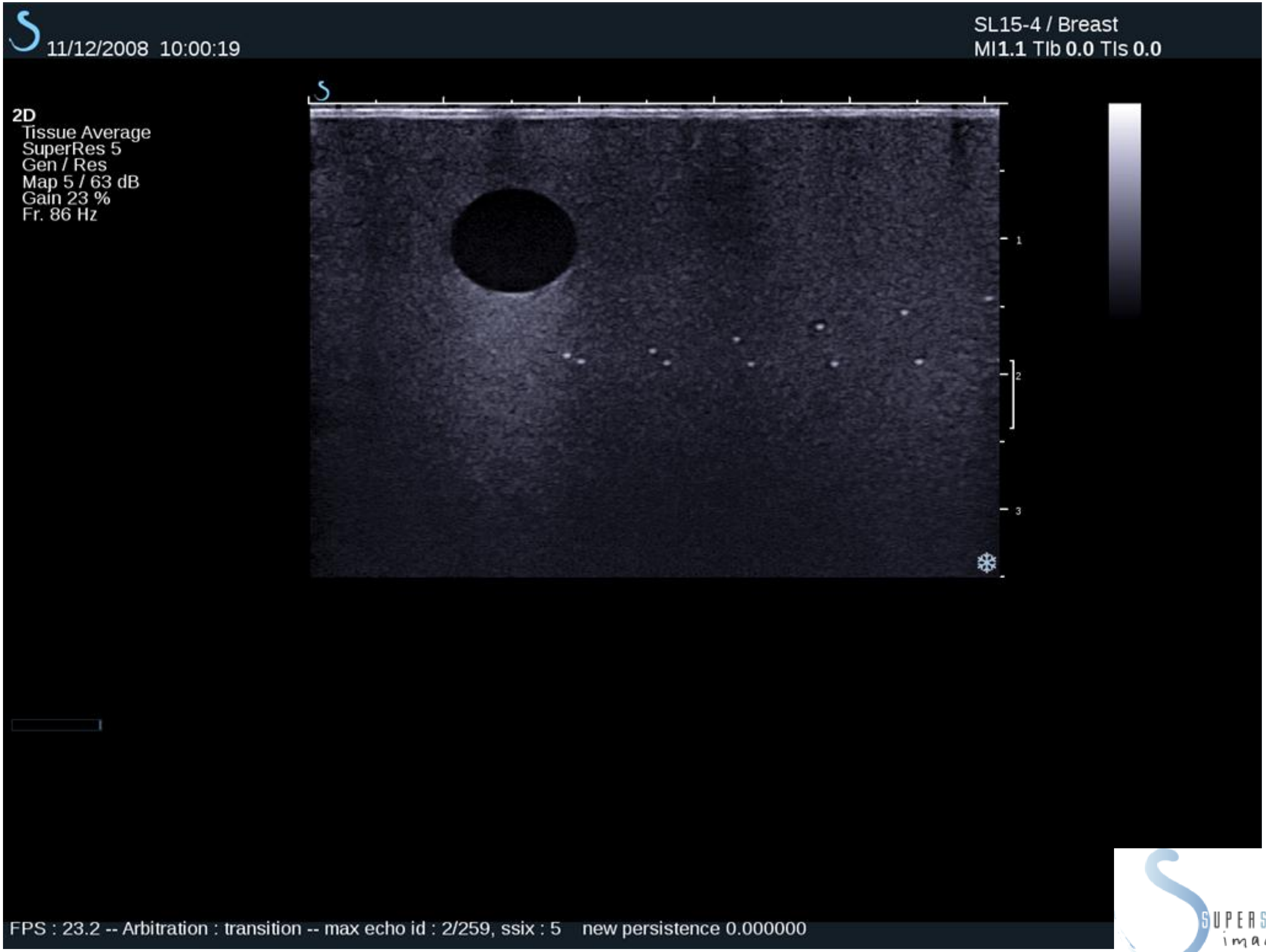
    signal = mean of the 10 images

    noise = standard deviation of the 10 images

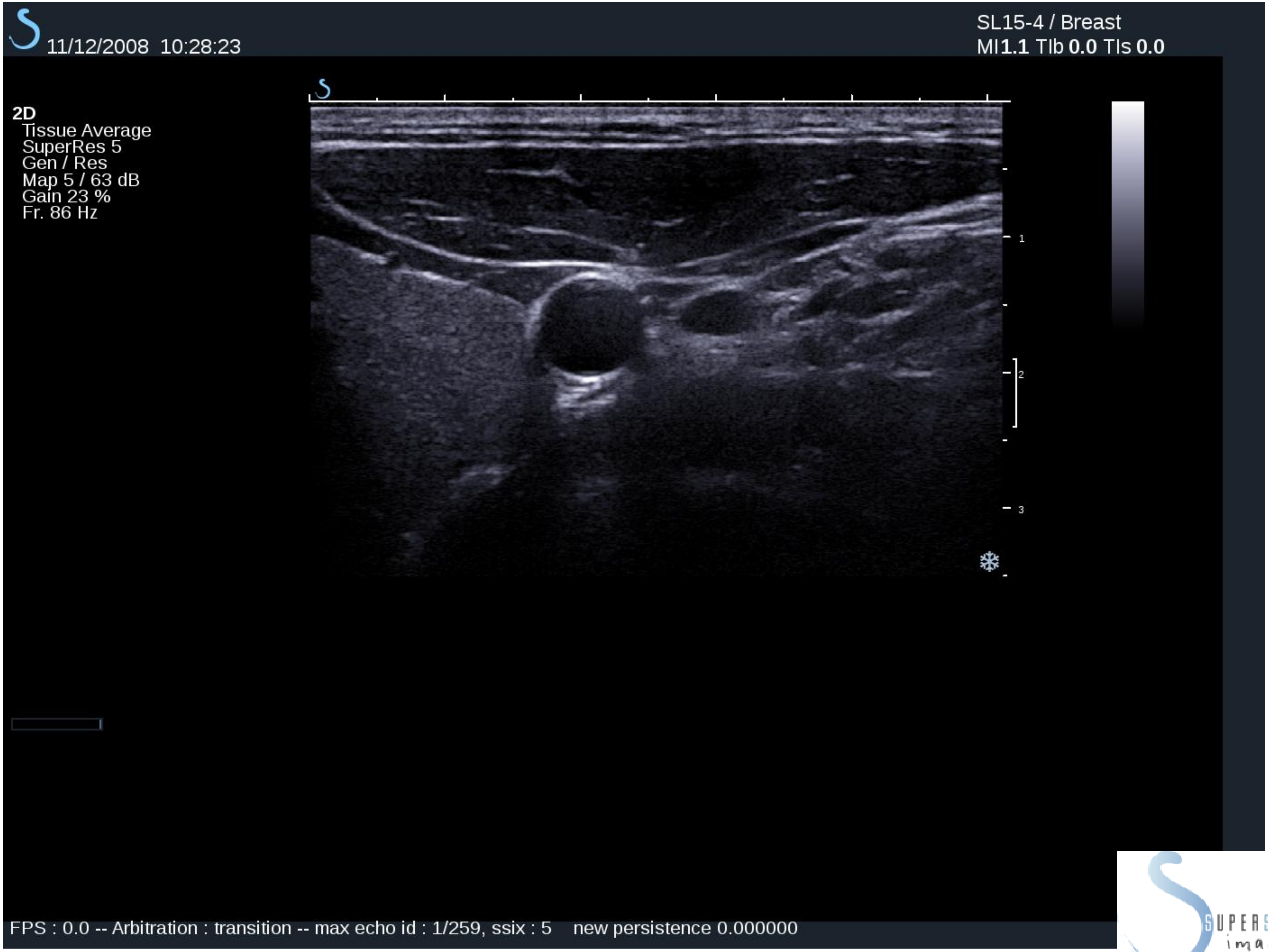



Better SNR using Plane Wave Coherent Compounding

# Implementation on Aixplorer® scanner (Supersonic Imagine)



# Implementation on Aixplorer® scanner (Supersonic Imagine)



# Ultrafast Frame Rates Give Access to New Information

## Ultrafast Ultrasonic Imaging

(typically more than 1000 fps)

**Tissue Motion**

**Blood Motion**

**Gray scale Modifications**

**Quantitative Elasticity Imaging**

Diagnosis Imaging

Temperature and necrosis Imaging

Imaging of natural vibrations

Muscle fibers stimulation

Cardiac Electromechanical waves

Arterial Pulse Wave

**Ultrafast Imaging of bubbles**

Cavitation threshold estimation

Information on gas dissolution

Imaging of Drug release

Enhanced Contrast Imaging

Superresolution Imaging

**Ultrafast Doppler Imaging**

Full field imaging of complex flows

Imaging of the micro-vascularization

(tumor vasc., brain ischemia,…)

Functional imaging of brain activation

# Quantitative Elasticity Imaging

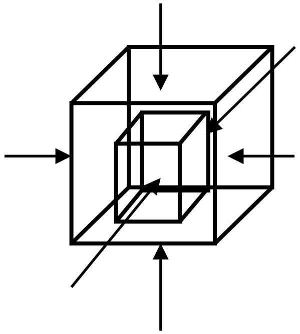
## From Transient Elastography to Shear Wave imaging :

**The multiwave approach**

# What kind of mechanical waves can propagate in soft tissues ?

Two types of waves related to the two mechanical coefficients **K** and **μ** used to define the elasticity of a solid material

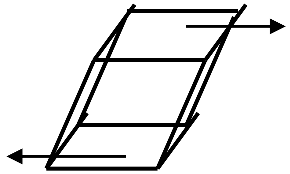
**K**



**K** Bulk Modulus (Compression) almost constant, of the order of **$10^9$ Pa,** Fluctuations ≈ 5%

Quasi incompressible medium

**μ**



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

(A. Sarvazian)

**K >> μ**

Young modulus

**E ≈ 3 μ**

# Human Body Seismology : Mechanical waves in soft tissues

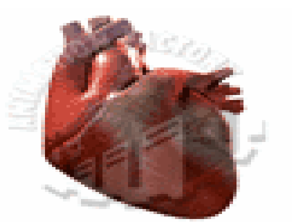
Compressional Waves propagate at $c_P \approx \sqrt{\frac{K}{\rho}}$ ($\approx 1500\ \mathrm{m.s^{-1}}$)

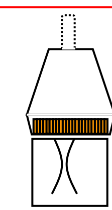
Shear waves propagates at $c_s = \sqrt{\frac{\mu}{\rho}}$ ($\approx 1\text{-}10\ \mathrm{m.s^{-1}}$)

Two kind of waves propagating at totally different speeds !!

At **Ultrasonic** frequency, only Compressional waves can propagate, at 5MHz, **wavelength = 0.3mm.**

At **Sonic** frequency, Shear waves can propagate < 1000 Hz (High Shear Viscosity), at 200 Hz, **large wavelength = 2cm**

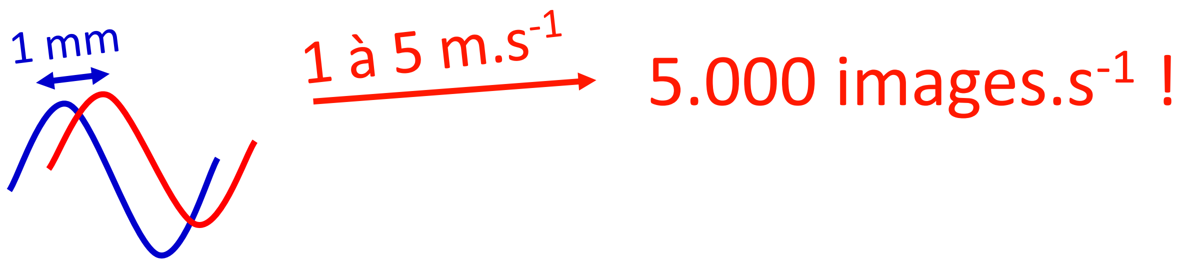




**Ultrasonic radiation force**

# Transient Elastography : Shear Wave Imaging - a Multiwave approach

- Generation of transient low frequency shear wave (10 Hz to 1000 Hz) with some microns amplitude

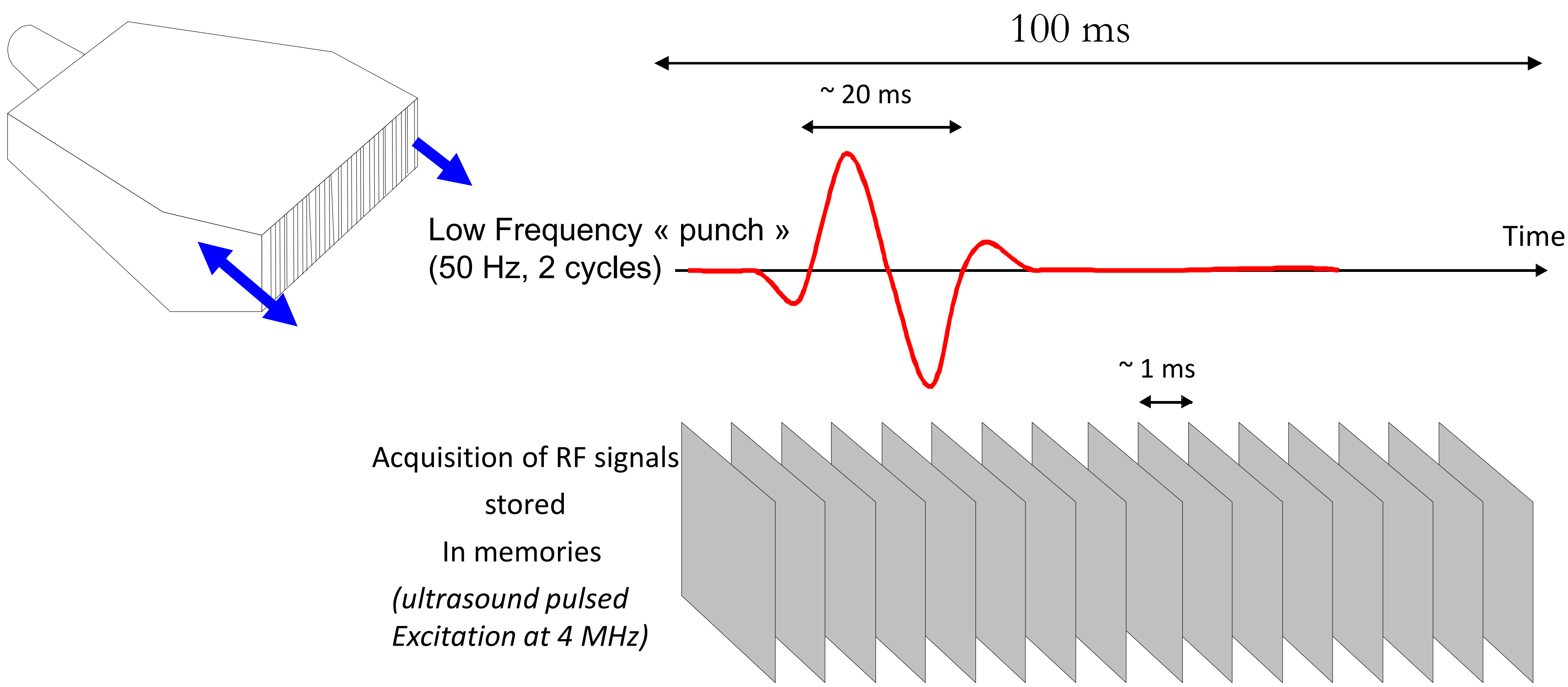



- One follows tissue motion induced by shear waves 5.000 times/s. Local measurement of the shear velocity and E ou μ are deduced by relation :

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

# The Transient Elastography Technique

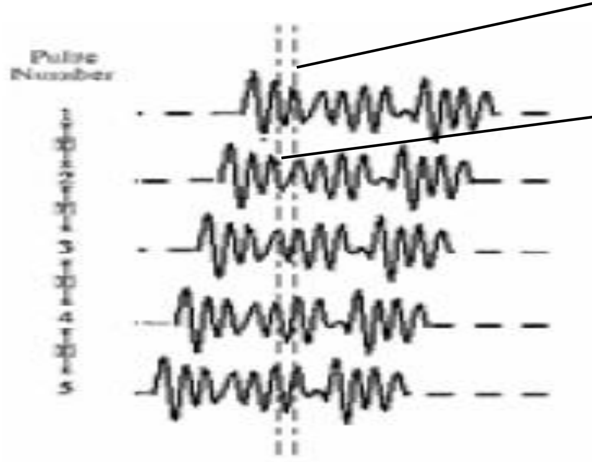
Shear wave generation + Ultrafast Imaging

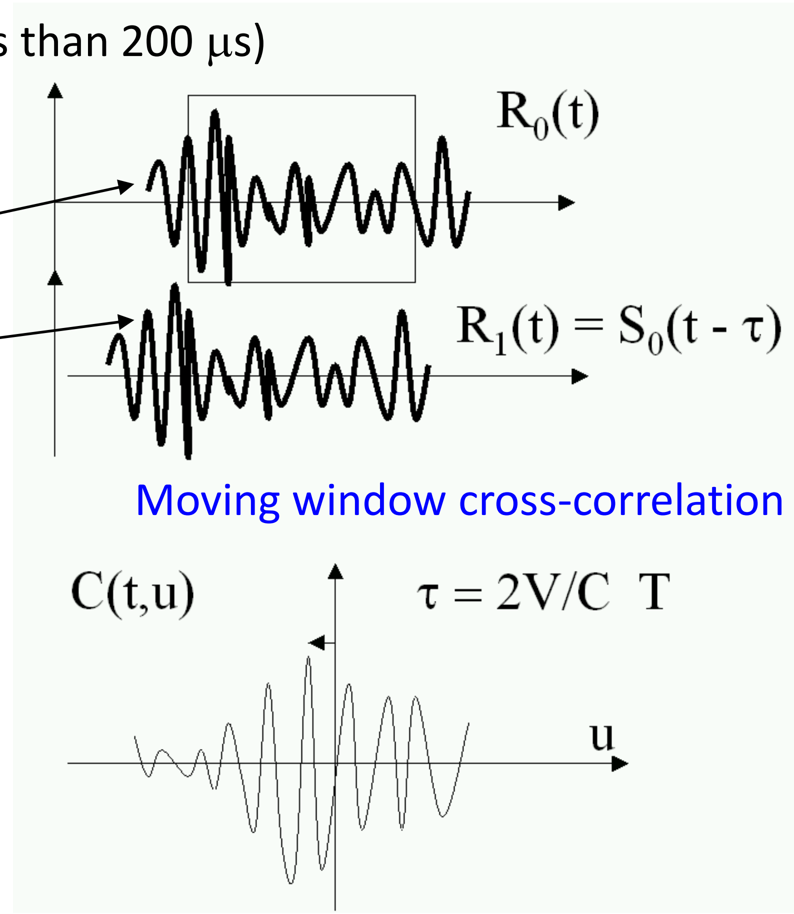


# How to measure the axial displacement induced by shear waves ?

Tissues behave as random distributions of scatterers.
One repeat ultrasonic shots at high rate (less than 200 μs)

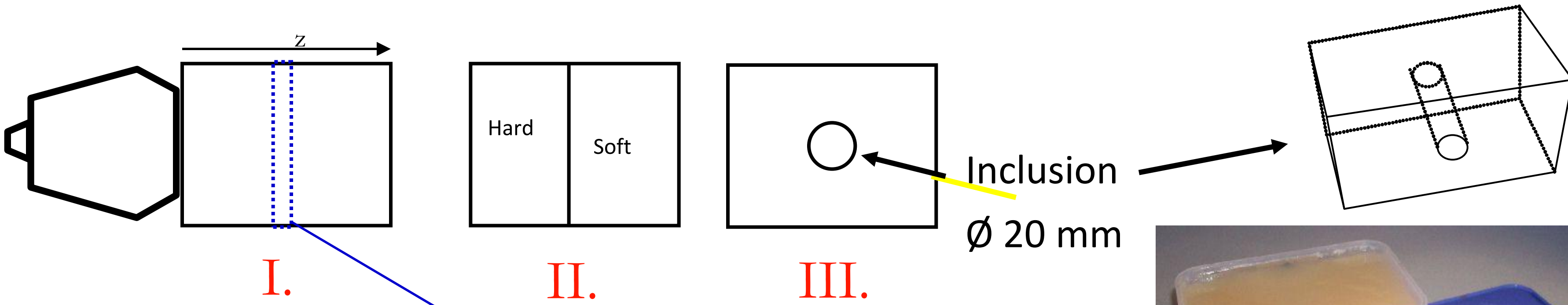
Tir 1
Tir 2
Tir 3
Tir 4
Tir 5

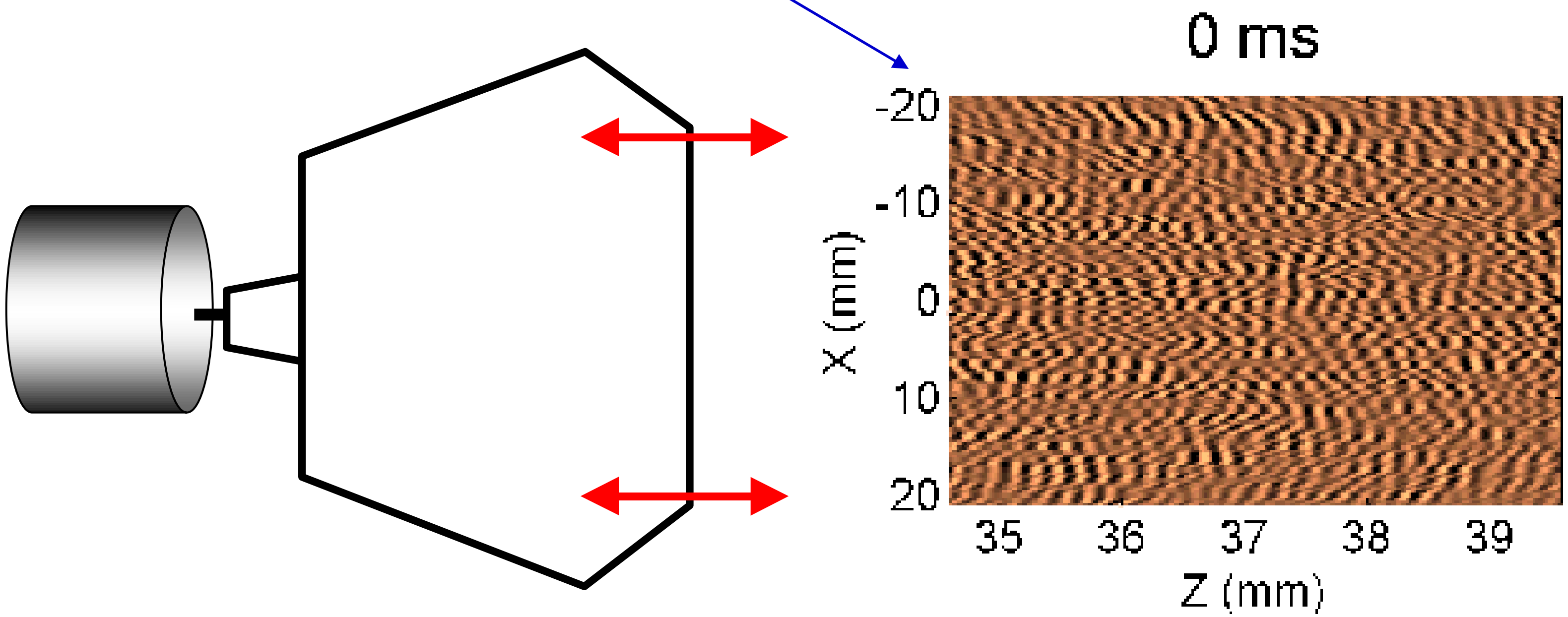





It is possible to measure between 2 shots (for example every 200 μs )
displacements between 1 and 100 μ ( particular velocity between 1 mm/s et 10 cm/s)

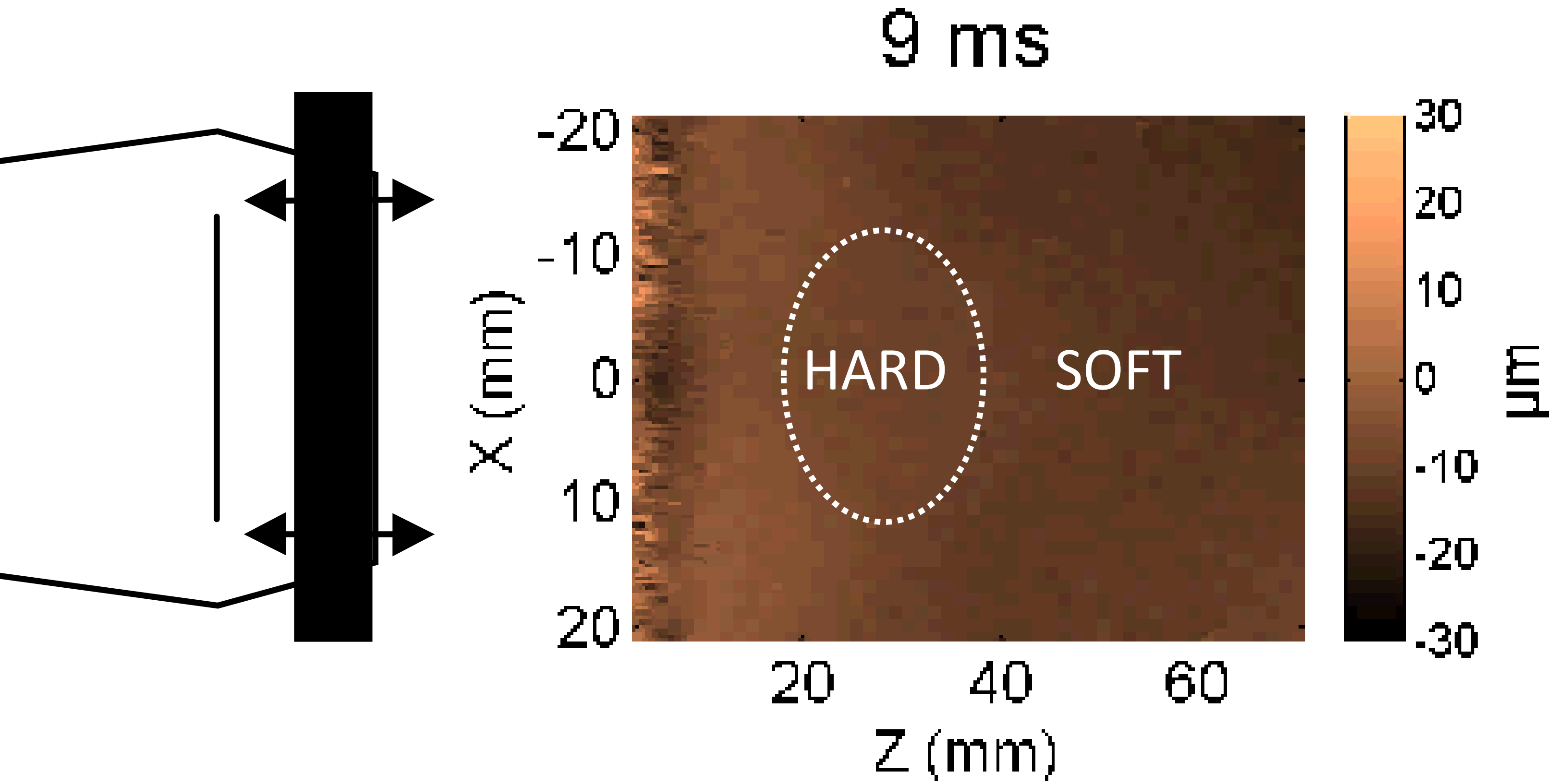
# Transient Elastography in Tissue Mimicking Phantoms



# Hard inclusion

Movie of Uz component



# A Simple Inversion Algorithm

## - Motion Equation : an ideal model : isotropic solid without dissipation

$$\rho \frac{\partial^2 \vec{u}}{\partial t^2} = (\lambda + \mu) \times \vec{\nabla}(\vec{\nabla}.\vec{u}) + \mu \Delta \vec{u}$$

Compressional shear

## - Assumptions:

1) The medium is considered as infinite, isotropic, purely elastic and locally homogeneous.

2) λ>>μ => the bulk wave propagates instantaneously, and then:

$$\rho \frac{\partial^2 u_z}{\partial t^2} = \mu \Delta u_z$$

3) $$\frac{\partial^2 u_z}{\partial y^2} << \frac{\partial^2 u_z}{\partial x^2} + \frac{\partial^2 u_z}{\partial z^2} => \Delta u_z \approx \frac{\partial^2 u_z}{\partial x^2} + \frac{\partial^2 u_z}{\partial z^2}$$

No diffraction outside the image plane

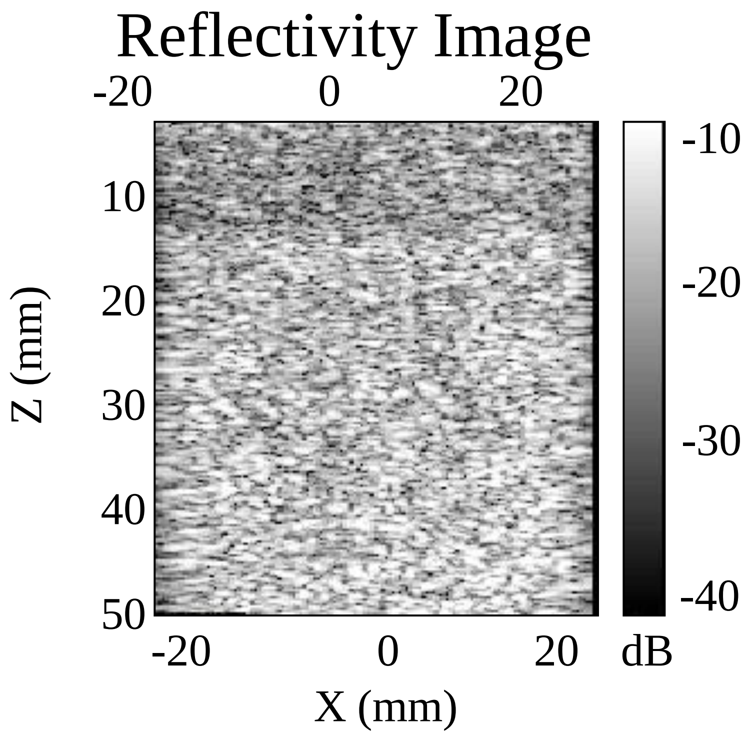
# Inverse Problem

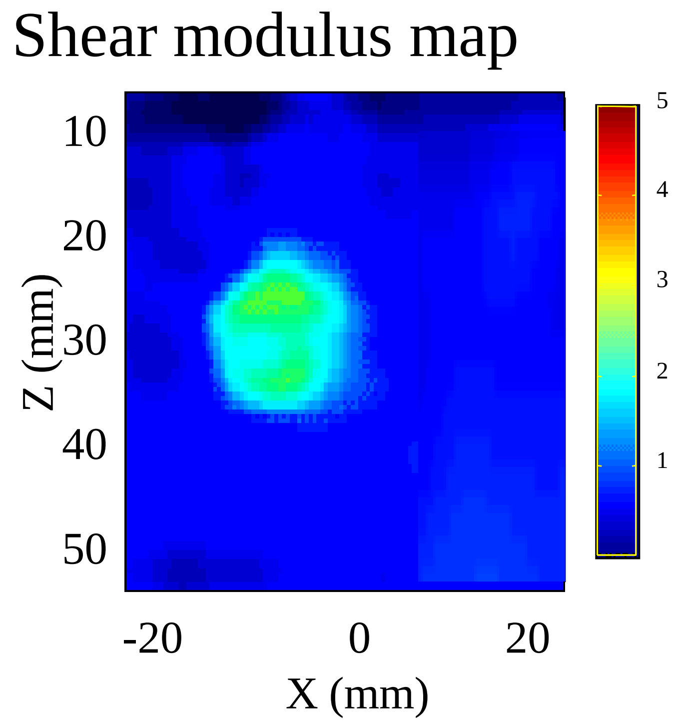
$$\rho \frac{\partial^2 u_z}{\partial t^2} = \mu \Delta u_z$$

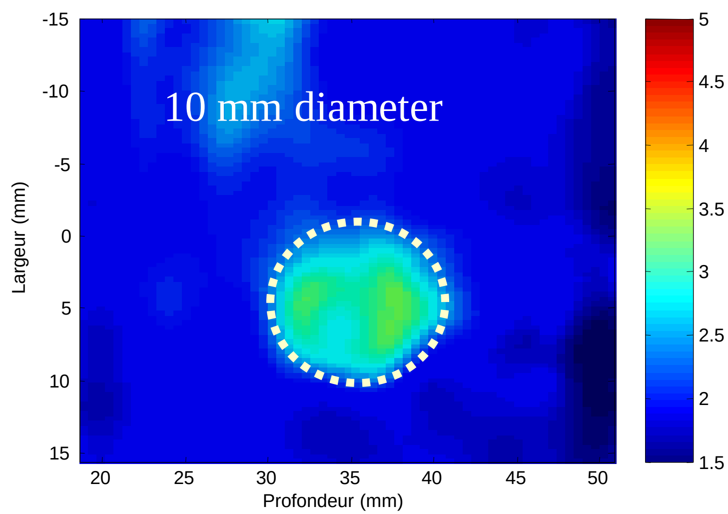
- Local inversion algorithm

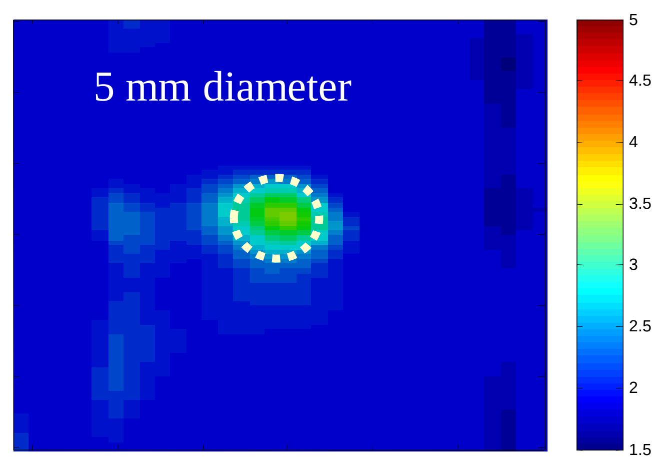
$$\mu(x,z) = \rho \frac{\left(\frac{\partial^2 u_z(x,z)}{\partial t^2}\right)}{\left(\frac{\partial^2 u_z(x,z)}{\partial x^2} + \frac{\partial^2 u_z(x,z)}{\partial z^2}\right)}$$

# Inverse Problem – Hard Inclusion



# Ultrafast Plane Wave Compound Imaging for Vector Tissue Motion Imaging

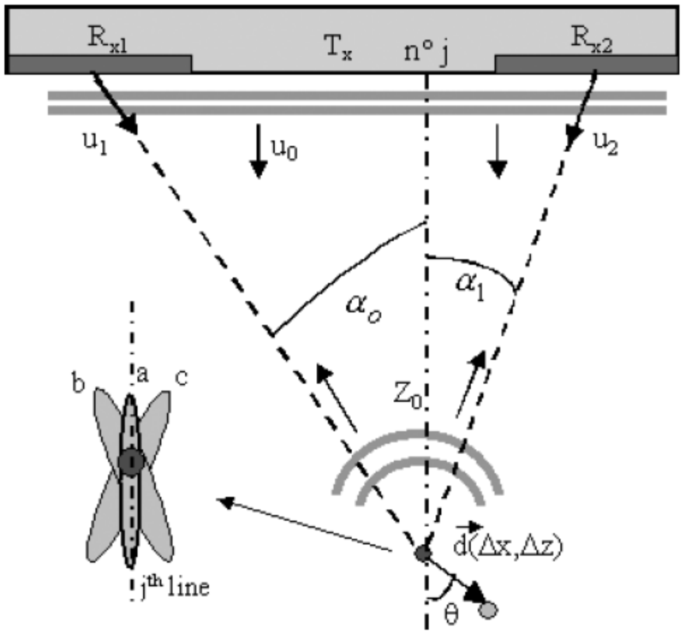
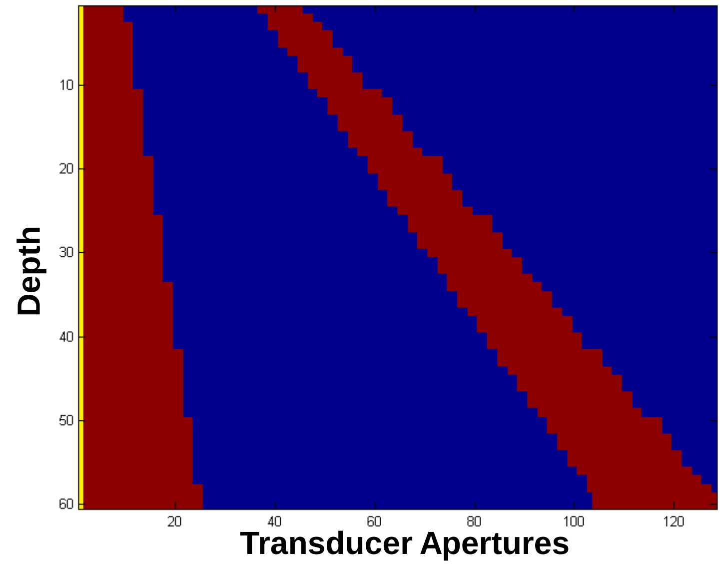
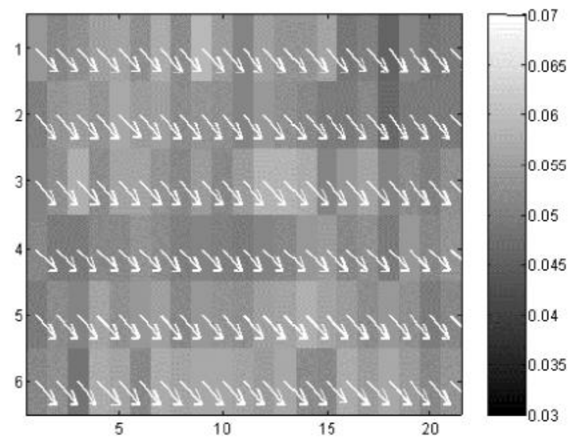



Fig. 3. Left and right subapertures performing two different left and right speckle images. The focal spot allowing one to perform a segment (at depth $Z_0$) of the $j^{th}$ line of the image is presented: (a) for a classical transmit-receive beamforming, (b) for the left subaperture receive beamforming, (c) for the right subaperture receive beamforming.



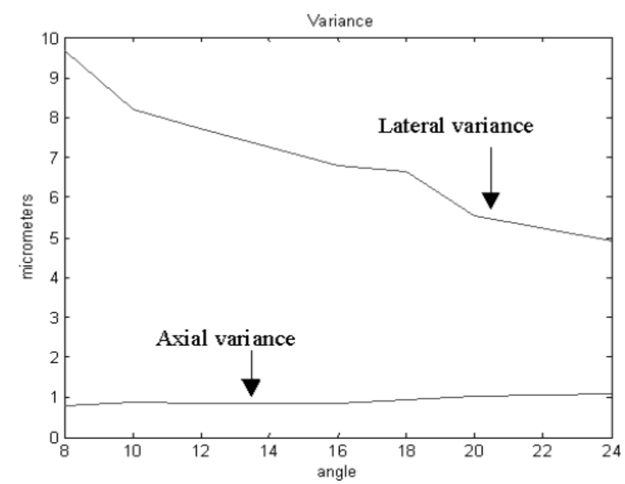



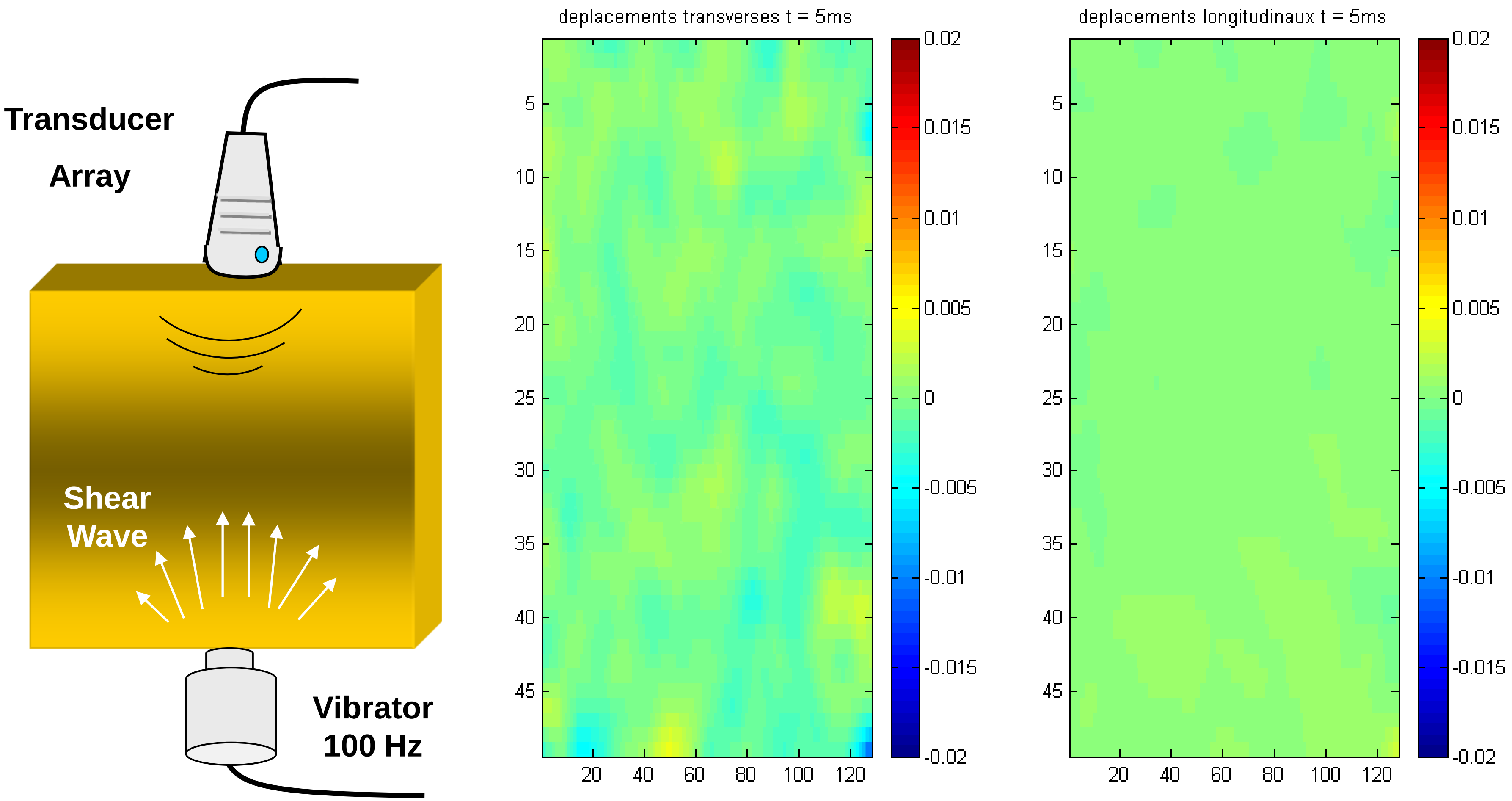

Fig. 10. Dependence of the lateral and longitudinal displacements variance with the angle between subapertures (in degrees). For a 50-$\mu$m displacement applied in both directions, the mean estimate of the lateral and longitudinal displacements are, respectively, 48 and 51 $\mu$m.

*Ultrafast compound imaging for 2D motion vector estimation : Application to transient elastography"*

**M. Tanter, J. Bercoff, M. Fink, IEEE Ultr., Ferr. And Freq. Ctrl, 49 (10), pp 1363-1374, 2002.**

# Ultrafast Compound Imaging for Vector Tissue Motion Imaging

## Experimental Proof of concept for Transient Elastography

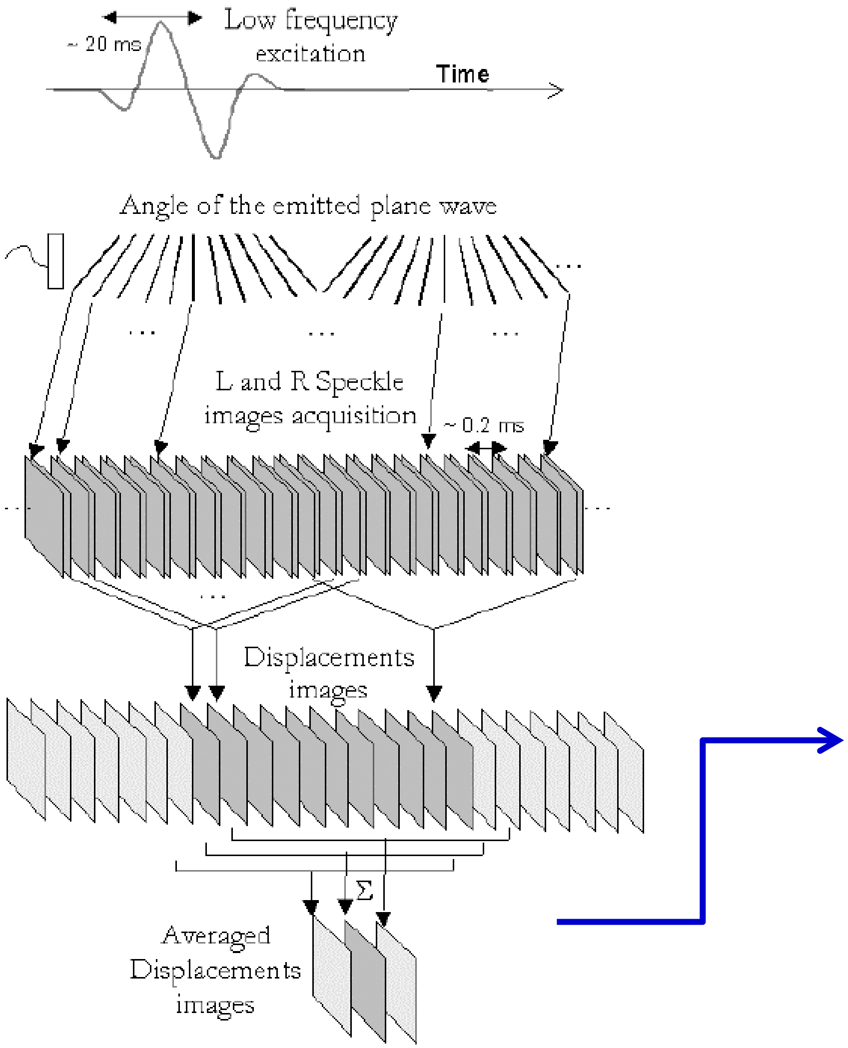



***Transient Shear wave at 2000 fps***

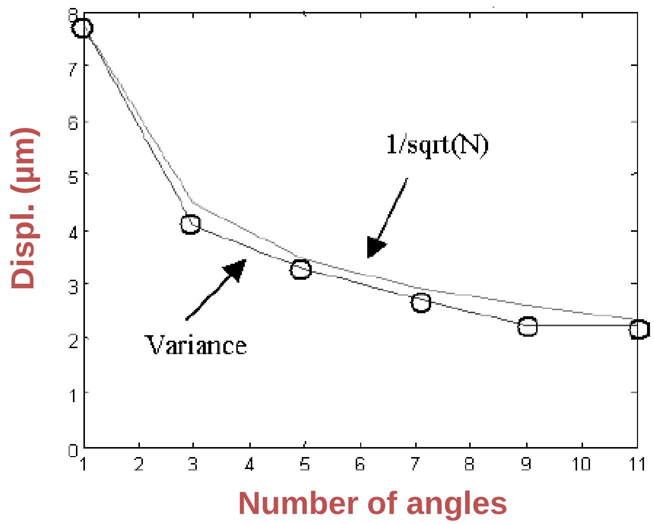
## The extension to Ultrafast Vector Doppler was also proposed in the 2002 paper


**Ultrafast compound imaging for 2D motion vector estimation : Application to transient elastography"**
**M. Tanter, J. Bercoff, M. Fink, IEEE Ultr., Ferr. And Freq. Ctrl, 49 (10), pp 1363-1374, 2002.**

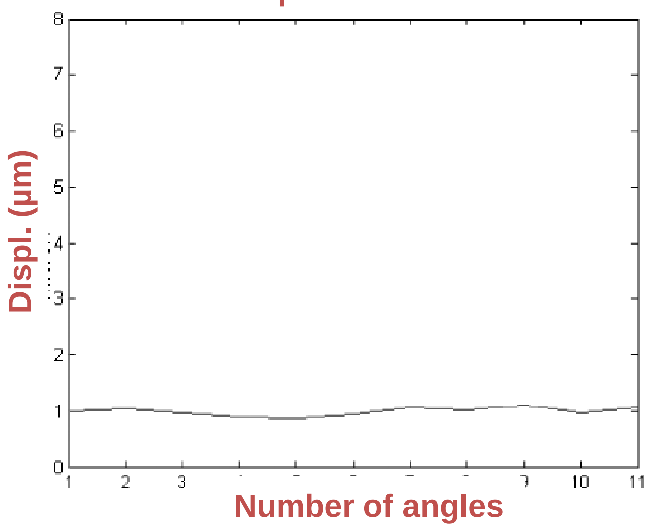
# Ultrafast Plane Wave Compounding improves Motion estimation




Lateral displacement variance




Axial displacement variance



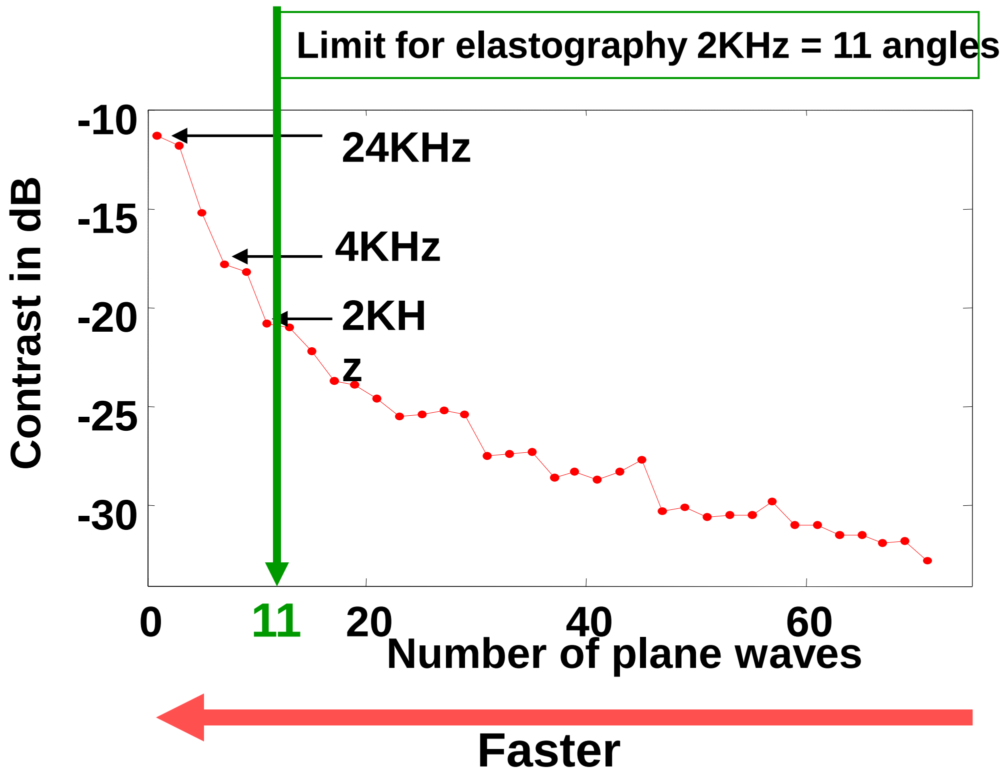

*Ultrafast compound imaging for 2D motion vector estimation : Application to transient elastography"*

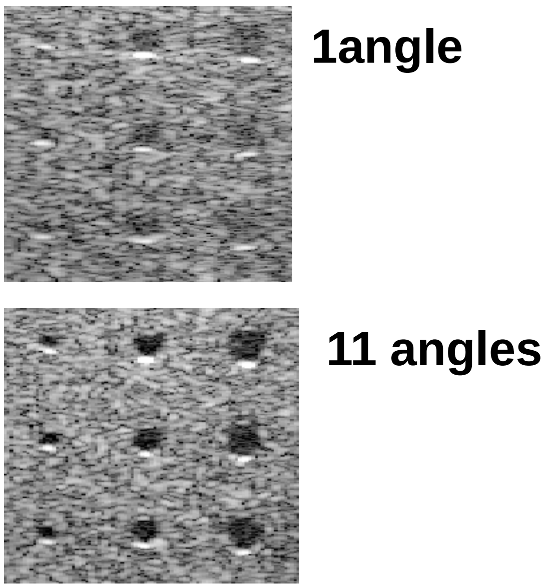
**M. Tanter, J. Bercoff, M. Fink, IEEE Ultr., Ferr. And Freq. Ctrl, 49 (10), pp 1363-1374, 2002.**

# Ultrafast imaging with Coherent Compounding

**Tradeoff between FRAME RATE and IMAGE QUALITY**

**Example in a 3cm depth image**

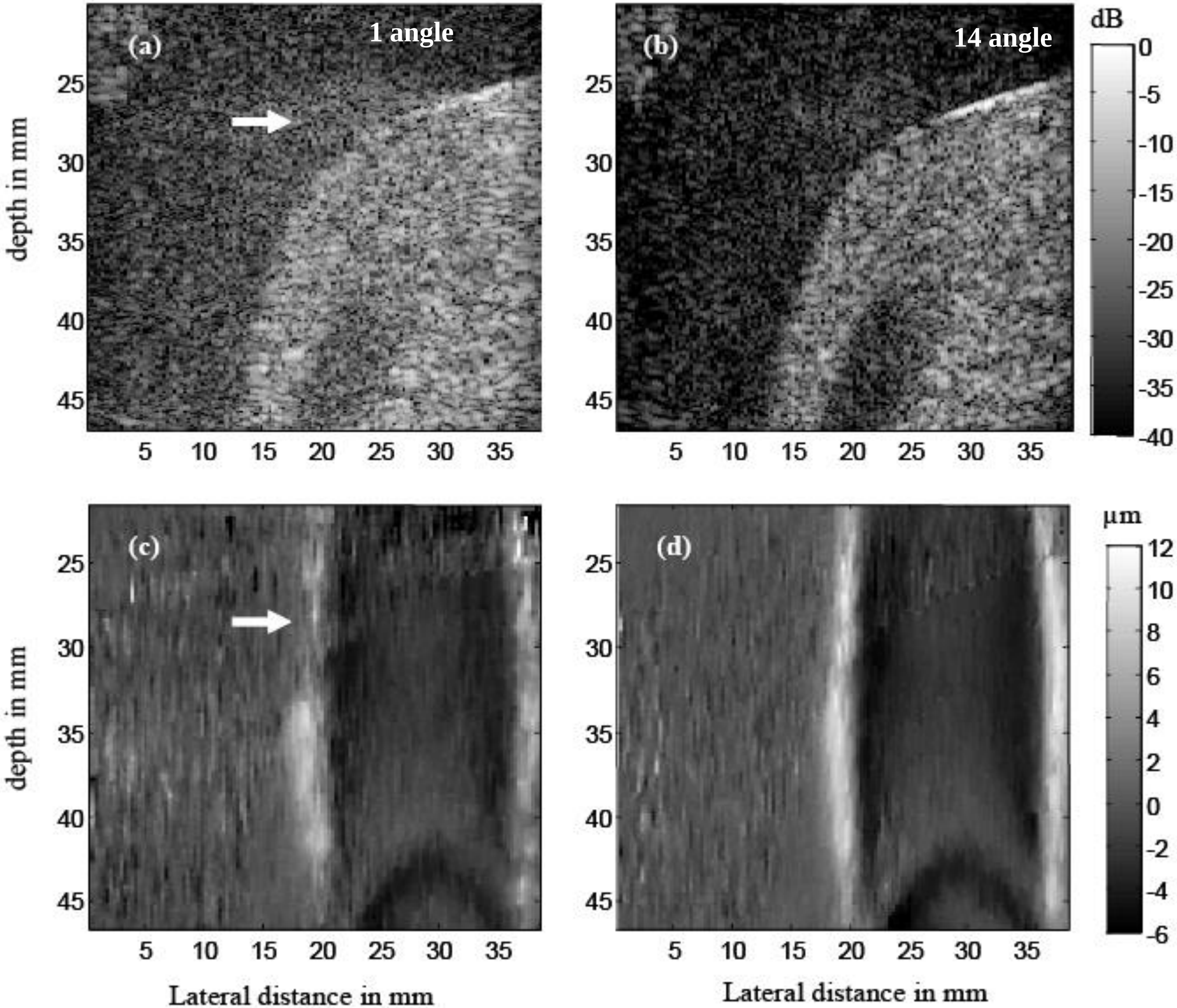



**10dB contrast Improvement using Ultrafast Compound for SSI sequence**

# Supersonic shear Imaging with Coherent compounding

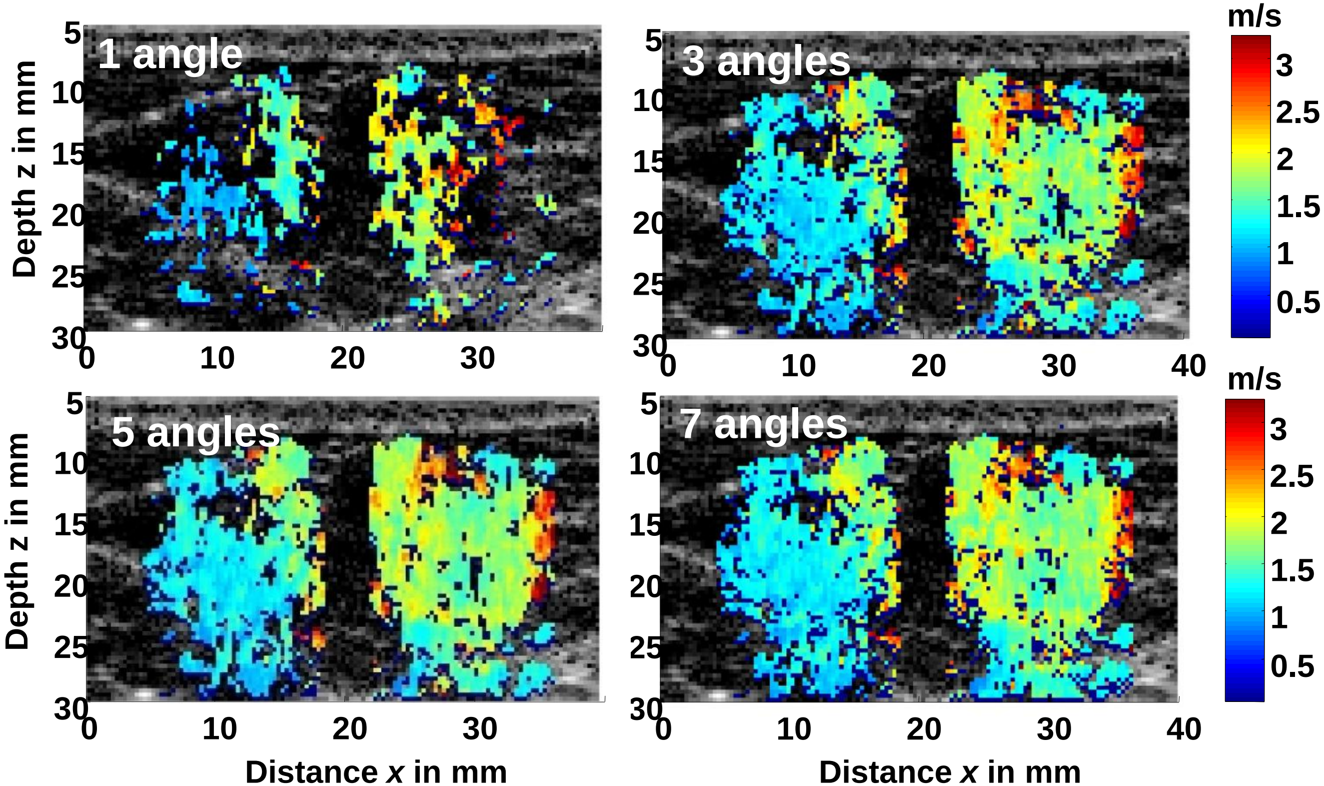
## Typical Experiment in Gelatin Phantoms



# In Vivo Breast Elasticity map using Coherent Compou

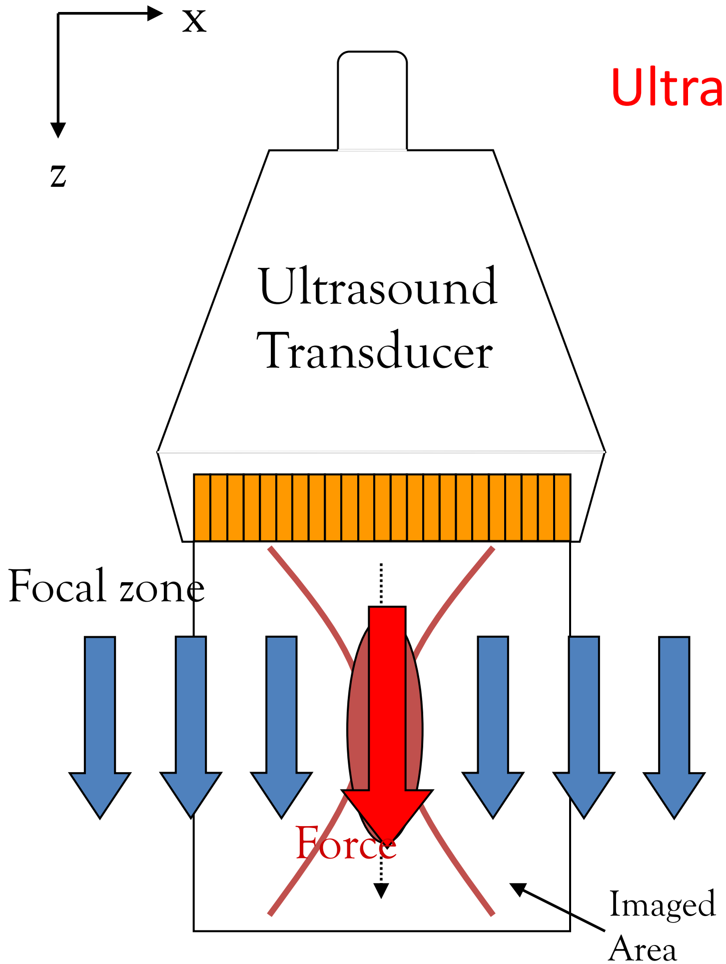
**Medium: In Vivo Breast (healthy volunteer)**
**1 pushing line in the middle of the image**

**Shear wave velocity maps**




**Strong Increase of the quality of the shear velocity maps**

# Transient Elastography and Ultrasonic Radiation Force



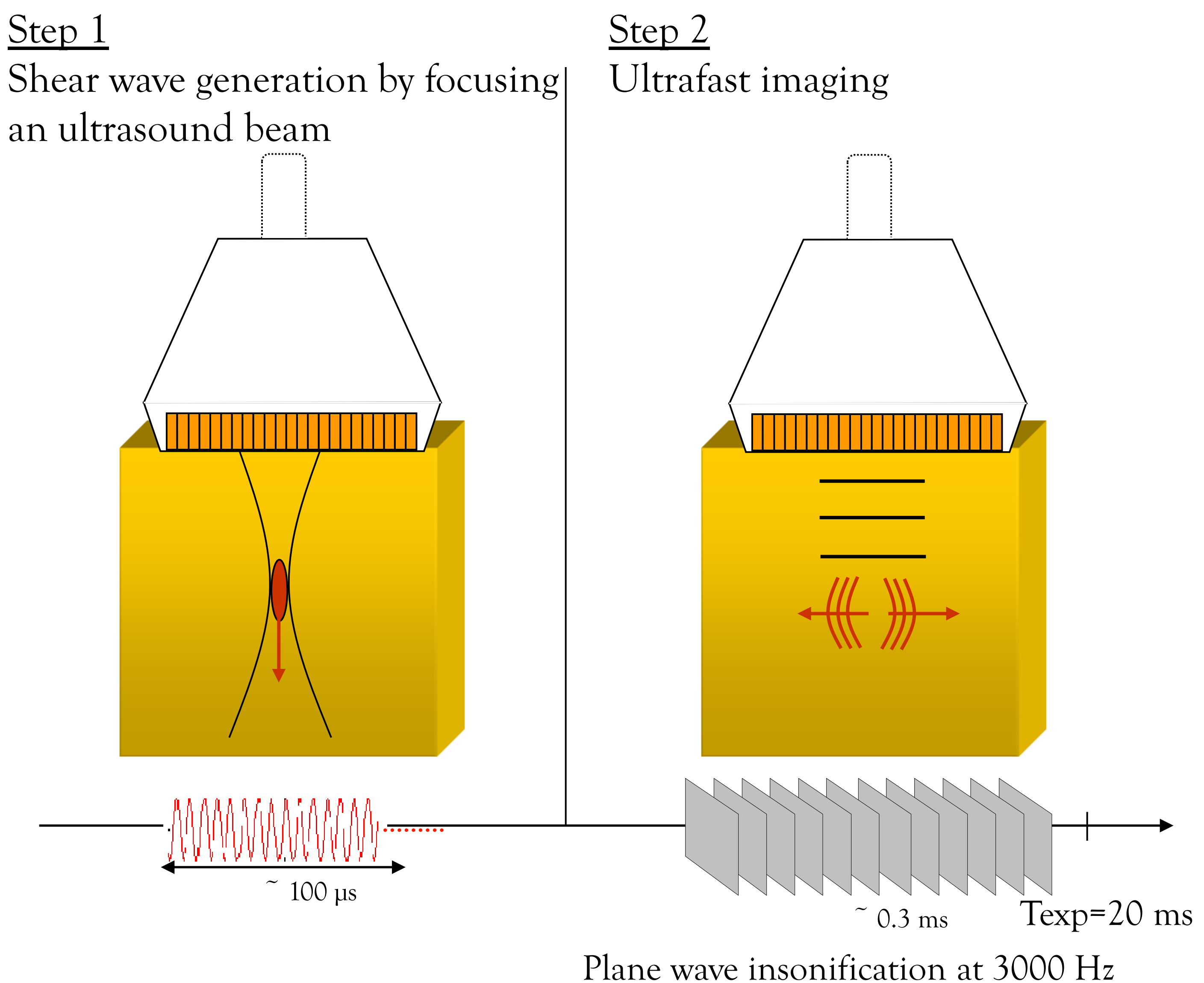

Ultrasonic Radiation Force
non-linear effect

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

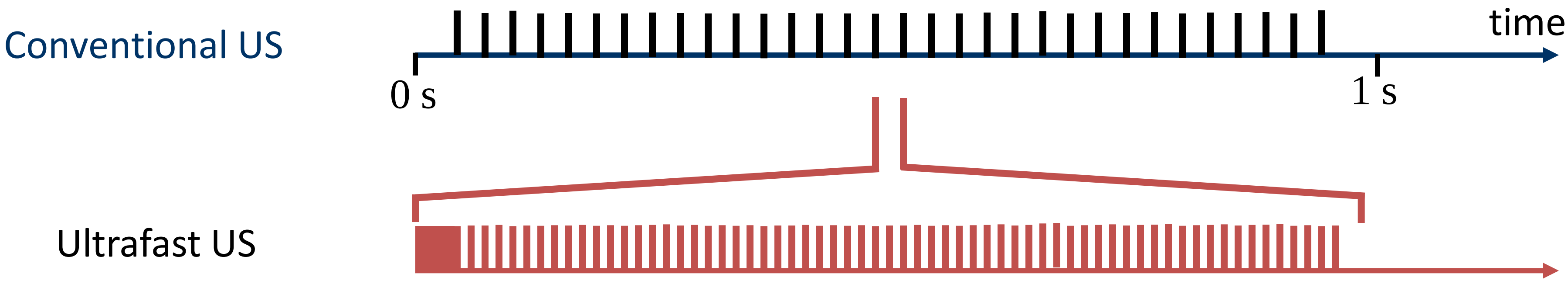
Typical ultrasonic bursts of 100 µs to create low frequency pushes (10 micrometers displacement)

*A . Sarvazyan, K Nigthingale, J Greenleaf, M. Fink, M Tanter*

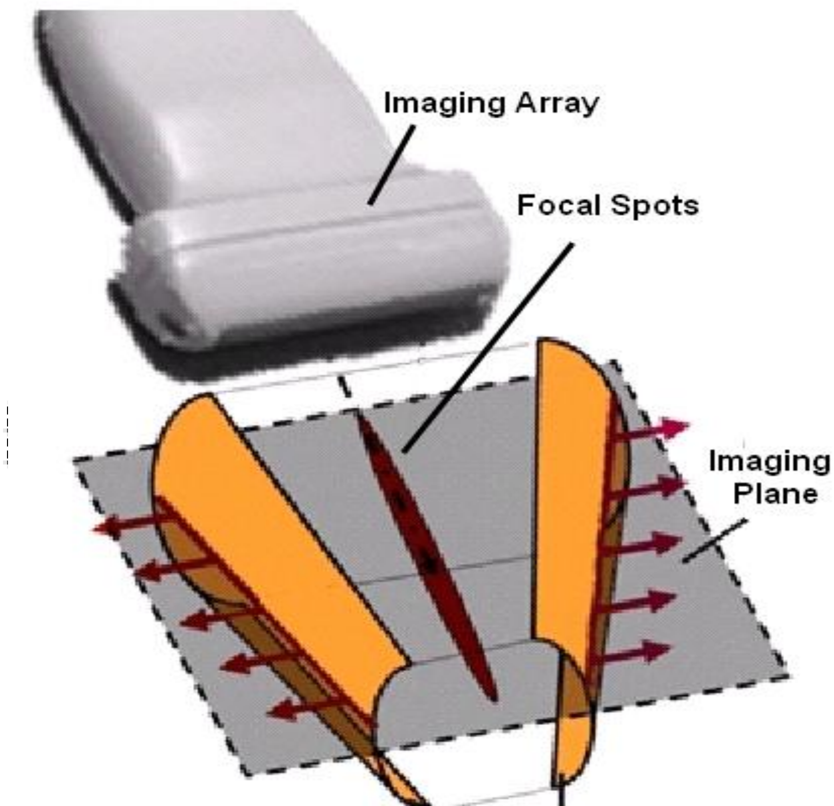
# Ultrafast Imaging and Acoustic Radiation Force



# The Supersonic Push !!!!!!!

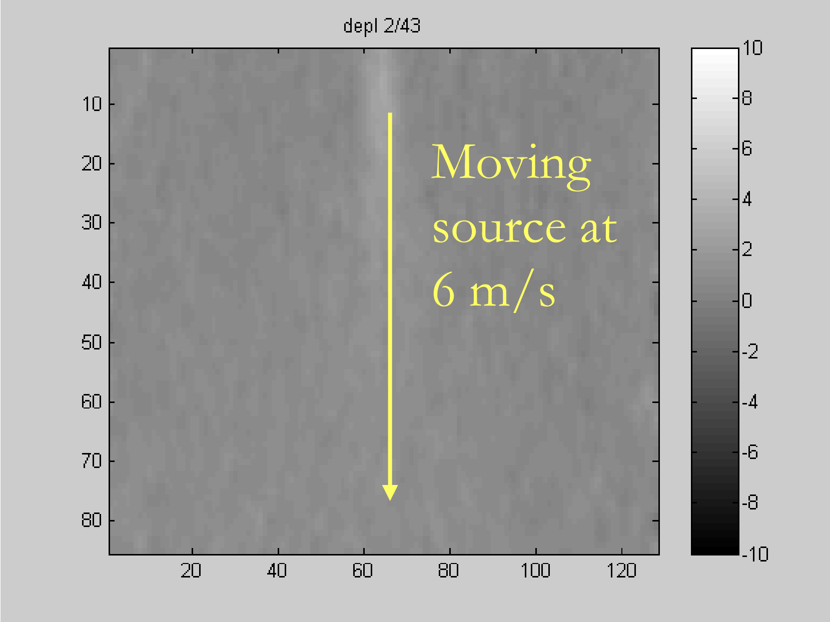



A 30 ms Experiment !!

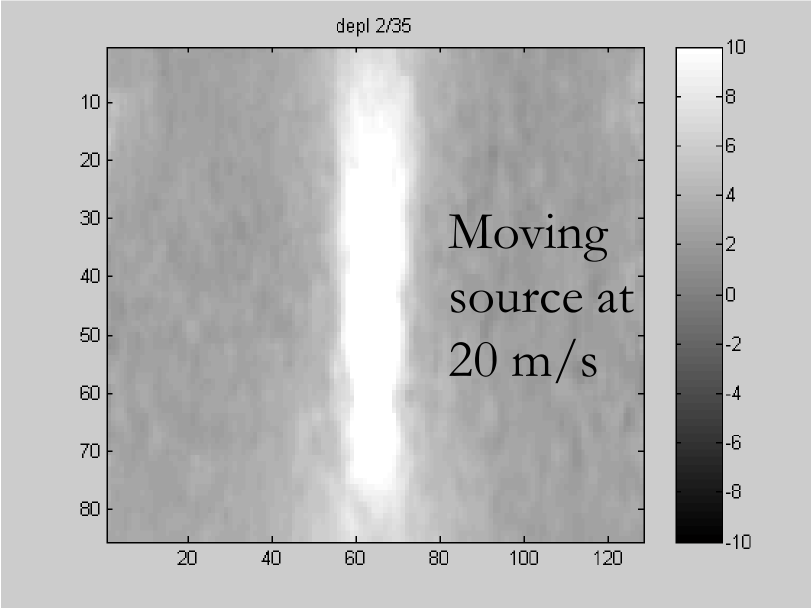



# Shear beamforming with a supersonic moving source

Plane wave generation in a 2m/s phantom

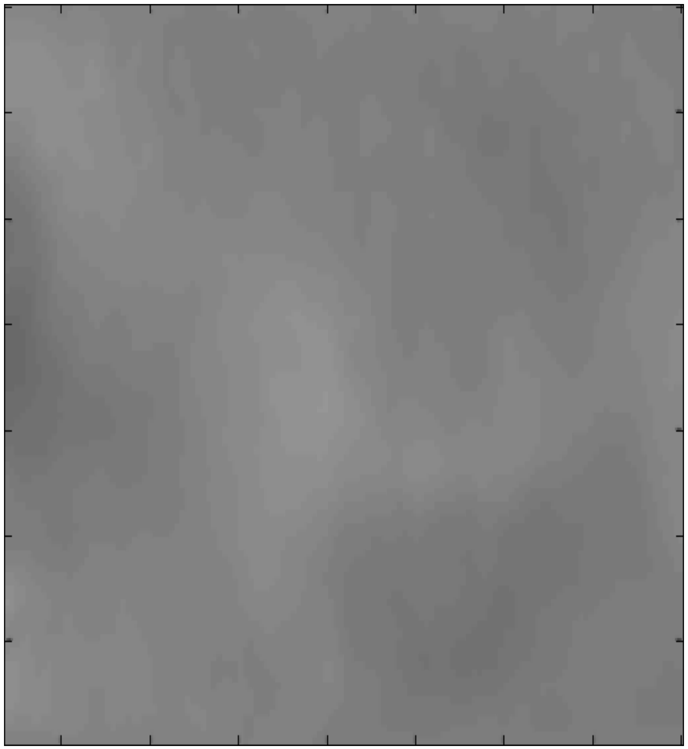


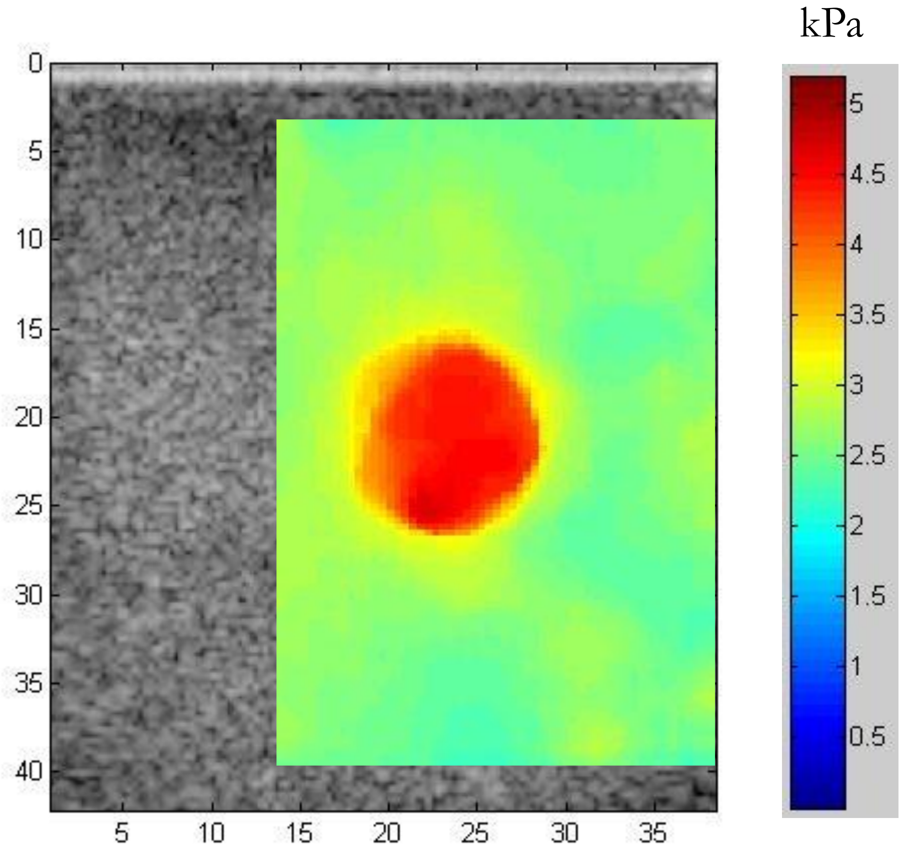

Mach 3




Mach 10

# Mapping  Elasticity : Inverse problem of Shear Wave Propagation






Movie Duration  20 ms

La résolution des ultrasons
Le contraste des ondes de cisaillement

# The goal of Elastography is to estimate tissue elasticity : Multiwave or not Multiwave ?

- **Mechanical excitation**

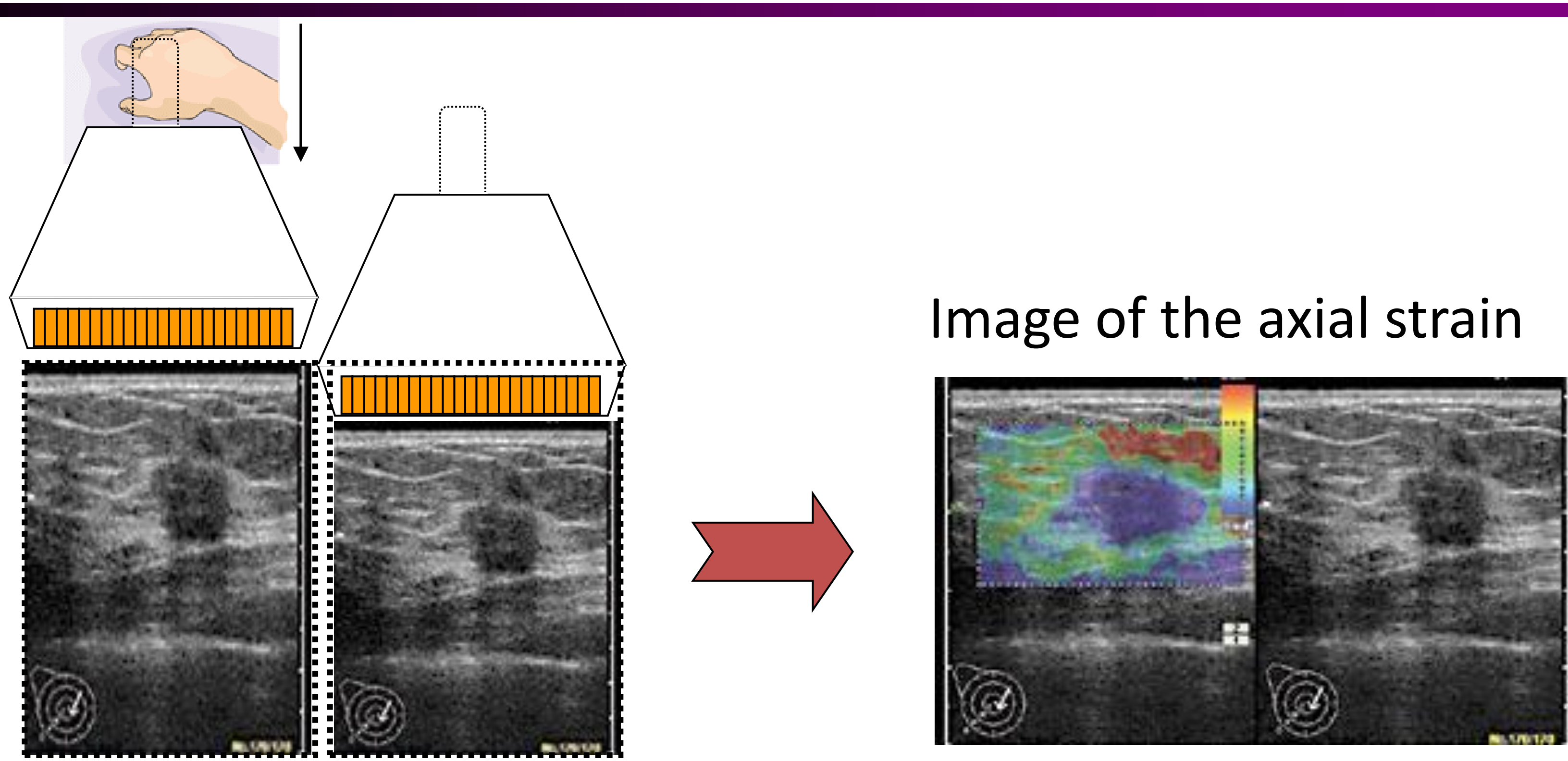
  - Static (*Ophir, Konofagou, Insana…*)
  - Dynamic / Harmonic (*Parker, Sato, Greenleaf, Levinson,…*)
  - Transient (*Fink, Tanter*)
  - Induced remotely by ultrasonic radiation force (*Sarvazyan, Trahey, Nightingale* (ARFI), *Greenleaf, Fink, Tanter*)

- **Imaging tissue displacements**

  - Ultrasound Speckle motion (*Sato, Parker, Levinson,Ophir, Fink…*)
  - Magnetic Resonance Imaging (*Greenleaf,…*)

# Static Elastography (J. Ophir)

**One create a static stress that induces a static strain.**
**On measure at all locations the strain (strain imaging)**

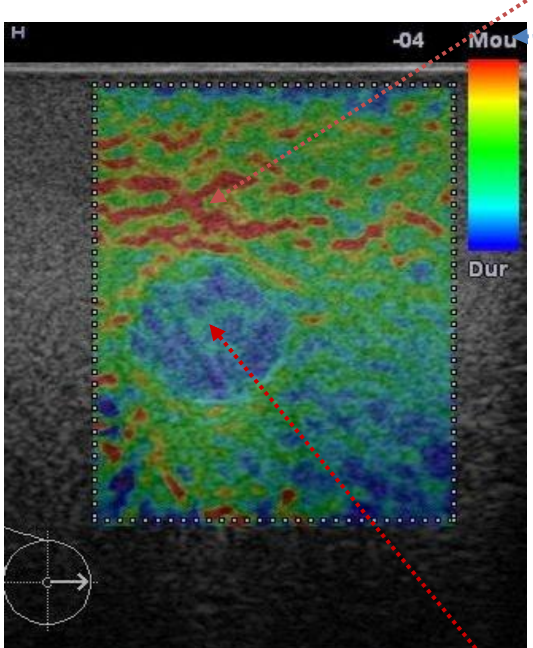


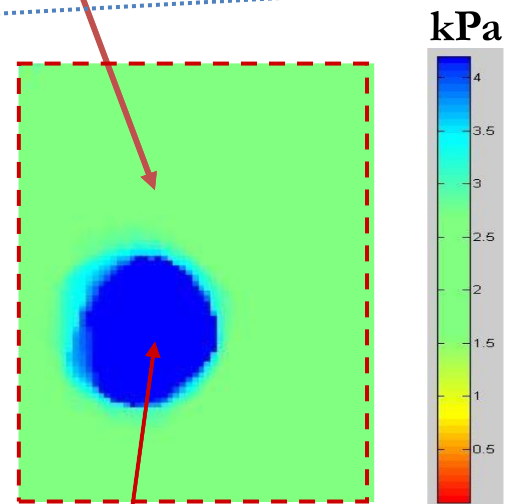

**<u>Hitachi, Medison, Siemens,Ultrasonix, Zonare, Toshoba…</u>**

# Comparison between the Supersonic Shear Wave Imaging and Static Elastography (strain imaging)

No compressional (pre-lesion) artefacts

Quantitative estimation of elasticity



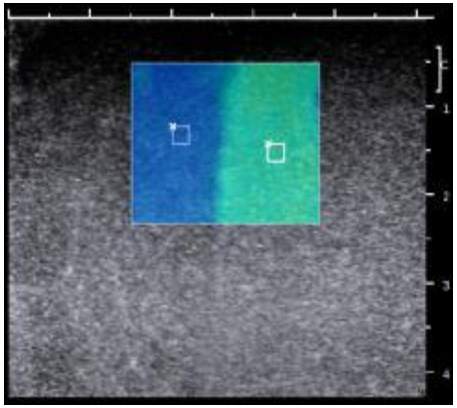




Much less elasticity variance in the inclusion (and outside)

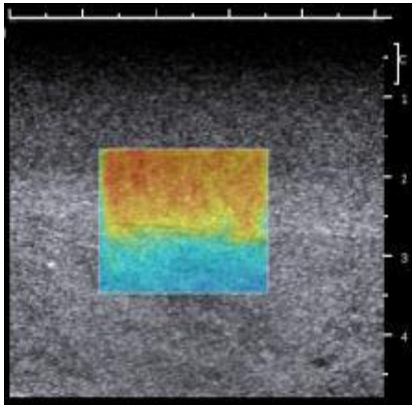
# Supersonic Shear Wave Imaging: Spatial resolution

Axial and lateral resolution in a two layers medium : around 1 mm

Lateral resolution



Axial resolution



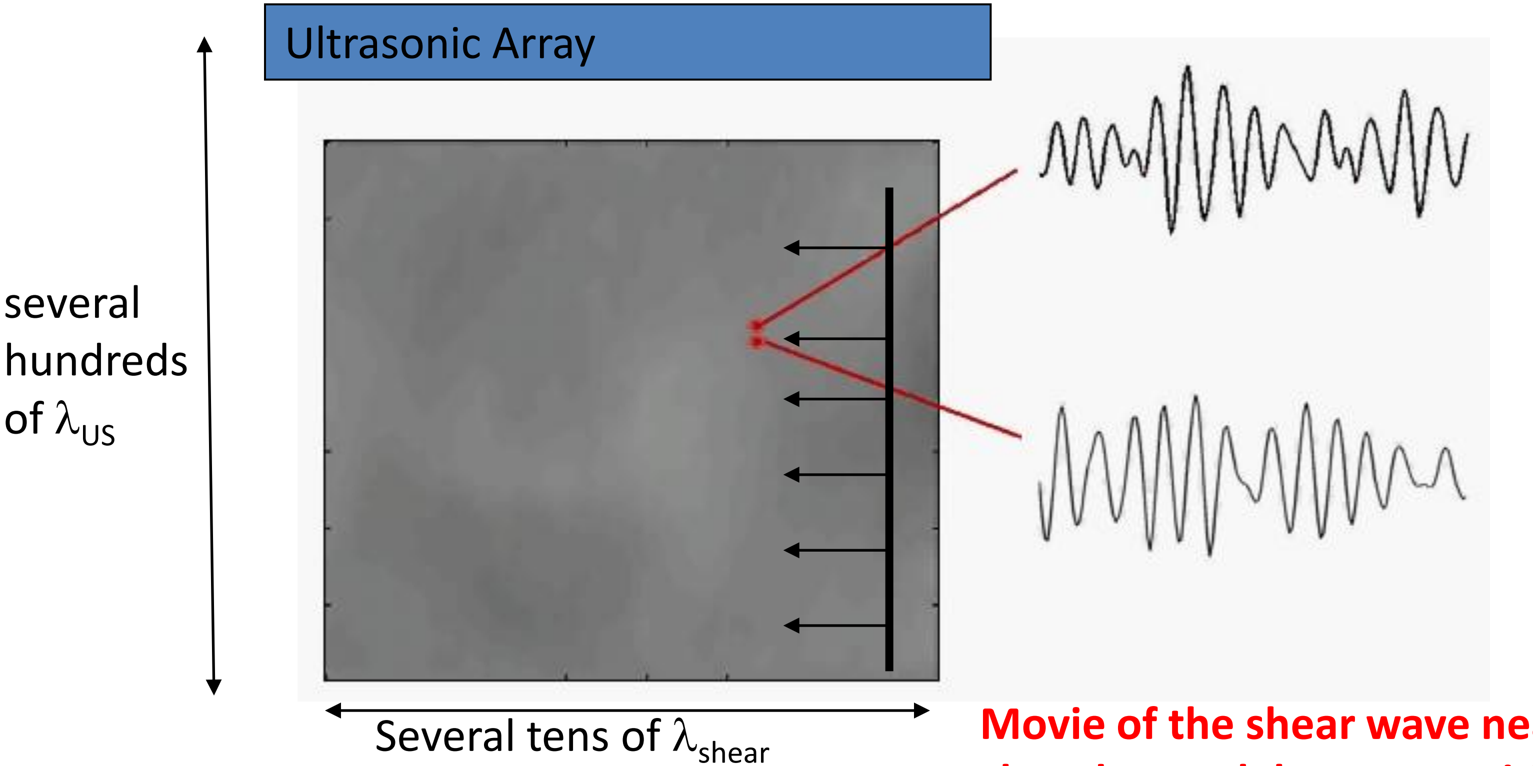
| Elasticity contrast | Axial Res (mm) | Lateral Res (mm) |
|---|---|---|
| 2 | 1 | 1.1 |
| 3 | 1.2 | 1.2 |
| 10 | 1.3 | 1.1 |

# Multiwave imaging and super-resolution

M. Fink, M. Tanter, "Multiwave Imaging and Superresolution"
Physics Today, 63(2), 28-33, Feb. 2010

**Shear wavelength : typicaly 10 mm**

**Spatial resolution on the shear modulus : 1 mm ($\lambda_{US}$)**




**Movie of the shear wave near-field closed to each heterogeneities**

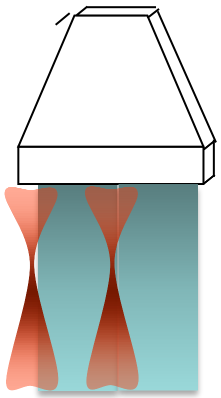
**Multi-Wave Imaging allows to get the Contrast of One Wave with the Resolution of the Second Wave**

# The Evolution of our Ultrafast Imaging Technology

# Safety and Efficiency issues in Elastography

## A Key difference between SSI and ARFI is ULTRAFAST IMAGING

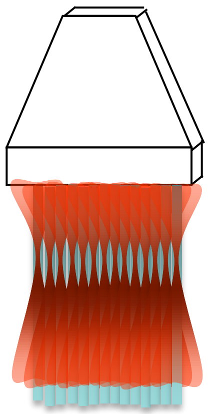
### SSI



« Flash » Imaging
+
Limited nb of « push »

**Real Time**
**Quantitative**
**No motion artefacts**

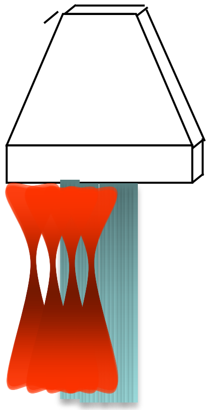
### ARFI



Imaging only at push location
+
High number of pushes

**Qualitative**

### ARFI- SWS



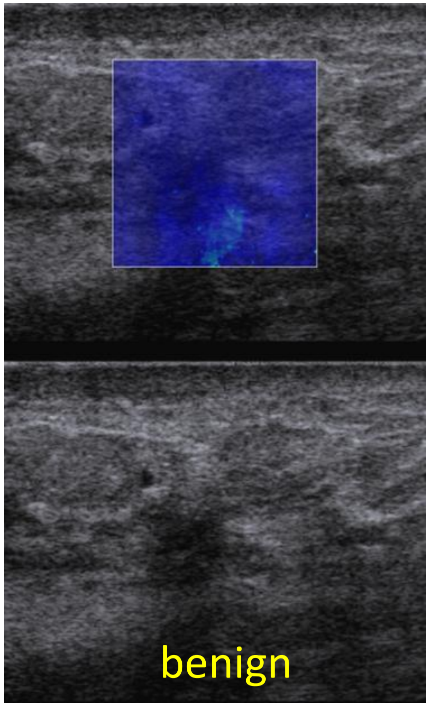
Synthetic building
of «flash» sequence
+ repeated local «Push»

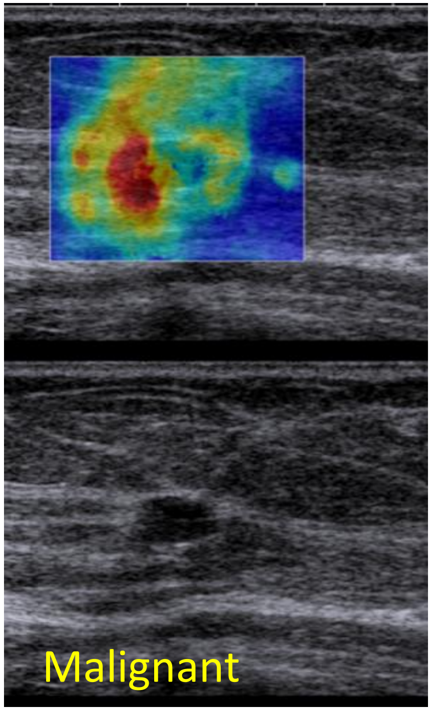
**Quantitative**
**Not Real Time**
**Potential motion Artefacts**

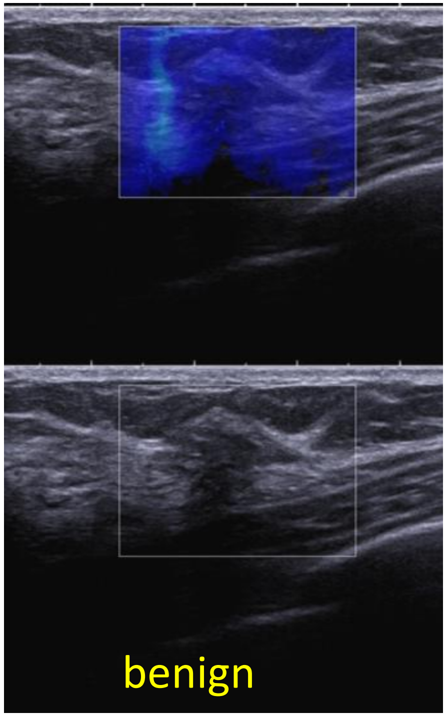
# Medical applications

- Breast
- Tyroid
- Liver
- Kidney
- Muscle
- **Vascular**
- **Cardiac**
- Eye
- Prostate
- Monitoring HIFU

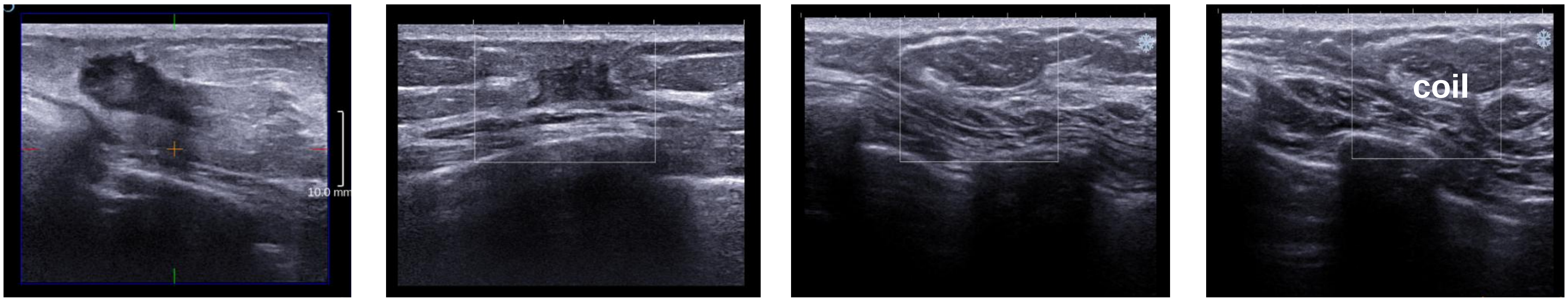
# Diagnostic impact in breast :



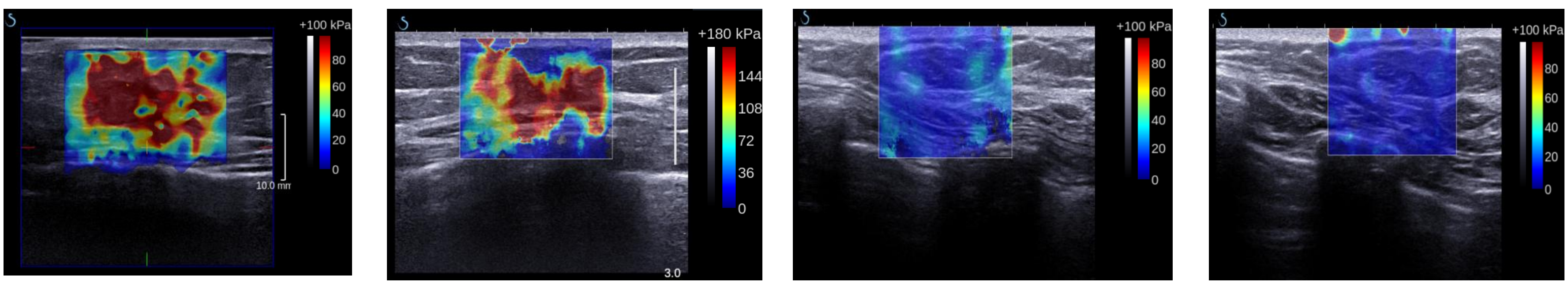



# Breast Chimiotherapy



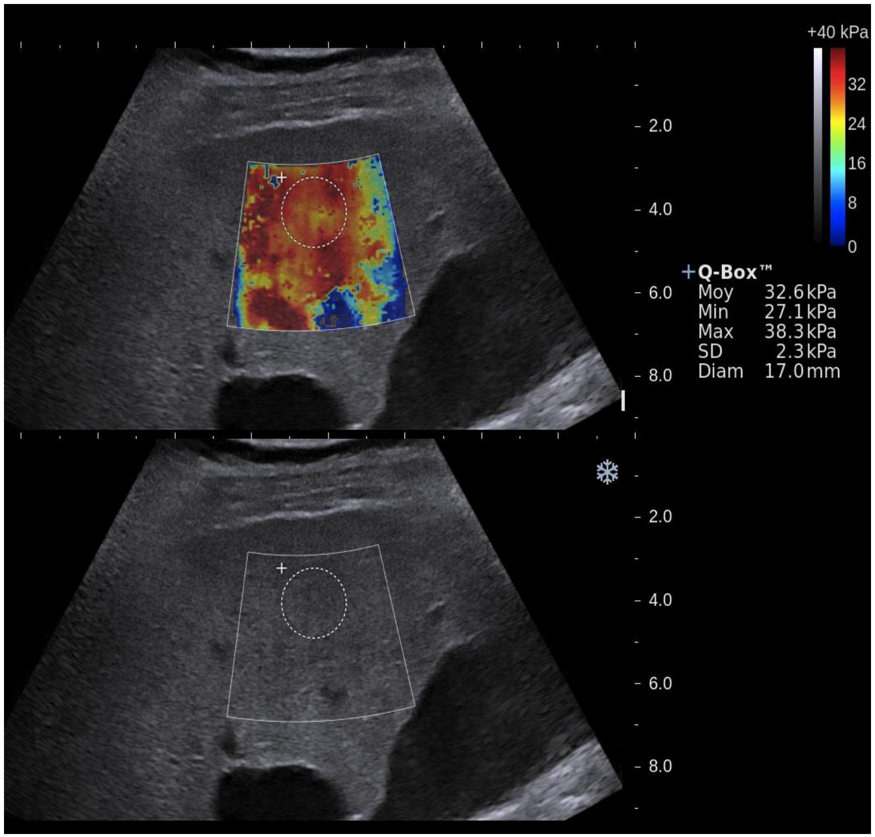

∅ = 2.04 cm | ∅ ≈ 1.80 cm | ∅ = 1.64 cm | ∅ ≈ 0.1 cm

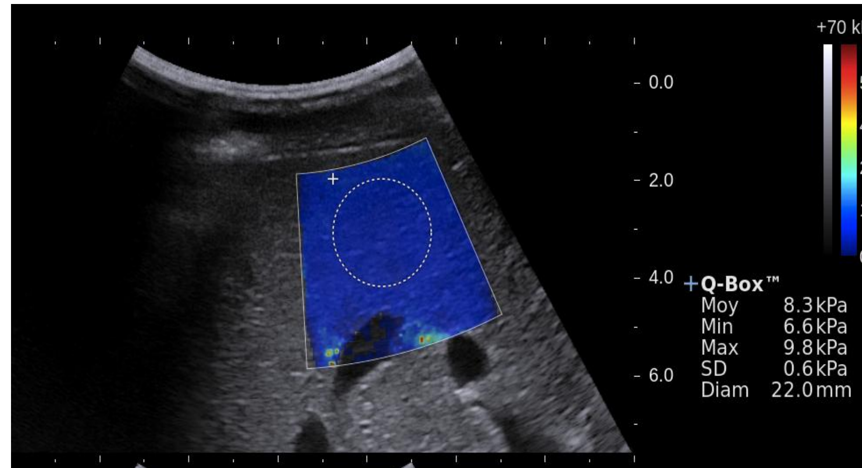


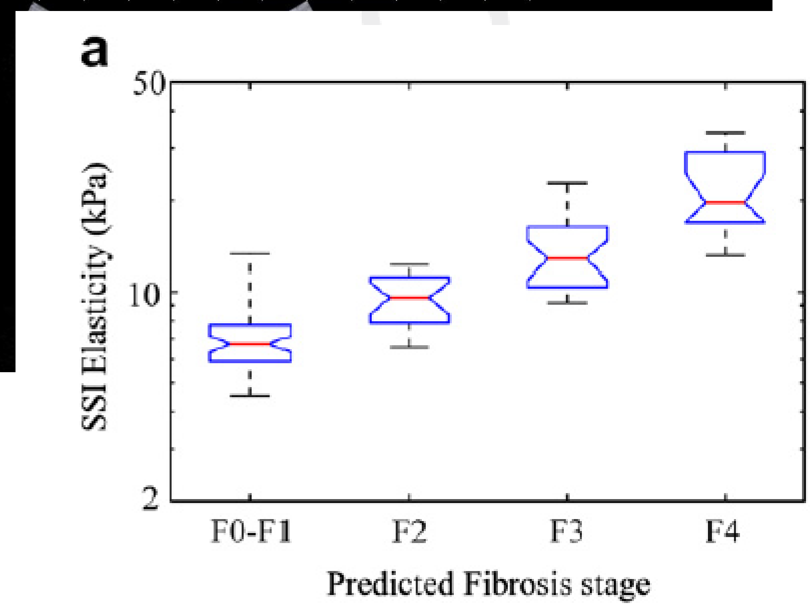

*June/2011* | *July/2011* | *August/2011* | *October/2011*

***(Collaboration A. Athanasiou, Curie Institute, Paris, France)***

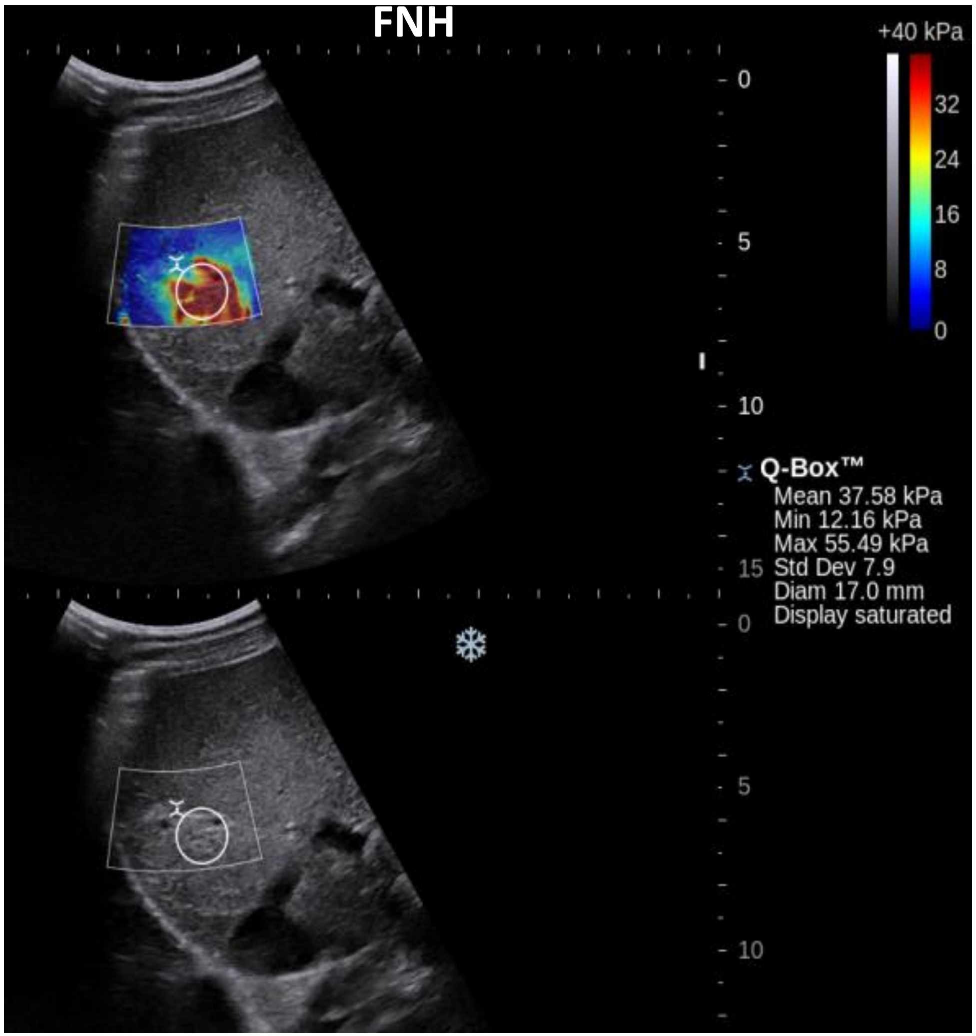
# Liver : Fibrosis and Cirrhosis

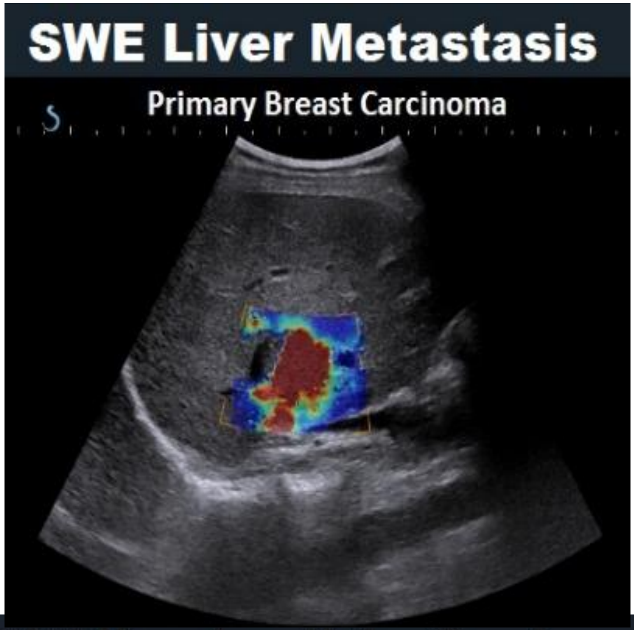


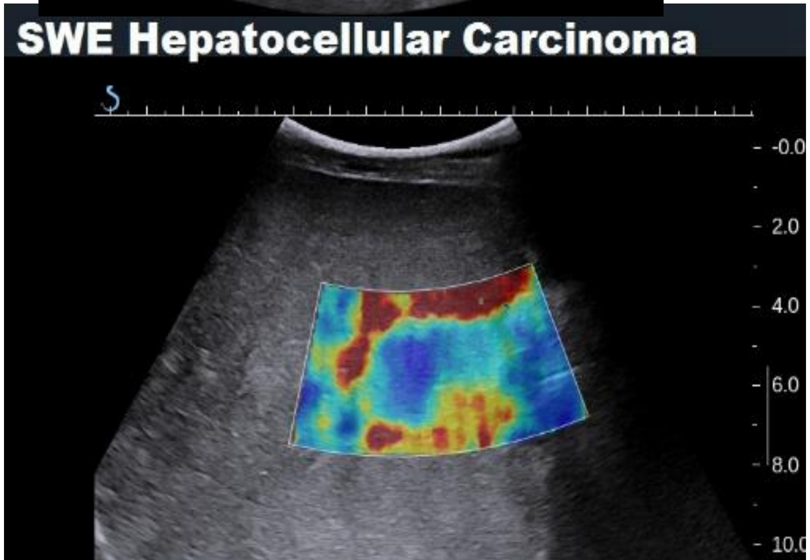



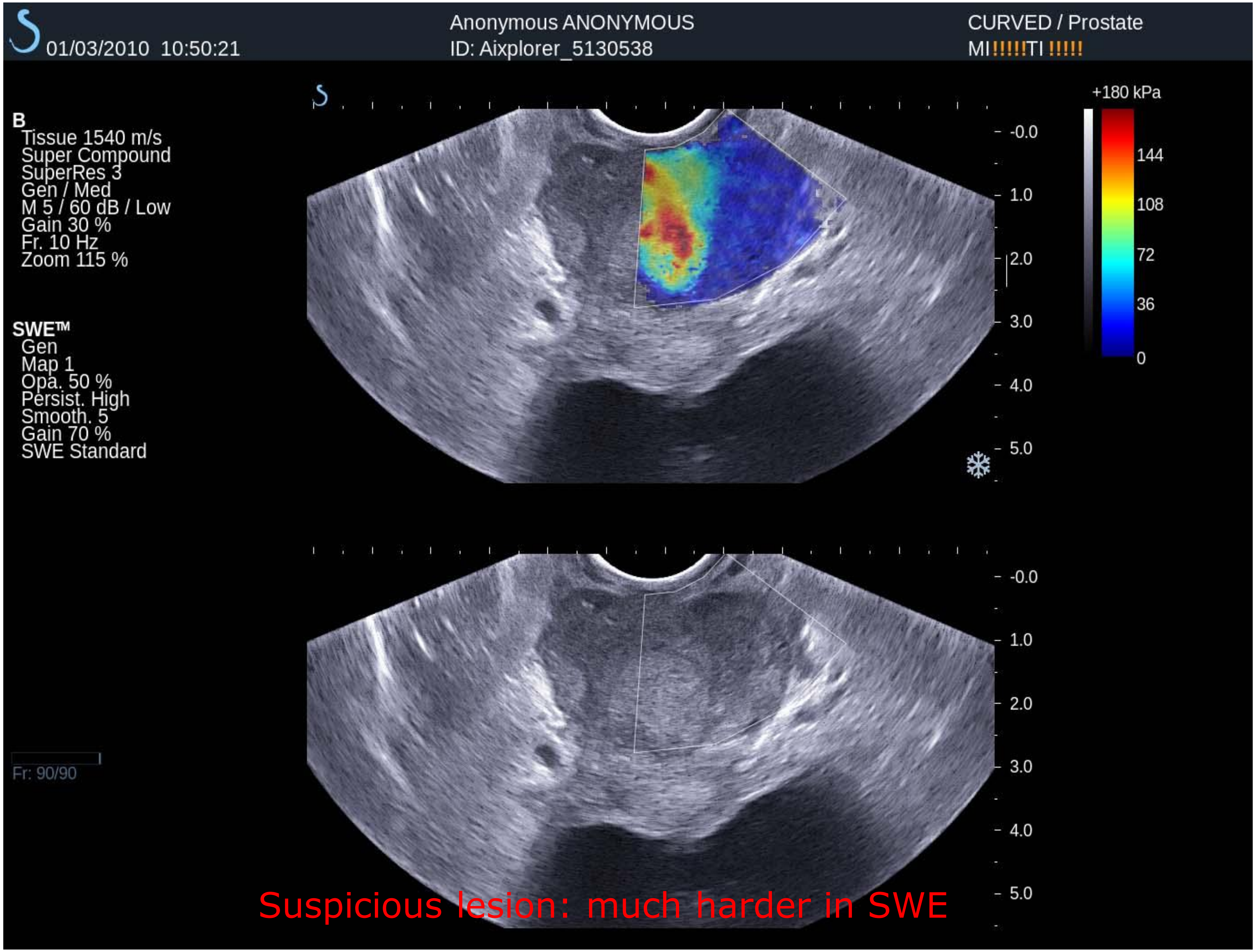
# Focal lesions in Liver : examples



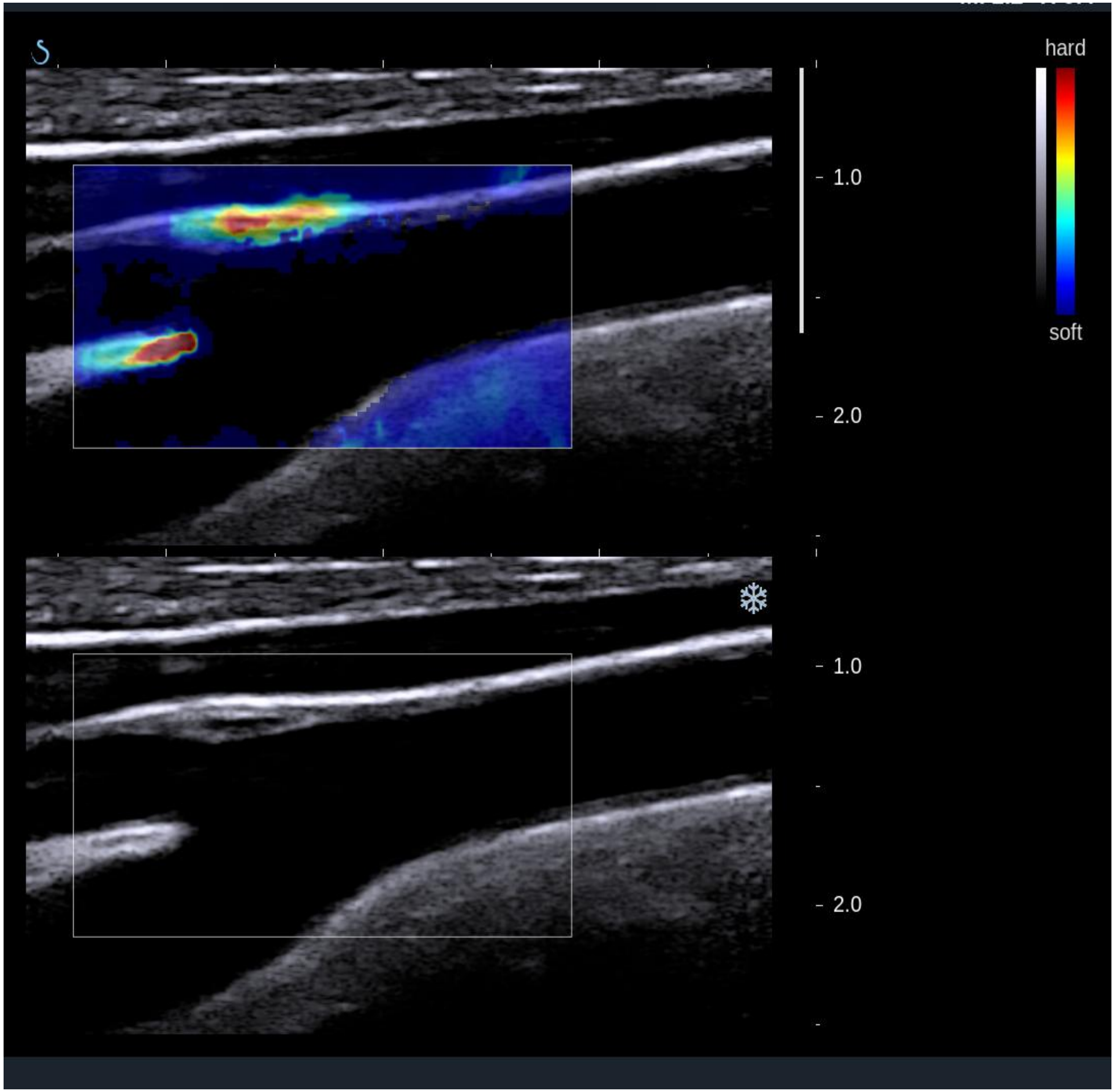



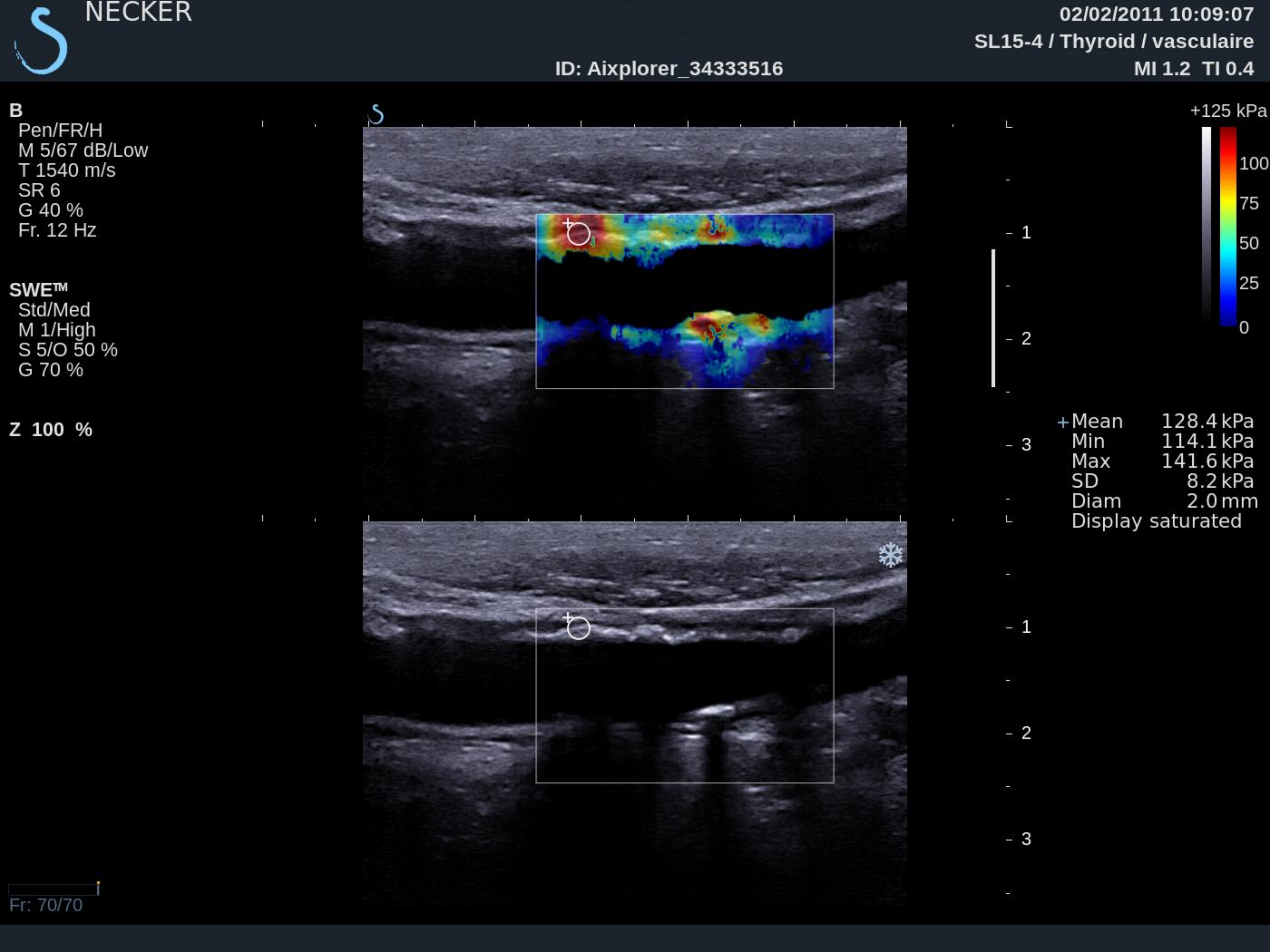



# Prostate – multiwave imaging

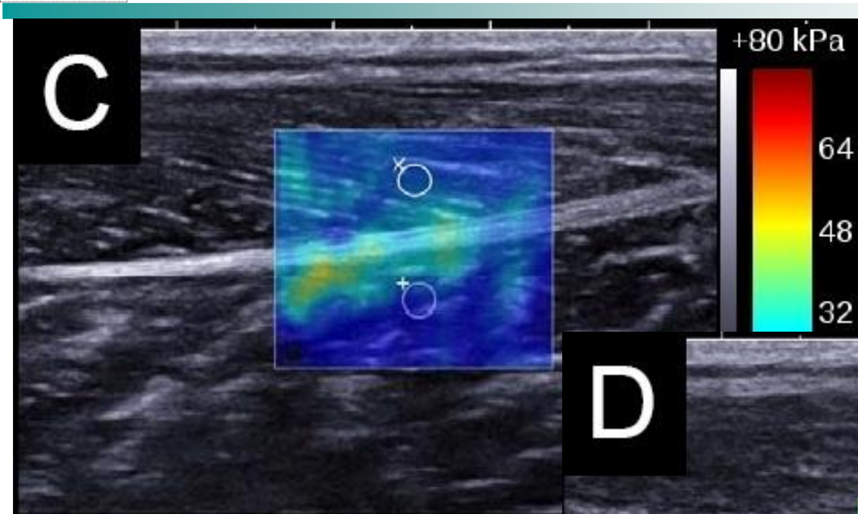


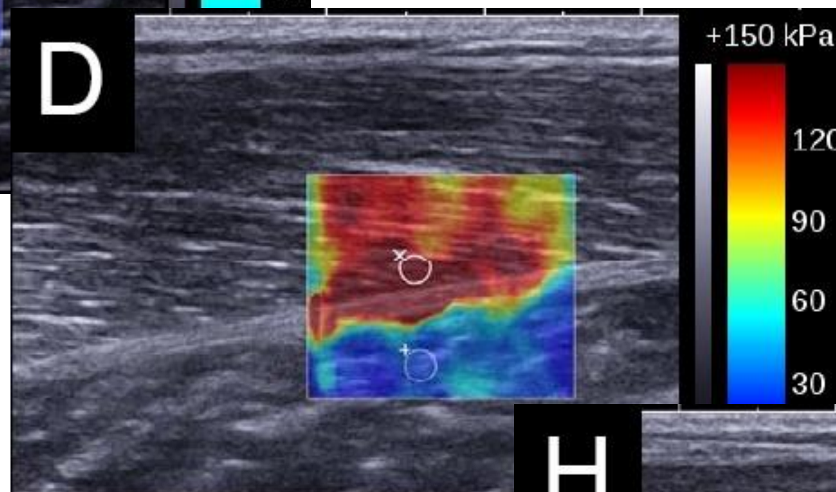
# Carotid Plaque Stifness

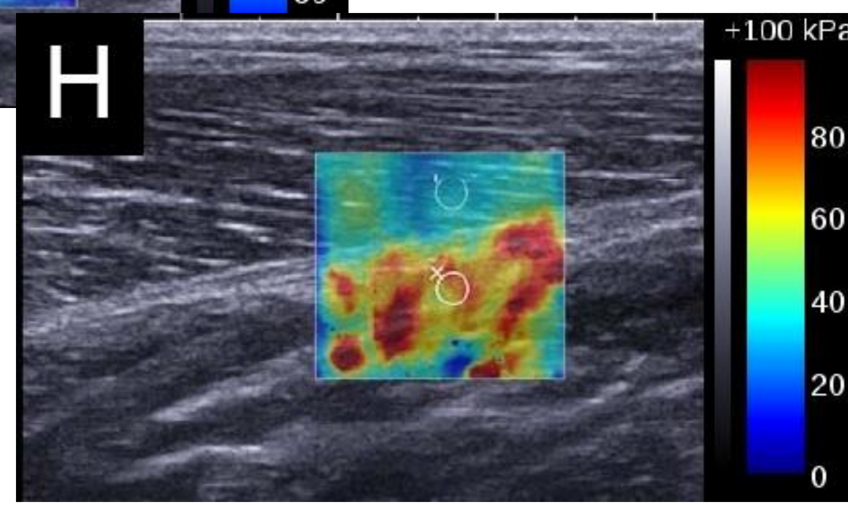



NECKER
02/02/2011 10:09:07
SL15-4 / Thyroid / vasculaire
ID: Aixplorer_34333516
MI 1.2 TI 0.4
B
Pen/FR/H
M 5/67 dB/Low
T 1540 m/s
SR 6
G 40 %
Fr. 12 Hz
SWE™
Std/Med
M 1/High
S 5/O 50 %
G 70 %
Z 100 %
+125 kPa
100
75
50
25
0
1
2
3
Mean 128.4 kPa
Min 114.1 kPa
Max 141.6 kPa
SD 8.2 kPa
Diam 2.0 mm
Display saturated
1
2
3
Fr: 70/70

# Dynamics of Muscle Contraction



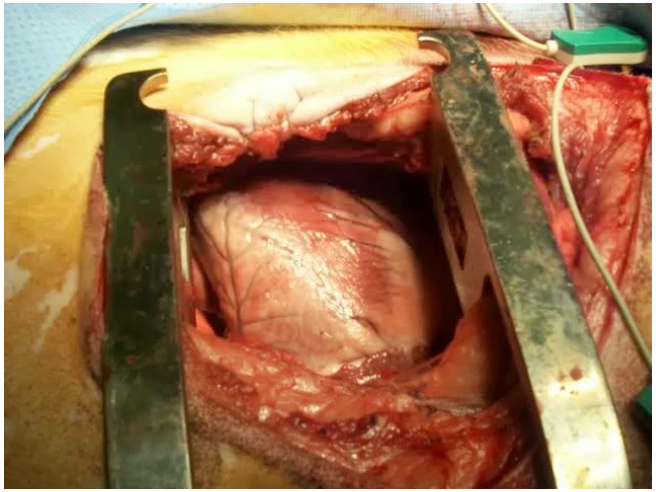

**Coll. M. Shinohara, K. sabra, Georgia Tech. University, Usa**

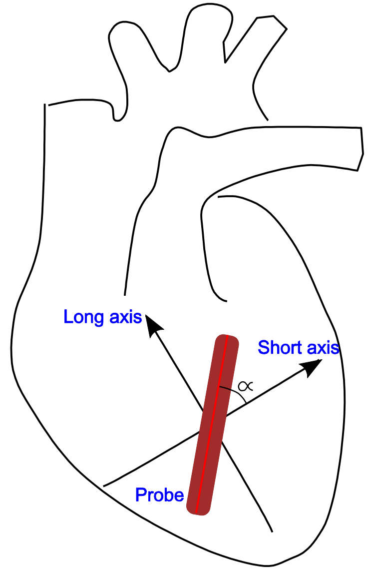
**Gastrocnemius Contraction**

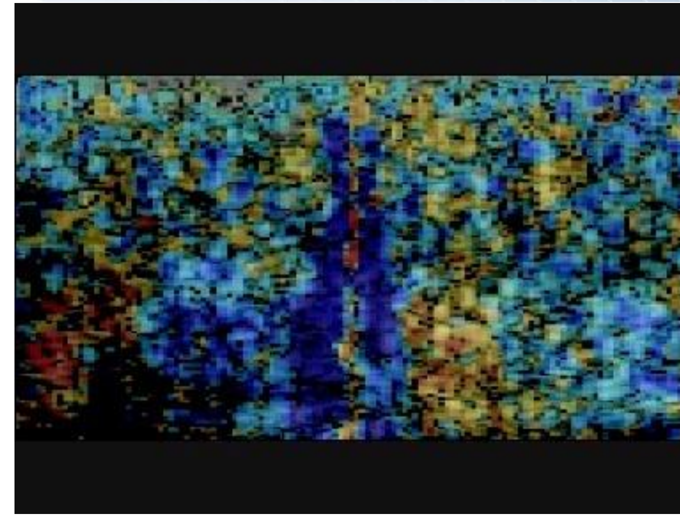
**Soleus Contraction**

Shinohara S., Sabra K., Genisson J.-L., Fink M., Tanter M.
"Real-time visualization of muscle stiffness distribution with ultrasound SWI during muscle contractions », Muscle and Nerve, June 2010

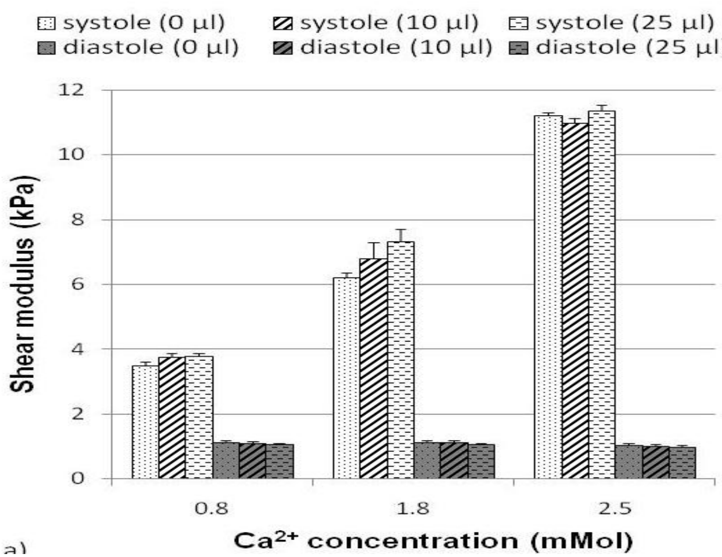
# Real Time Elasticity Changes of *in vivo* Cardiac Muscle (Sheep Model)

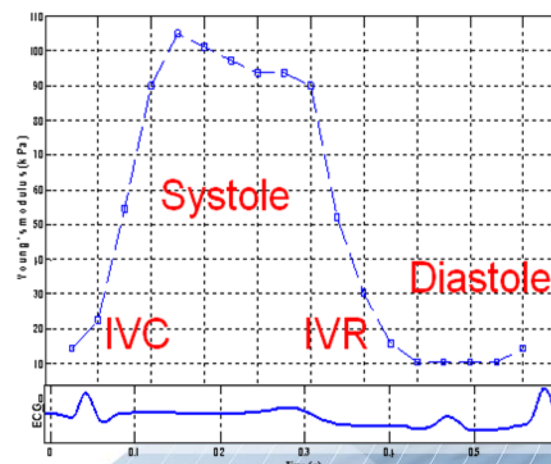




**5000 fps**



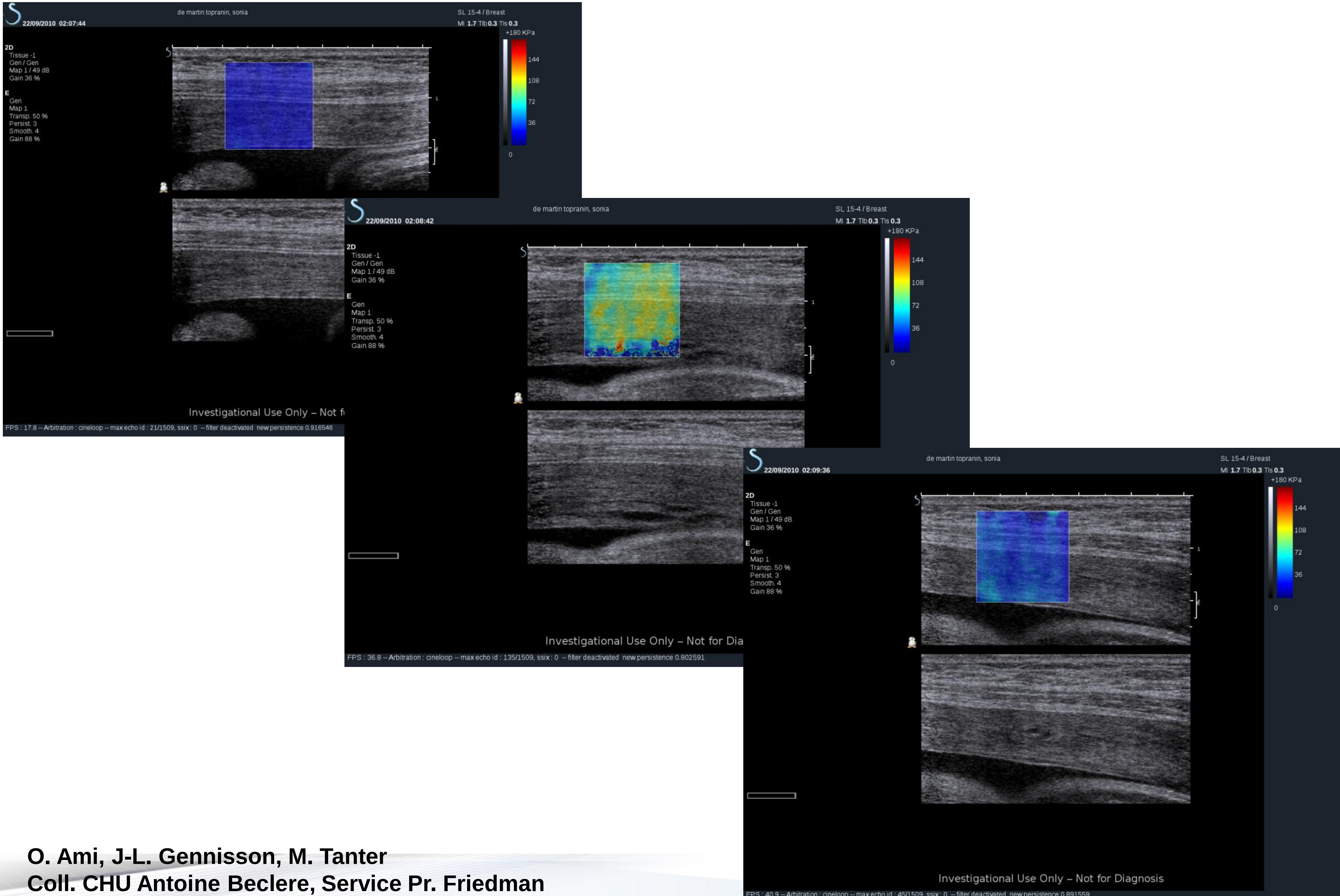




**Pernot M, Matteo P., Couade M., Crozatier B., Fischmeister R., Tanter M.**
**Journal of the American College of Cardiology , *2011***

**M. Couade, M. Pernot, P. Matteo, B. Crozatier, R. Fischmeister and M. Tanter**
**Ultr. Med. Biol., Oct. 2010**

Institut Langevin
ondes et images

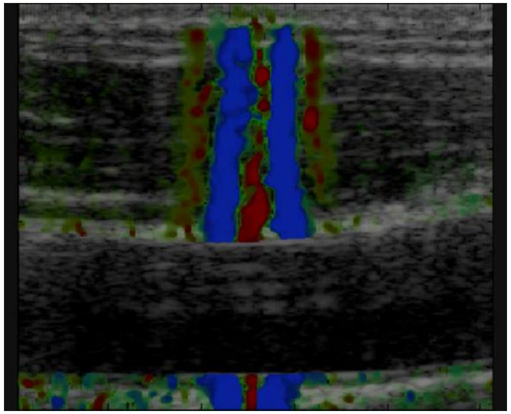
# Quantitative Monitoring of Uterin Contraction during Pregnancy

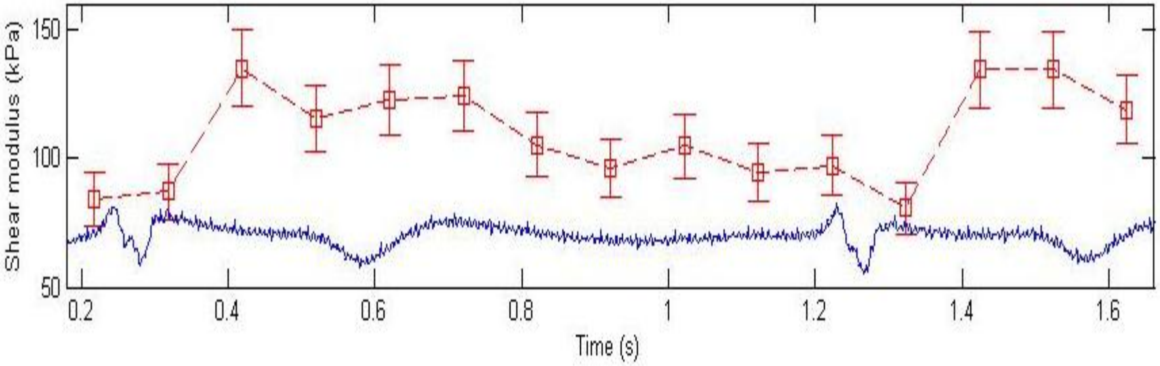



**O. Ami, J-L. Gennisson, M. Tanter**
**Coll. CHU Antoine Beclere, Service Pr. Friedman**

# The arterial stiffness varies with blood pressure (diastole/systole) - Carotid

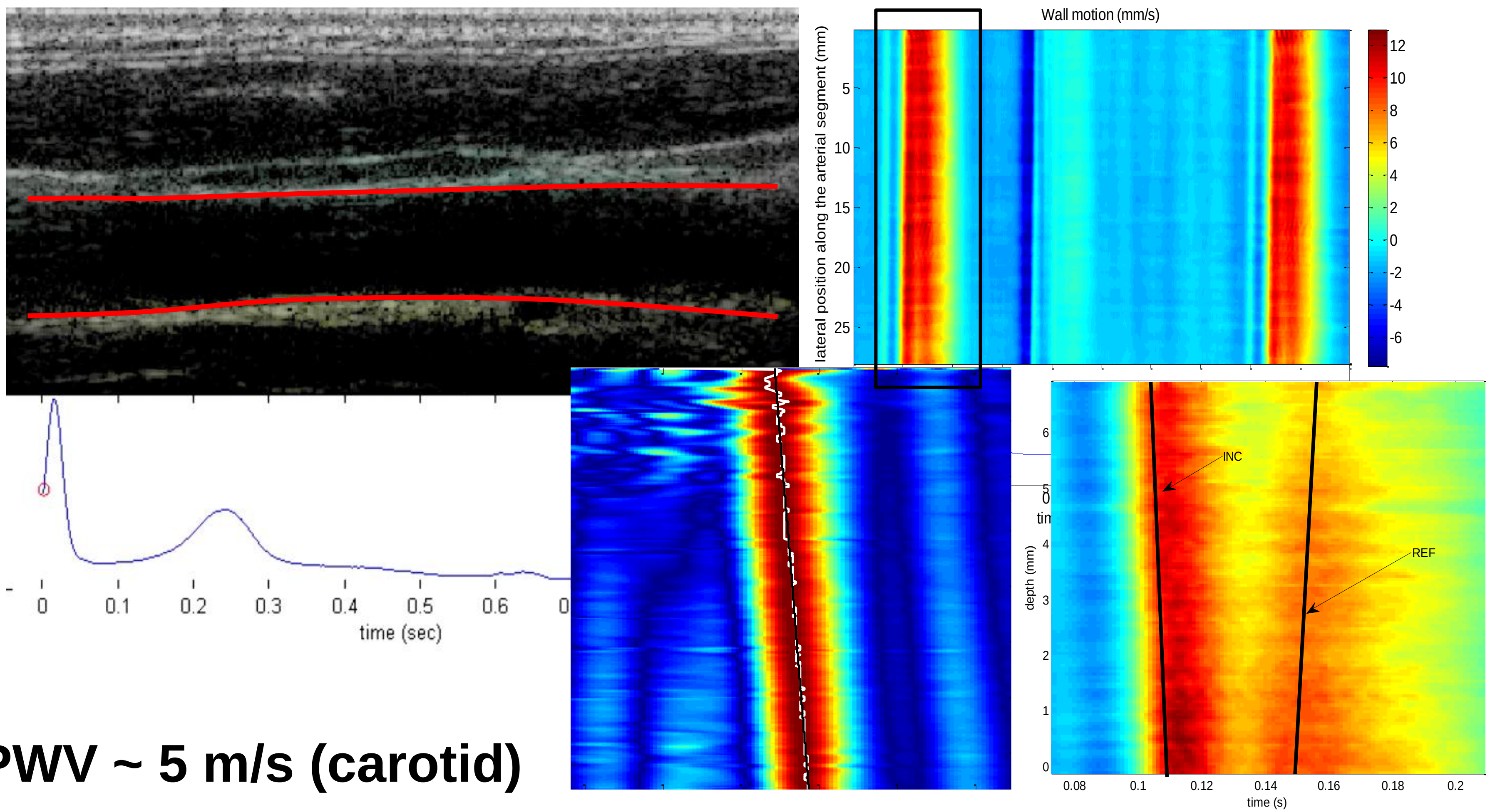
- **13 successive 20 ms experiment every 120 ms = 13 elasticity per cardiac cycle**





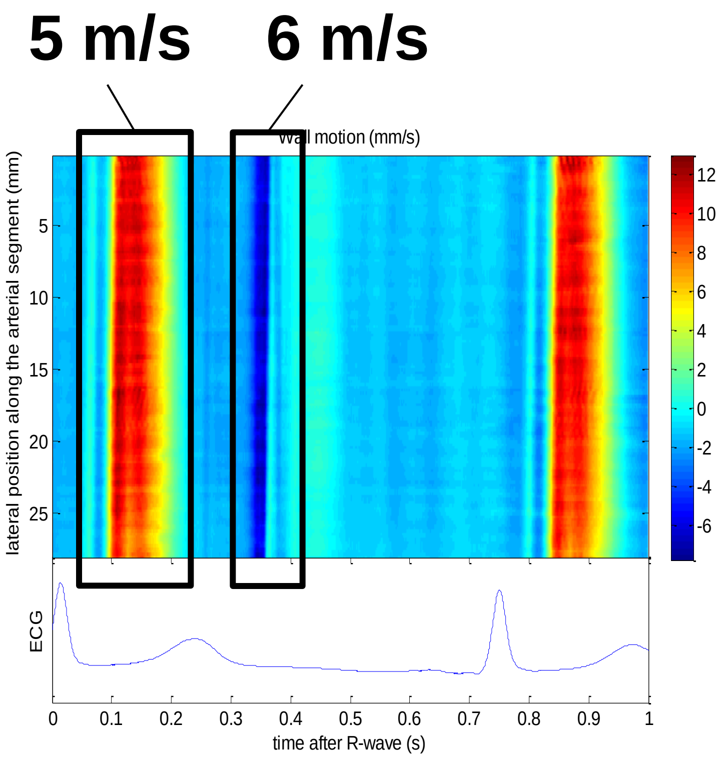
# Ultrafast imaging of the pulse wave along the carotid

- Frame rate : 3.000 frames/second




**PWV ~ 5 m/s (carotid)**

# Local estimation of PWV using ultrafast imaging



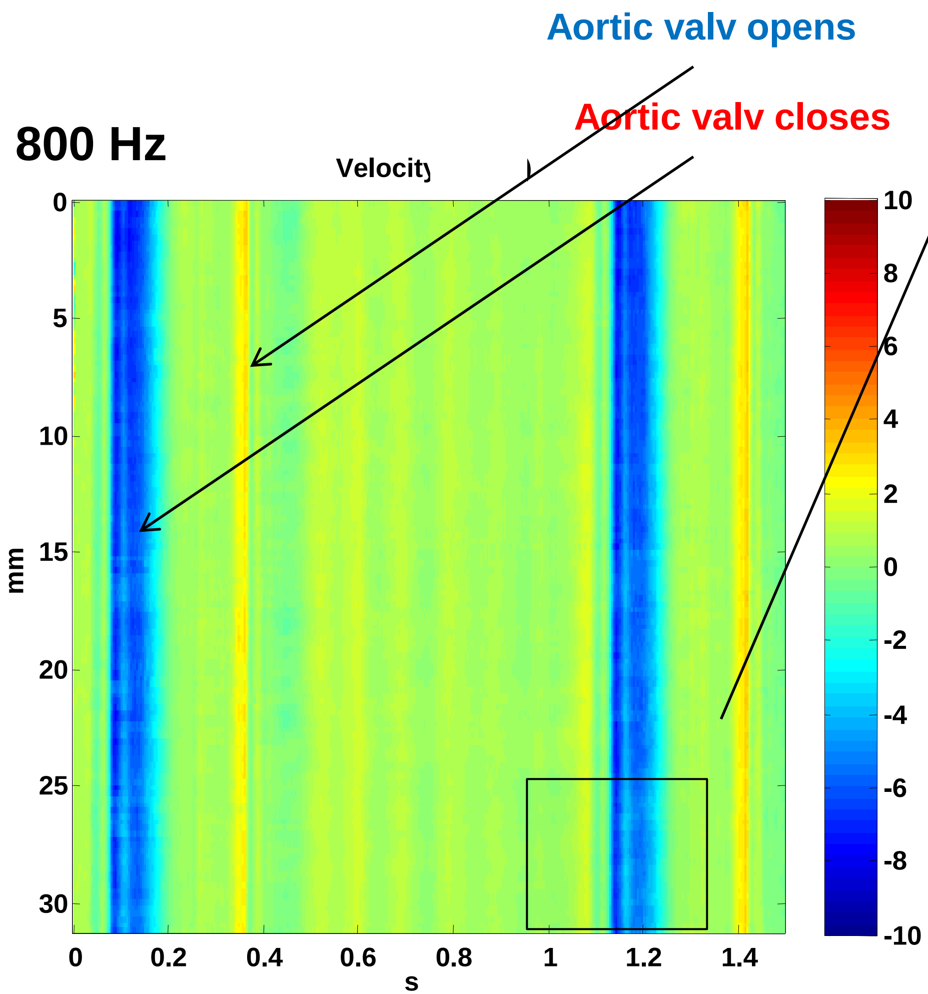

**≠ propagation speed**
**=**
**≠ elasticity**

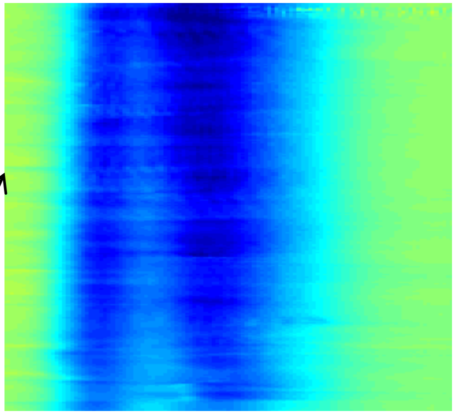
**Two estimations per cardiac cycle**

# PWV measured by ultrafast imaging

## PWV estimation using ultrafast scanner

**800 Hz**



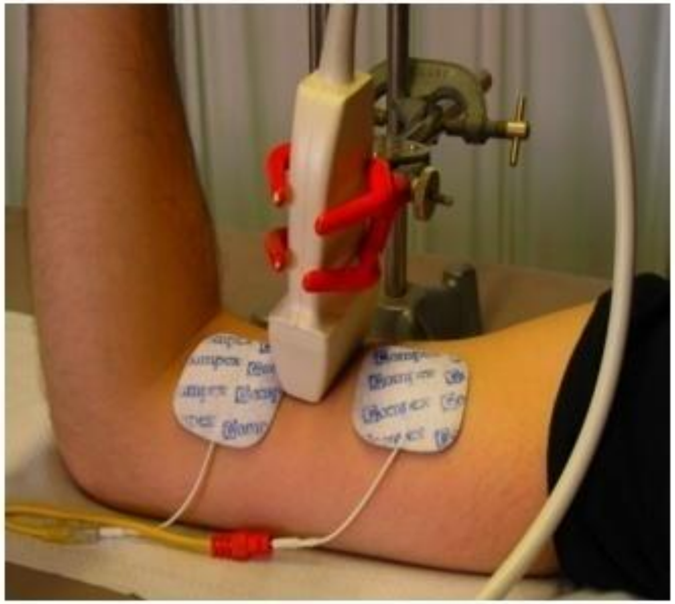



| | Opening | closing |
|---|---|---|
| Average over 19 volonteers | 5 m/s | 6 m/s |
| Std over 19 volonteers | 1 m/s | 1.1 m/s |
| Volonteer 1 (10x) | Opening | Closing |
| **Average 1** | 5,1 m/s | 6,3 m/s |
| **Standard Dev 1** | 0.46 m/s | 0.4 m/s |

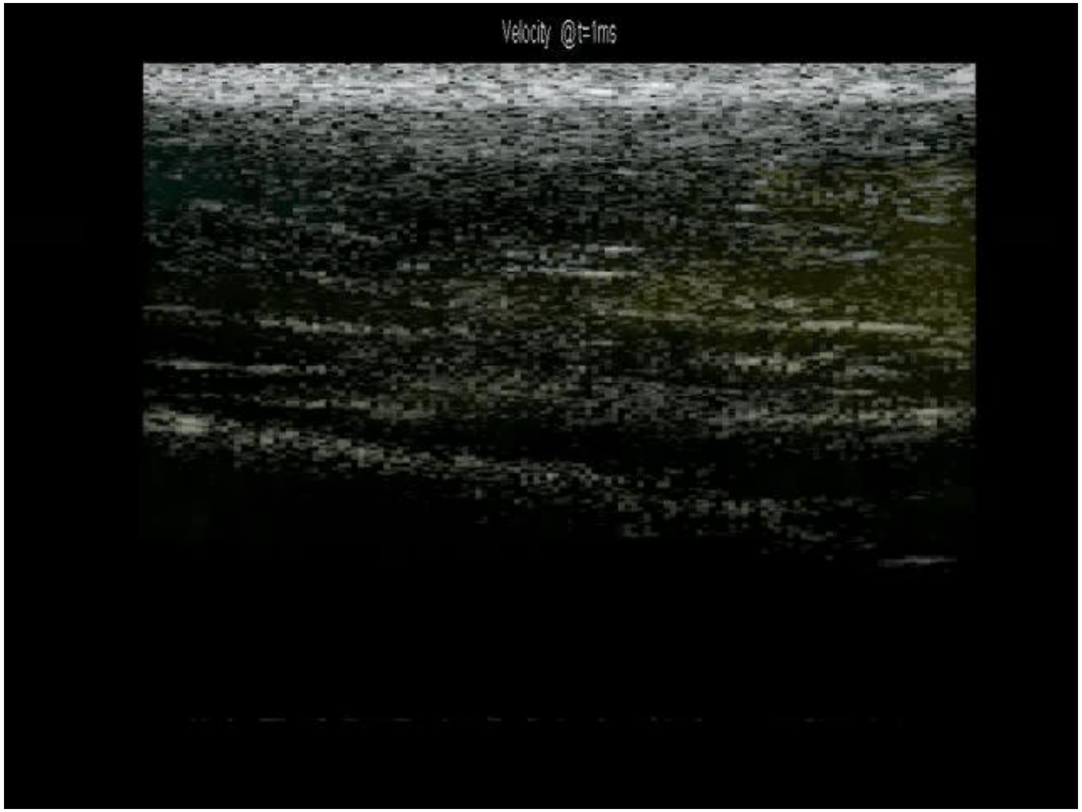
**Couade, M.; Pernot, M.; Messas, E.; Emmerich, J.; Hagege, A.; Fink, M. & Tanter, M. (2011), 'Ultrafast imaging of the arterial pulse wave', *Irbm* 32(2), 106--108.**

# Ultrafast Imaging of Intrinsic waves

# Ultrafast Ultrasonic Imaging of Muscle fibers activation



**Our body is the ground of many transient phenomena at time scales of the order of milliseconds**



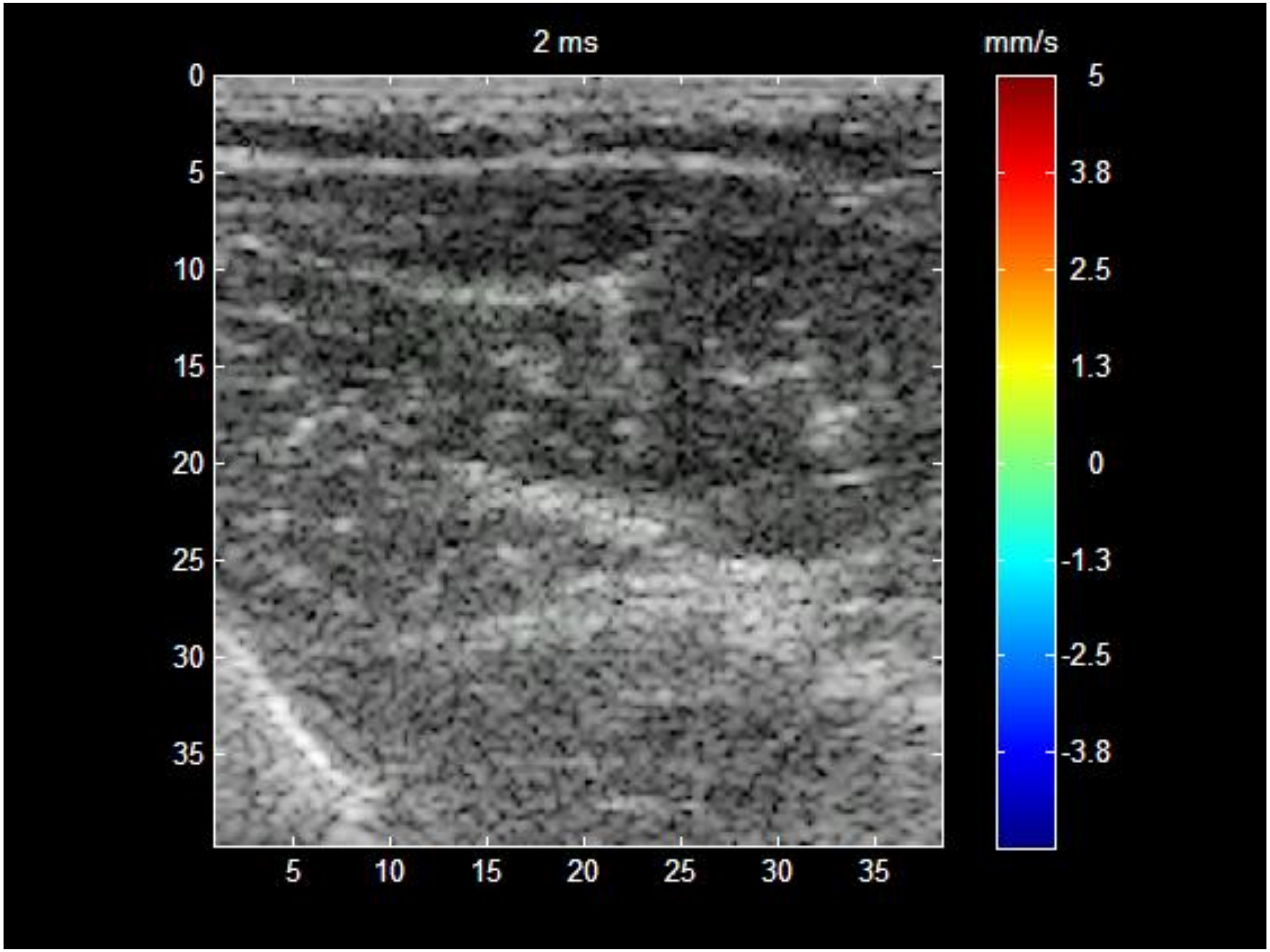

**2000 images/s**

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


**Deffieux, T.; Gennisson, J.-L.; Tanter, M.; Fink, M. Nordez, A.**
**'Ultrafast imaging of in vivo muscle contraction using ultrasound', *Applied Physics Letters* 89(18), 2006**

**Deffieux T, Gennisson JL, Tanter M, et al. IEEE TRANSACTIONS ON ULTRASONICS, 55 (10), Pages: 2177-2190, OCT 2008**

# Ultrafast Localization of activated muscle fiber bundles

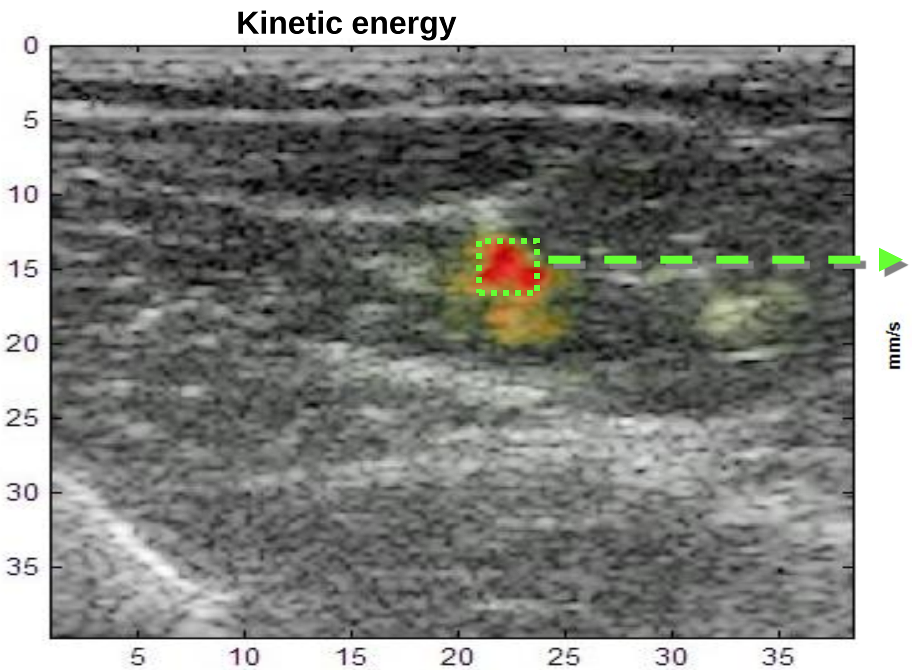


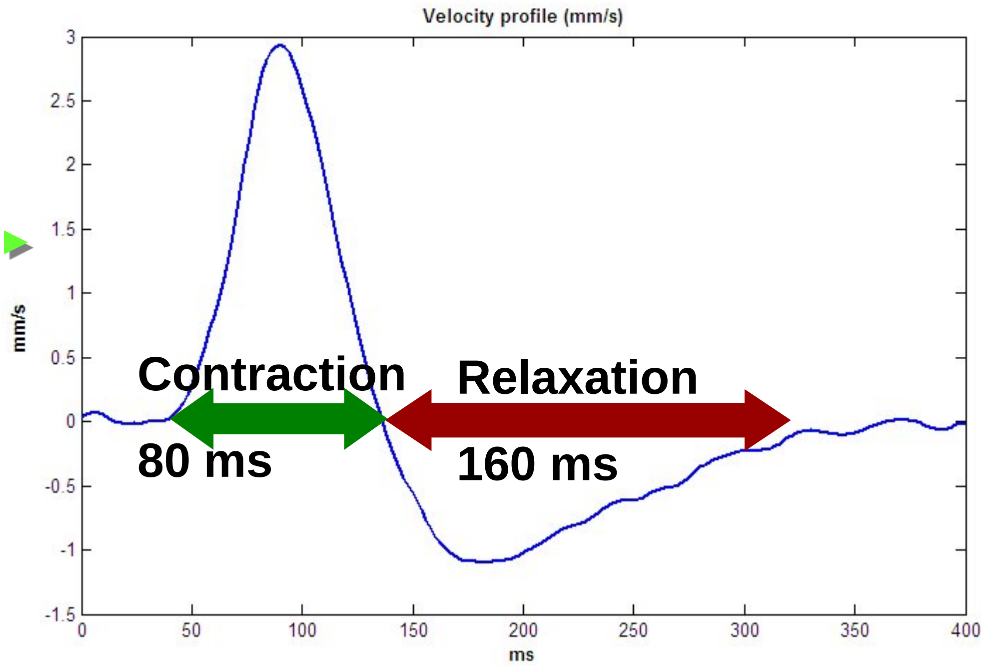

Deffieux, T.; Gennisson, J.-L.; Tanter, M.; Fink, M. Nordez, A.
'Ultrafast imaging of in vivo muscle contraction using ultrasound', *Applied Physics Letters* 89(18), 2006

Deffieux T, Gennisson JL, Tanter M, et al. IEEE TRANSACTIONS ON ULTRASONICS, 55 (10), Pages: 2177-2190, OCT 2008

# Ultrafast Localization of activated muscle fiber bundles

## Localization and time profile of contraction

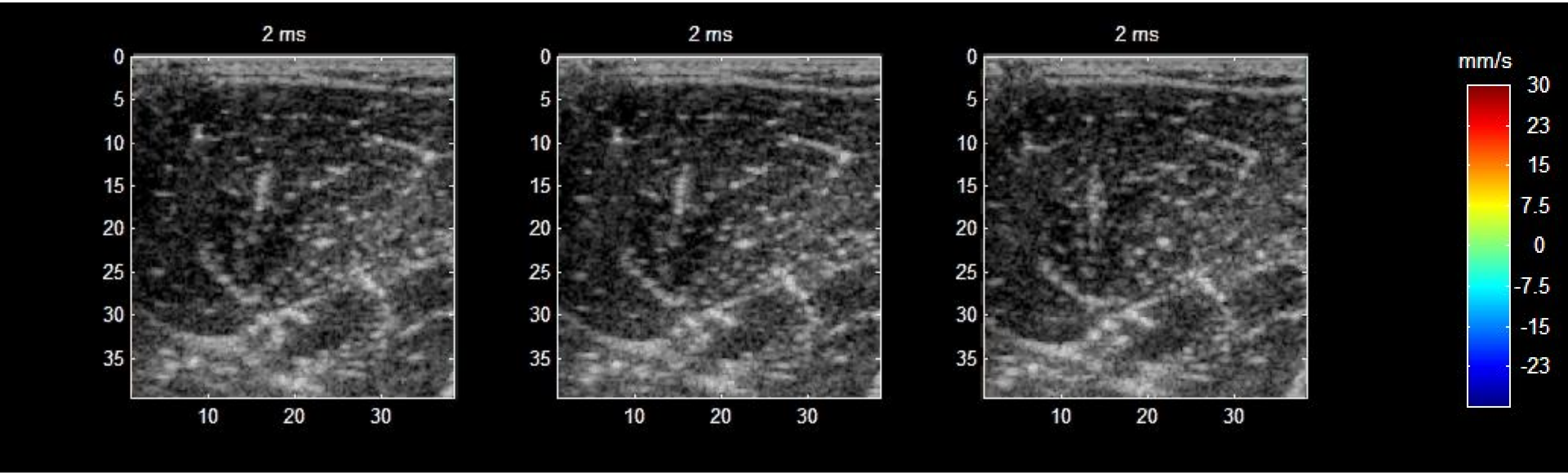



Deffieux, T.; Gennisson, J.-L.; Tanter, M.; Fink, M. Nordez, A.
'Ultrafast imaging of in vivo muscle contraction using ultrasound', *Applied Physics Letters* 89(18), 2006

Deffieux T, Gennisson JL, Tanter M, et al. IEEE TRANSACTIONS ON ULTRASONICS, 55 (10), Pages: 2177-2190, OCT 2008

# Effect of electro stimulation amplitude on the contraction

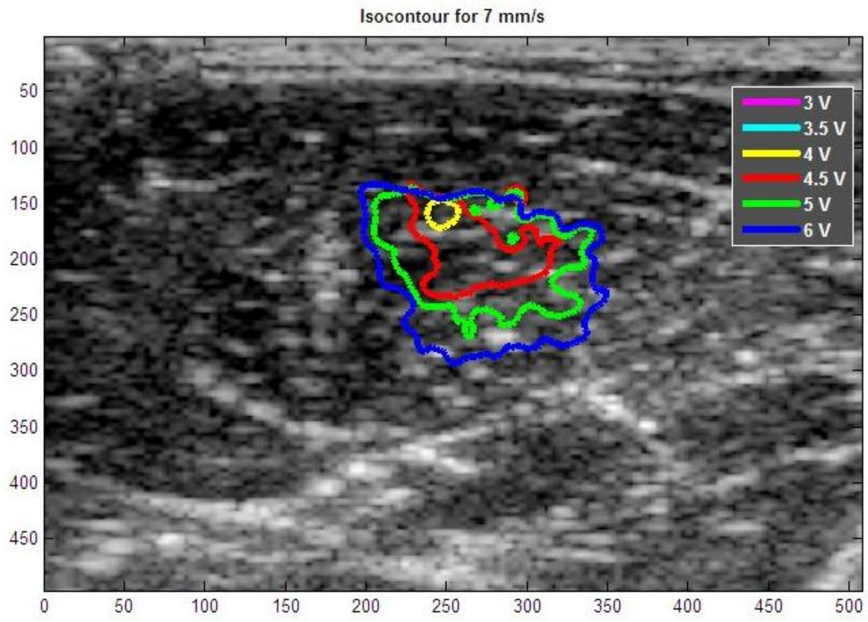


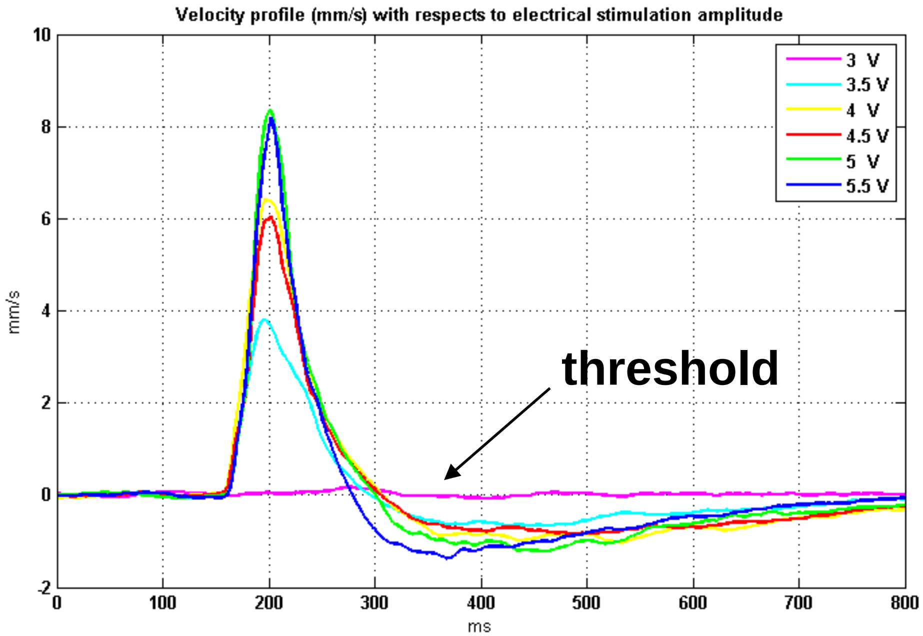

**3.5 V** **4.5 V** **5.5 V**

**Deffieux, T.; Gennisson, J.-L.; Tanter, M.; Fink, M. Nordez, A.**
**'Ultrafast imaging of in vivo muscle contraction using ultrasound', *Applied Physics Letters* 89(18), 2006**

**Deffieux T, Gennisson JL, Tanter M, et al. IEEE TRANSACTIONS ON ULTRASONICS, 55 (10), Pages: 2177-2190, OCT 2008**

# Effect of electro stimulation amplitude on the contraction





Deffieux, T.; Gennisson, J.-L.; Tanter, M.; Fink, M. Nordez, A.
'Ultrafast imaging of in vivo muscle contraction using ultrasound', *Applied Physics Letters* 89(18), 2006

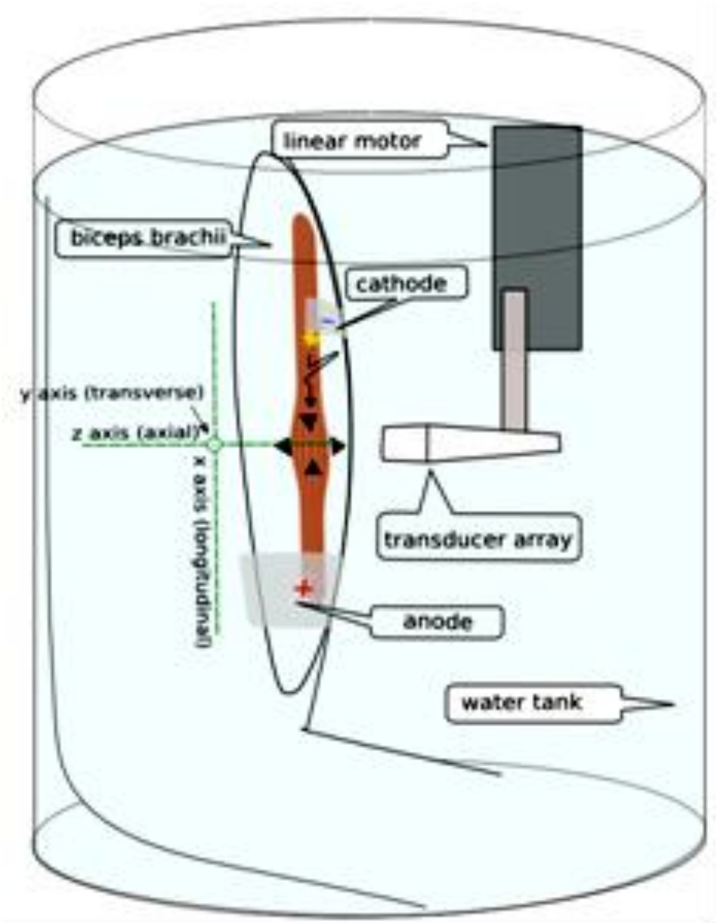
Deffieux T, Gennisson JL, Tanter M, et al. IEEE TRANSACTIONS ON ULTRASONICS, 55 (10), Pages: 2177-2190, OCT 2008

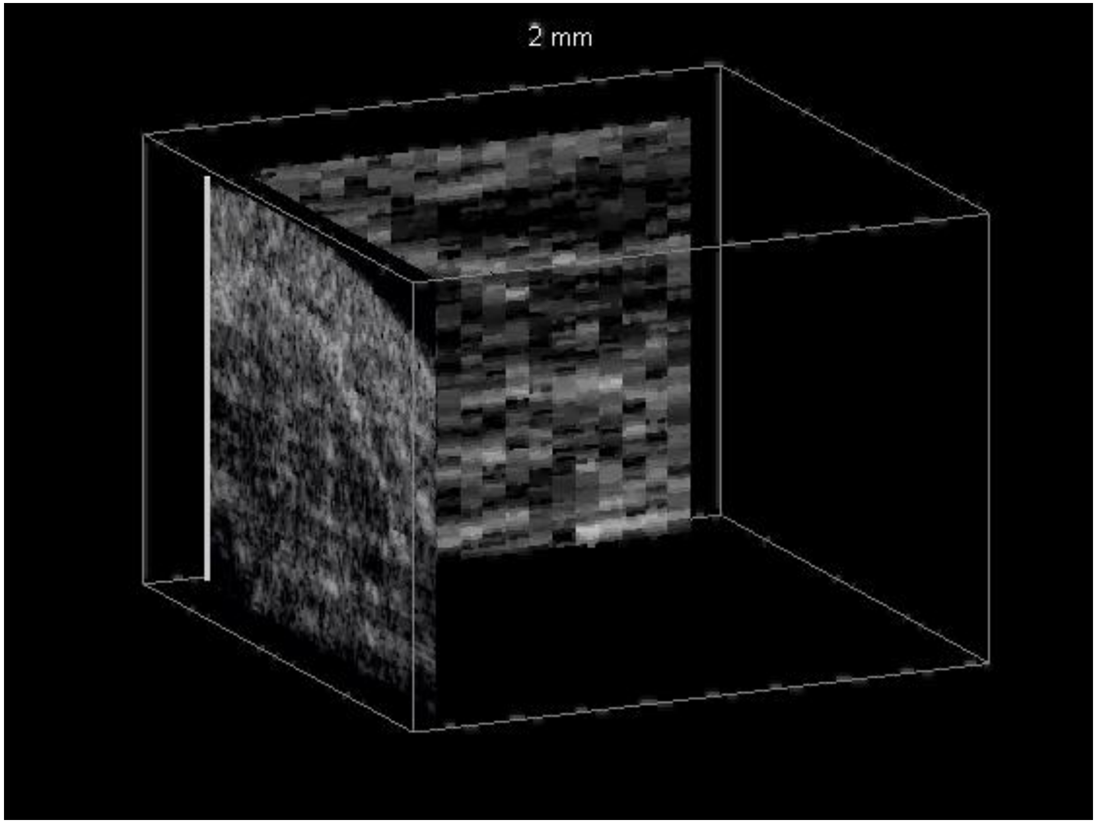
# 3D Ultrafast imaging of muscle electrostimulation

## 3D linear Scan with triggered acquisition/electrostimulation

**22 translations with a 2 mm step**

**3D Scan volume : 35x35x44 $mm^3$**





**Deffieux, T.; Gennisson, J.-L.; Tanter, M.; Fink, M. Nordez, A.**
**'Ultrafast imaging of in vivo muscle contraction using ultrasound', *Applied Physics Letters* 89(18), 2006**

**Deffieux T, Gennisson JL, Tanter M, et al. IEEE TRANSACTIONS ON ULTRASONICS, 55 (10), Pages: 2177-2190, OCT 2008**

# Electromechanical waves in the heart

Myocardial rapid velocity distribution, Kanai, H; Koiwa, Y
ULTRASOUND IN MEDICINE AND BIOLOGY, 27(4), 481-498, 2001

Left ventricular transmural systolic function by high-sensitivity velocity measurement "phased-tracking method" across the septum in doxorubicin cardiomyopathy, Koiwa, Y; Kanai, H; et al.
ULTRASOUND IN MEDICINE AND BIOLOGY, 28, 11-12 , 1395-1403, 2002

**First ultrasonic imaging of mechanical Waves**

Electromechanical imaging of the myocardium at normal and pathological states
Pernot, M; Konofagou, IEEE International Ultrasonics Symposium Location: Rotterdam, 2005

ECG-gated, mechanical and electromechanical wave imaging of cardiovascular tissues in vivo
Pernot, Mathieu; Fujikura, Kana; Fung-Kee-Fung, Simon D.; et al., ULTRASOUND IN MEDICINE AND BIOLOGY, 33 (7), 1075-1085, 2007

Noninvasive electromechanical wave imaging and conduction velocity estimation in vivo
Konofagou, Elisa; Luo, Jianwen; Saluja, Deepak; et al. IEEE ULTRASONICS SYMPOSIUM , 969-972,2007

**First US imaging of Electro- mechanical Waves (ECG Gated)**

Ultrafast imaging of the heart using circular wave synthetic imaging with phased arrays
Couade M., Hagege, A.-A. ; Fink, M. IEEE Ultrasonics Symposium, pp 515-518, 2009.

**First ultrafast imaging of single heartbeat**

H. Kanai: "Propagation of Vibration Caused by Electrical Excitation in the Normal Human Heart"
*Ultrasound in Medicine & Biology* Vol. 35, No. 6, pp. 936-948 (June 2009)

Electromechanical Wave Imaging for Noninvasive Mapping of the 3D Electrical Activation Sequence in vivo, Provost, Jean; Lee, Wei-Ning; Fujikura, Kana; et al., CIRCULATION, 122(21), 2010

Physiologic Cardiovascular Strain and Intrinsic Wave Imaging, Konofagou, Elisa; Lee, Wei-Ning; Luo, Jianwen; et al., ANNUAL REVIEW OF BIOMEDICAL ENGINEERING, VOL 13 Book Series: Annual Review of Biomedical Engineering, 13,477-505, 2011

Imaging the electromechanical activity of the heart in vivo,
Provost, Jean; Lee, Wei-Ning; Fujikura, Kana; et al., P.N.A.S., 108(21), 2011

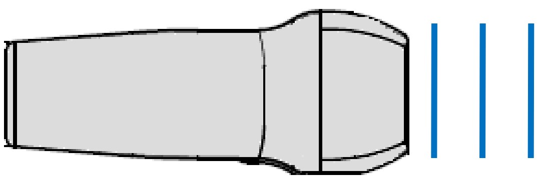
**ECG Gated US imaging Of Electromechanical waves**

Single-heartbeat electromechanical wave imaging using temporally unequispaced acquisition sequences,
Provost, Jean; Thiebaut, Stephane; Luo, Jianwen; et al., Phys. Med. Biol., 57(4), 2012

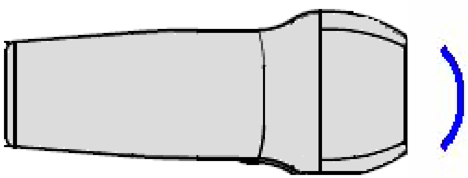
**Ultrafast imaging of single hearbeat**

# Use of circular waves to increase field of view

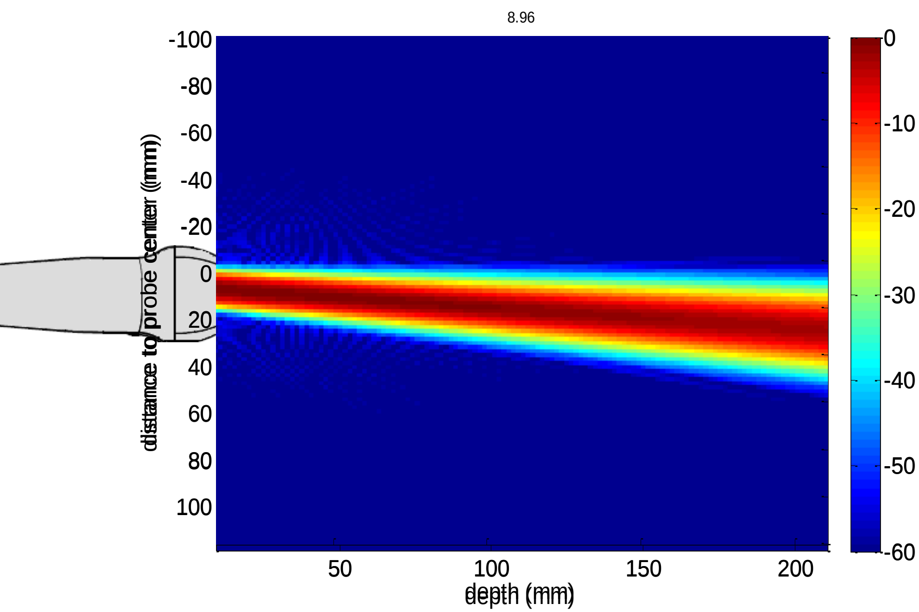
## Flat transmit

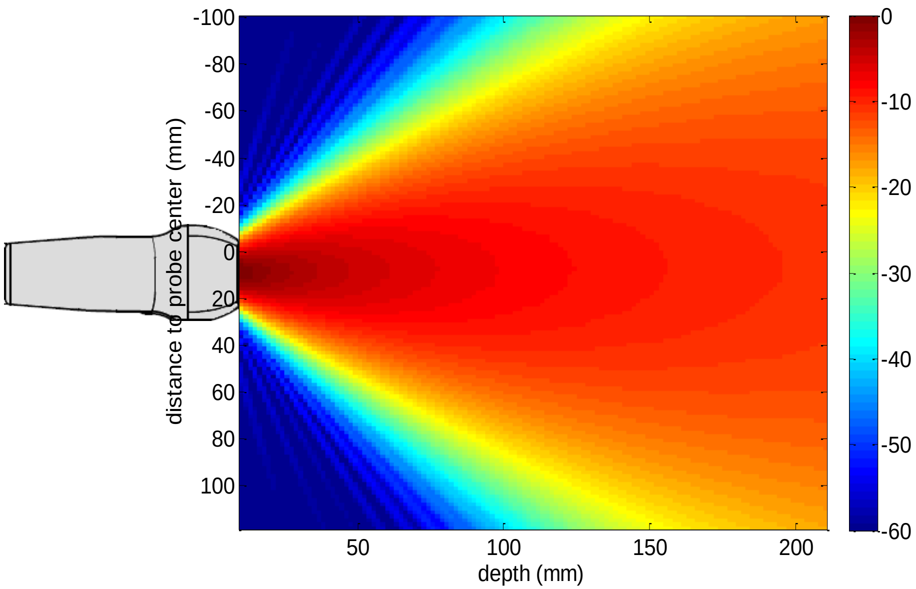


- Circular transmit



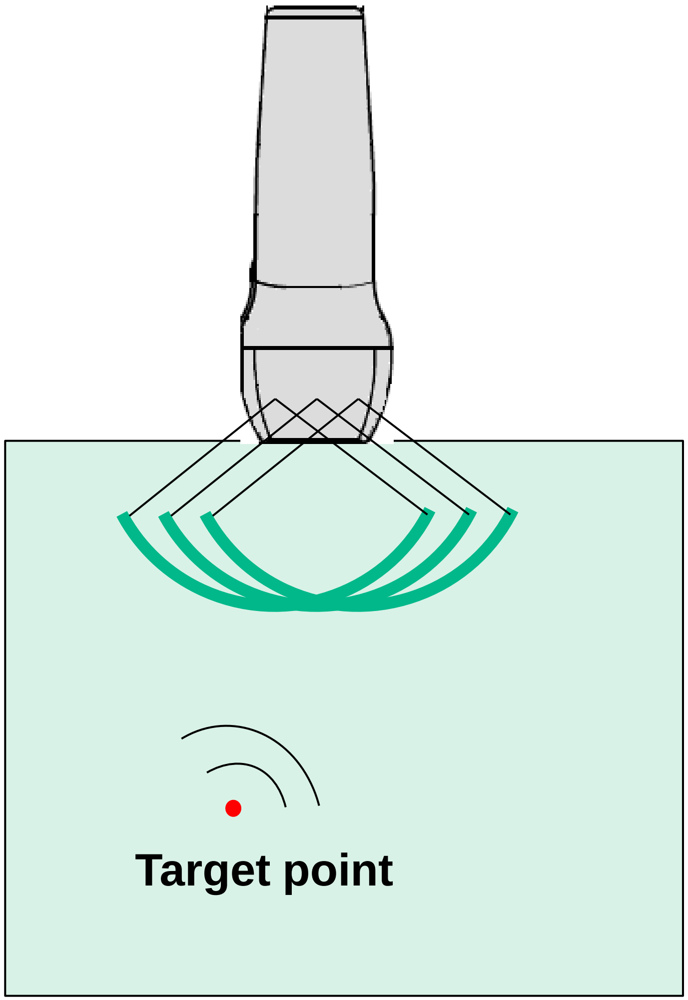
**Andresen et al. UFFC 2006 Symposium**

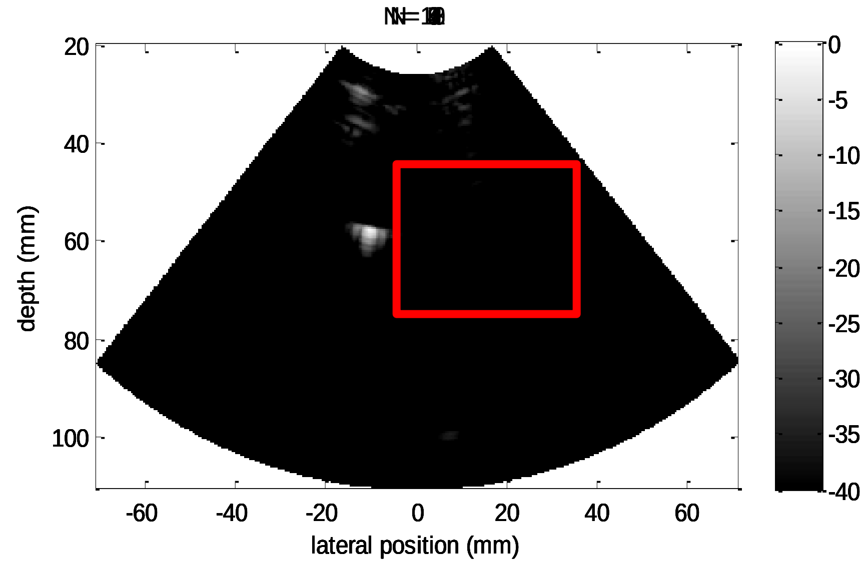


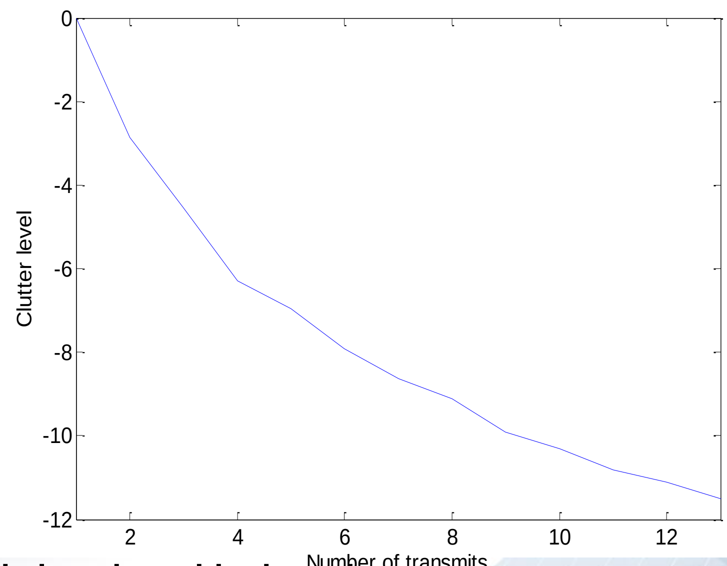




**Ultrafast imaging of the heart using circular wave synthetic imaging with phased arrays**
**Couade M., Hagege, A.-A. ; Fink, M. IEEE Ultrasonics Symposium, pp 515-518, 2009.**
**Papadacci C., Pernot M., et al. IEEE IUS, Dresden, 2012**

# Synthetic imaging with circular waves

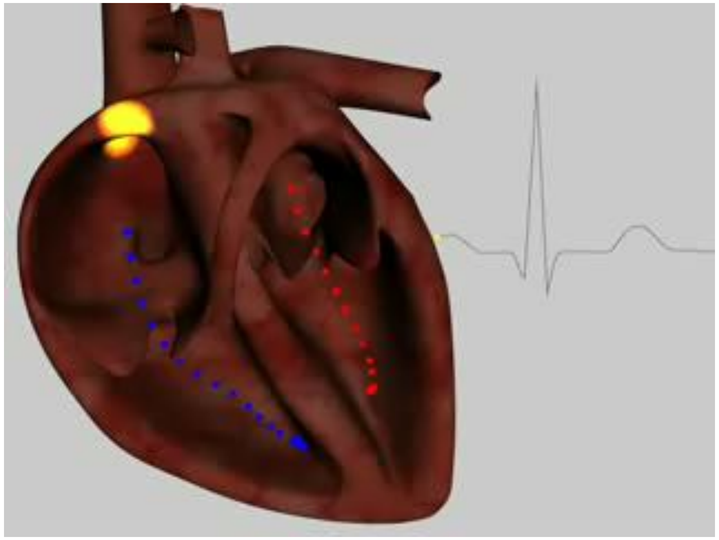


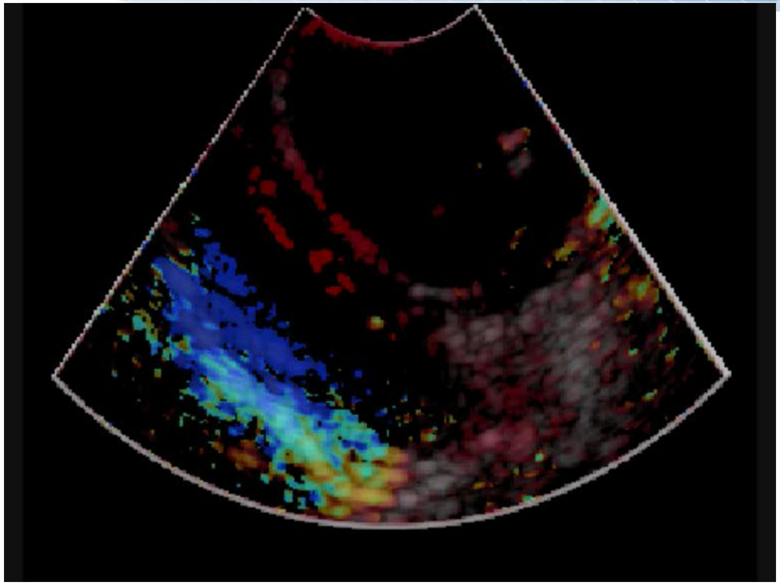




**Ultrafast imaging of the heart using circular wave synthetic imaging with phased arrays**
**Couade M., Hagege, A.-A. ; Fink, M. IEEE Ultrasonics Symposium, pp 515-518, 2009.**

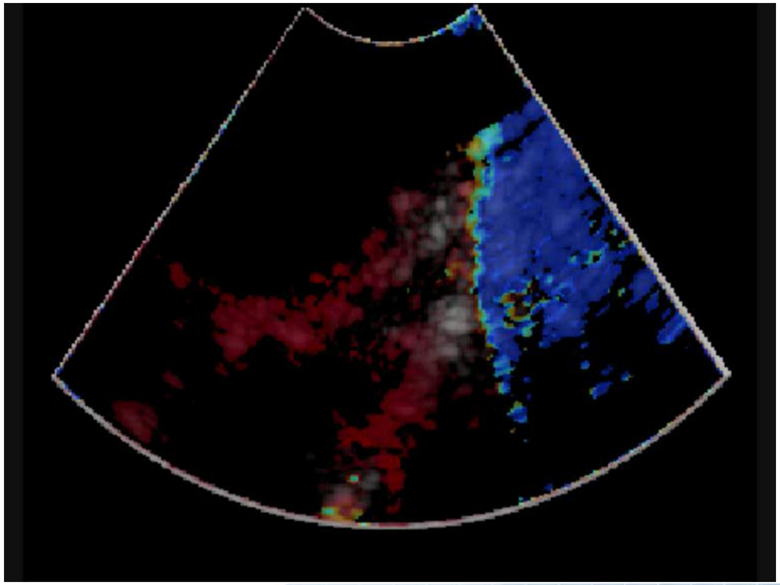
# Ultrafast Imaging of Heart Transient Vibrations





**Short Axis**

Hiroshi Kanai: "Propagation of Vibration Caused by Electrical Excitation in the Normal Human Heart" *Ultrasound in Medicine & Biology* Vol. 35, No. 6, pp. 936-948 (June 2009)



**Ultrafast Imaging of *in vivo* heart potentials**
**(Wide field of view during a single cardiac cycle)**

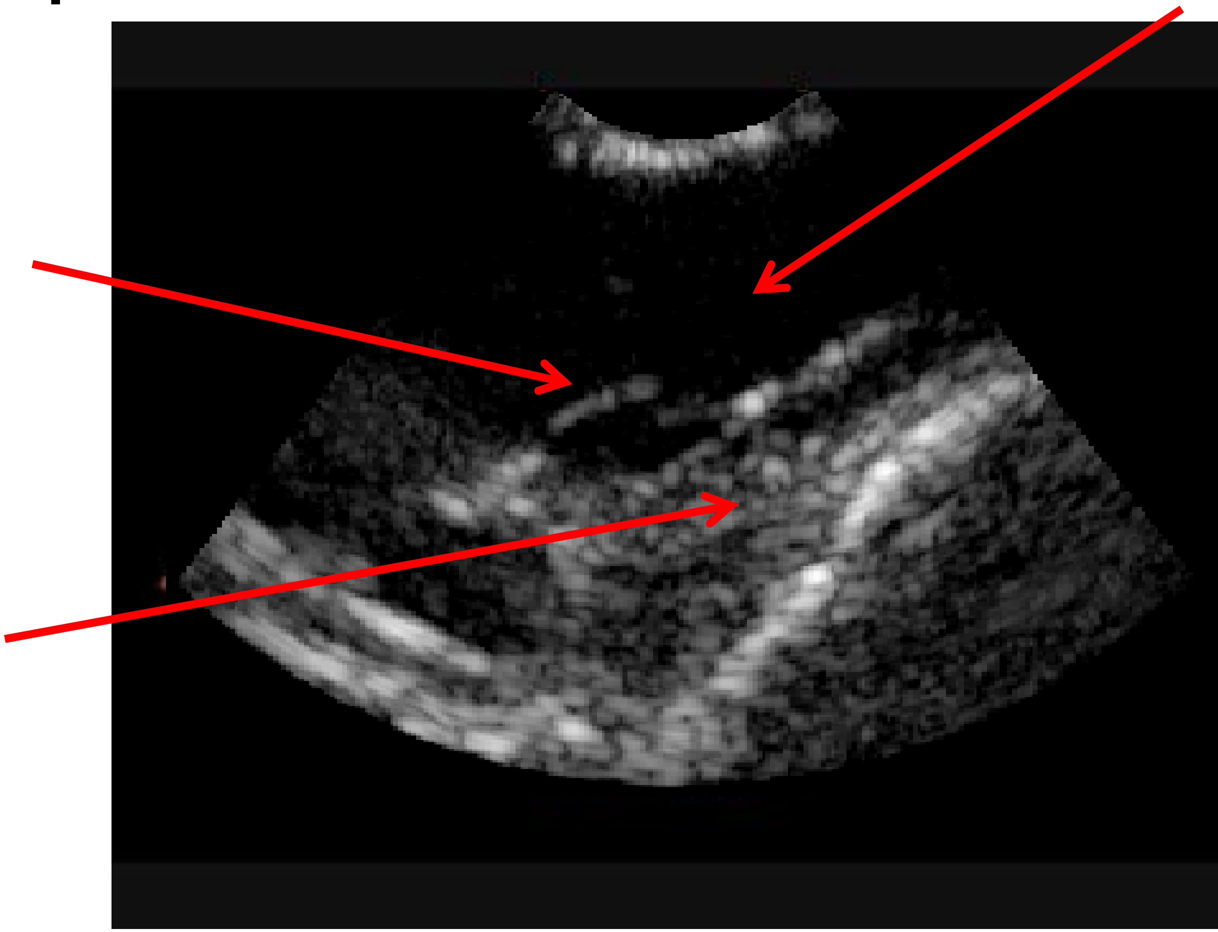
**in vivo Sheep experiments**
**Phased Array, fc = 3.3 MHz**
**Field of View 8 cm**
**1600 frames per second**

**Long Axis**

Ultrafast imaging of the heart using circular wave synthetic imaging with phased arrays
Couade M., Hagege, A.-A. ; Fink, M. IEEE Ultrasonics Symposium, pp 515-518, 2009.

# Ultrafast Imaging the heart sound propagation

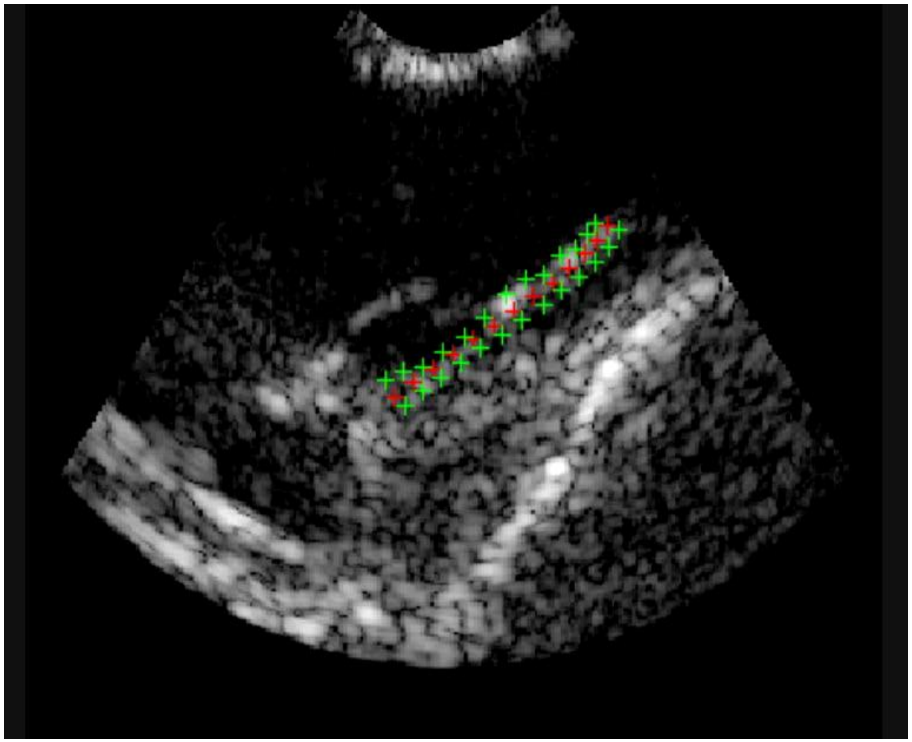
- **TDI cineloop**



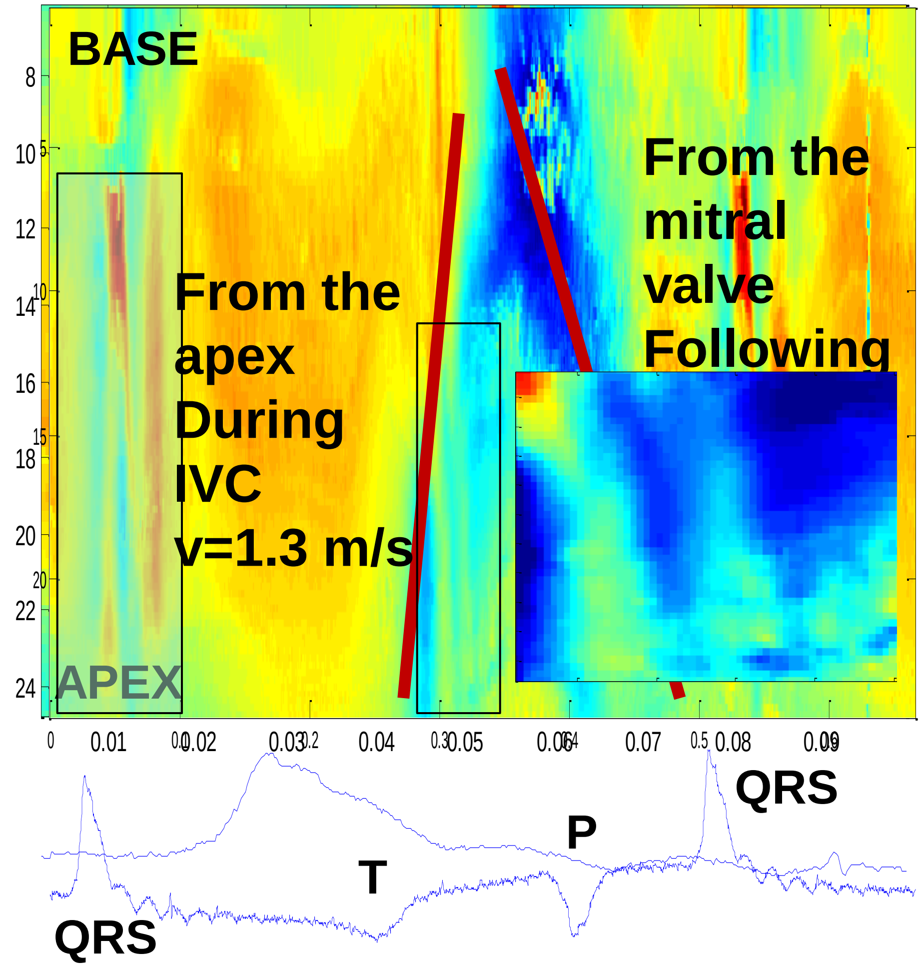

**Ultrafast imaging of the heart using circular wave synthetic imaging with phased arrays**
**Couade M., Hagege, A.-A. ; Fink, M. IEEE Ultrasonics Symposium, pp 515-518, 2009.**

# Wall tracking with 2D speckle tracking combined with TDI

**Wall tracking**



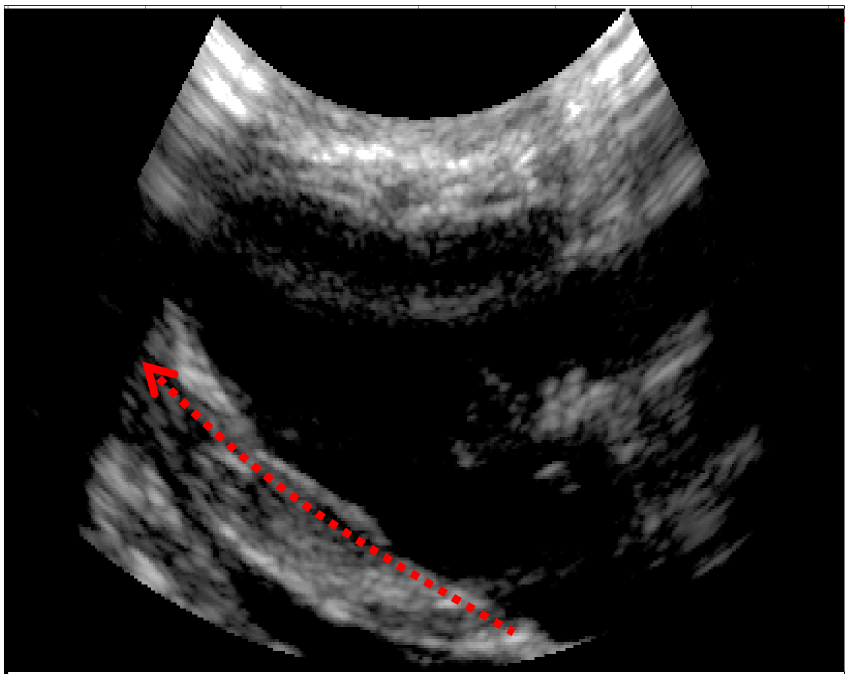
**TDI signal along the tracked wall**

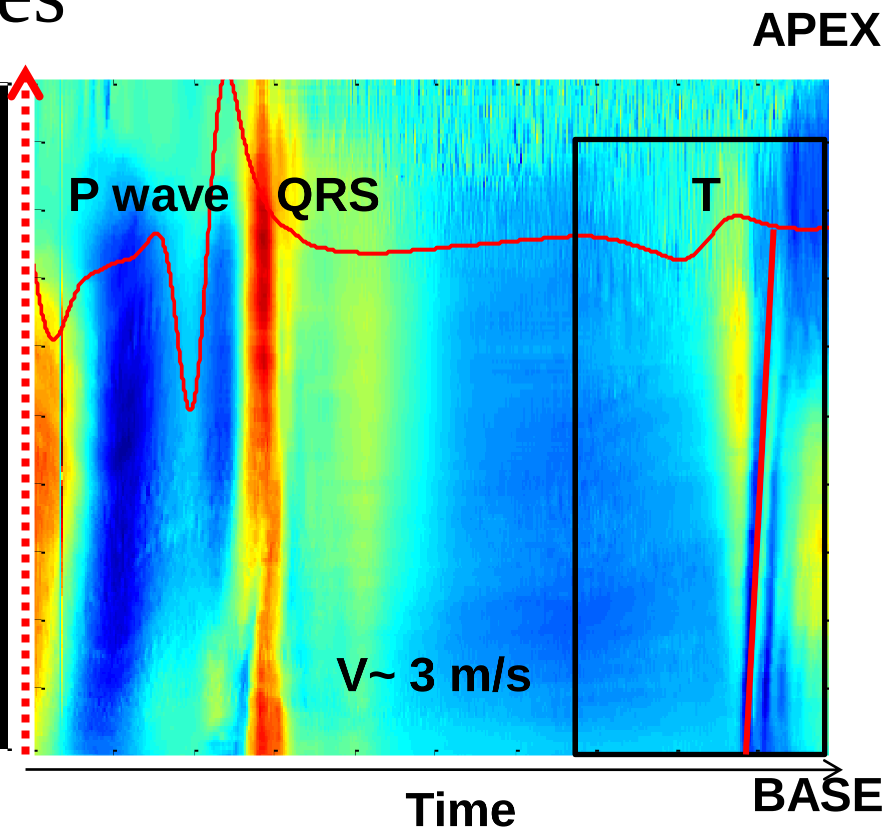



Ultrafast imaging of the heart using circular wave synthetic imaging with phased arrays
Couade M., Hagege, A.-A. ; Fink, M. IEEE Ultrasonics Symposium, pp 515-518, 2009.

# Aortic valve closure

- Long Axis View, signal along the septum
- FR = 1600 Hz, 800 frames



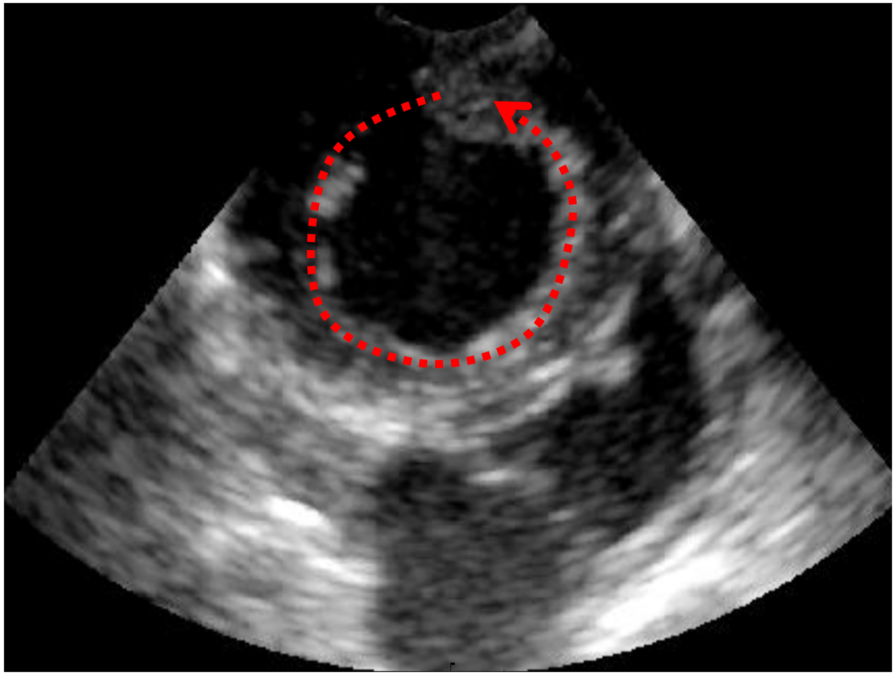


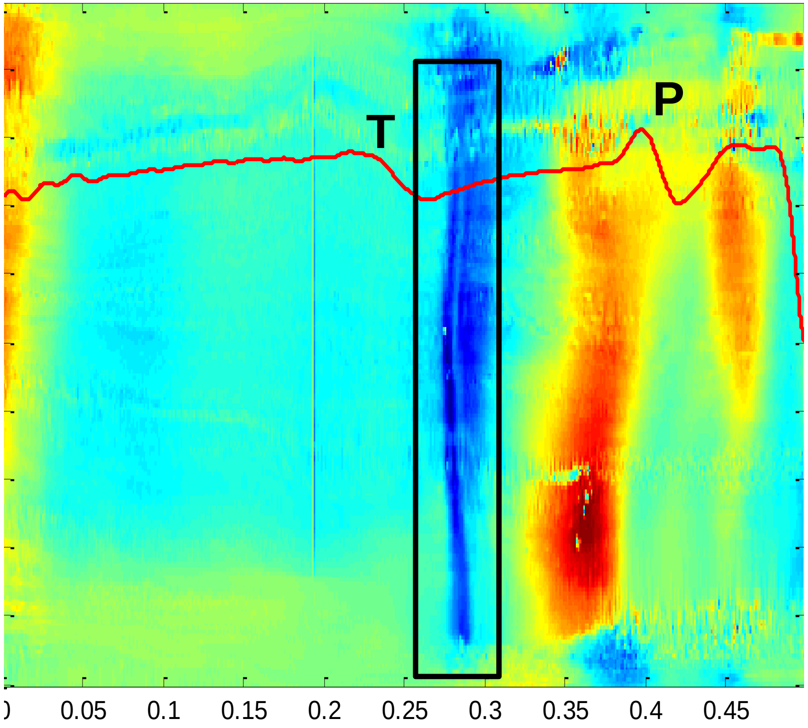

Couade M., «Application of ultrafast imaging in cardiology», PhD Thesis, Paris 7 University, 2011

Ultrafast imaging of the heart using circular wave synthetic imaging with phased arrays
Couade M., Hagege, A.-A. ; Fink, M. IEEE Ultrasonics Symposium, pp 515-518, 2009.

# Aortic valve closure

- FR = 1600 Hz, 800 frames
- Propagation of the heart sound from the aortic valve (short axis view)






Couade M., «Application of ultrafast imaging in cardiology», PhD Thesis, Paris 7 University, 2011

# Ultrafast Imaging of Acoustic Cavitation

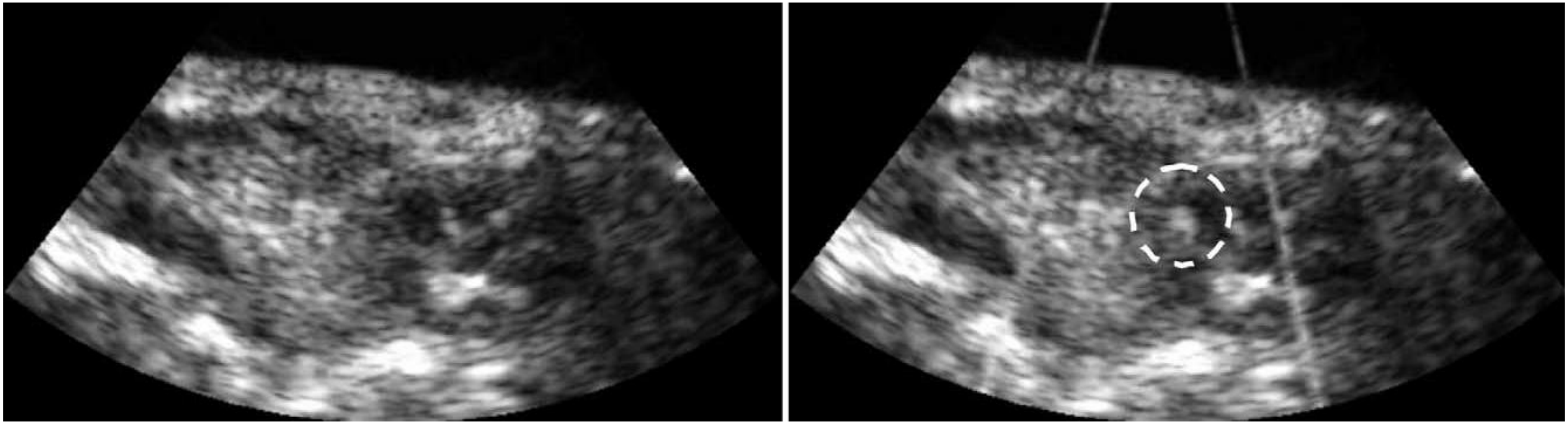
Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events Induced by Short Pulses of High-Intensity Ultrasound', *Ieee Transactions On Ultrasonics Ferroelectrics and Frequency Control* 58(3), 517--532.

# Introduction- Ultrafast Imaging of Acoustic Cavitation

## Active detection of cavitation events in HIFU treatments

### > Bubbles as scatterers

**Conventional B-mode imaging :hyperechogenic region in the treated region**



**Acoustically induced bubbles**

*Roberts, WW; Hall, TL; Ives, K; et al. Journal of Urology, 175 (2): 734-738, 2006*

**(+) localization of the bubbles**

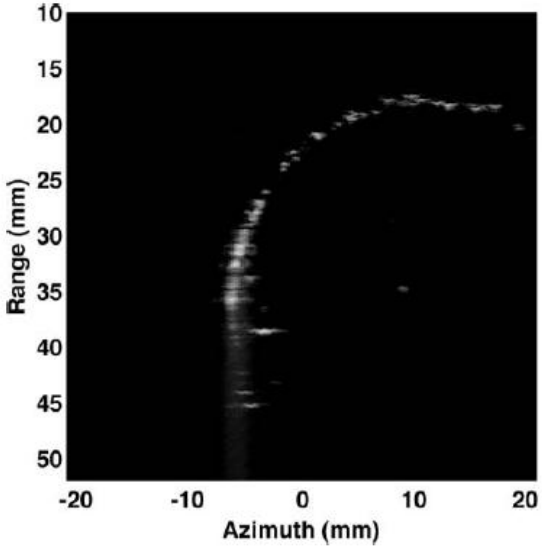
**(-) only large number of bubbles can be detected (bubble clouds)**

# Introduction- Ultrafast Imaging of Acoustic Cavitation

## Passive detection and localization of cavitation events in HIFU

### > Detection of the acoustic emission of the cavitation events

**Passive imaging in saline solution (520-kHz CW),**




**B-scan**

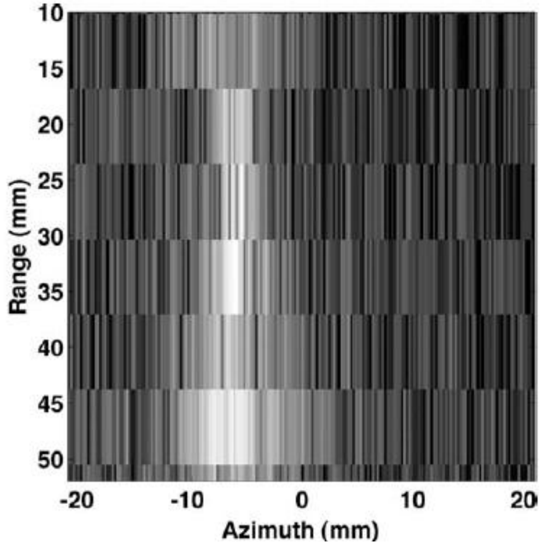



**Image formed from passive recording**

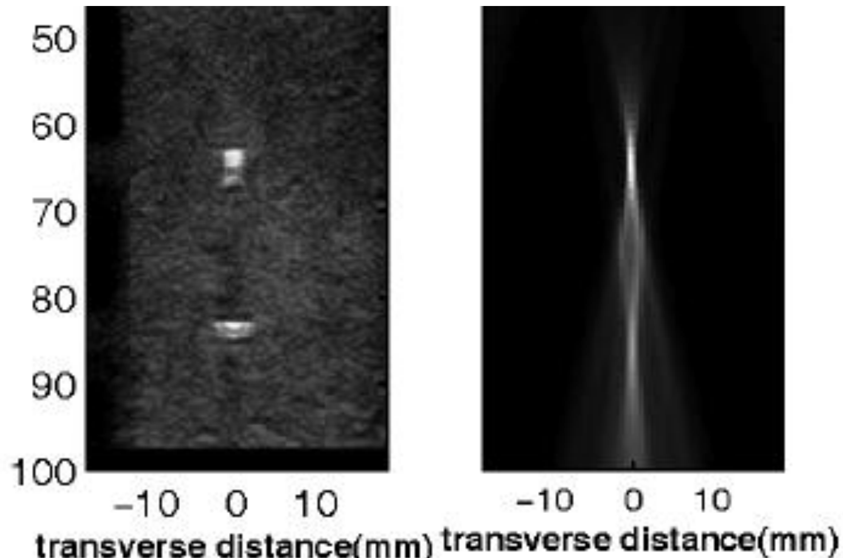
**Passive cavitation imaging with ultrasound arrays, Vasant A. Salgaonkar, Saurabh Datta, Christy K. Holland, and T. Douglas Mast J. Acoust. Soc. Am., 2009**

# Introduction- Ultrafast Imaging of Acoustic Cavitation

## Passive detection and localization of cavitation events in HIFU

### > Detection of the acoustic emission of the cavitation events

**Passive mapping of two disjoint cavitation regions produced by insonifying an agar phantom with two talc suspensions**




**B-scan** **Passive source intensity map**

**Passive Spatial Mapping of Inertial Cavitation During HIFU Exposure**
**M. Gyongy *and C. Coussios* IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, 2010**

**(+) localization of the cavitation events**
**(-) poor axial resolution**

# Impact of Ultrafast Imaging in cavitation detection imaging

***Why to study acoustic cavitation***

***using ultrafast ultrasound imaging ?***

*In Vivo* mapping of single cavitation events generated with high amplitude short ultrasonic excitation of tissue

- For monitoring early stages of **therapeutic applications** :

    - cavitation-enhanced heating

    - histotripsy

  > *location of the first bubbles leading to the initial cloud*

- For evaluating the nucleation threshold in vivo (investigate safety in **diagnostic applications**)

# Impact of Ultrafast Imaging in cavitation detection imaging

## Potential in Therapeutic Ultrasound (HIFU, Histotripsy, RF ablation)

**Active Imaging with an ultrasonic array**

- Not sensitive to single cavitation events (bubble clouds)

Improvement for single event detection : *subtraction of a reference image+ ultrafast imaging technique (9KHz imaging rate)*

**Passive imaging with an ultrasonic array**

Farny, CH; Holt, RG; Roy, RA, UMB , 35 (4): 603-615 APR 2009

Salgaonkar, VA; Datta, S; Holland, CK; et al, JASA 126 (6): 3071-3083 DEC 2009

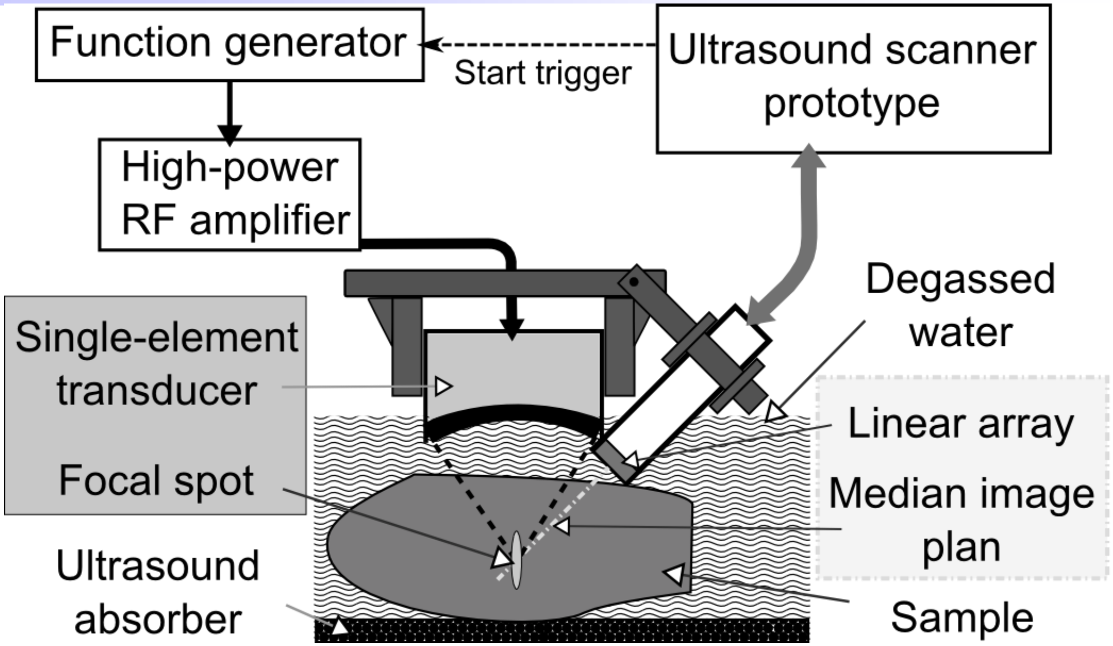
Gyongy, M; Coussios, CC IEEE TBME, 57 (1): 48-56 JAN 2010

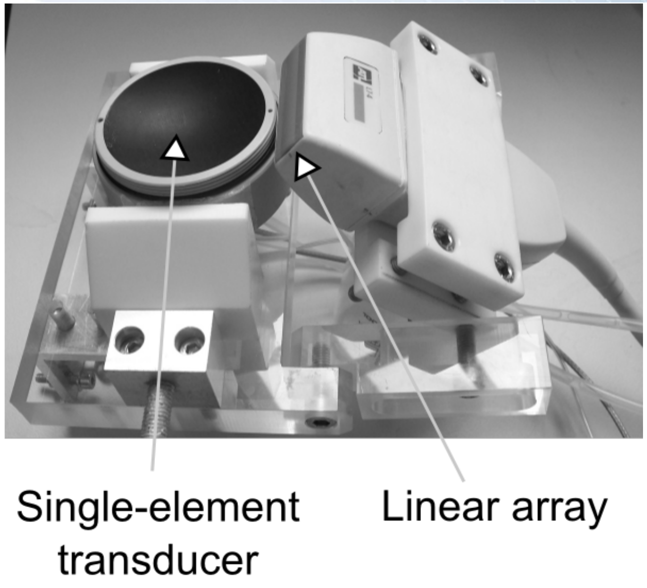
> no time origin, localization submitted to diffraction limit (both in lateral and axial dimension)

Improvement for single event detection : *synchronized detection*

*(no integration in time: improved axial resolution)*

# Ultrafast Cavitation Imaging




## HIFU single element transducer (Imasonic, France)

660kHz central frequency

Focal distance: 45 mm, f#=1

*driven by:* function generator + 300W or 5kW amplifier

## Standard ultrasound imaging linear array (L7-4, Phillips)

128 transducers, pitch 0.3 mm, bandwidth: 4-7MHz

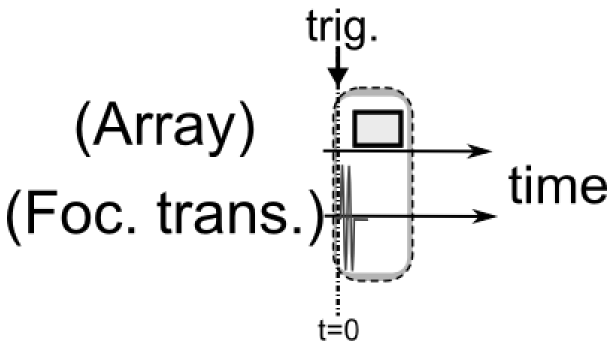
*driven by:* SuperSonic protoype programmable channels both in receive (64 channels) and transmit (128 channels)

# Passive Imaging In vitro experiment: gelatin phantom

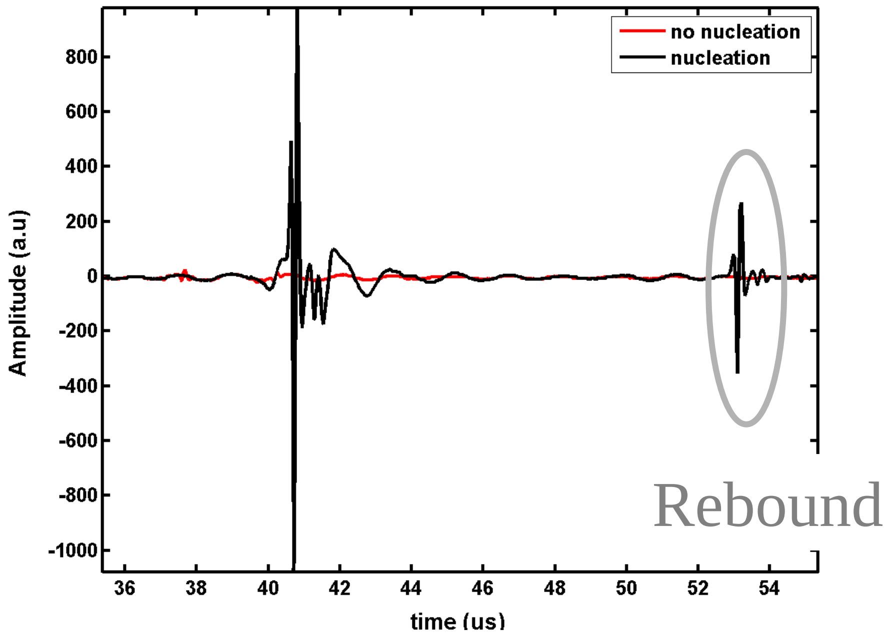
Phantom : 5% (w/v) gelatin gel > free of scatterer

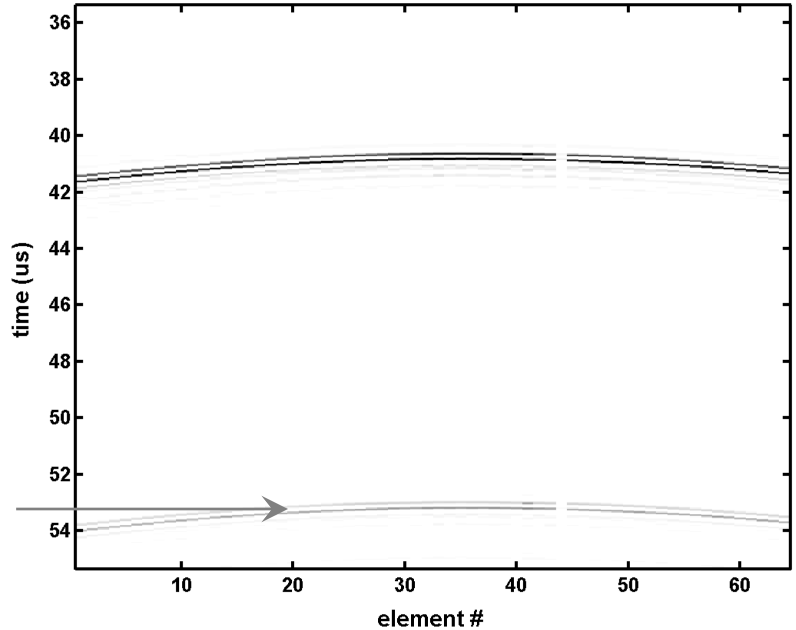
High amplitude excitation : 2cy. @ 660 kHz,
- 6.4 MPa negative peak

Synchronization with the emission:
passive recording starts 22 µs after the transmit




First case: one nucleated bubble

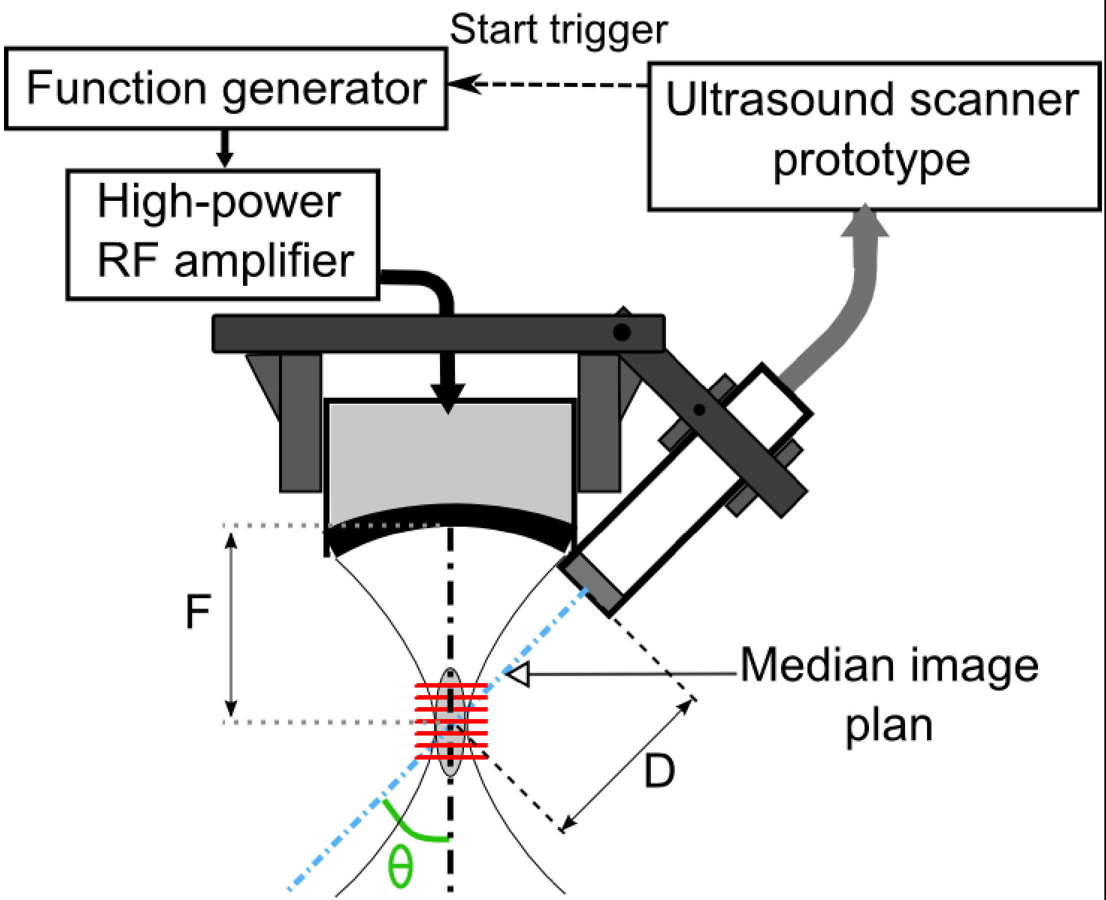



RF data on the element # 32

High frequency wave-front

# Ultrafast Passive receive beamforming




## Model for beamforming :

**Geometry:**

✓ D measured by imaging actively an hydrophone tip at focal point

✓ θ set equal to 45°

**Wave propagation:**

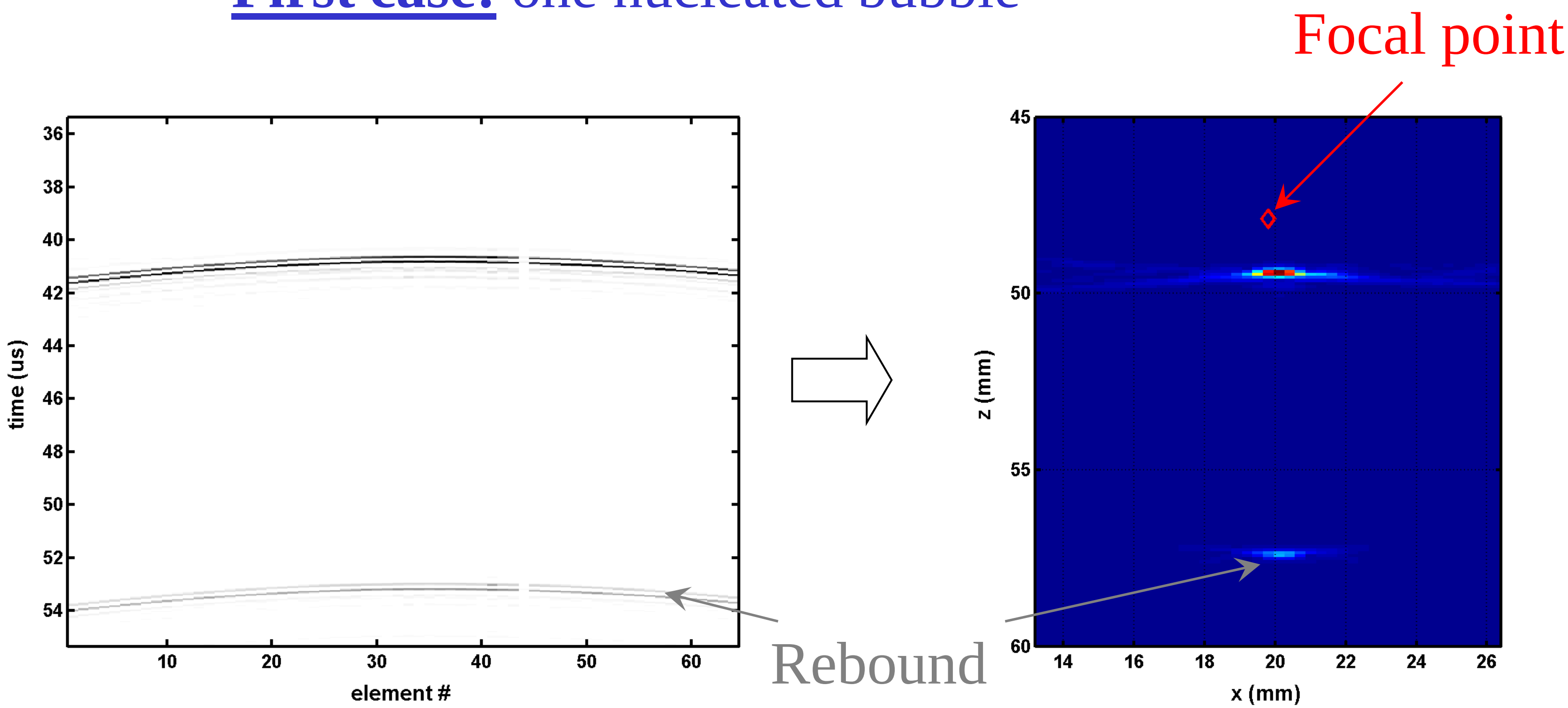
✓ plane wave-front in the focal spot of the single element

✓ immediate response of nuclei

**Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.**

# Passive Imaging In vitro experiment: gelatin phantom

## **First case:** one nucleated bubble



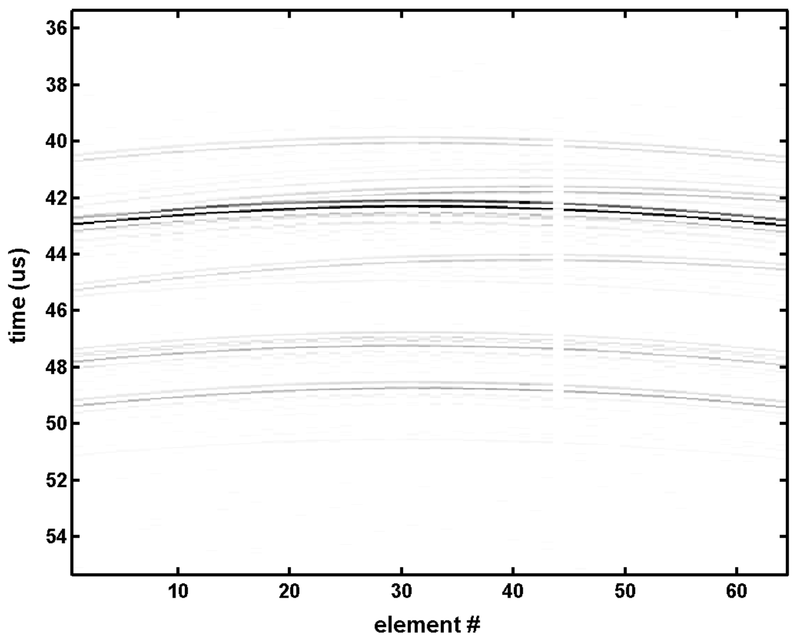

High frequency wave-front

Beamformed RF data

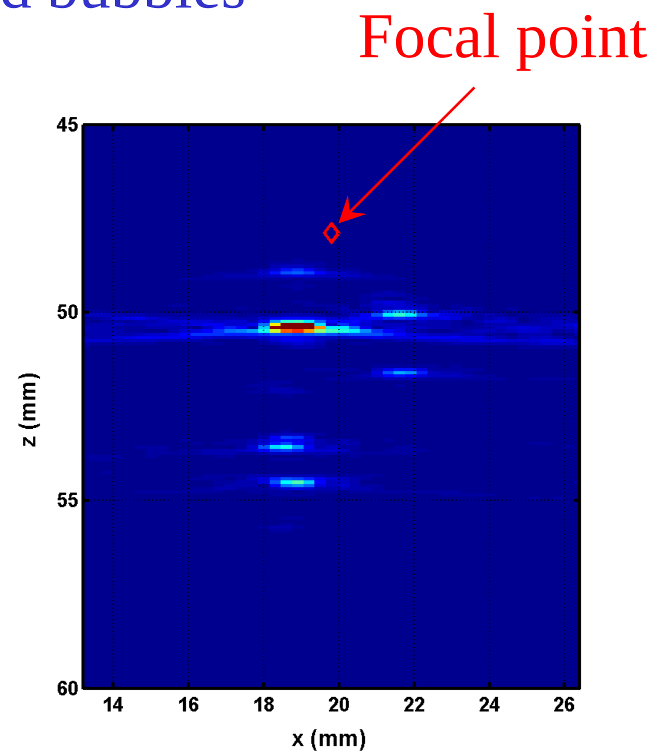
**Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.**

# Passive Imaging In vitro experiment: gelatin phantom

**Second case:** several nucleated bubbles




High frequency wave-front




Beamformed RF data

**Questions :** How many bubbles ? How accurate are the locations ?


**Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.**

# Standard Active Cavitation Detection (ACD)

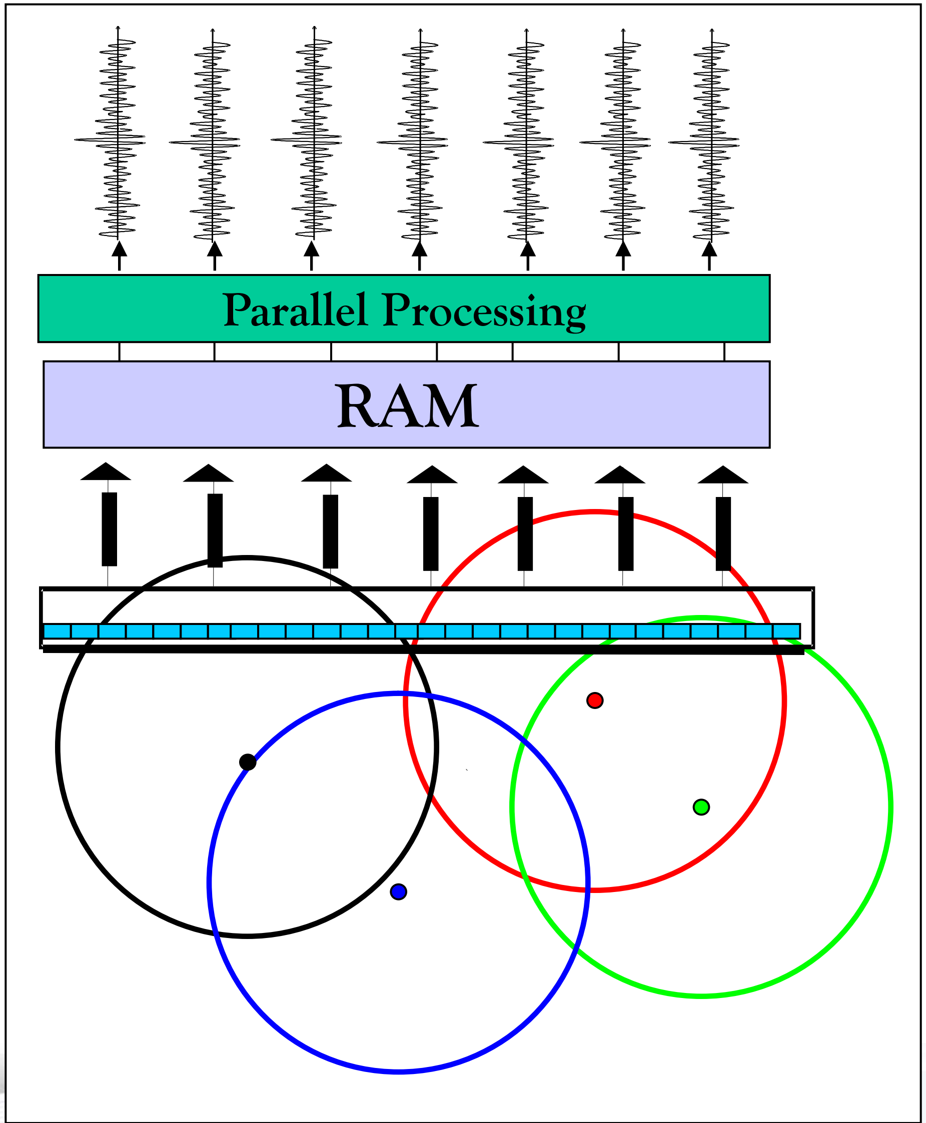
**B-mode imaging :** maximum frame rate 100Hz > possible dissolution of bubble before the 1st image

Improvement for single event detection : *ultra-fast imaging up to 9kHz*

Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.

# Standard Active Cavitation Detection (ACD)

**B-mode imaging :** maximum frame rate 100Hz > possible dissolution of bubble before the 1st image

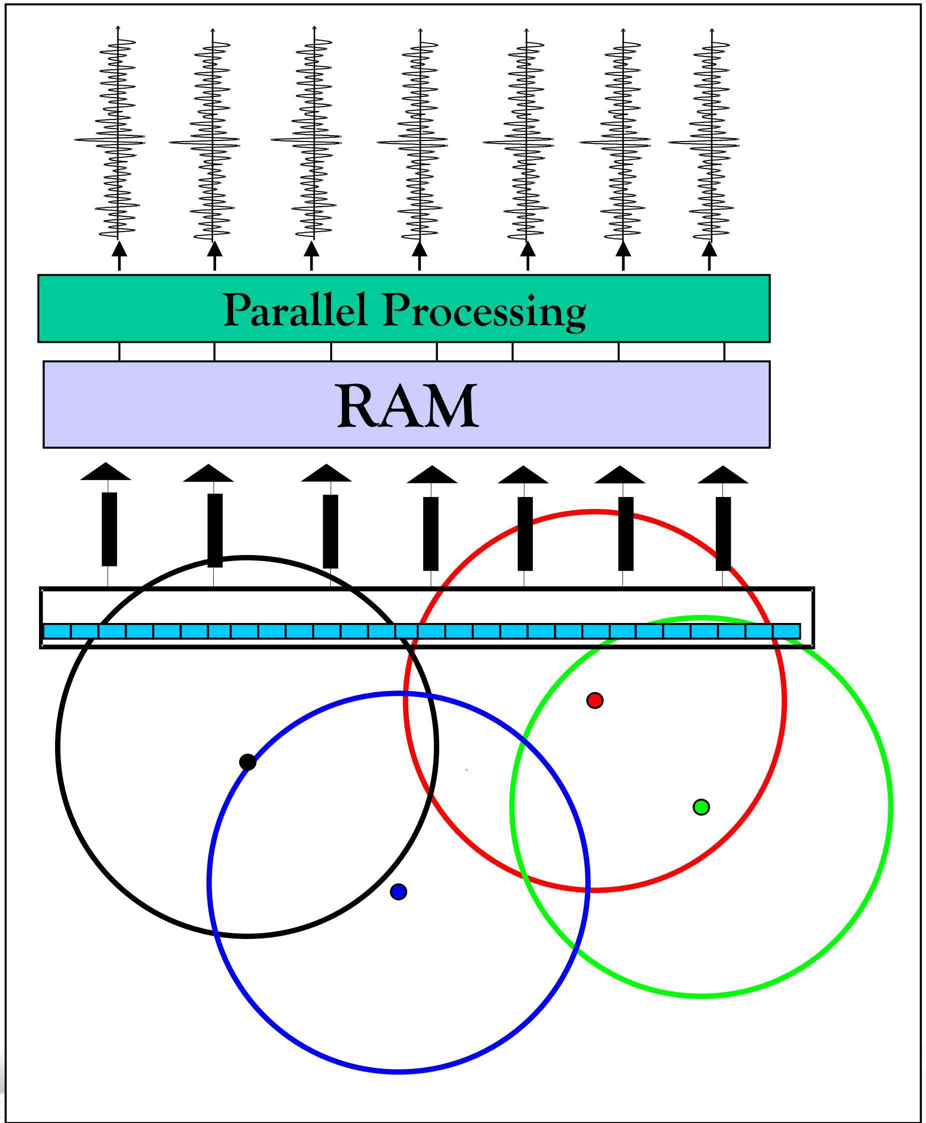



Improvement for single event detection :

*ultra-fast imaging up to 9 kHz here*

# Standard Active Cavitation Detection (ACD)

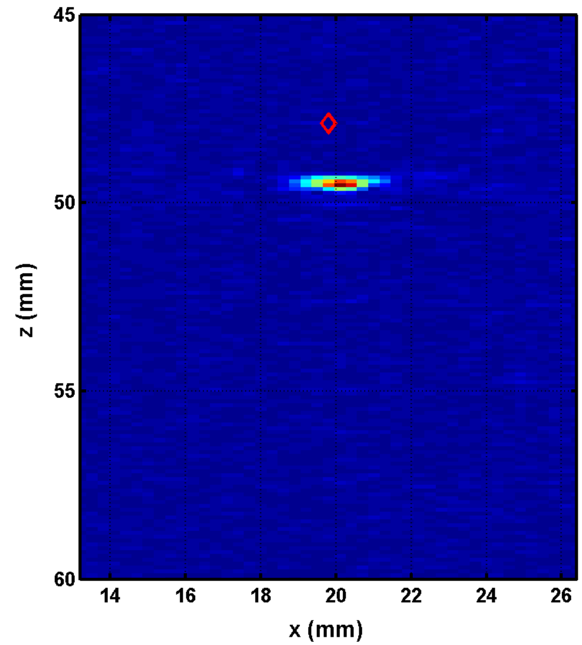
**B-mode imaging :** maximum frame rate 100Hz > possible dissolution of bubble before the 1st image




Improvement for single event detection :

*ultra-fast imaging up to 9 kHz here*

Plane wave : 1 cy. , 6MHz

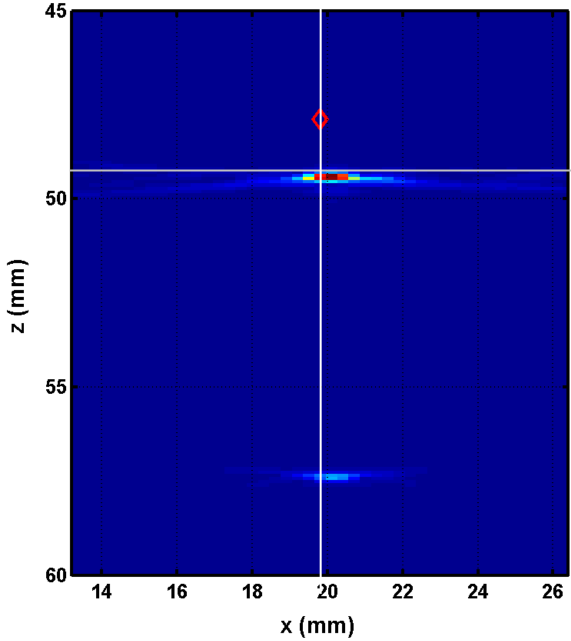



330 µs after the high amplitude excitation

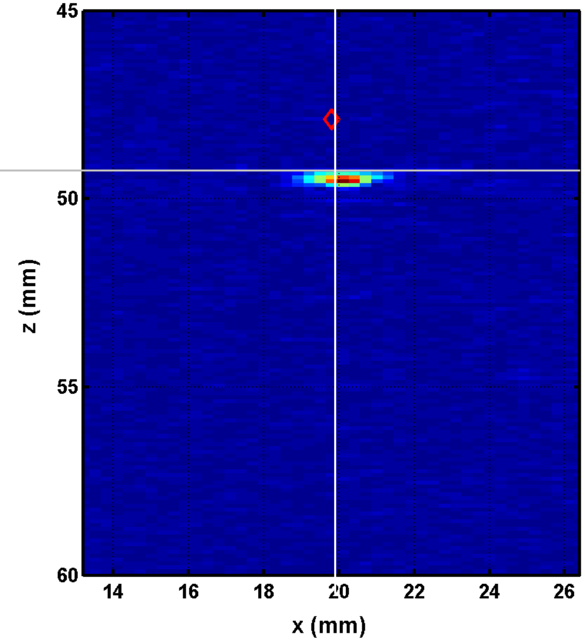
# Comparison passive and active detection

## **First case :** one nucleated bubble

Passive image




Active image




330 µs after the high amplitude excitation

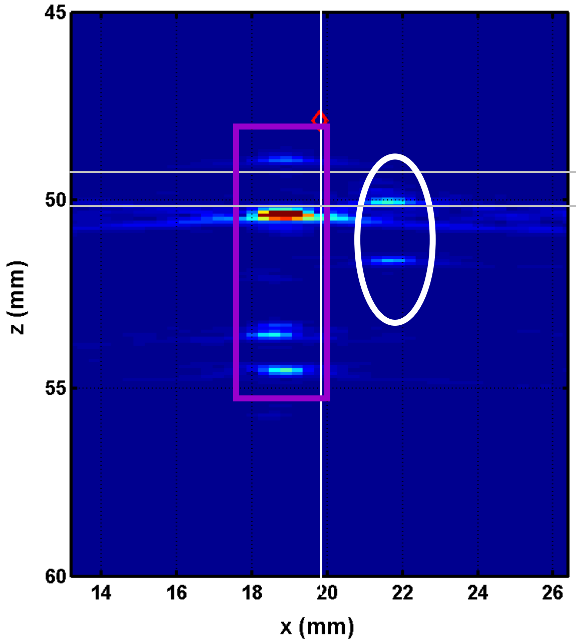
⇨ Good spatial agreement between active and passive imaging

**Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.**

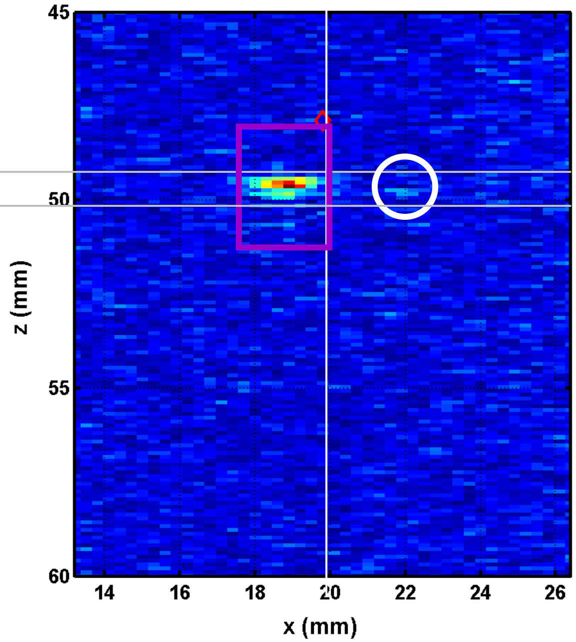
# Comparison passive and active detection

## **Second case :** several nucleated bubbles

Passive image




Active image

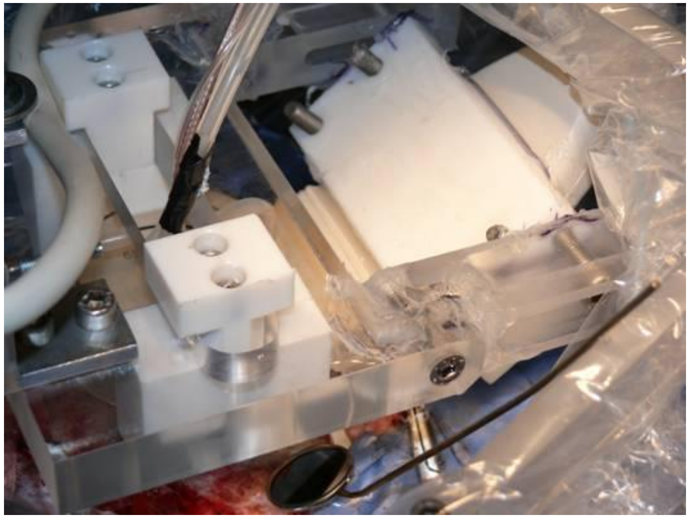



⇨ Only 2 bubbles in the active image and 1mm axial agreement :

- the assumptions for passive beamforming are not exact
- complex passive signature of nucleating bubble (rebound, collapse…)

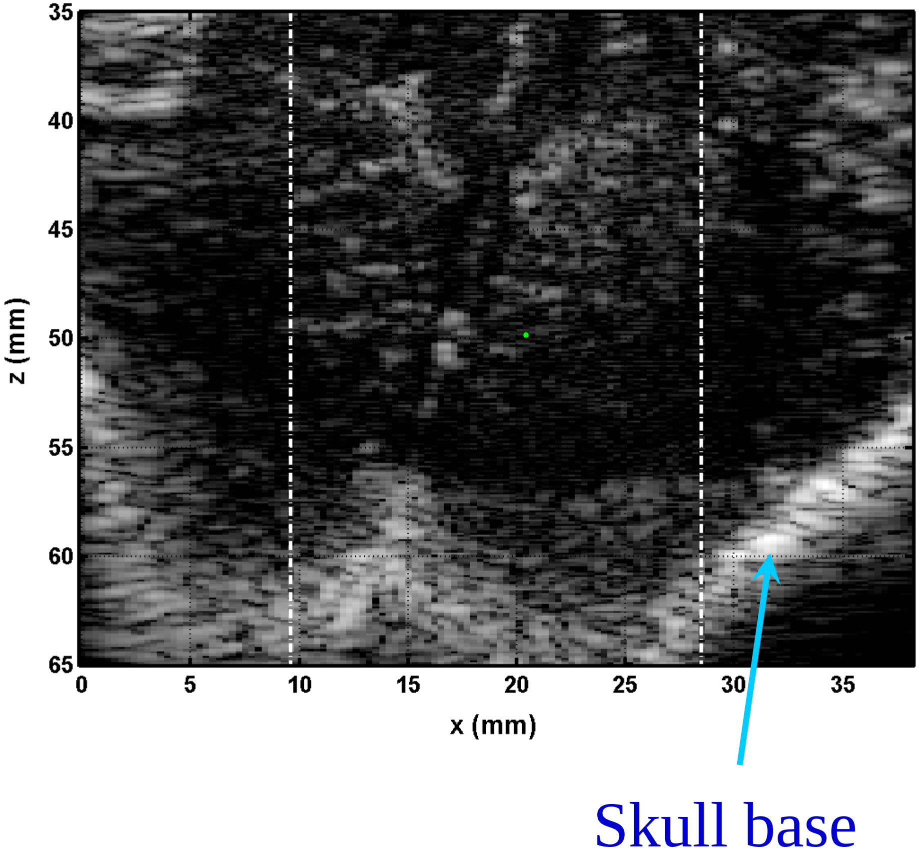
> Passive images more complex, but qualitative agreement

# In vivo experiments on sheep brain

**Ultrafast Imaging is key for *In vivo* determination of the acoustic cavitation threshold**

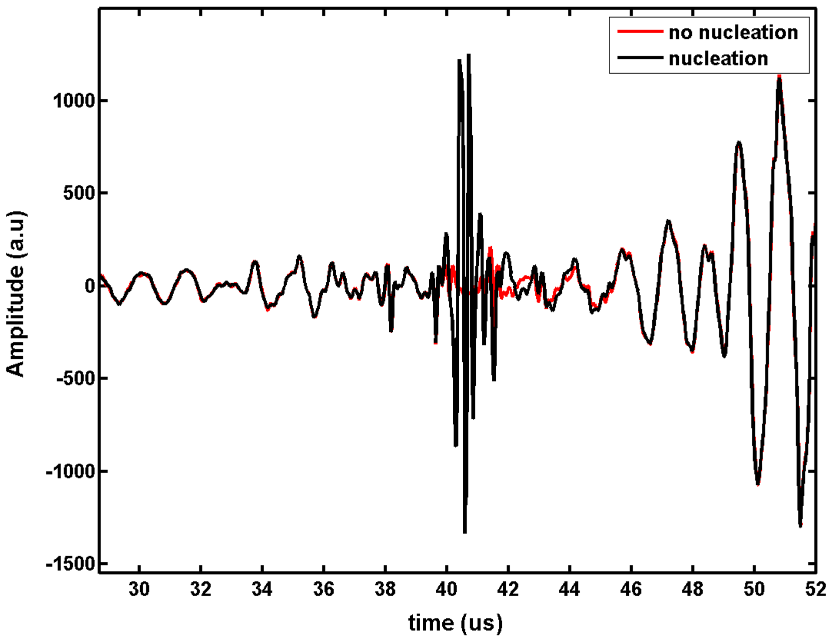
Bmode image



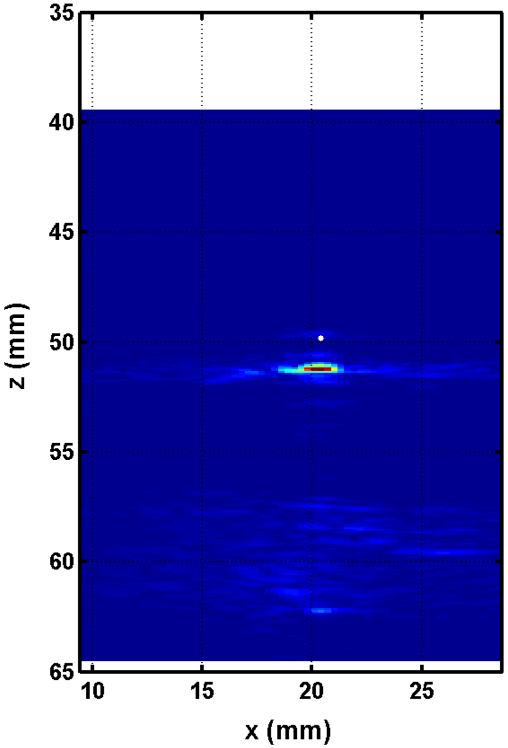

Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.

# In vivo experiments on sheep brain

High amplitude excitation : 2cy. @ 660 kHz,
up to - 20 MPa negative peak pressure




RF data on the element # 32



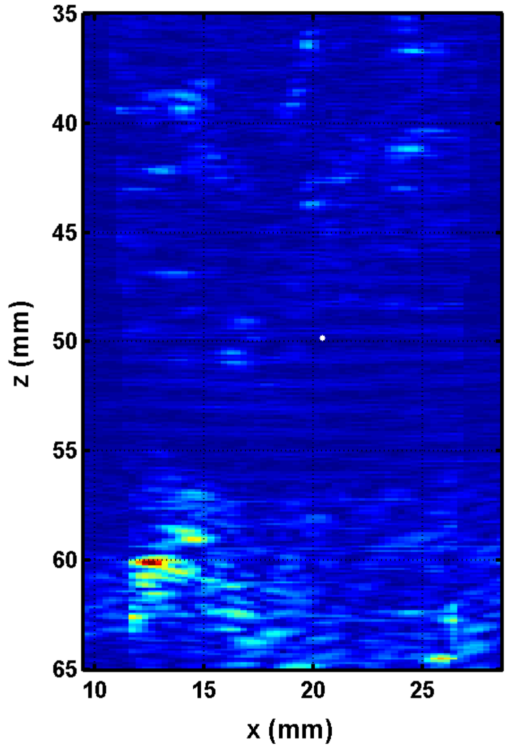

Passive image

Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.

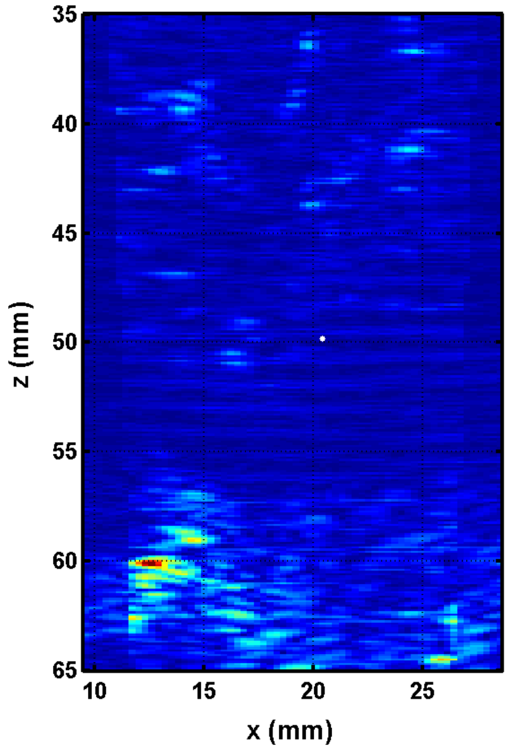
# In vivo experiments on sheep brain

Active images 550 µs after the high amplitude excitation

No nucleation



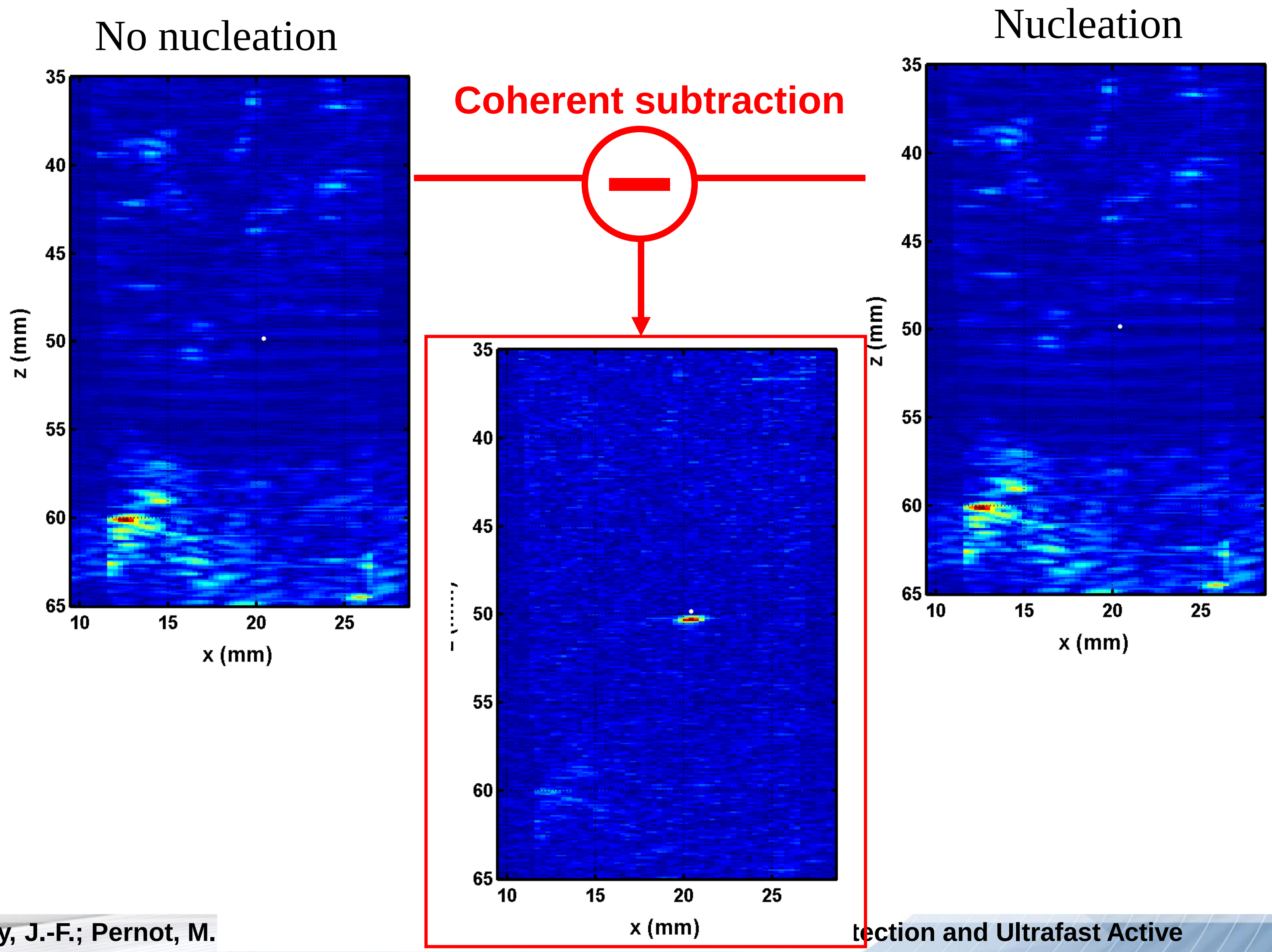

Nucleation




Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.

# In vivo experiments on sheep brain

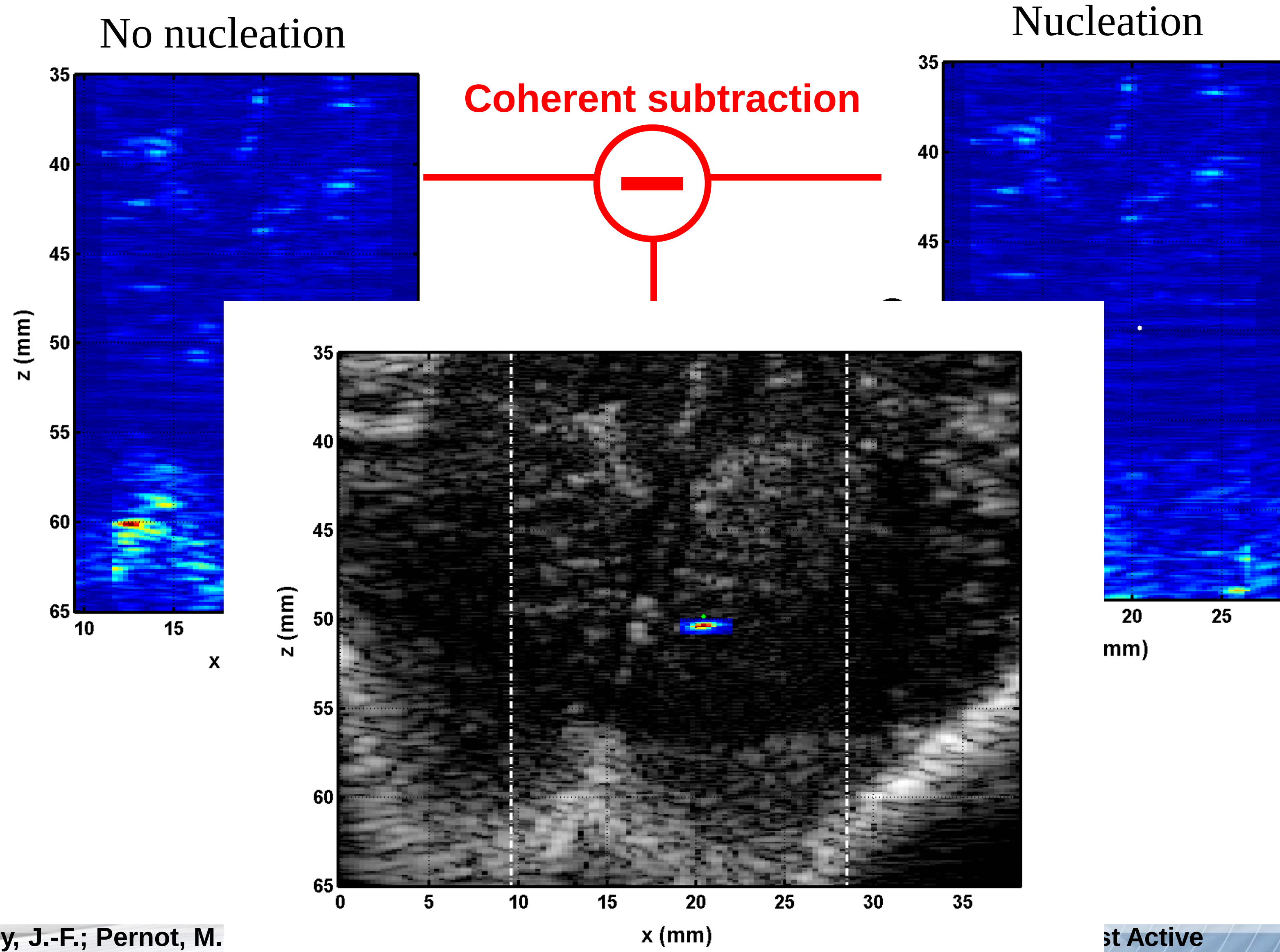
## Active images 550 µs after the high amplitude excitation




Gateau, J.; Aubry, J.-F.; Pernot, M. ...tection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.

# In vivo experiments on sheep brain

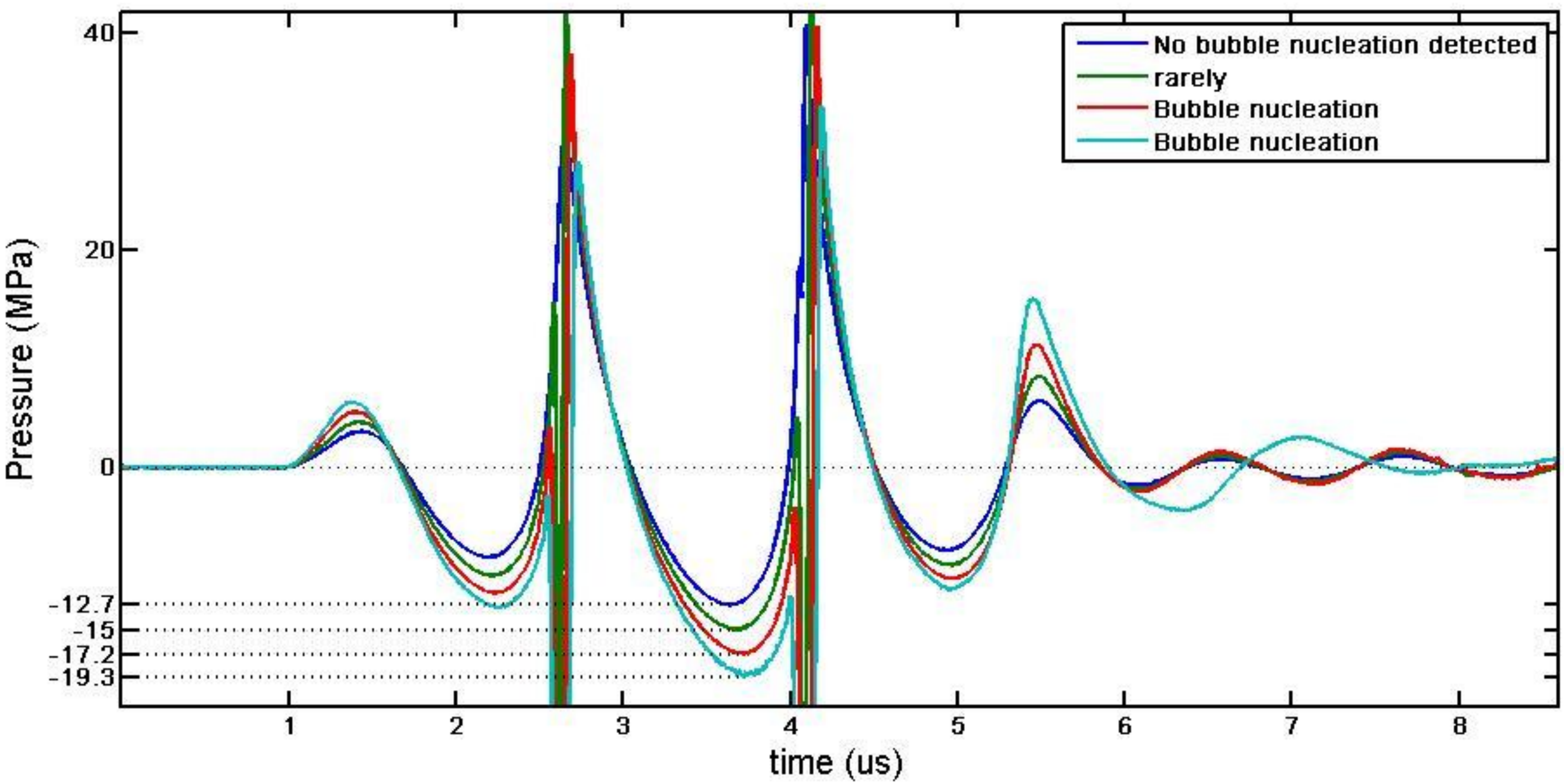
## Active images 550 µs after the high amplitude excitation




Gateau, J.; Aubry, J.-F.; Pernot, M. … st Active
Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.

# In vivo estimation of the cavitation threshold sheep brain

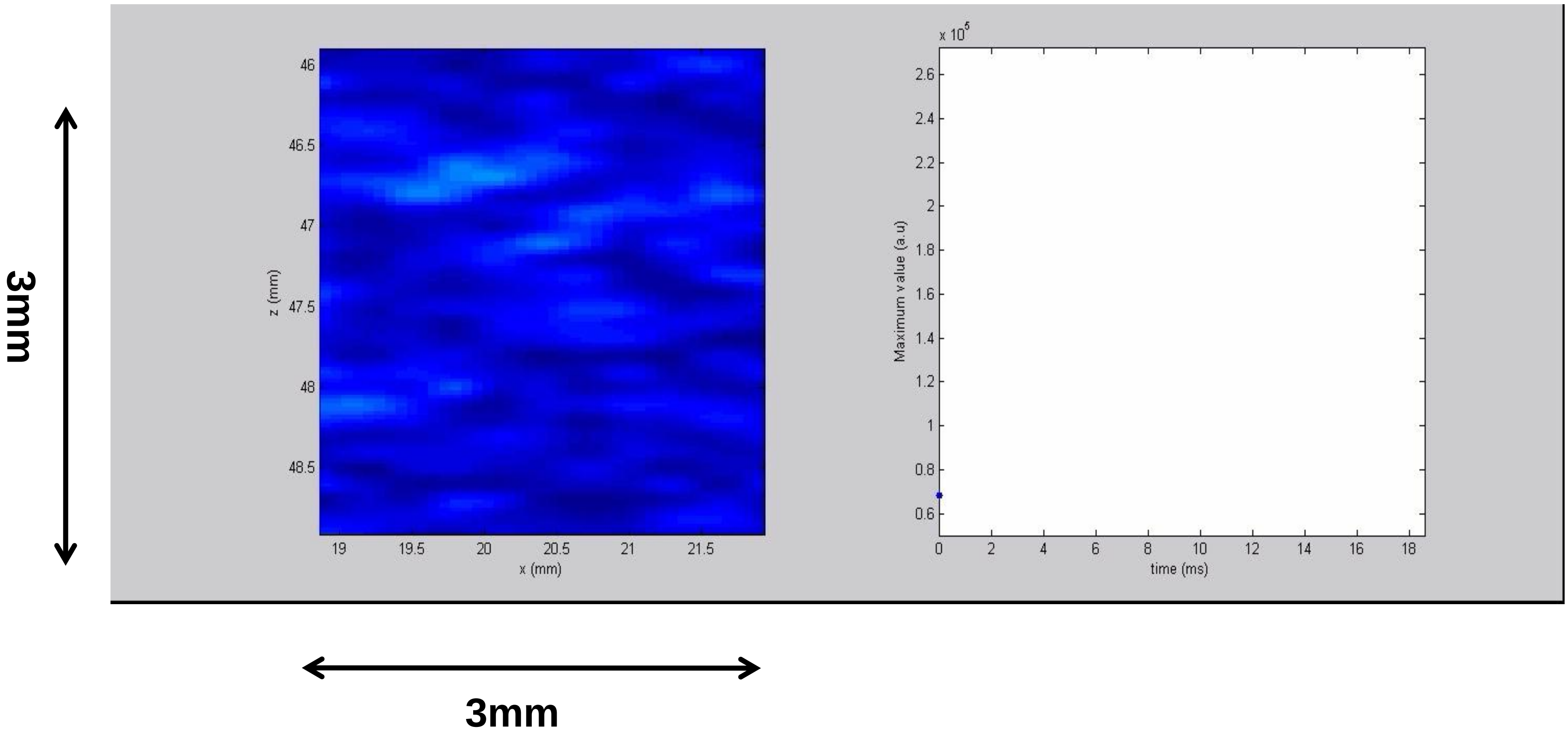
**Statistical study on 4 sheeps: 100 different sonications in the brain**
**Experiments still ongoing**
**Cavitation threshold : between -15MPa and -17.2MPa (660kHz)**




**Calibration of the 600kHz transducer with an heterodyne interferometer**

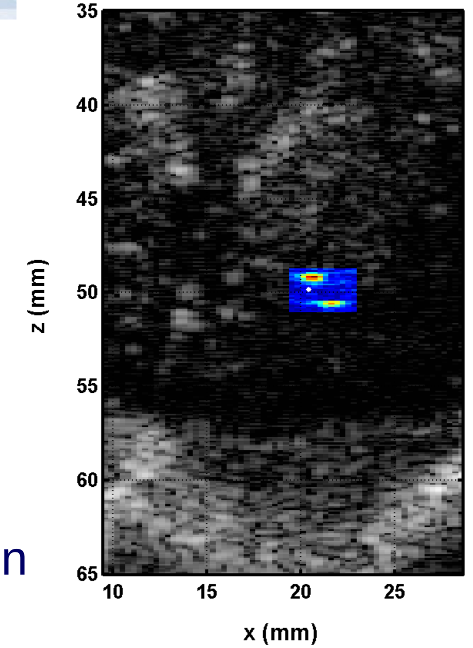
# Ultrafast Imaging of bubble dynamics

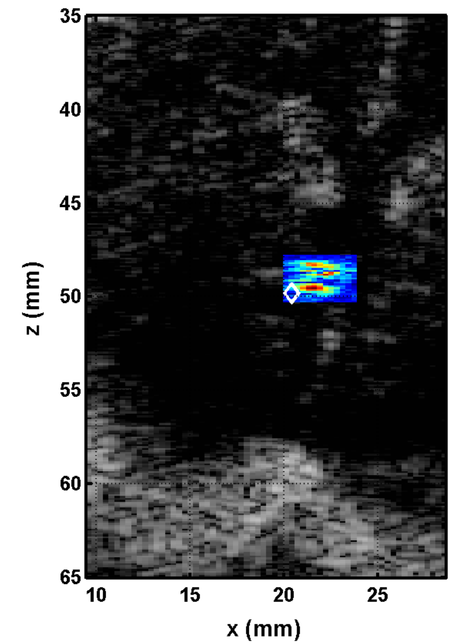
## Use of the high imaging frame rate to follow the bubble dynamics




Gateau, J.; Aubry, J.-F.; Pernot, M.; Fink, M. & Tanter, M. (2011), 'Combined Passive Detection and Ultrafast Active Imaging of Cavitation Events', *Ieee UFFC* 58(3), 517--532.

# Summary - Ultrafast Imaging of Acoustic Cavitation




- Single bubble nucleation events were detected and localized passively and actively with an axial resolution of less than 0.3 mm

- Active detection is performed even in scattering media

- Small number of events can be separated

- Combination of passive and active detection provides information on the nucleation event and the induced bubbles Cavitation threshold in vivo in brain: between -15MPa and -17.2MPa (660kHz) (still ongoing)

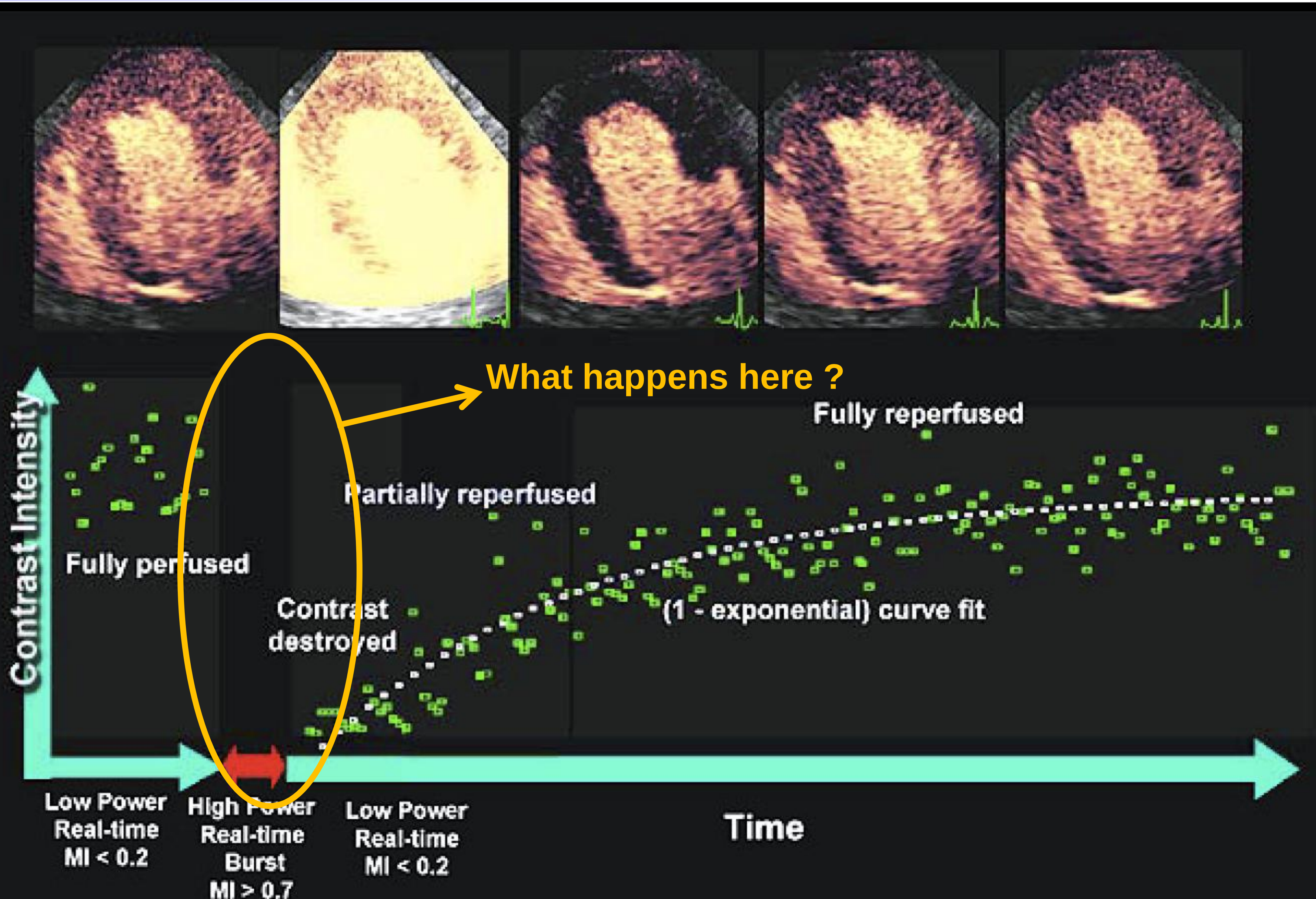
- Active high frame rate :
  - reach PRF in the kHz range > step by step formation a bubble cloud
  - follow the dynamics of the induced bubble

Applications : study the nuclei population *in vivo* and monitor the initiation phase of bubble cloud formation for cavitation therapies

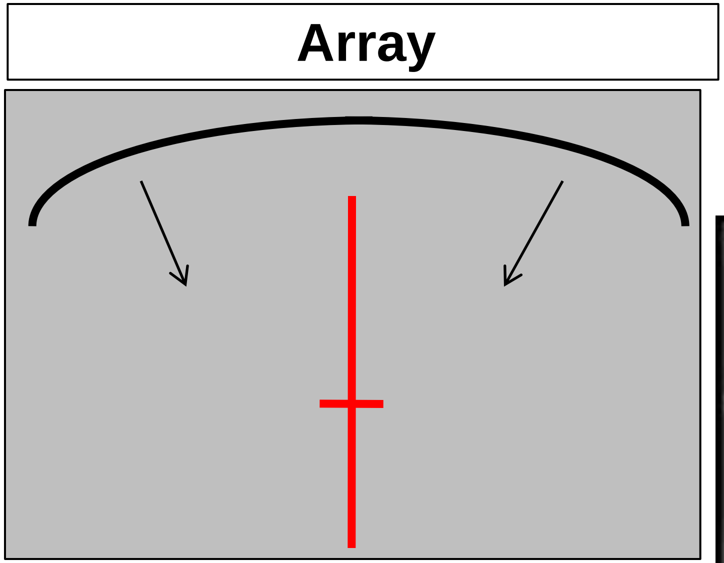
# Ultrafast Imaging of contrast agents disruption

Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.

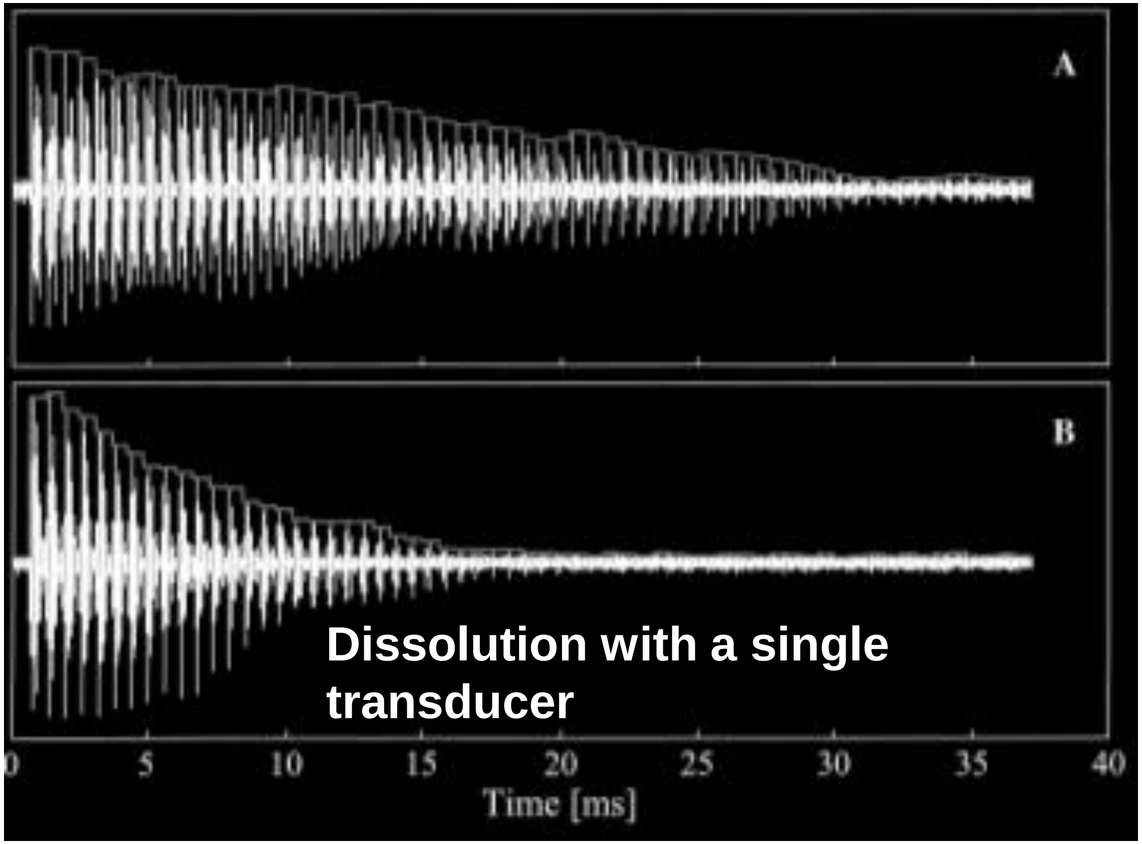
# Context – Conventional ultrasonic imaging of Blood Perfusion



# Conventional imaging is too slow to image dissolution over an entire image



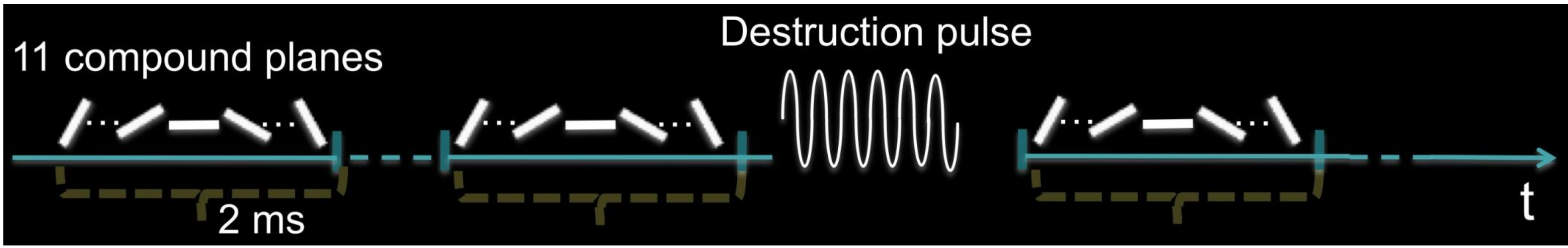

Single Imaging line
At ultrafast frame rate

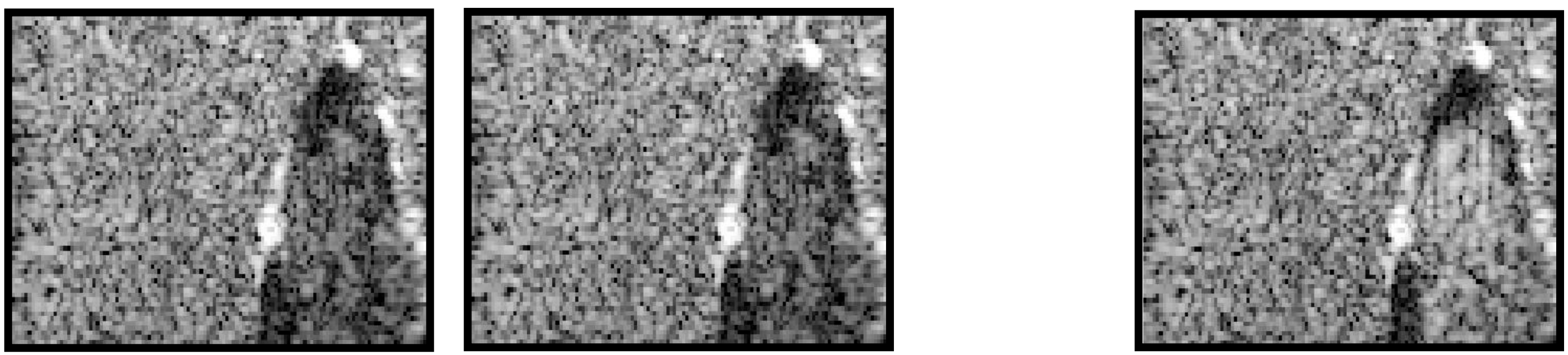



Bouakaz et al. 2009

# Plane wave compounding increases SNR and reduces frame rate to 500 Hz

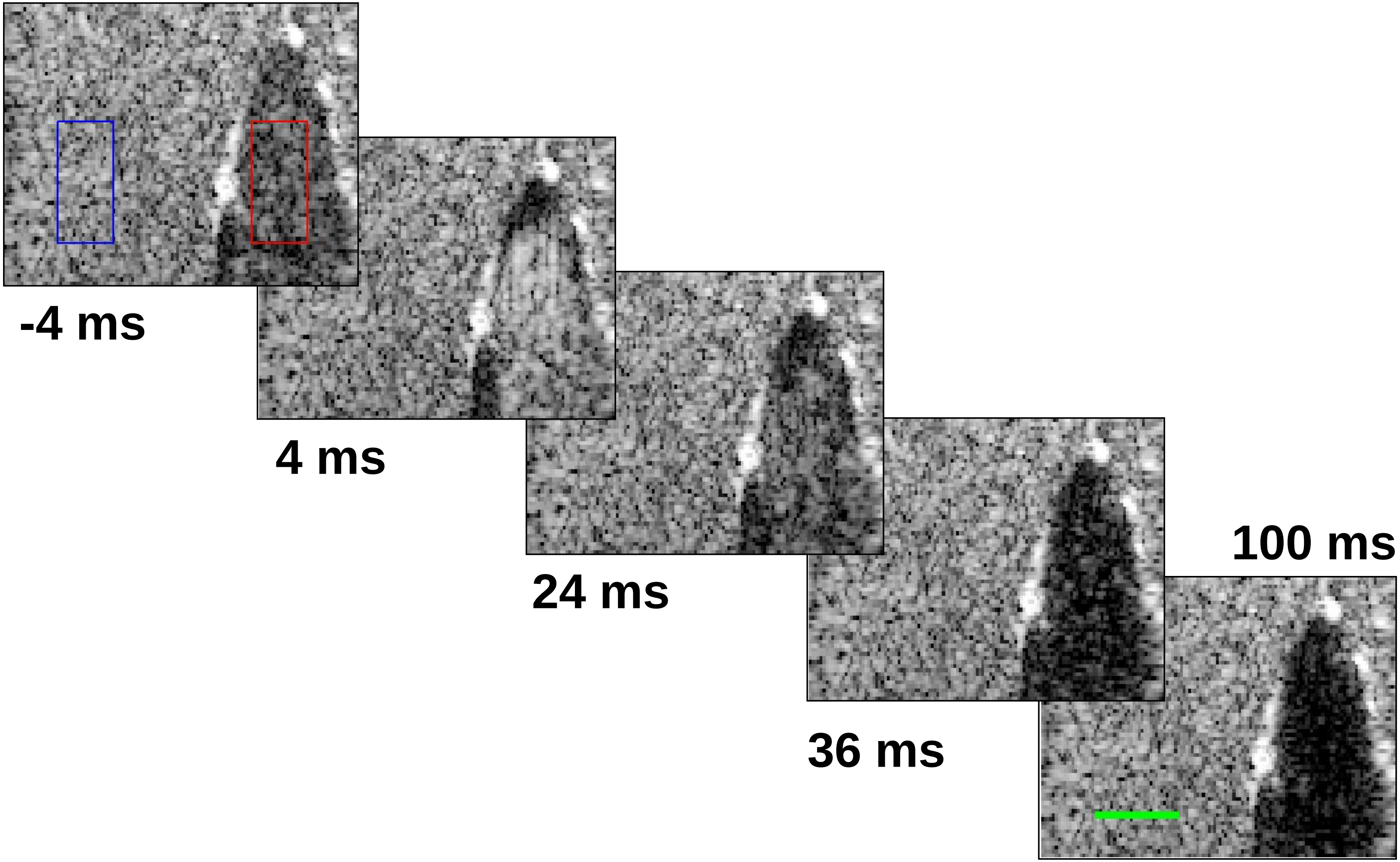
## Pulse sequence used for contrast agents dissolution imaging



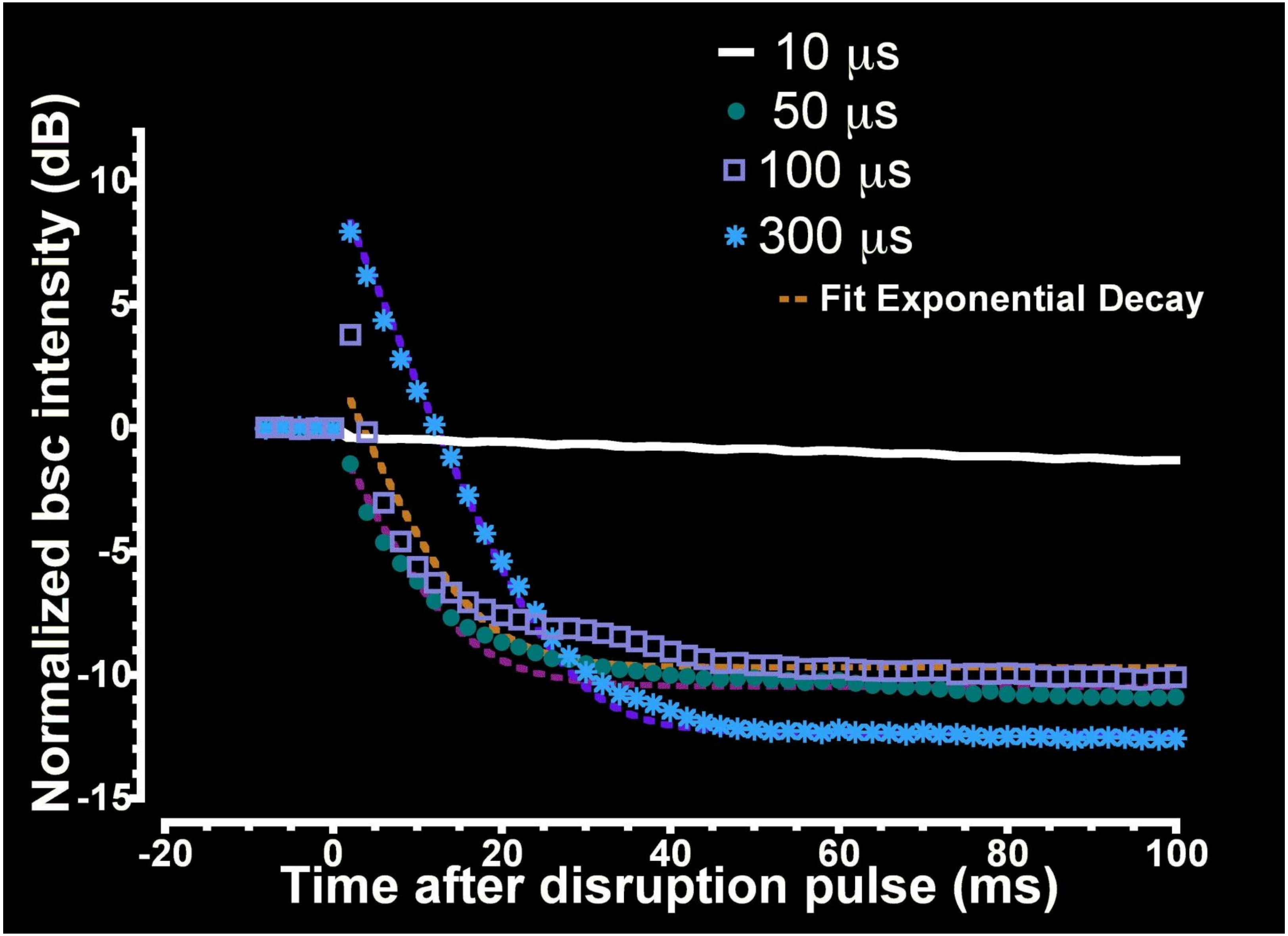
Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.

# The process of dissolution in the wall-less vessel is observable over 100 ms



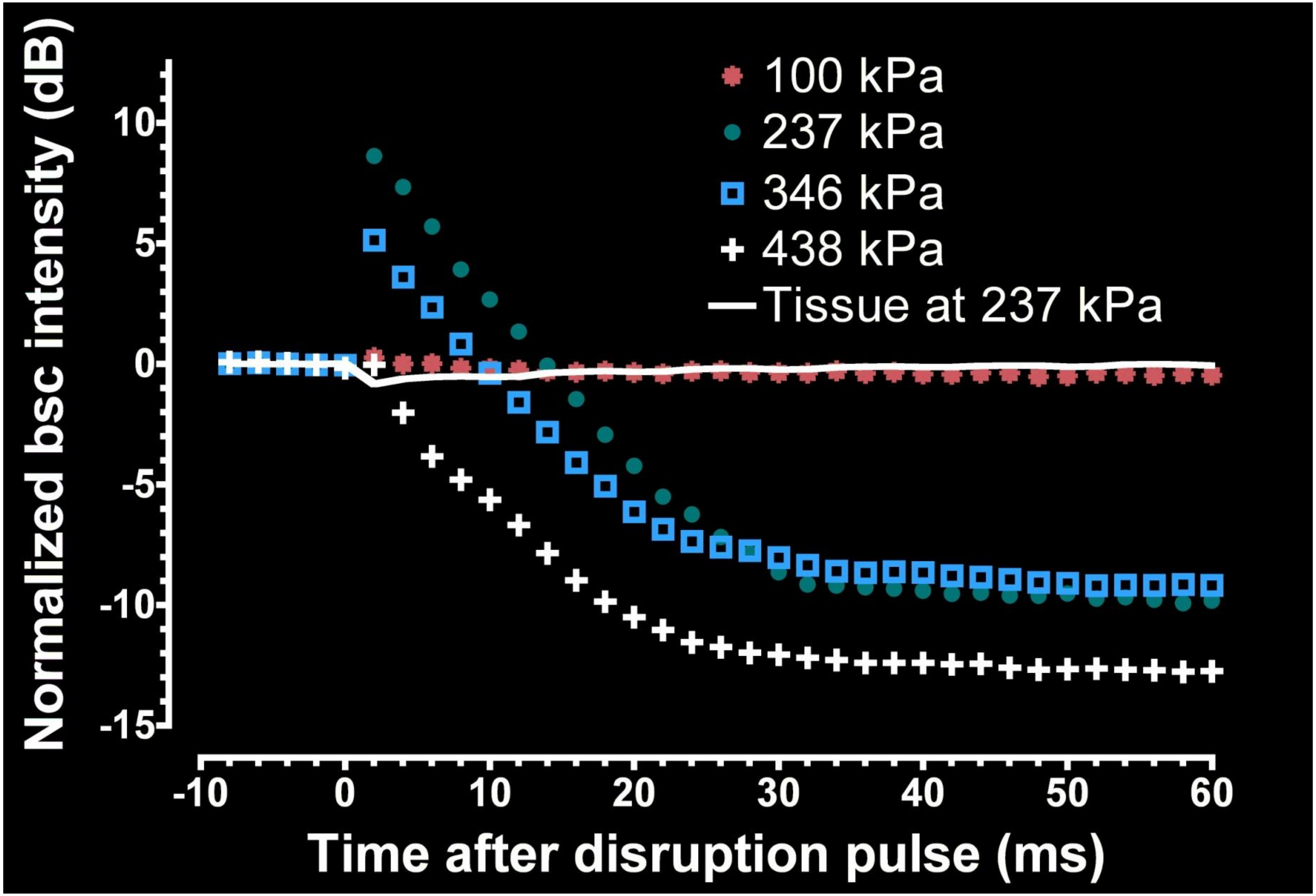

Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.

# The dissolution curves in 2D are similar to those measured with single transducers

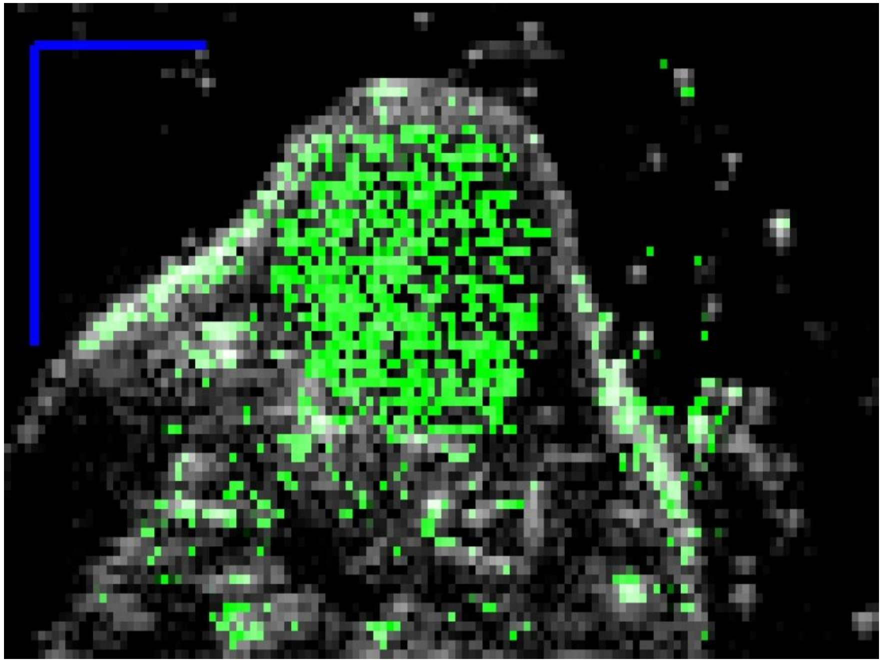



Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.

# The dissolution curves depends on disruption pulse length and amplitude

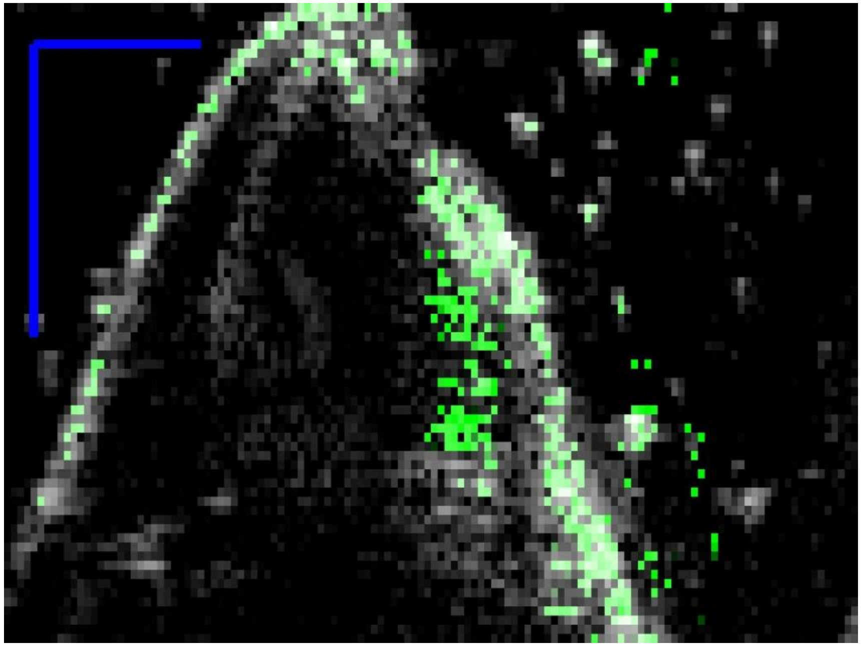


# Distinguishing bound and unspecific microbubbles is a challenge in molecular imaging with ultrasound



**Tumor-targeted Microbubbles**

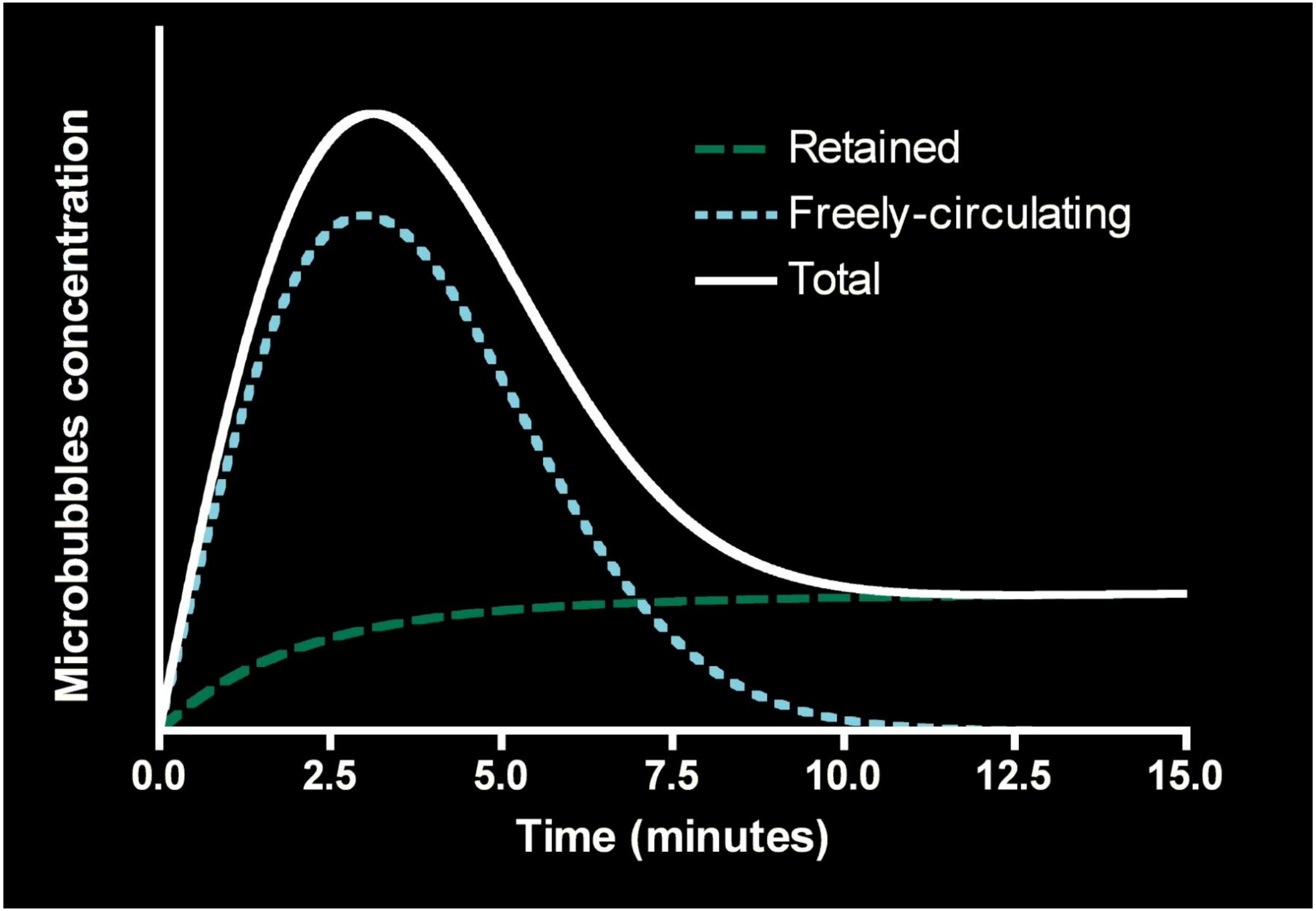
**(StBx Shiga Toxin)**



**Control microbubbles**

**Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.**

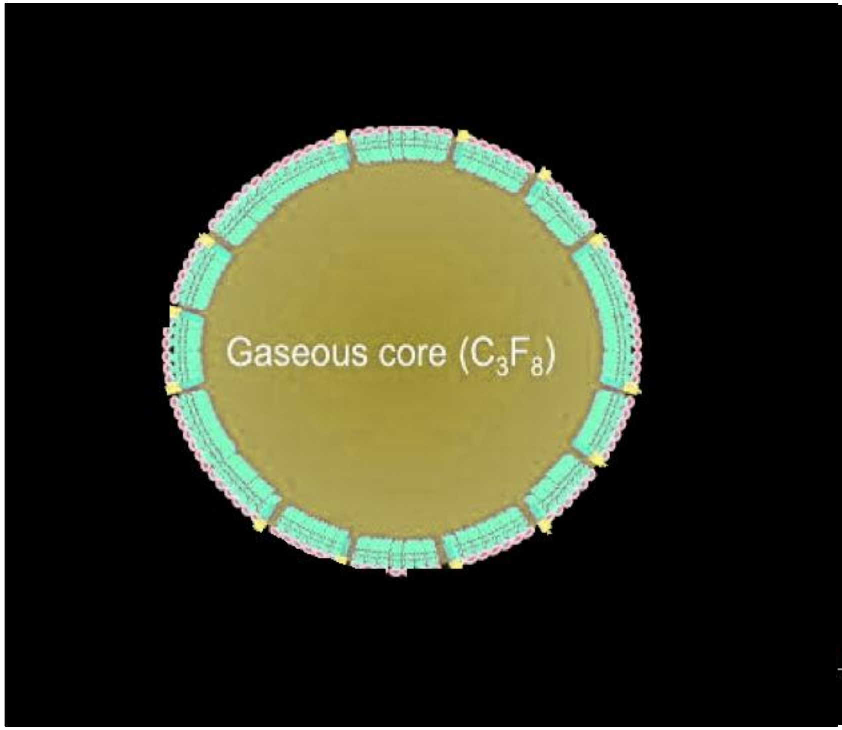
# Bound and unspecific microbubbles are distinguished through their clearance time in the tumor



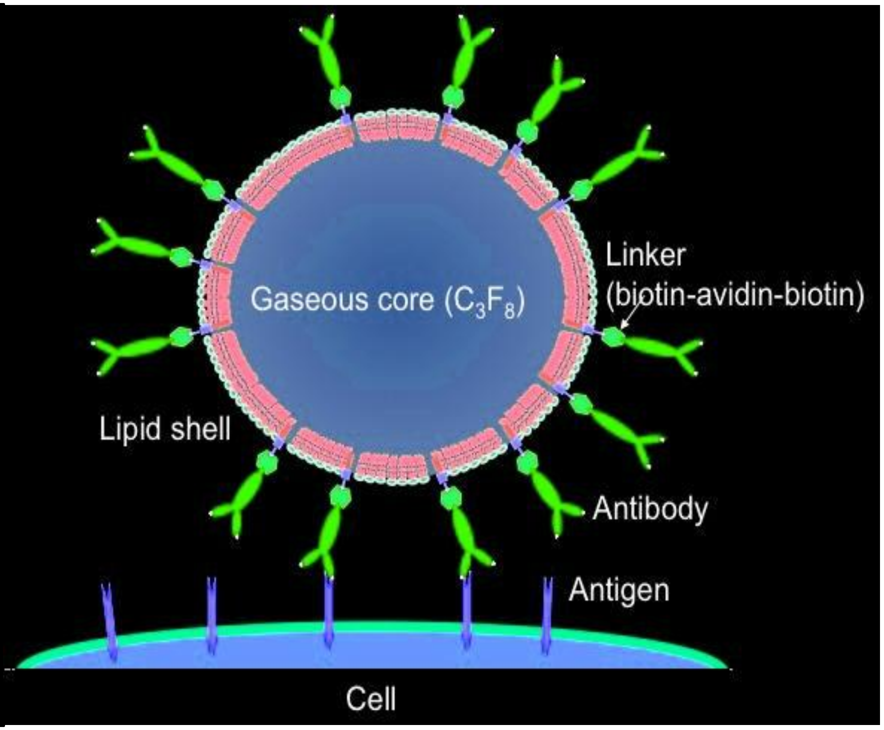

Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.

# The physical environment affects the acoustic response of microbubbles

***Hypothesis*: The dissolution time after disruption changes in the "bound state".**



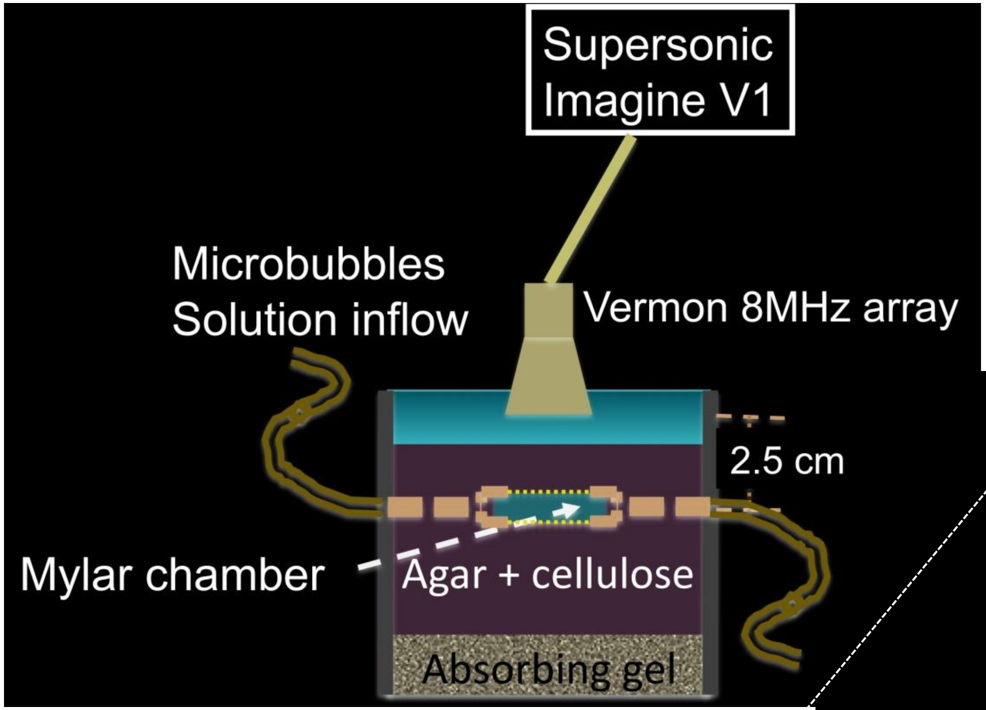

**Free Bubbles**




**Targeted microbubbles**

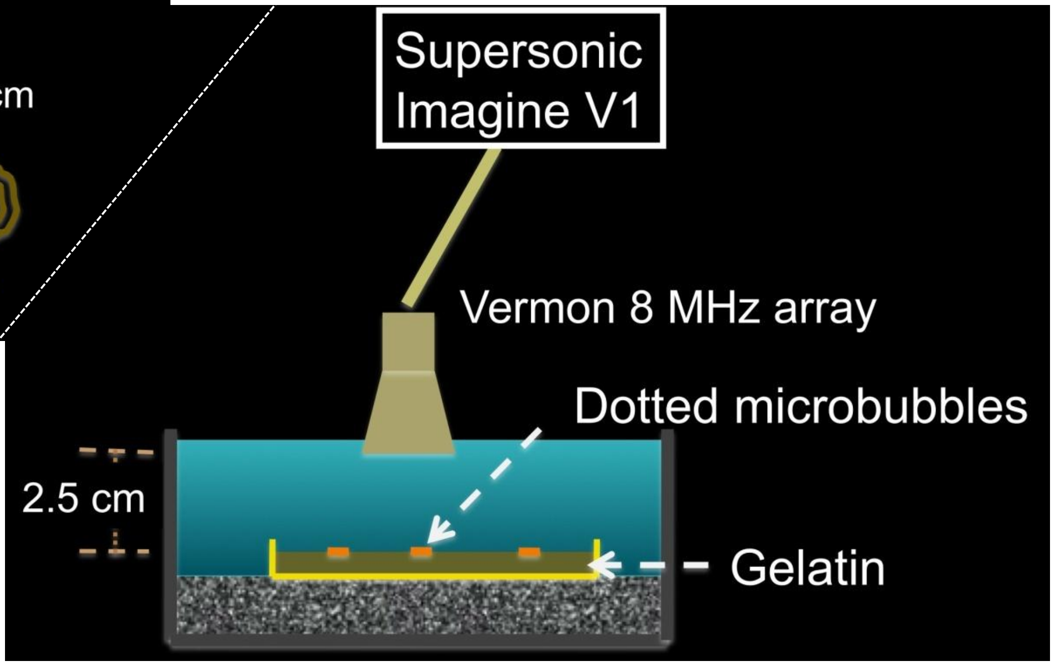

**Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.**

# Dissolution imaging is performed with an elastography apparatus on two parallel setup



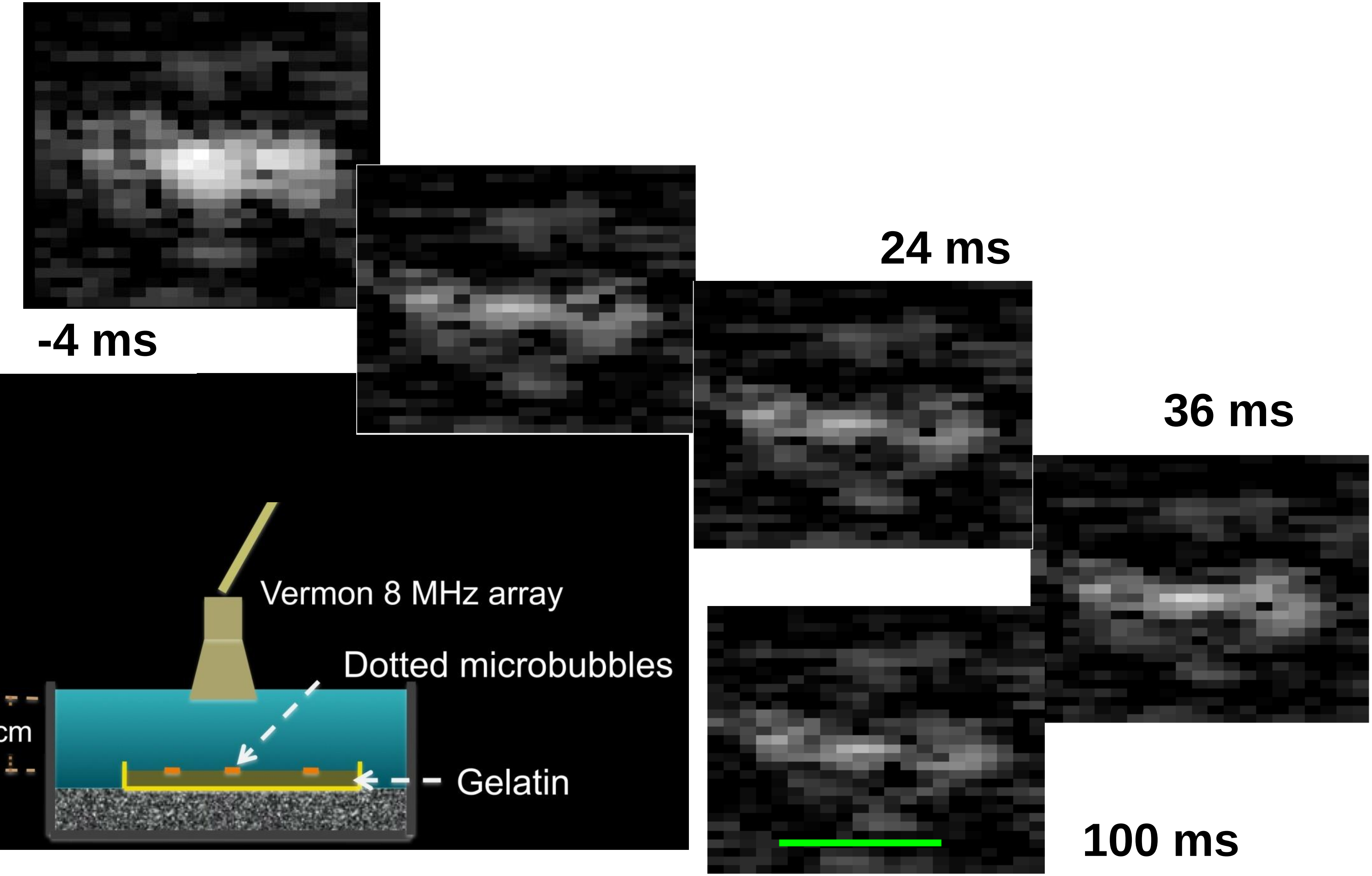

**Bound setup**

**Flowing setup**



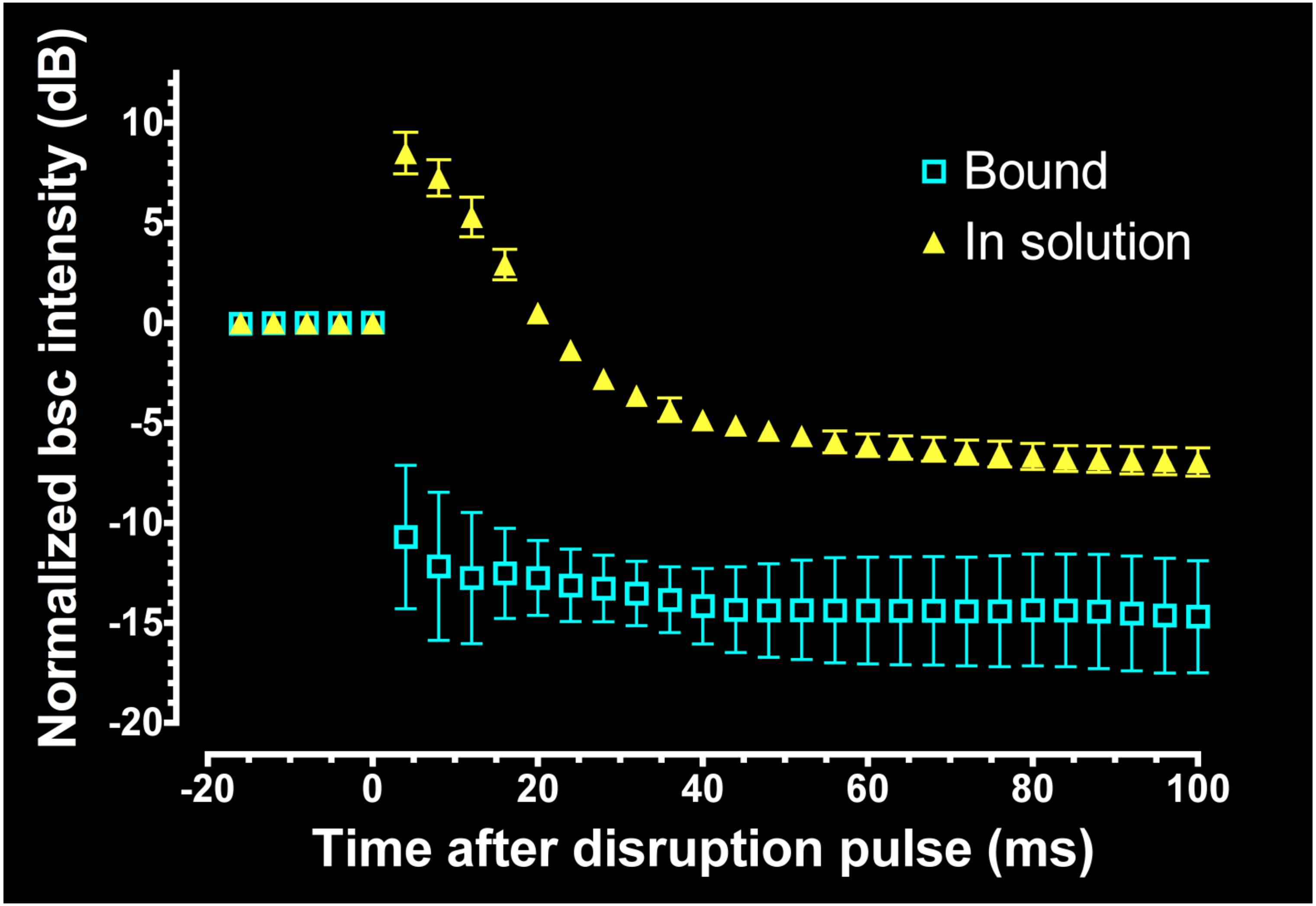

**Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.**

# The process of dissolution is also observable on a dot of targeted microbubbles




Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.

# Targeted microbubbles dissolve faster than freely moving microbubbles.



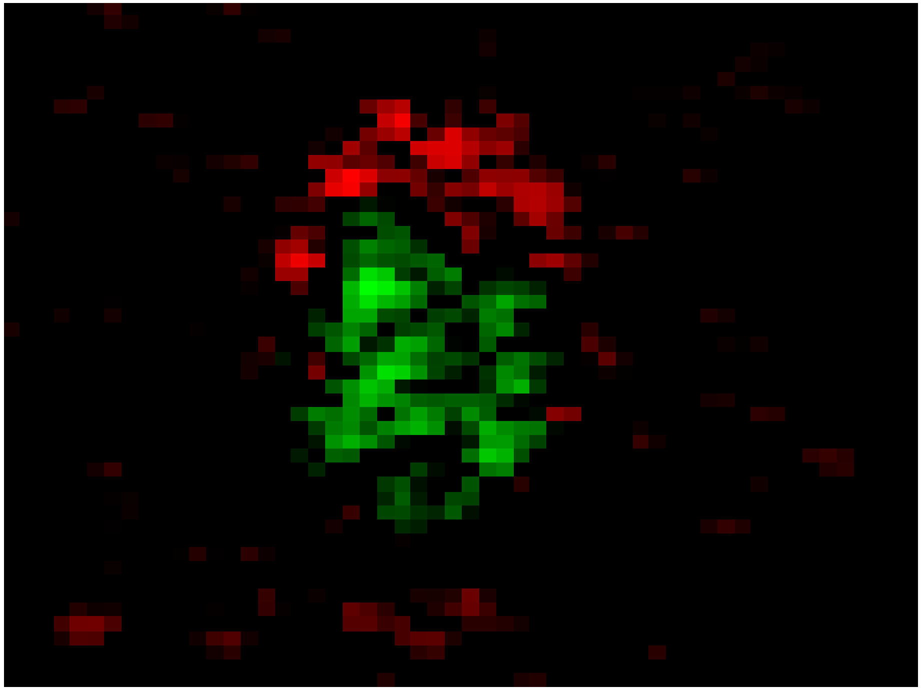


Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.

Couture, O.; Dransart, E.; Dehay, S.; Nemati, F.; Decaudin, D.; Johannes, L. & Tanter, M. (2011), 'Tumor Delivery of Ultrasound Contrast Agents Using Shiga Toxin B Subunit', *Molecular Imaging* 10(2), 135--143.

# Dissolution imaging gives access to new types of contrast enhancement

## *Impact of ultrafast imaging for contrast agents imaging*



- Differentiate bound from unspecific microbubbles

- Fast events are dependent on the geometry of the environment

- Pulses schemes (PI, AM, …) can be applied to entire frames

- Frame rate accelerates with calculations capacity

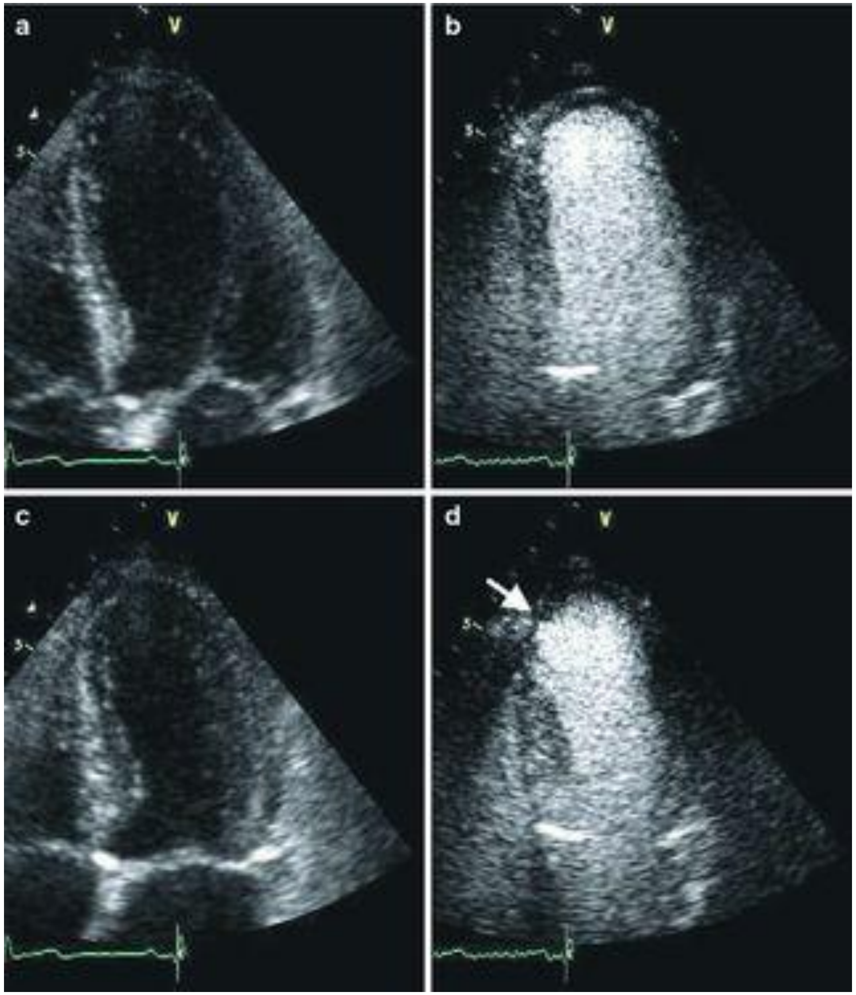

Couture, O.; Bannouf, S.; Montaldo, G.; Aubry, J.-F.; Fink, M. & Tanter, M. (2009), 'Ultrafast Imaging of Ultrasound Contrast Agents', *Ultrasound In Medicine and Biology* 35(11), 1908--1916.

Couture, O.; Dransart, E.; Dehay, S.; Nemati, F.; Decaudin, D.; Johannes, L. & Tanter, M. (2011), 'Tumor Delivery of Ultrasound Contrast Agents Using Shiga Toxin B Subunit', *Molecular Imaging* 10(2), 135--143.

# Ultrafast Contrast Imaging

‘Ultrasound Contrast Plane Wave Imaging’
O. Couture, M. Fink, M. Tanter, IEEE Trans. Ultr. Ferr. Freq. Ctrl., in press, 2012

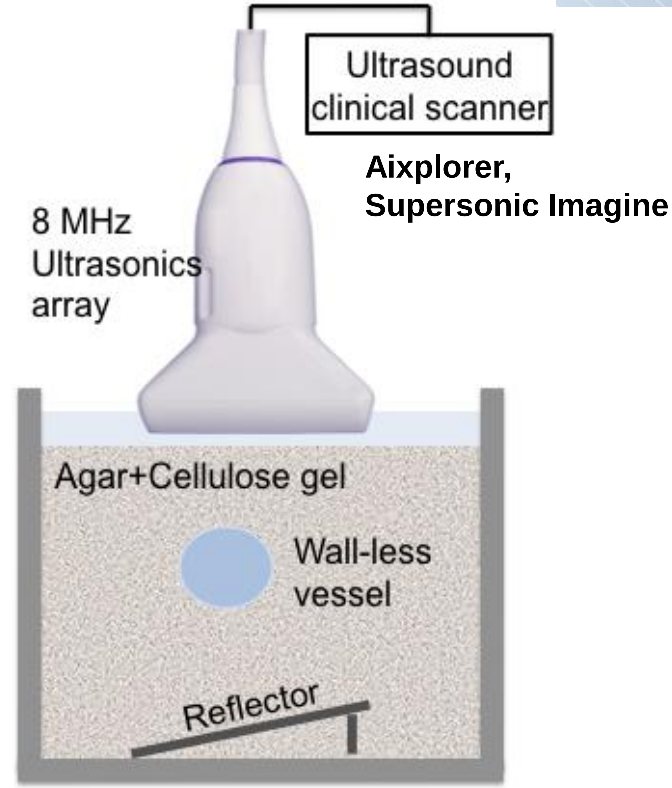
# Microbubbles are used to image vascularization and measure perfusion

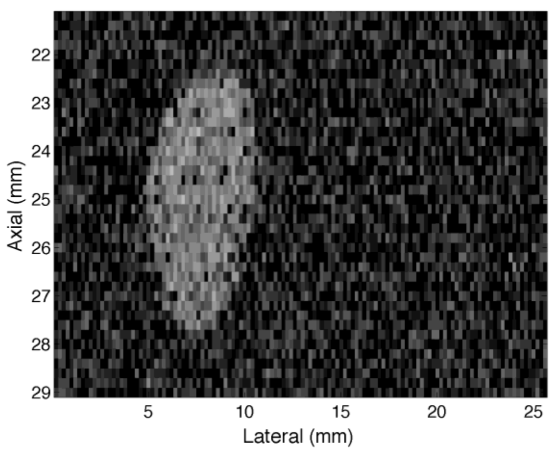



# Ultrafast Contrast Plane Wave Imaging produces a much better contrast

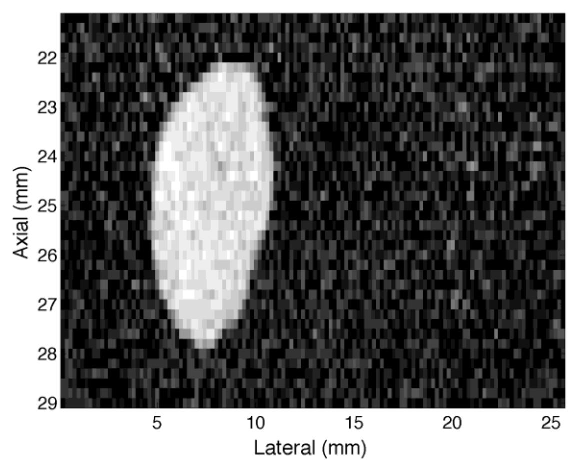
**Different Contrast schemes**

| Pulse | 1 | 2 | 3 | Linear comb. | Non-linear |
|---|---|---|---|---|---|
| Linear | | 1 | | | — |
| Pulse-Inversion | 1 | | -1 | — | |
| Amplitude Modulation | 1/2 | 1 | 1/2 | — | |
| Contrast Pulse Sequencing | 1/2 | -1 | 1/2 | — | |




**Conventional focused CPS**

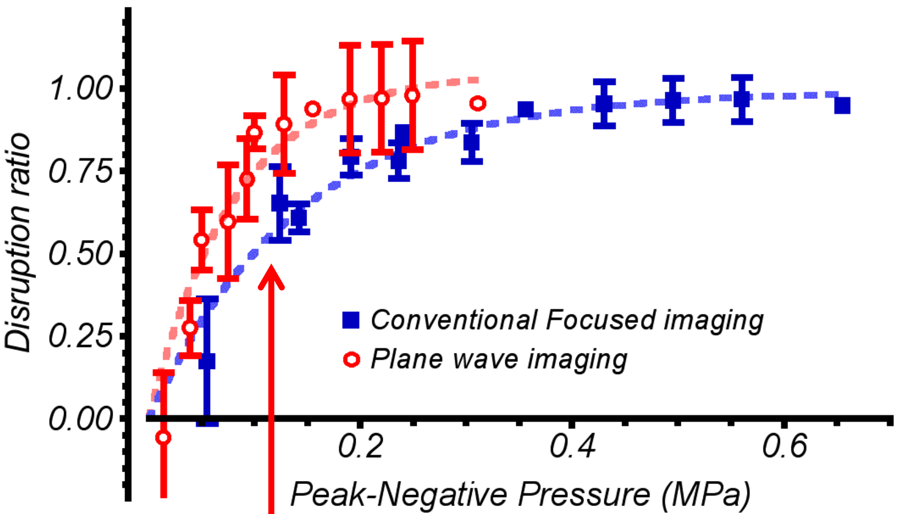


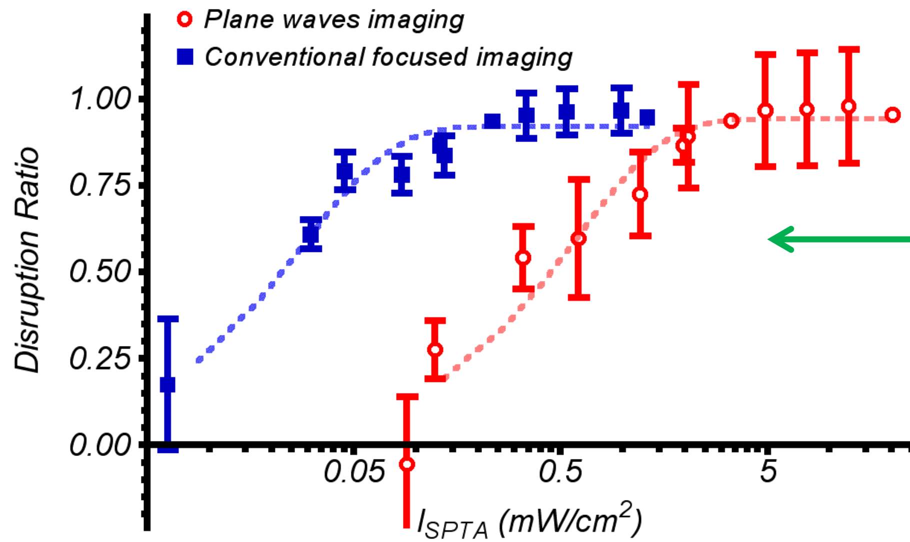

**Plane Wave CPS**

**Images obtained for a similar disruption ratio of microbubbles (25 % disruption after 100 images or focused: 55 kPa peak-negative pressure and Plane waves = 40 kPa).**

**'Ultrasound Contrast Plane Wave Imaging'**
**O. Couture, M. Fink, M. Tanter, IEEE Trans. Ultr. Ferr. Freq. Ctrl., in press, 2012**

# Ultrafast Contrast Plane Wave Imaging spreads the acoustic intensity in time



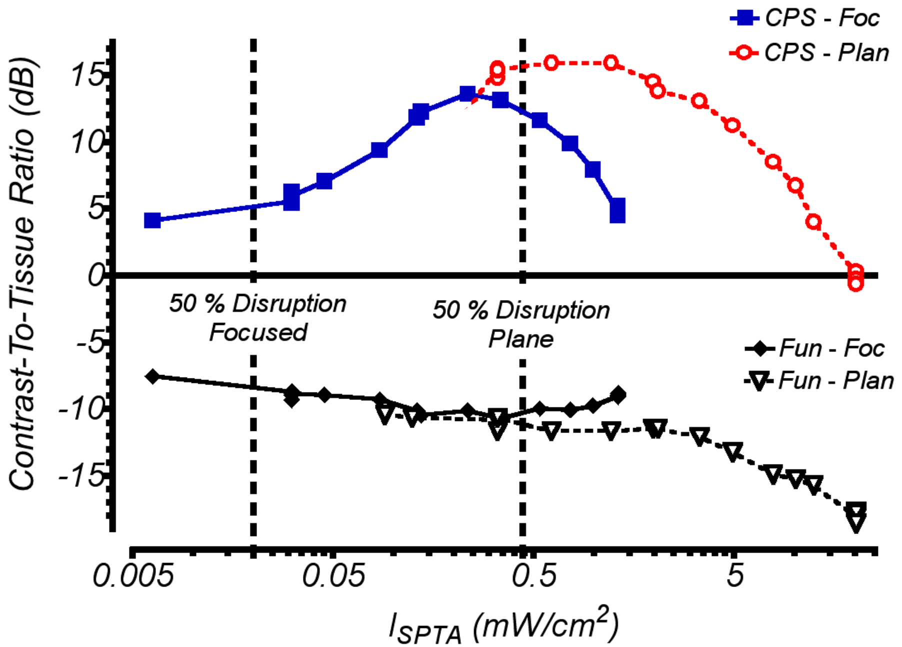

**Disruption ratio obtained after 100 images. The ratio is calculated from the intensity of the microbubble echo before and after the full sequence. In plane-wave imaging, each pixel is insonified 121 times rather than a single time in focused imaging.**

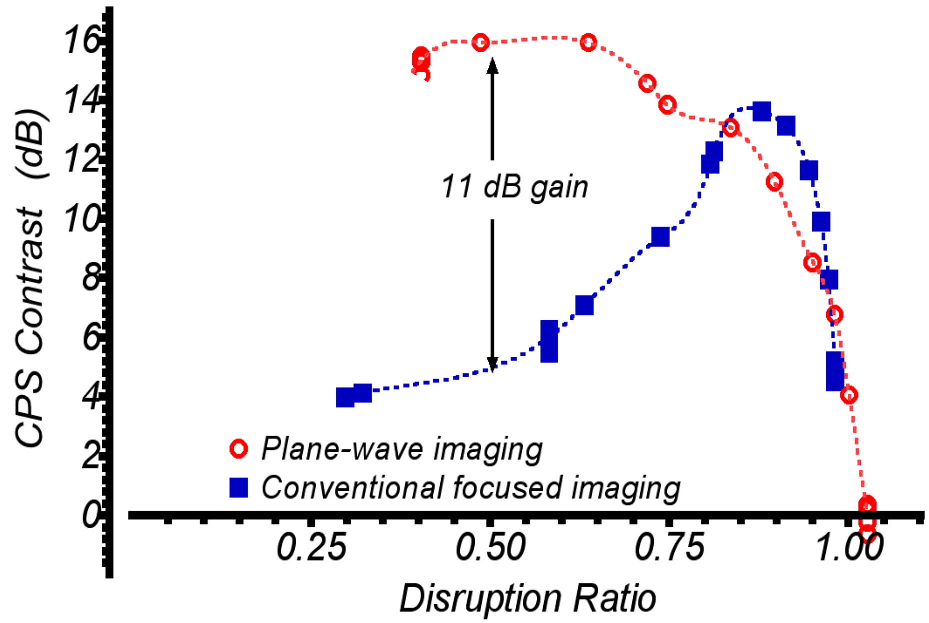
**Hence, at the same peak-negative pressure, plane-wave imaging disrupts slightly more bubbles.**

**But Plane-wave imaging spread the energy over more pulses at lower pressure. Microbubbles being sensitive to the peak-negative pressure, rather than the total energy, the 50% disruption point is only observed at 0.47 mW/cm2 for plane-wave imaging as compared to 0.02 mW/cm2 for focused pulses.**

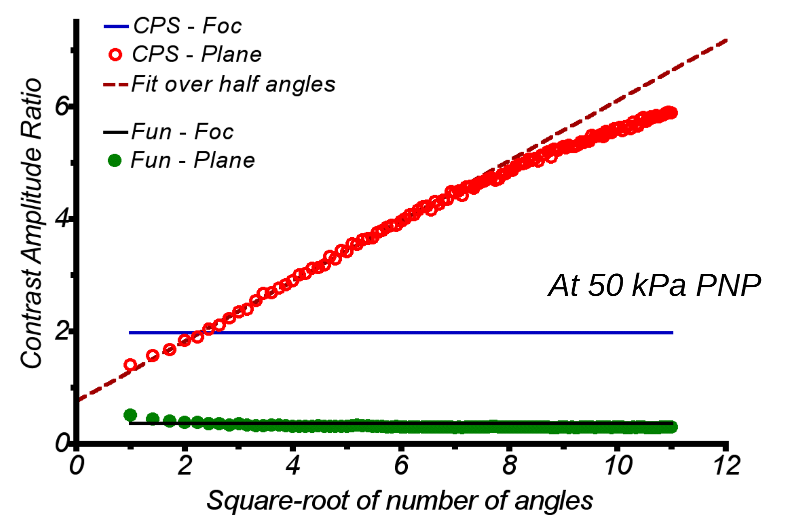
**Less acoustic energy can be emitted with focused pulses before microbubbles disruption occurs.**

# Ultrafast Contrast Imaging keeps a high CTR while preserving bubbles



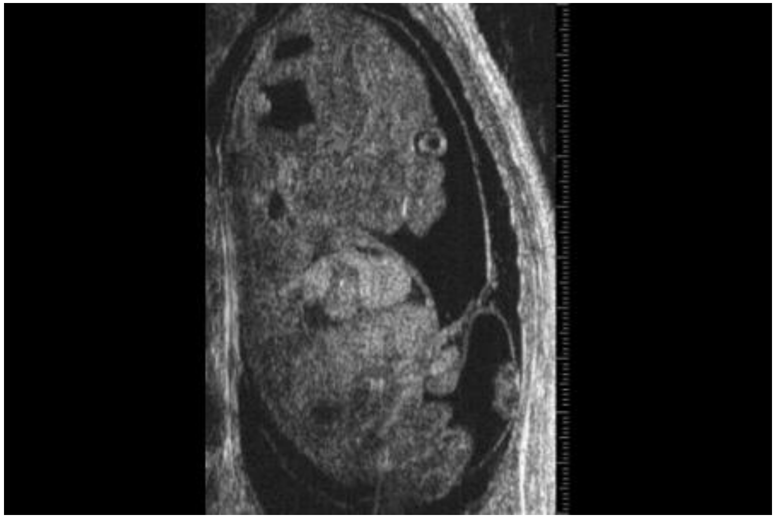




$$\frac{CTR_{PlaneWave}}{CTR_{Focused}} \sim \sqrt{N_{angles}}$$



# Ultrafast Ultrasound for Contrast Superresolution Imaging

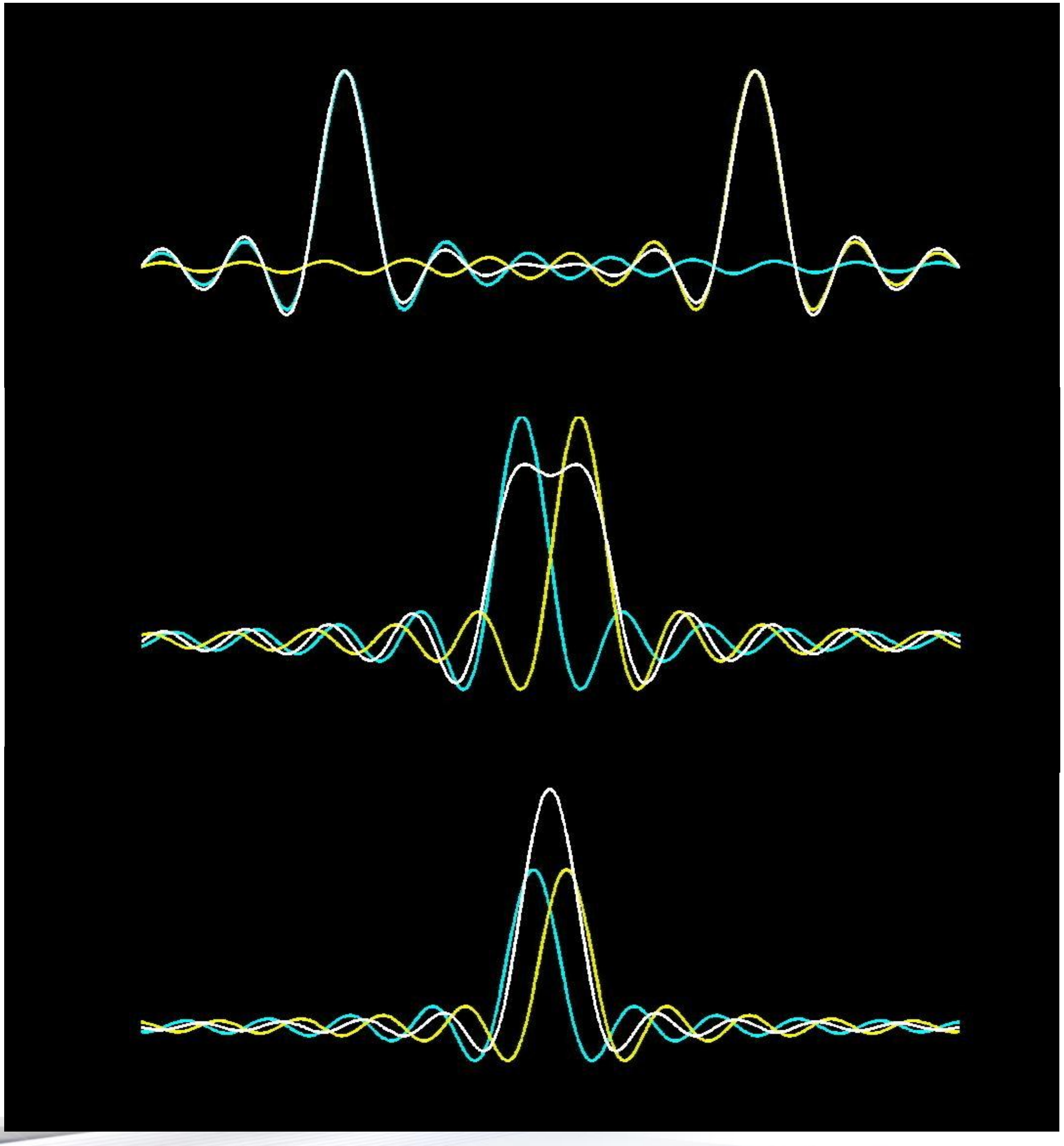
# Ultrasound imaging is still limited by the trade-off between resolution and penetration



**Mouse embryo at 40 MHz**
**Penetration ≈ 1 cm**

**Human fœtus at 5 MHz**
**Penetration ≈ 10 cm**

# Imaging resolution is limited by the wavelength

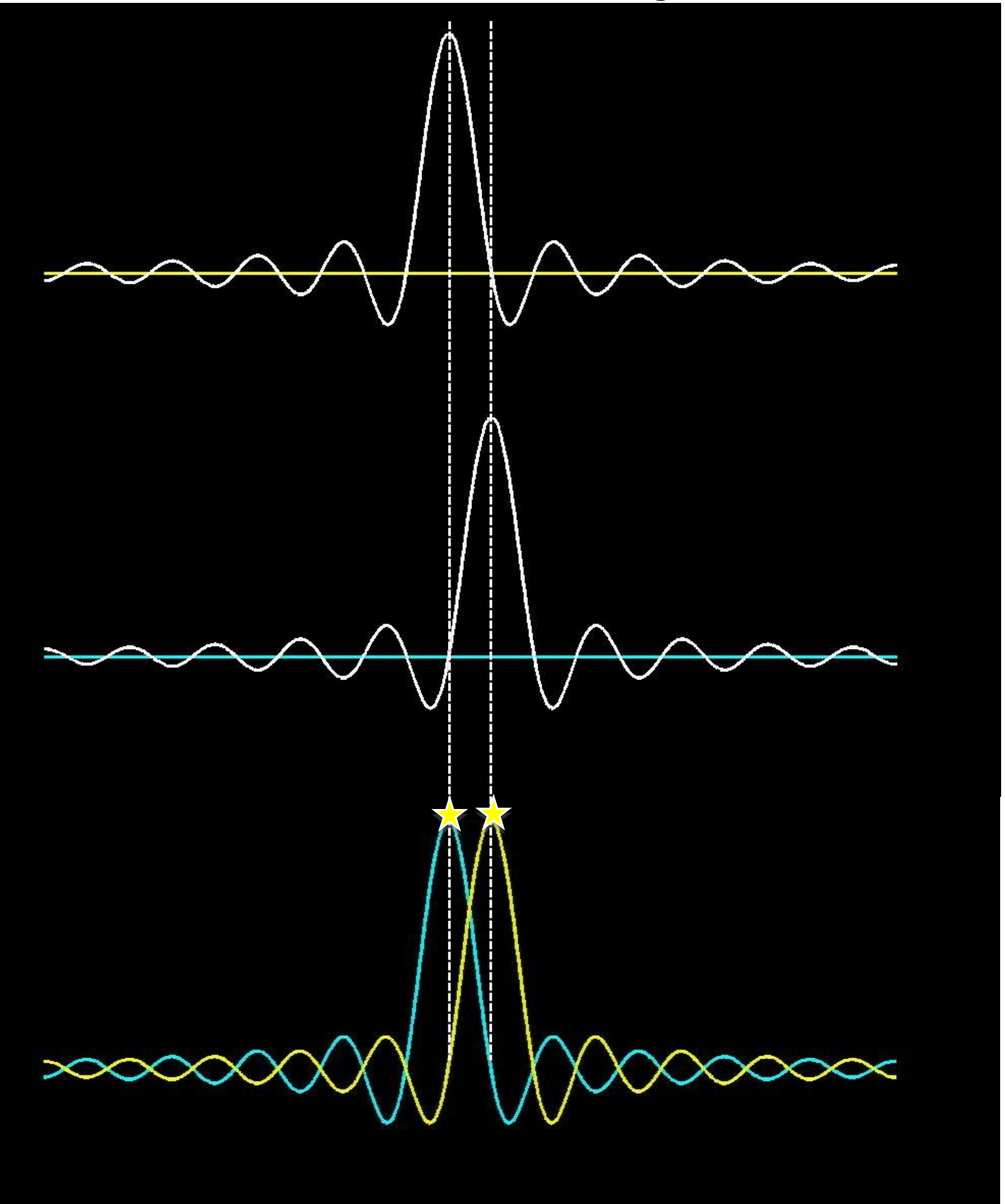


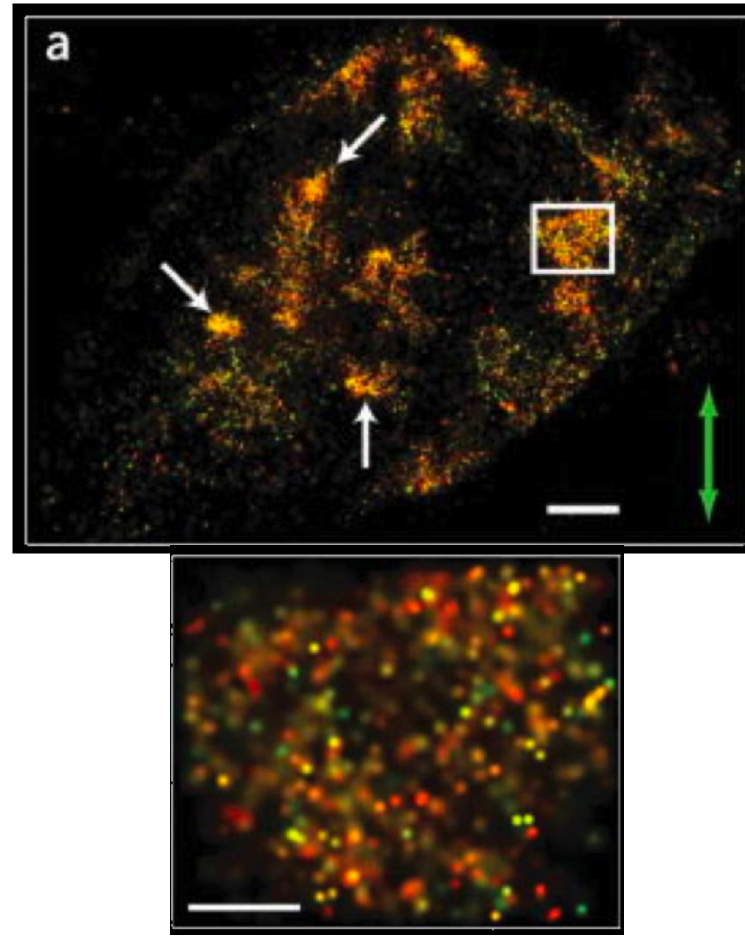
**Two distincts sources**

**Rayleigh criterion**

**Two indistinguishable sources**

# Sources become distinguishable when they are activated separately

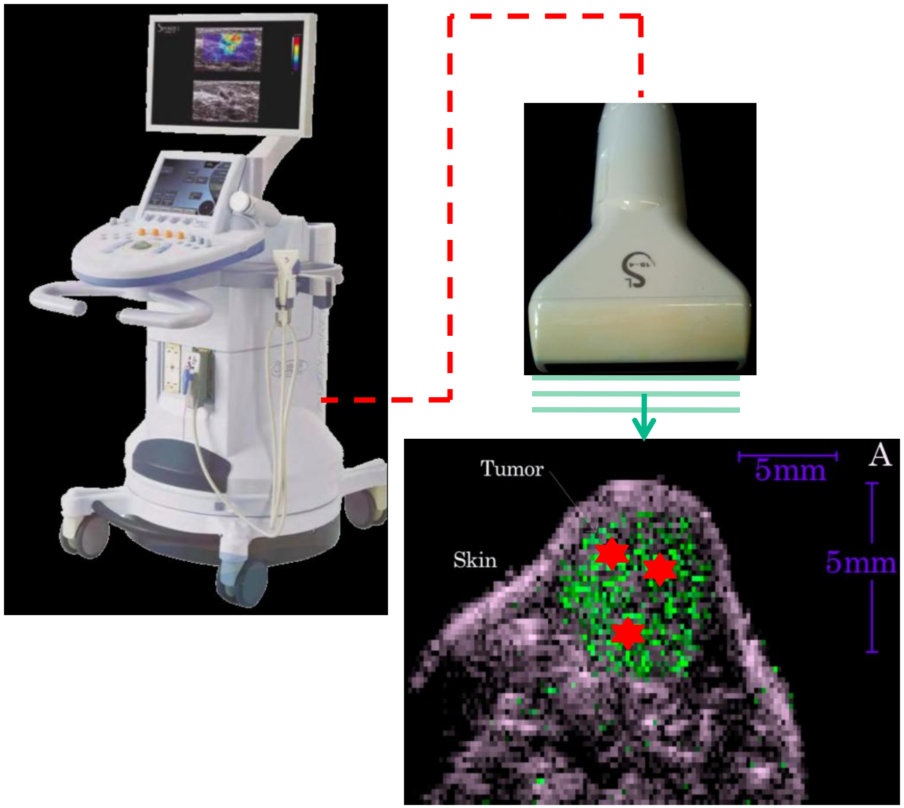





**P-FPALM image of a fixed fibroblast (scale bar = 1 µm).**

**Gould et al. Nat Methods 2008. (Hess group)**

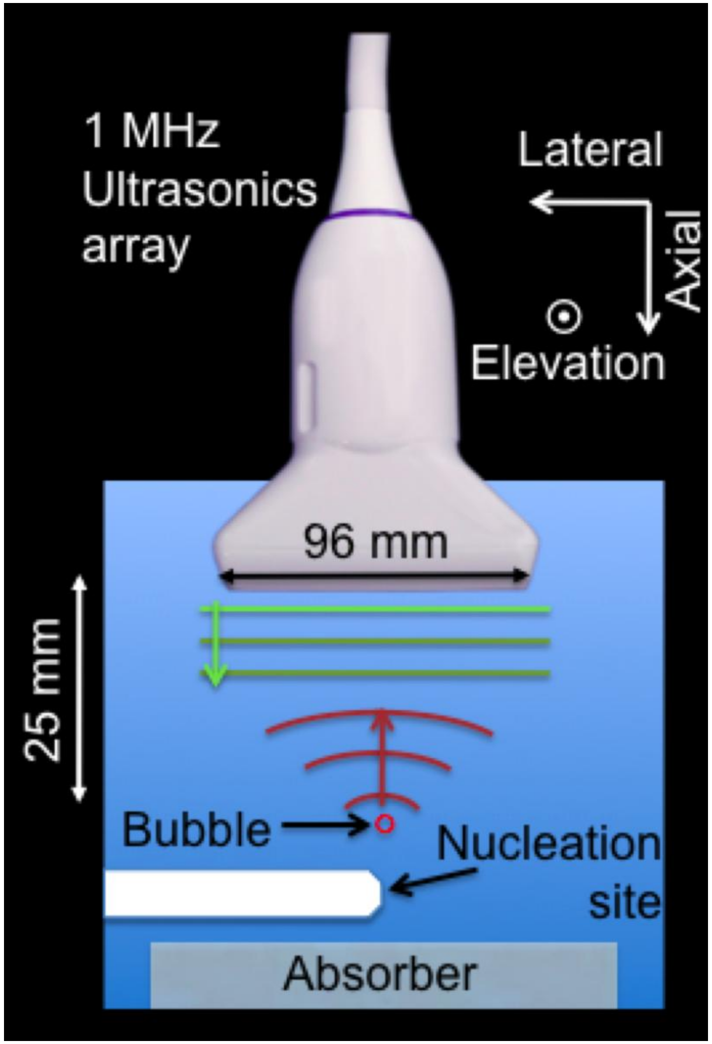
# Ultrafast (plane-wave) imaging shows distinct events in-vivo

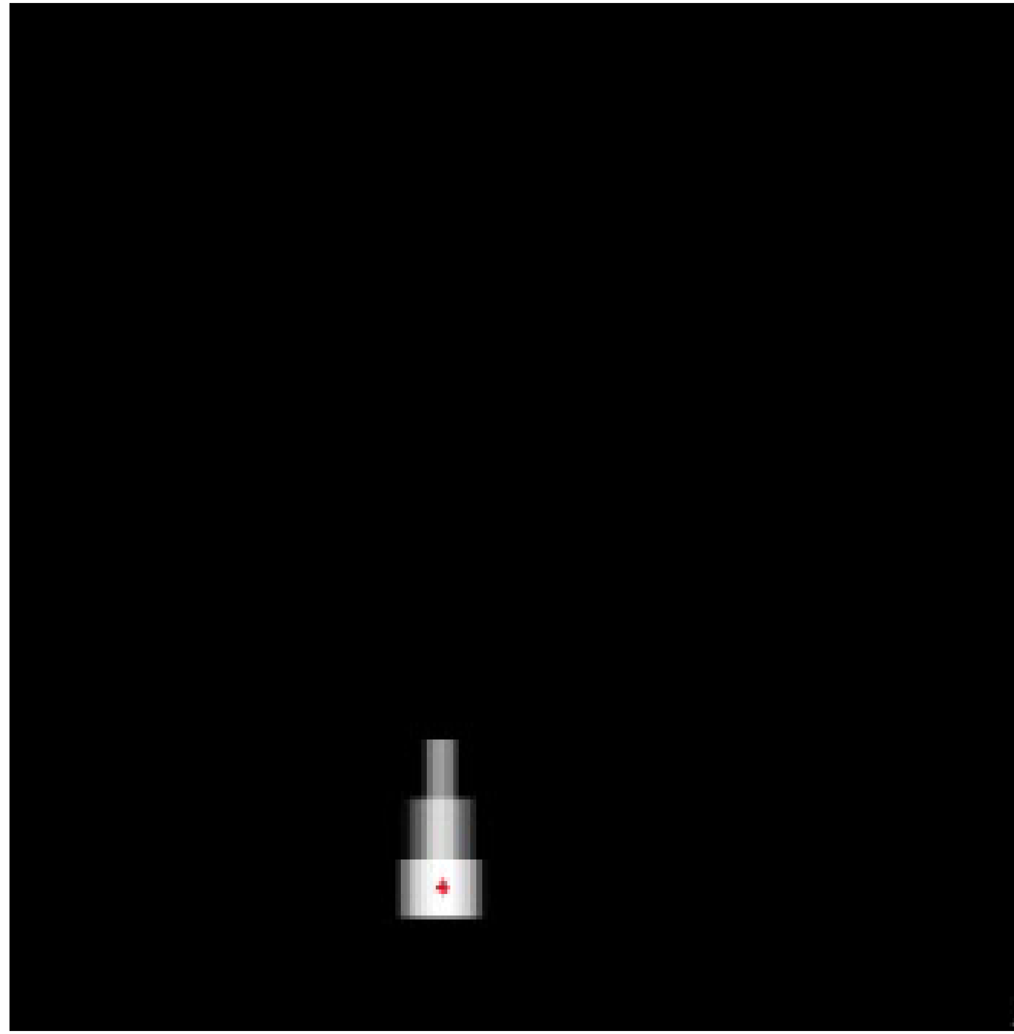



Frame Rate: 5000 kHz

**‘Microbubbles Ultrasonic Super Localization Imaging »**
**O. Couture, M. Fink, M. Tanter, Proc. IEEE, Orlando, 2011**

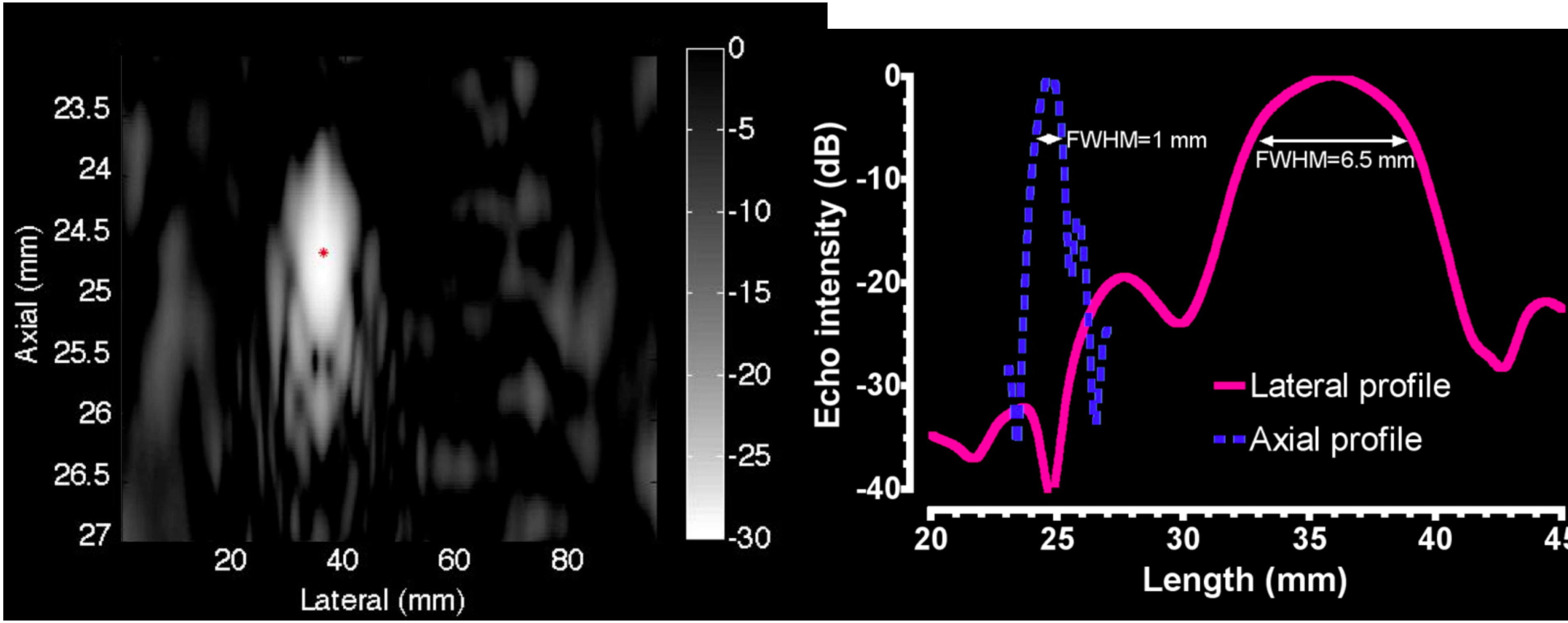
# A bubble is an ideal punctual source



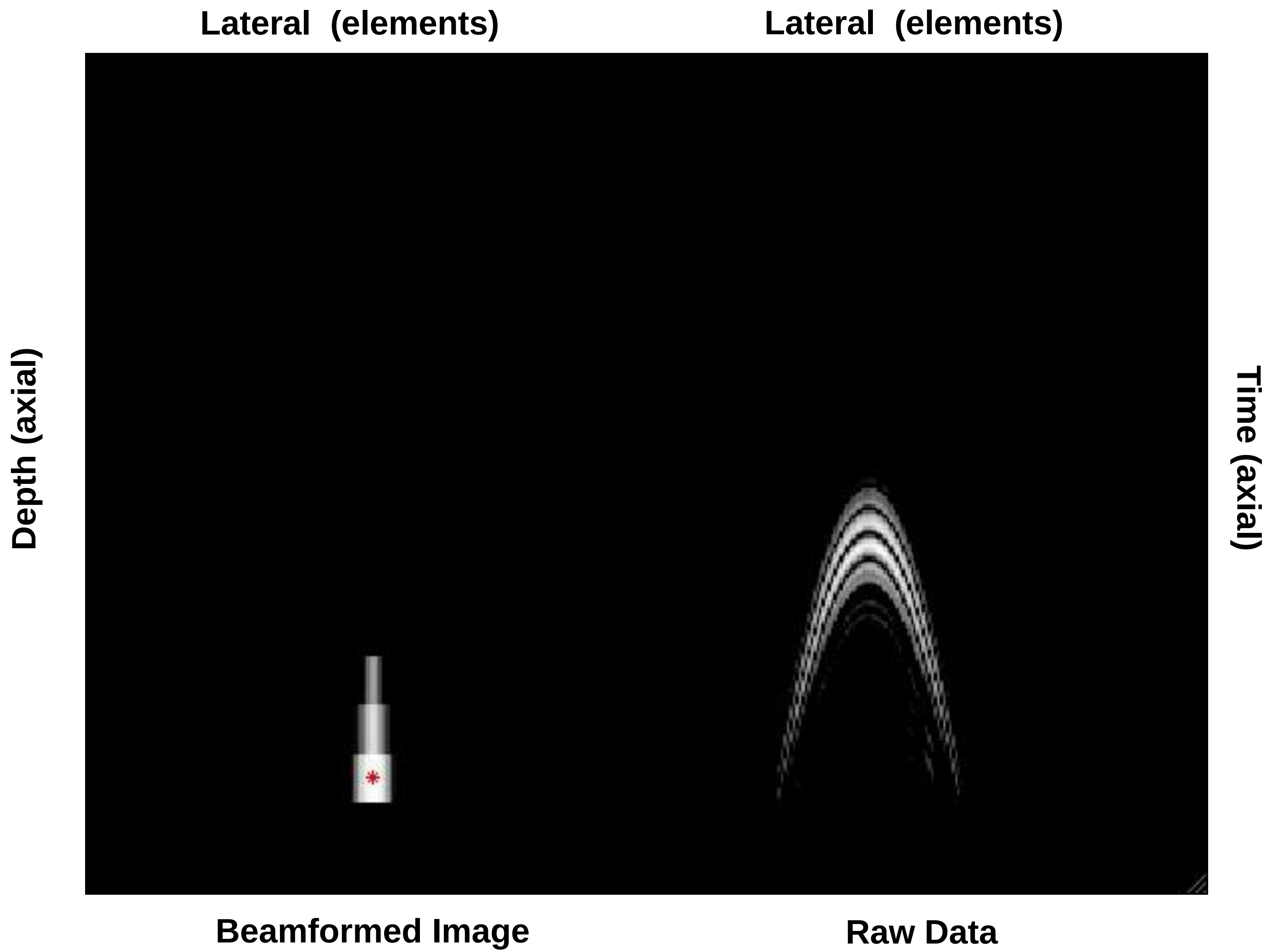
‘Microbubbles Ultrasonic Super Localization Imaging »
O. Couture, M. Fink, M. Tanter, Proc. IEEE, Orlando, 2011

# A punctual source defines the classical resolution limit after the beamforming process




'Microbubbles Ultrasonic Super Localization Imaging »
O. Couture, M. Fink, M. Tanter, Proc. IEEE, Orlando, 2011

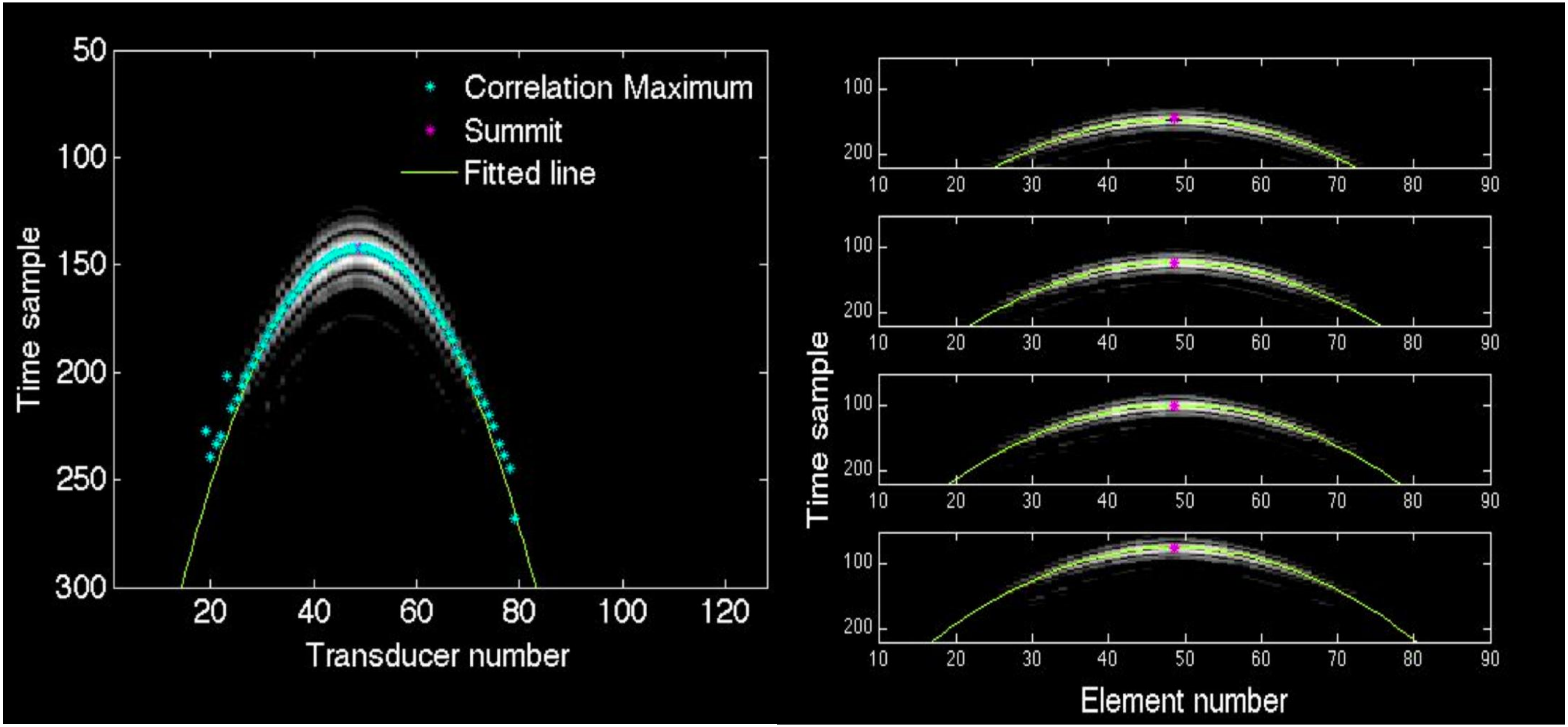
# A punctual source generates a parabola on the RF signals (Bscan)




'Ultrasound Contrast Plane Wave Imaging'
O. Couture, M. Fink, M. Tanter, IEEE Trans. Ultr. Ferr. Freq. Ctrl., in press, 2012

# Fitting the arrival times parabola localizes the bubble

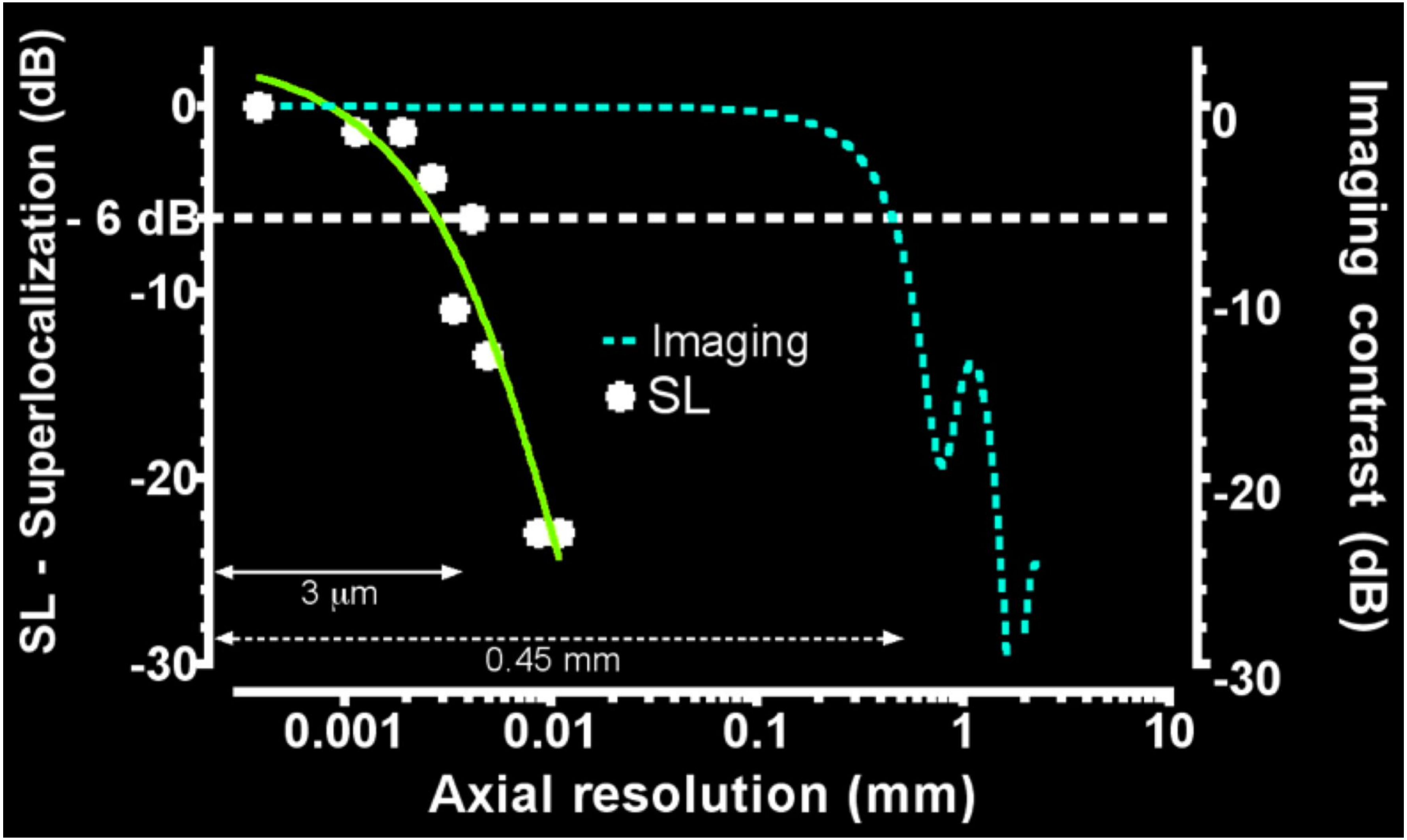
$$delay = \frac{\sqrt{depth\_of\_bubble^2 + (x - lateral\_position)^2}}{speed\_of\_sound}$$




**Spatial Localization precision is much better than conventional imaging**

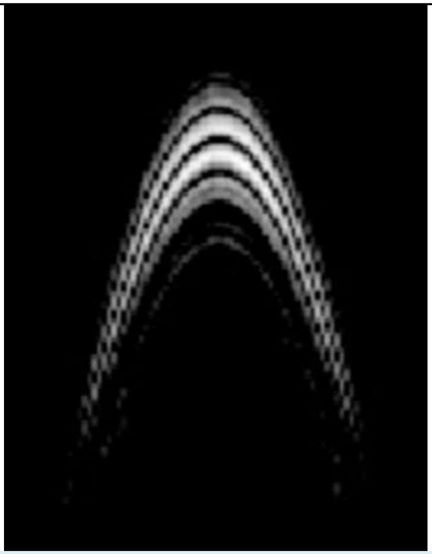
**'Ultrasound Contrast Plane Wave Imaging'**
**O. Couture, M. Fink, M. Tanter, IEEE Trans. Ultr. Ferr. Freq. Ctrl., in press, 2012**

# Axial “resolution” goes from 1 mm to 6 µm




‘Microbubbles Ultrasonic Super Localization Imaging »
O. Couture, M. Fink, M. Tanter, Proc. IEEE, Orlando, 2011

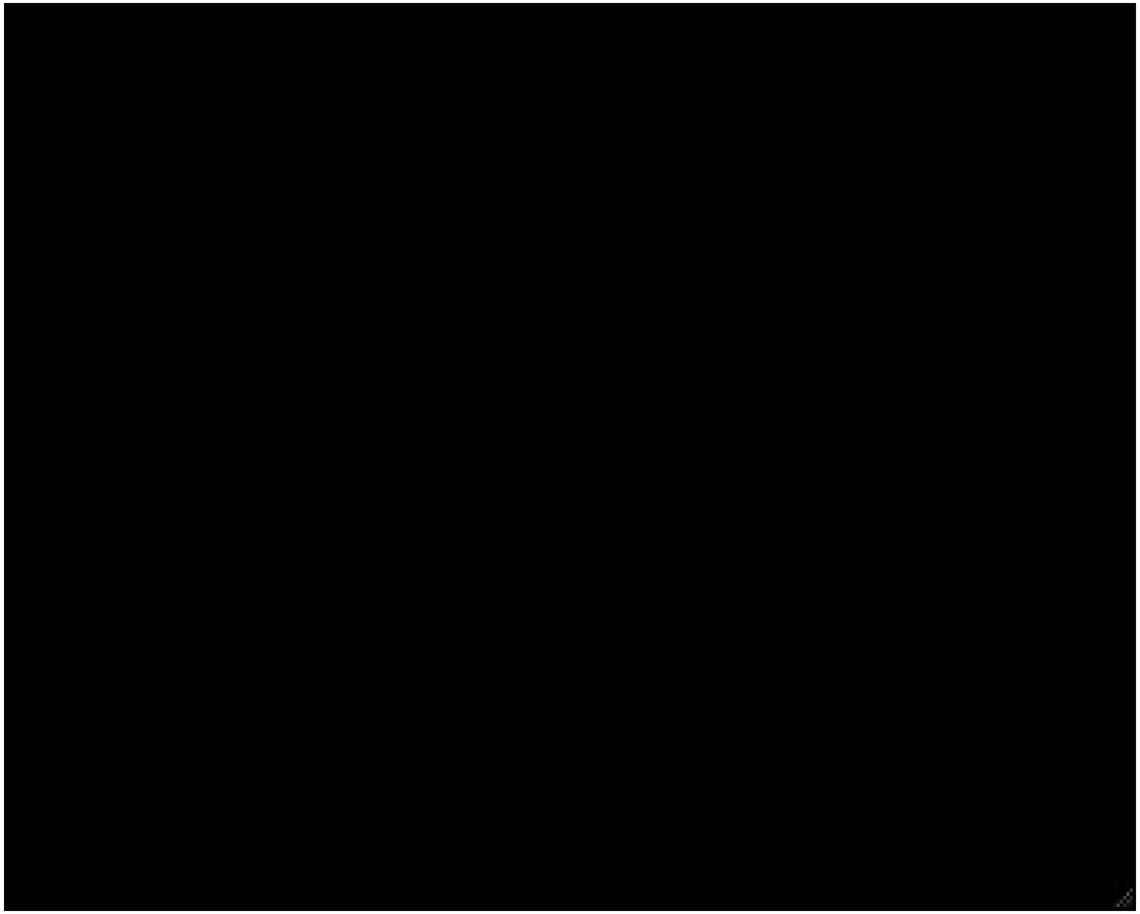
# *Microbubble ultrasound super-localization imaging (MUSLI) improves resolution 100-fold*



| 1.5 MHz | λ / 2 | EXP. | Simulation |
|---|---|---|---|
| AXIAL | 500 µm | 6 µm | 4.5 µm |
| LATERAL | | 40 µm | 11 µm |

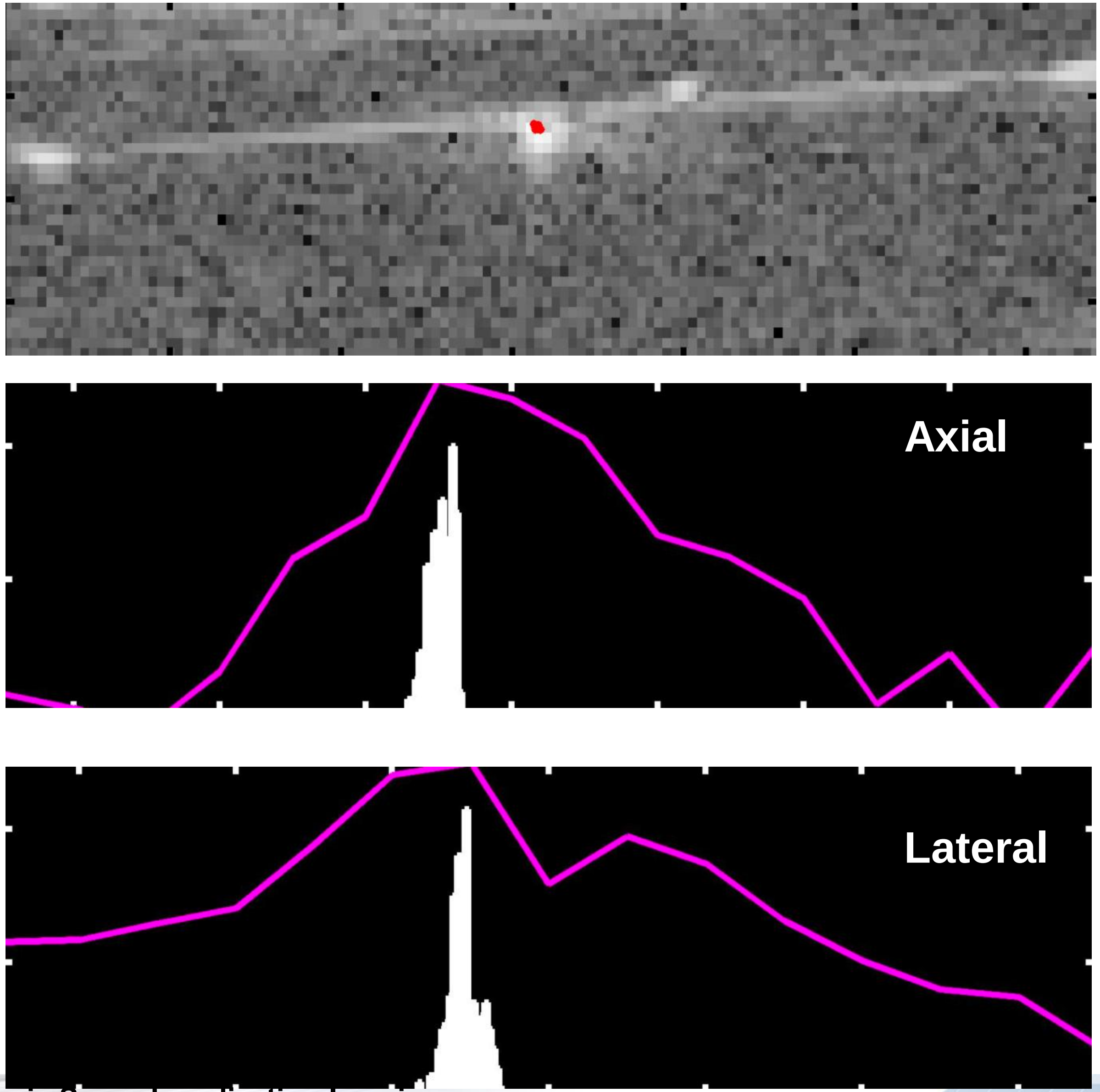
‘Microbubbles Ultrasonic Super Localization Imaging »
O. Couture, M. Fink, M. Tanter, Proc. IEEE, Orlando, 2011

# Experimental proof of concept in 2D with microchannels

**'Microbubbles Ultrasonic Super Localization Imaging »**
**O. Couture, M. Fink, M. Tanter, Proc. IEEE, Orlando, 2011**

# MUSLI can resolve a microchannel carrying microbubbles

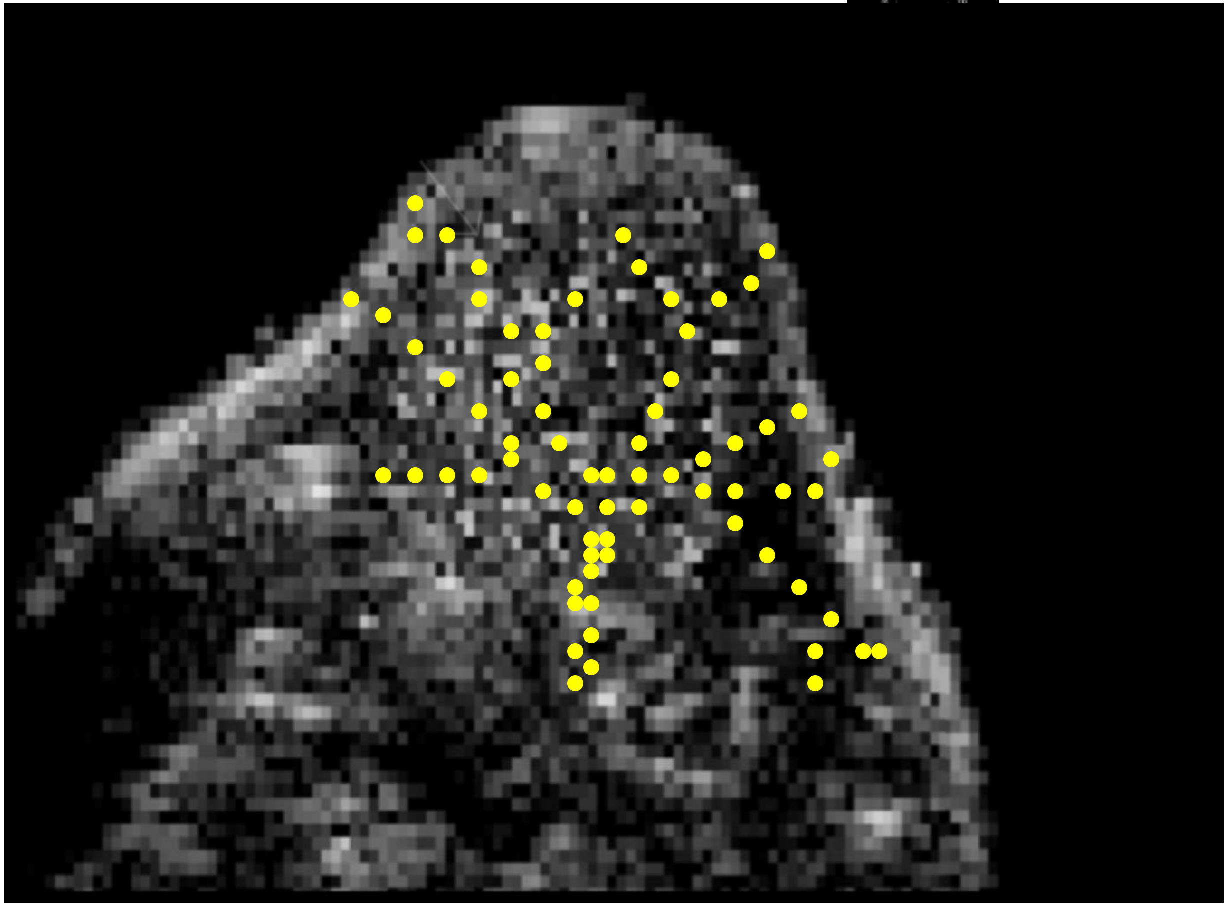



'Microbubbles Ultrasonic Super Localization Imaging »
O. Couture, M. Fink, M. Tanter, Proc. IEEE, Orlando, 2011

# Microbubbles ultrasound super-localization imaging could resolve capillaries at low frequencies

**λ / 2 = 500 µm**

**= 6 µm**



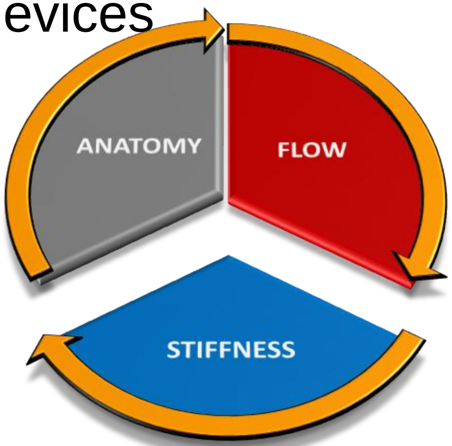
**'Microbubbles Ultrasonic Super Localization Imaging »**
**O. Couture, M. Fink, M. Tanter, Proc. IEEE, Orlando, 2011**

# Ultrafast Doppler Imaging

# SWE

- ShearWave Elastography (SWE) provides an additional information to the user: tissue stiffness

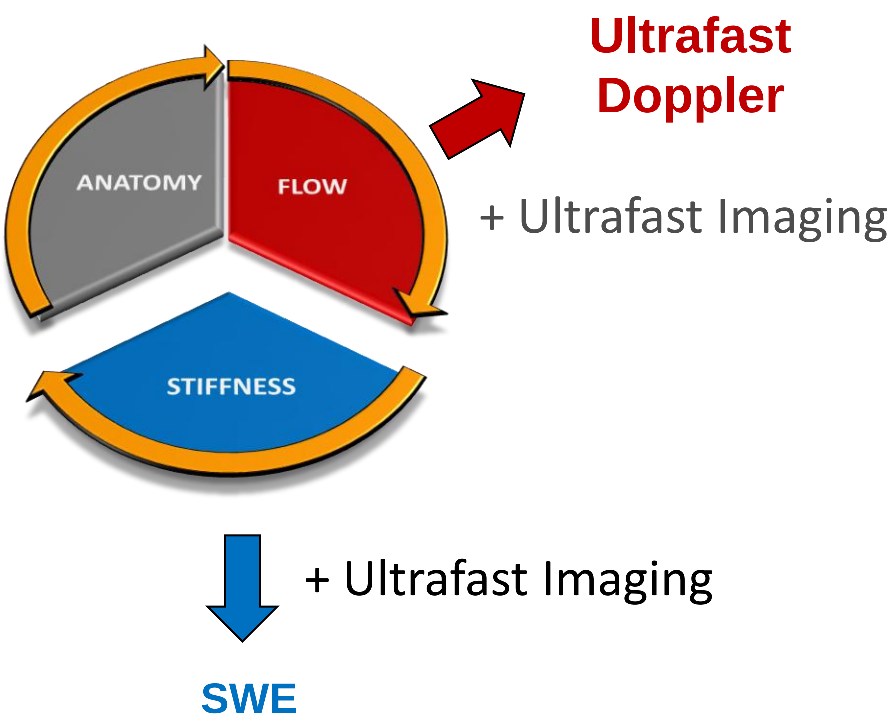
- SWE completes the information circle of ultrasound devices




| | | | | |
|---|---|---|---|---|
| ✓ | **B-mode** | **→** | **ANATOMY** | **(1970s – 1980s)** |
| ✓ | **Doppler** | **→** | **FLOW** | **(1980s – 1990s)** |
| ✓ | **Elastography** | **→** | **STIFFNESS** | **(2000s – 2010s)** |

- SWE has key advantages compared to other elastography techniques
  - Automated stress generation
  - Quantitative imaging (2D/3D)
  - Real time

# Can we reinvent conventional ultrasound modes with an Ultrafast imaging system ?

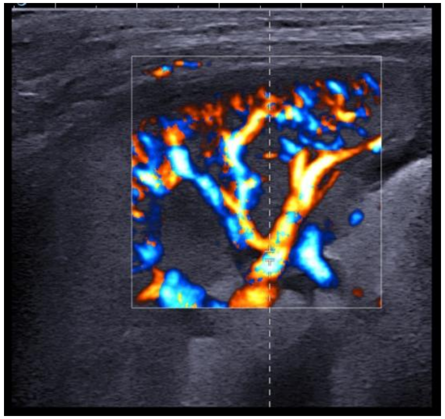



Bercoff, J.; Montaldo, G.; Loupas, T.; Savery, D.; Meziere, F.; Fink, M. & Tanter, M. (2011), 'Ultrafast Compound Doppler Imaging: Providing Full Blood Flow Characterization', *Ieee Trans. Ultr. Ferr. Frq. Ctrl,* 58(1)

# Doppler imaging today: two separate modes

## 1) Color Flow Imaging

- Real time imaging of flow
- Display the mean velocity per pixel in a color coded representation
- Used for detection of flow or localization of flow abnormalities



## 2) Spectral Doppler

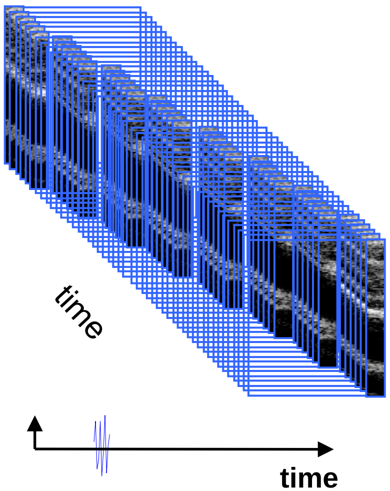
- Full quantification of flow velocity per Fourier analysis
- Available at on given location


**Imaging** **AND** **Quantification**

SuperSonic imagine
The Theragnostic Company™

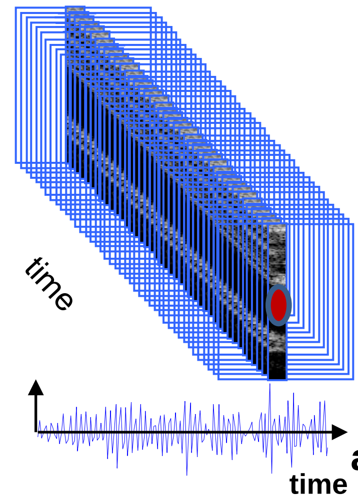
# Conventional vs Ultrafast Doppler sequences

- Conventional CFI



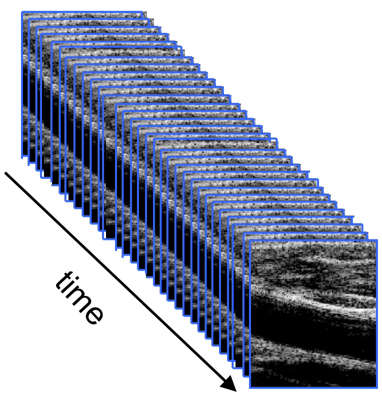

Only 10 points per pixel
Mean Velocity estimation

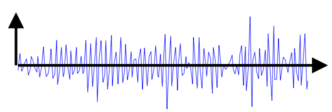
- Conventional PW




50- 150 points per pixel
**at a given sample volume**

- Ultrafast Doppler



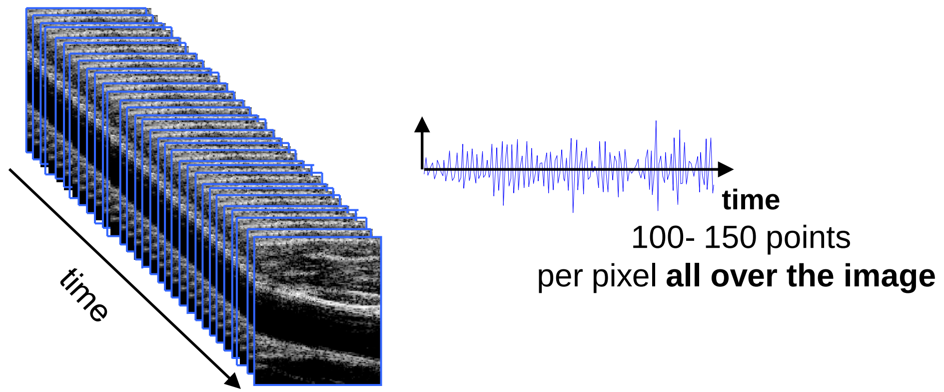



50- 150 points
per pixel **all over the image**

**Ultrafast allow gathering of complete Doppler information for all pixels**

# Leveraging Ultrafast Doppler Data

- Ultrafast Doppler




1) Increase color flow imaging performances

   + Sensitivity: improve slow flow detection

   + Frame rate: finer flow dynamics analysis

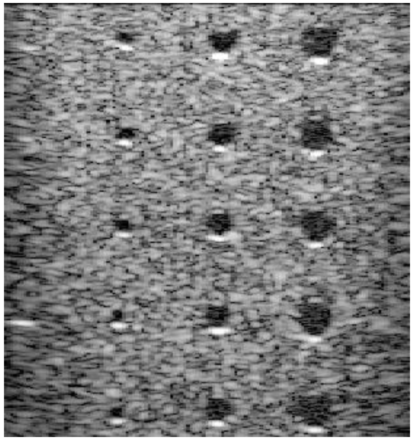
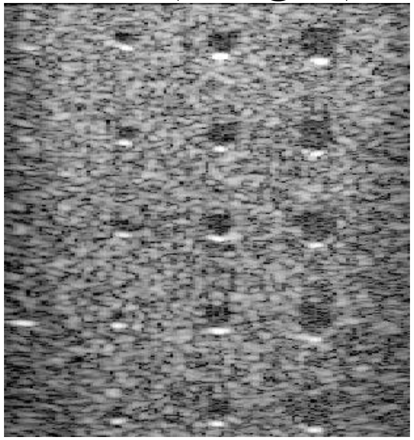
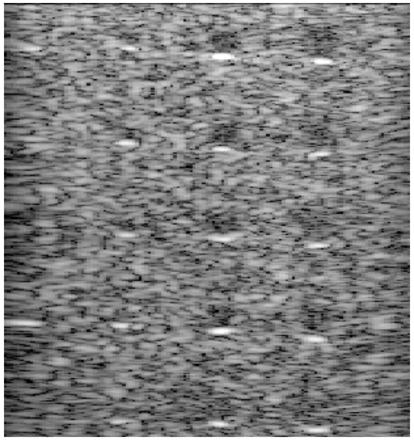
   + Consistency: All pixels shown are synchroneous.

2) Quantification => PW (spectral analysis) everywhere

**Bercoff, J.; Montaldo, G.; Loupas, T.; Savery, D.; Meziere, F.; Fink, M. & Tanter, M. (2011), 'Ultrafast Compound Doppler Imaging: Providing Full Blood Flow Characterization',** ***Ieee Trans. Ultr. Ferr. Frq. Ctrl,*** **58(1)**

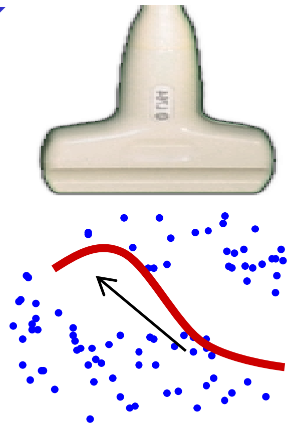
# A Trade-off between Speed and Sensitivity

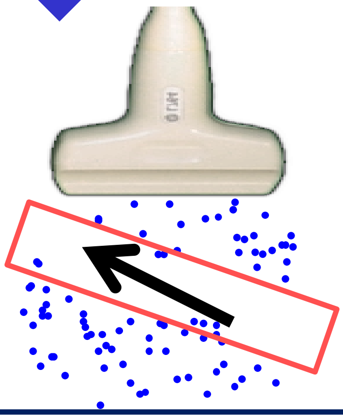
**FASTER** →

| 1kHz (17 angles) | 3 kHz (5 angles) | 18 kHz (1 angle) |
|---|---|---|
|  |  |  |

**Application 2:**
**Small vessels**

**Slow flow ~mm/s**
**SENSITIVITY**





**Application 1:**
**Carotid Artery**

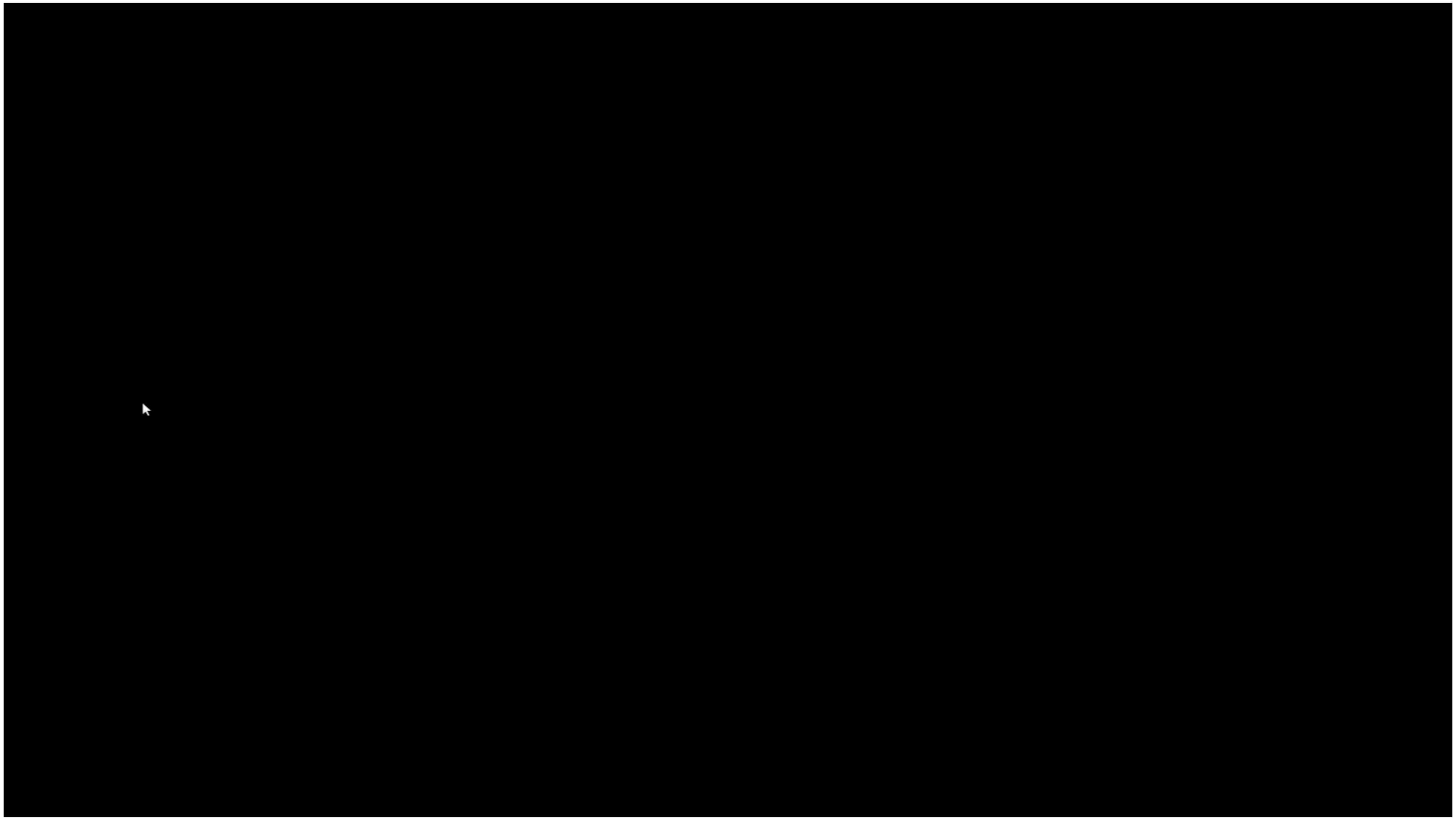
**Rapid flow >10cm/s**
**ULTRAFAST**

# Ultrafast Doppler mode presentation
## Workflow

Standard CFI (live) → UltraFast™ Doppler Acquisition → Prospective cineloop: 2-4 seconds of Doppler data → Flow analysis and Quantification

**Bercoff, J.; Montaldo, G.; Loupas, T.; Savery, D.; Meziere, F.; Fink, M. & Tanter, M. (2011), 'Ultrafast Compound Doppler Imaging: Providing Full Blood Flow Characterization',** ***Ieee Trans. Ultr. Ferr. Frq. Ctrl,*** **58(1)**

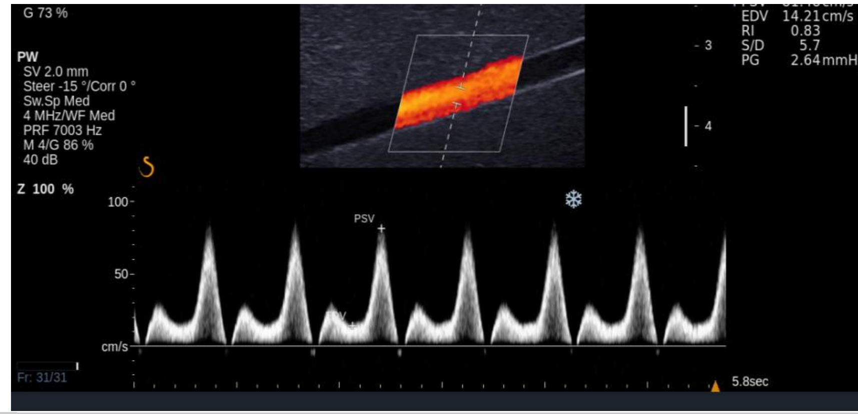
# Ultrafast Doppler: Full Retrospective analysis

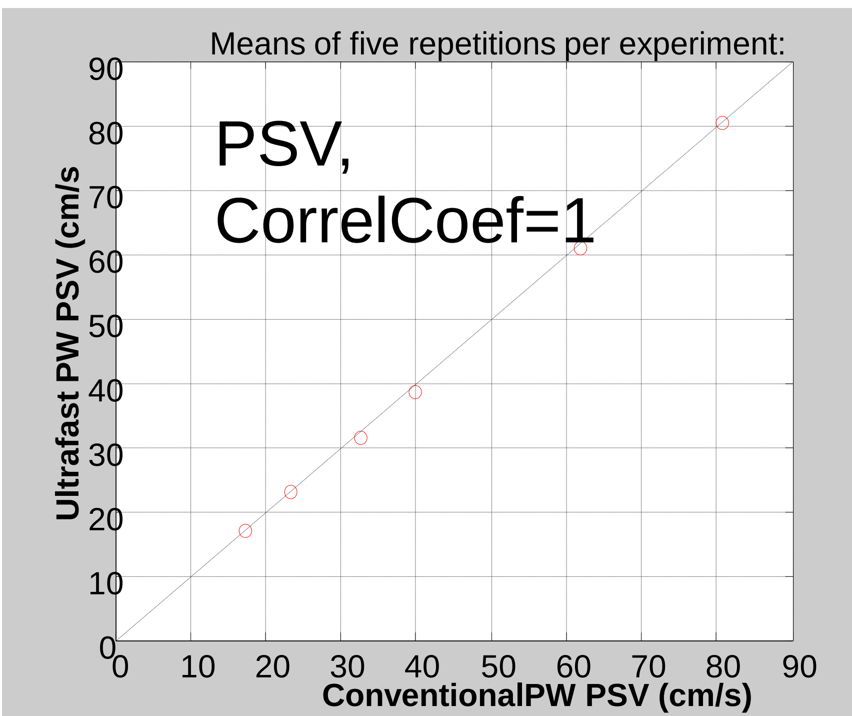


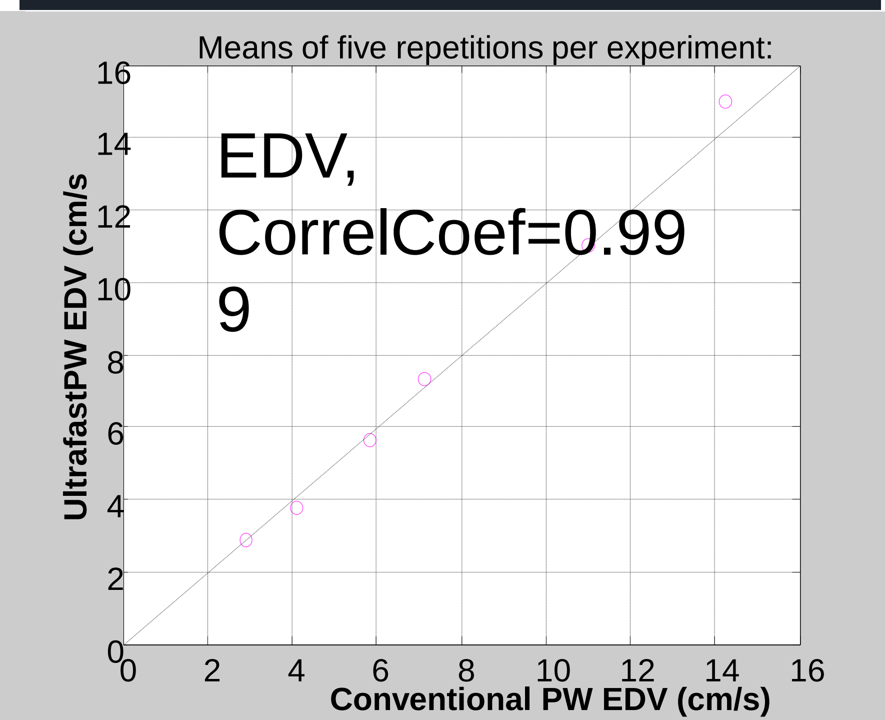
Bercoff, J.; Montaldo, G.; Loupas, T.; Savery, D.; Meziere, F.; Fink, M. & Tanter, M. (2011),
'Ultrafast Compound Doppler Imaging: Providing Full Blood Flow Characterization', *Ieee Trans. Ultr. Ferr. Frq. Ctrl,* 58(1)

# Ultrafast Doppler: Quantitative Validation

- Ultrafast PW vs Conventional PW



# Example

All images are courtesy of J.P. Henry

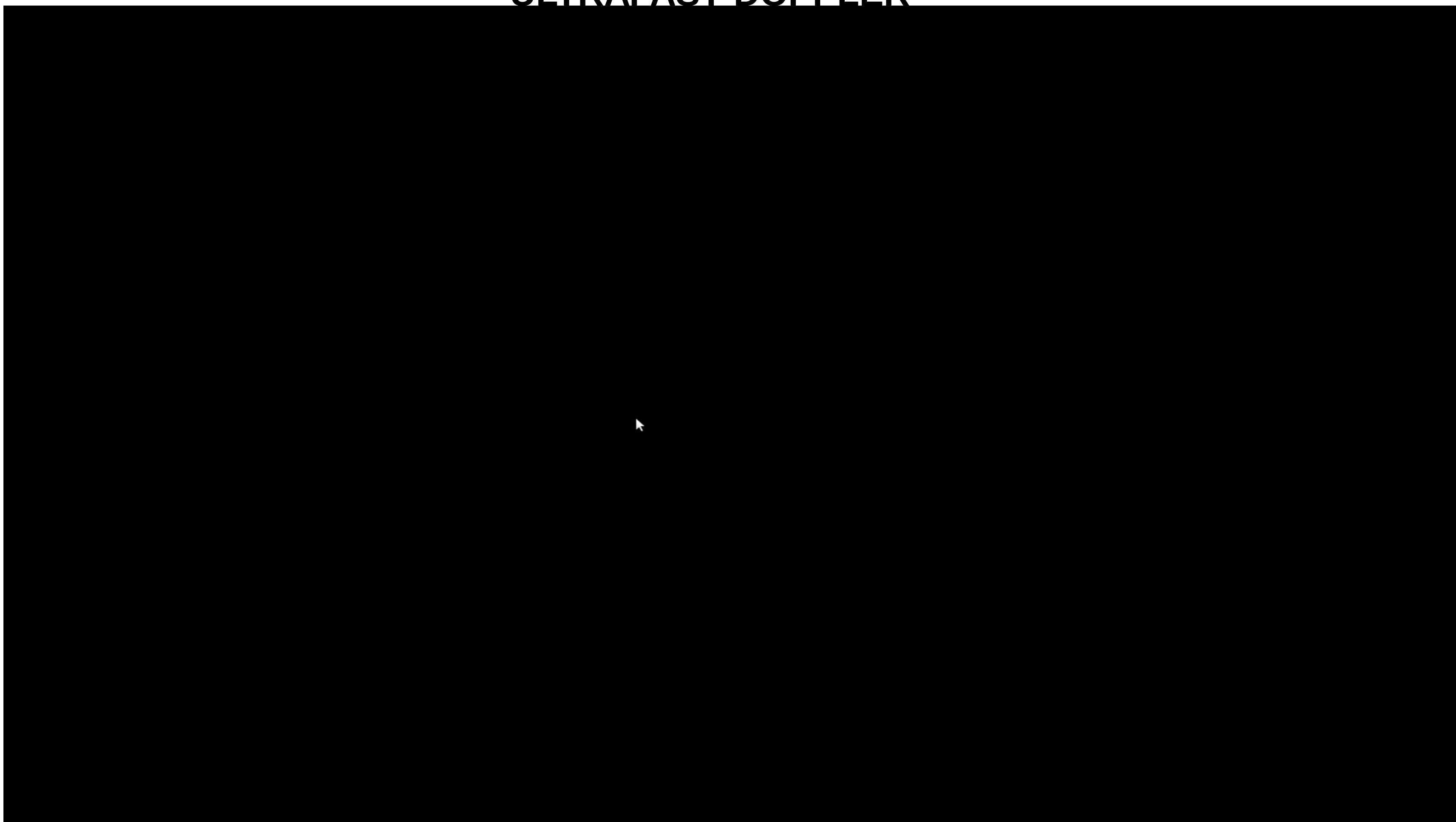
# Improving visualisation of hemodynamics

**STANDARD CFI**

**Bercoff, J.; Montaldo, G.; Loupas, T.; Savery, D.; Meziere, F.; Fink, M. & Tanter, M. (2011), 'Ultrafast Compound Doppler Imaging: Providing Full Blood Flow Characterization',** ***Ieee Trans. Ultr. Ferr. Frq. Ctrl,*** **58(1)**

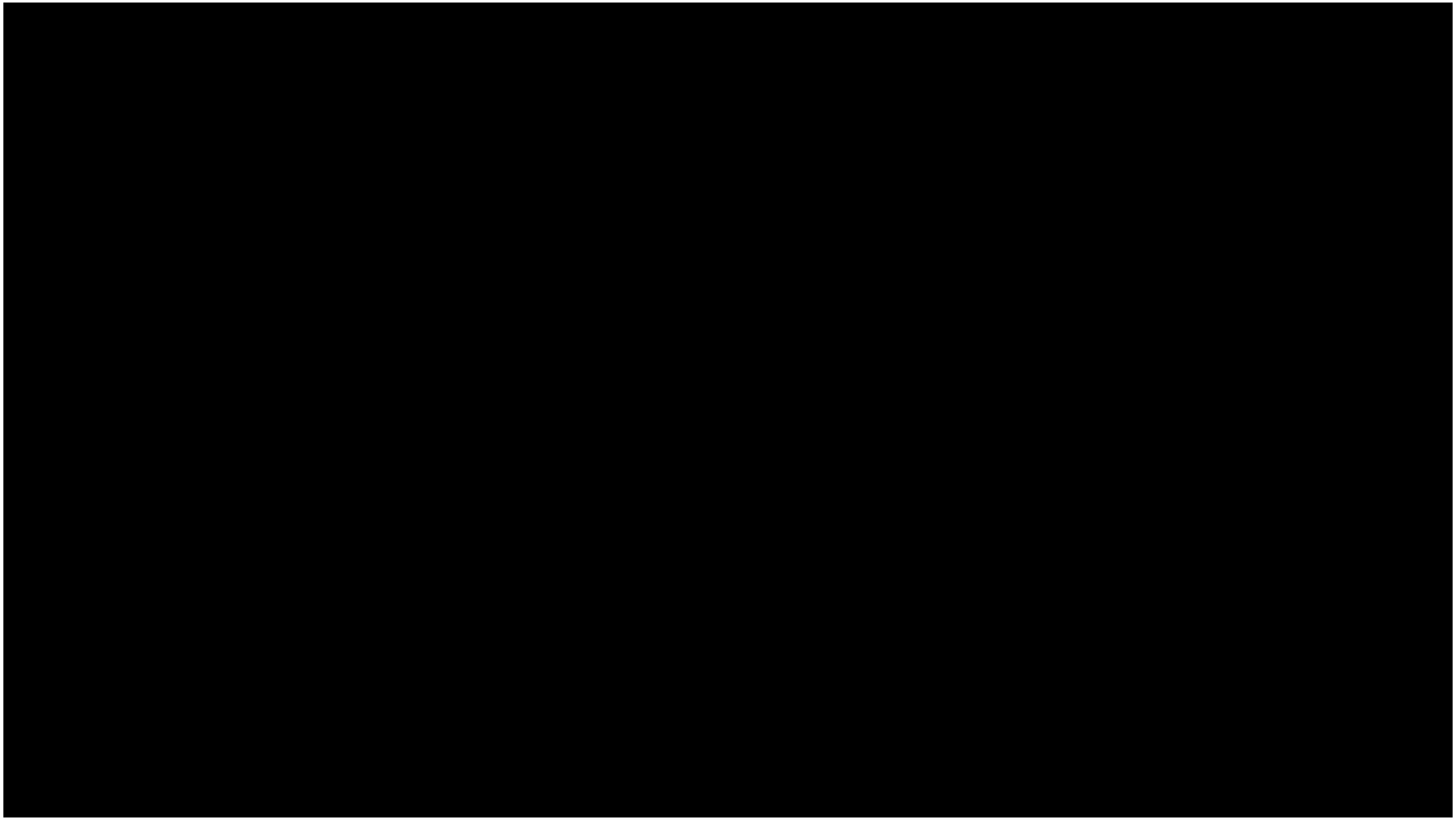
# Improving visualisation of hemodynamics

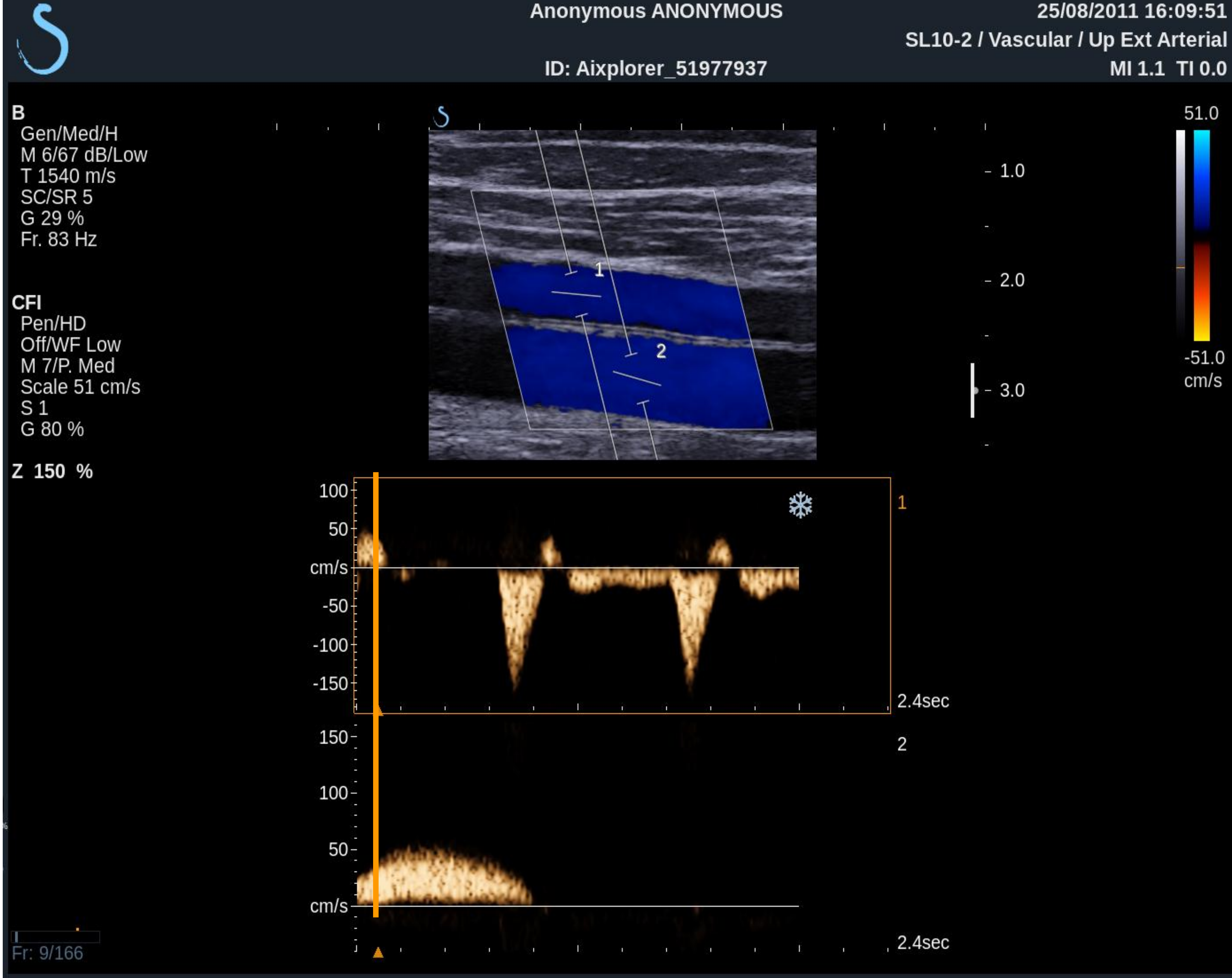
**ULTRAFAST DOPPLER**

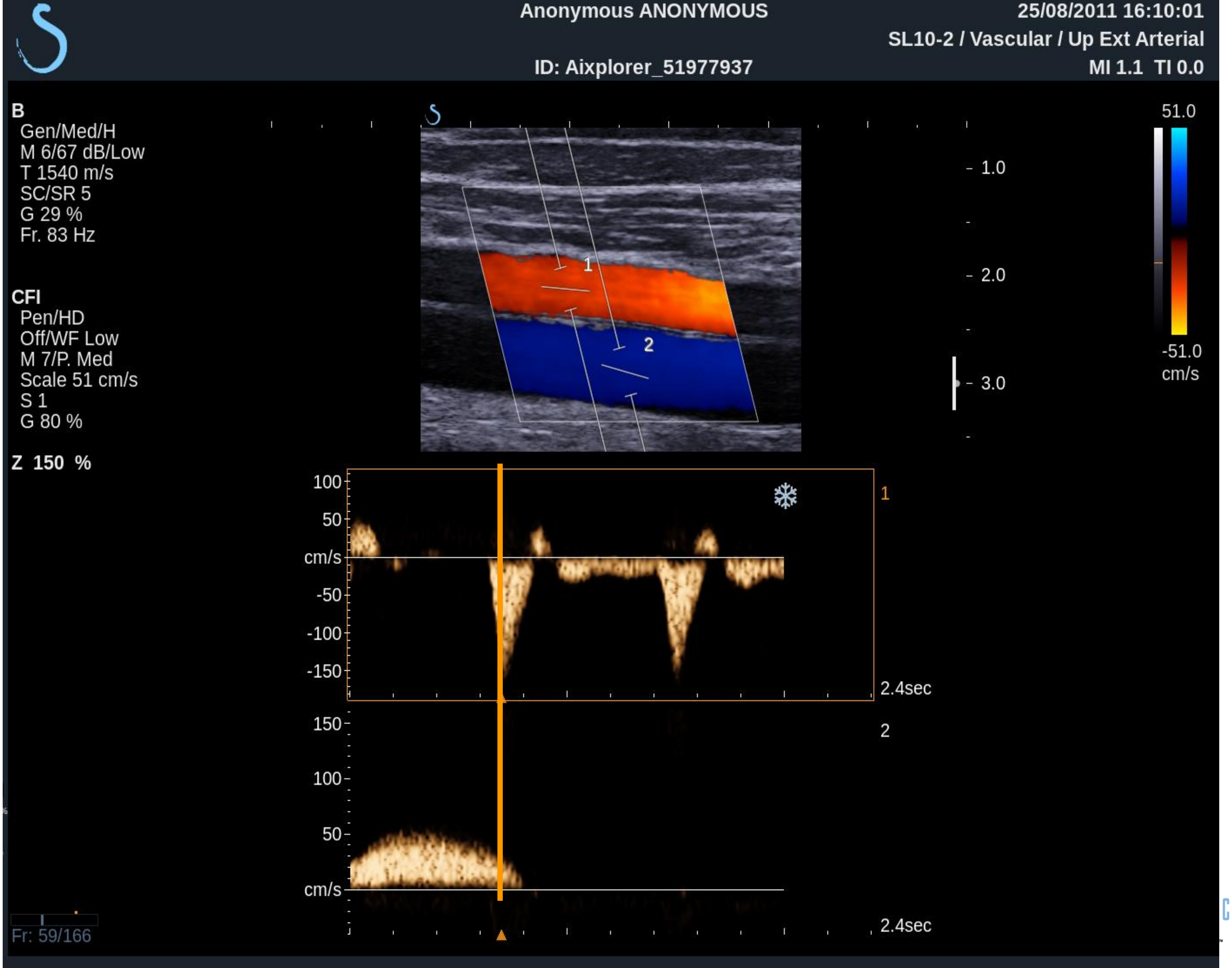


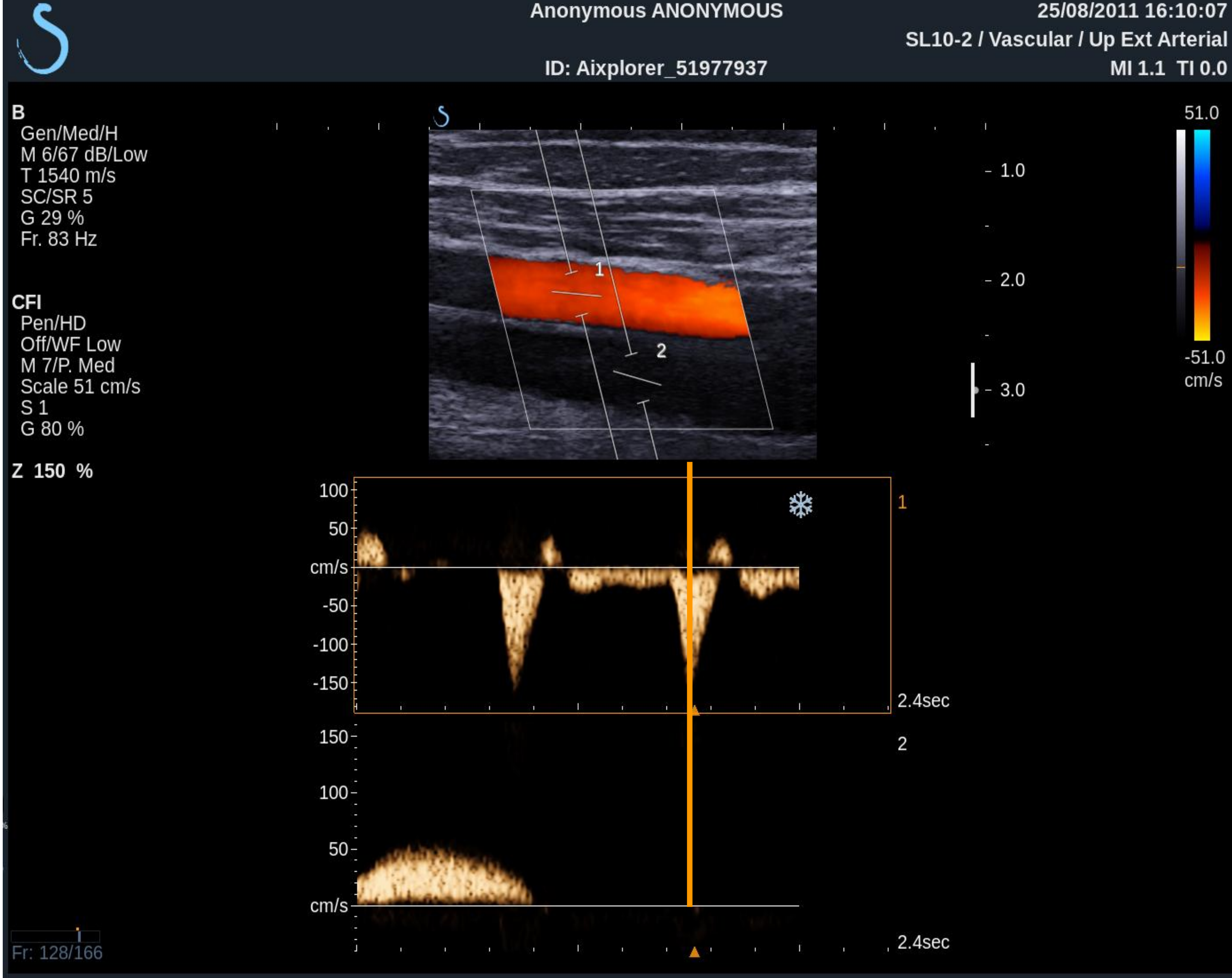
**Bercoff, J.; Montaldo, G.; Loupas, T.; Savery, D.; Meziere, F.; Fink, M. & Tanter, M. (2011), 'Ultrafast Compound Doppler Imaging: Providing Full Blood Flow Characterization', *Ieee Trans. Ultr. Ferr. Frq. Ctrl,* 58(1)**

# Full flow Characterization




Anonymous ANONYMOUS
ID: Aixplorer_51977937
25/08/2011 16:09:51
SL10-2 / Vascular / Up Ext Arterial
MI 1.1 TI 0.0
B
Gen/Med/H
M 6/67 dB/Low
T 1540 m/s
SC/SR 5
G 29 %
Fr. 83 Hz
CFI
Pen/HD
Off/WF Low
M 7/P. Med
Scale 51 cm/s
S 1
G 80 %
Z 150 %
Fr: 9/166
51.0
-51.0
cm/s
1.0
2.0
3.0
1
2
100
50
cm/s
-50
-100
-150
2.4sec
1
150
100
50
cm/s
2.4sec
2


Anonymous ANONYMOUS
ID: Aixplorer_51977937
25/08/2011 16:10:01
SL10-2 / Vascular / Up Ext Arterial
MI 1.1 TI 0.0
B
Gen/Med/H
M 6/67 dB/Low
T 1540 m/s
SC/SR 5
G 29 %
Fr. 83 Hz
CFI
Pen/HD
Off/WF Low
M 7/P. Med
Scale 51 cm/s
S 1
G 80 %
Z 150 %
1.0
2.0
3.0
51.0
-51.0
cm/s
1
2
100
50
cm/s
-50
-100
-150
2.4sec
150
100
50
cm/s
2.4sec
Fr: 59/166


Anonymous ANONYMOUS
ID: Aixplorer_51977937
25/08/2011 16:10:07
SL10-2 / Vascular / Up Ext Arterial
MI 1.1 TI 0.0
B
Gen/Med/H
M 6/67 dB/Low
T 1540 m/s
SC/SR 5
G 29 %
Fr. 83 Hz
CFI
Pen/HD
Off/WF Low
M 7/P. Med
Scale 51 cm/s
S 1
G 80 %
Z 150 %
51.0
-51.0
cm/s
1.0
2.0
3.0
1
2
100
50
cm/s
-50
-100
-150
2.4sec
150
100
50
cm/s
2.4sec
Fr: 128/166

# Ultrafast Vector Doppler Imaging

*Courtesy of Jørgen Arendt Jensen*

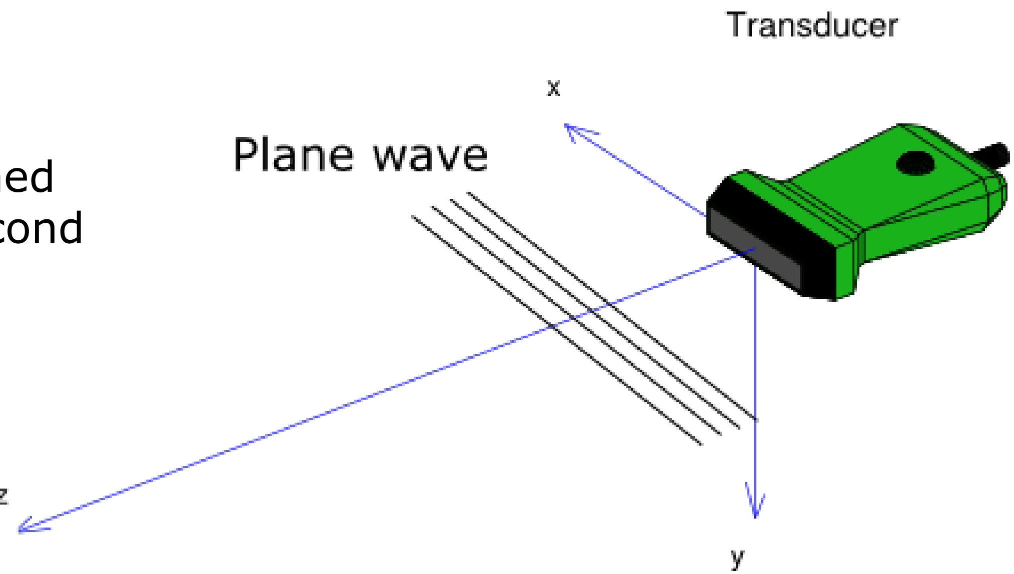
**Center for Fast Ultrasound Imaging**
**Department of Electrical Engineering**
**Technical University of Denmark**

# Fast plane wave imaging

- Single plane wave emitted
- Full image reconstructed from single emission
- Very fast imaging can be attained with thousand of image per second

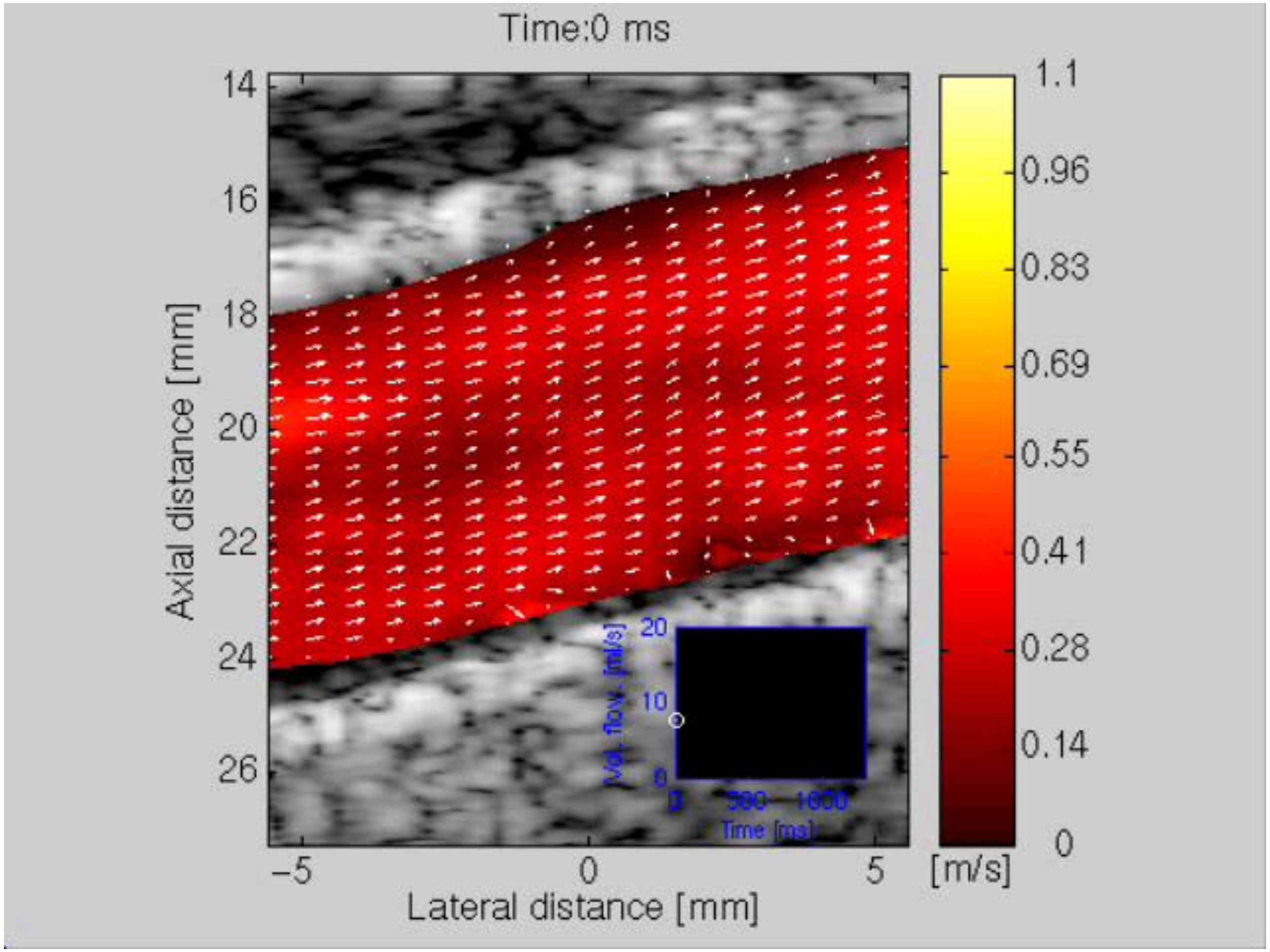
- Flow imaging with excellent temporal resolution
- Vector flow imaging possible

- Implemented on the RASMUS experimental scanner
- Frame rate of more than 100 Hz

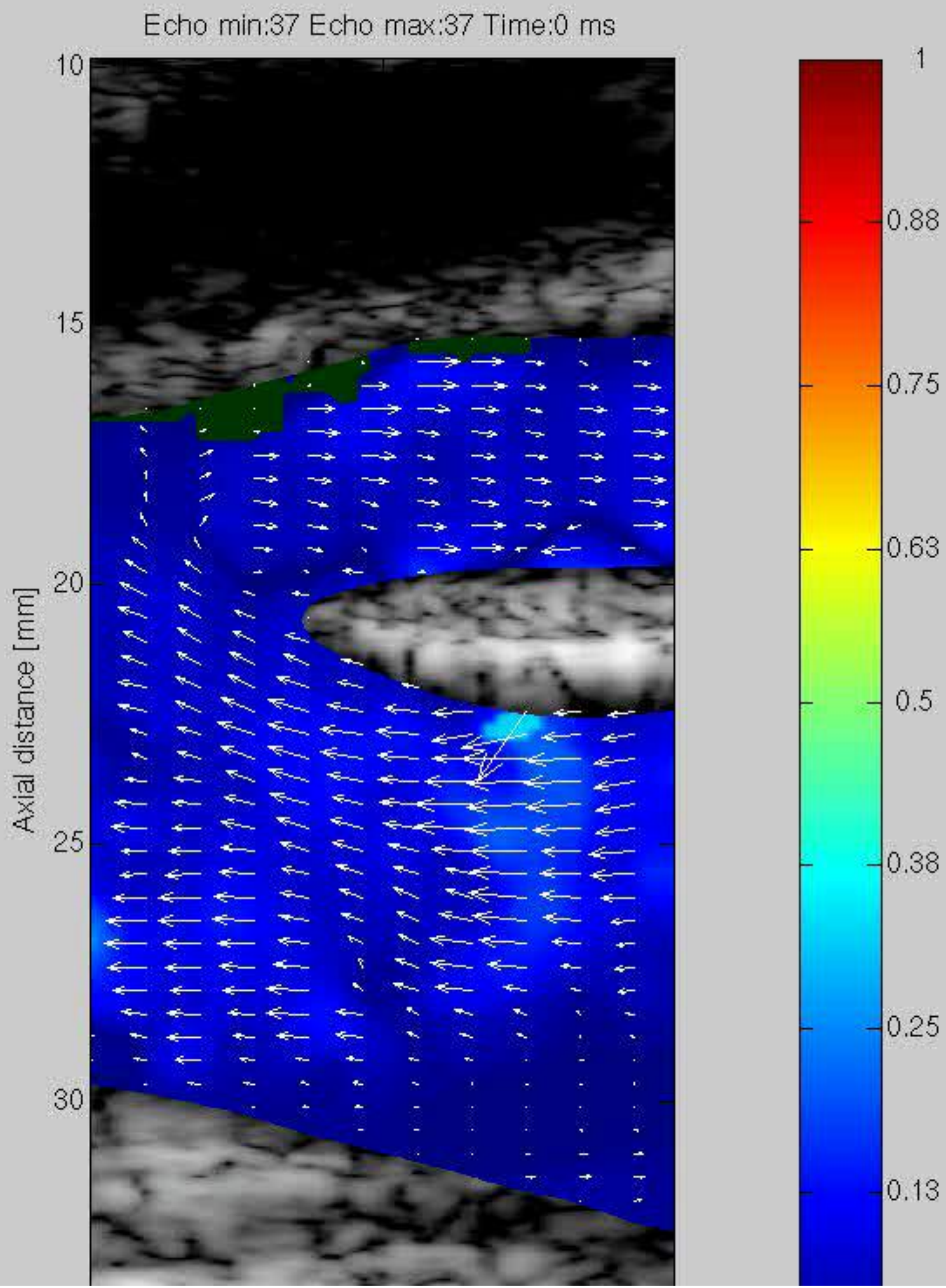



Udesen et al: *'High Frame-Rate Blood Vector Velocity Imaging Using Plane Waves: Simulations and Preliminary Experiments*', IEEE UFFC, vol 55, no. 8, pp. 1729-1743, 2008.

# Frame rate : 100 Hz, Common carotid artery

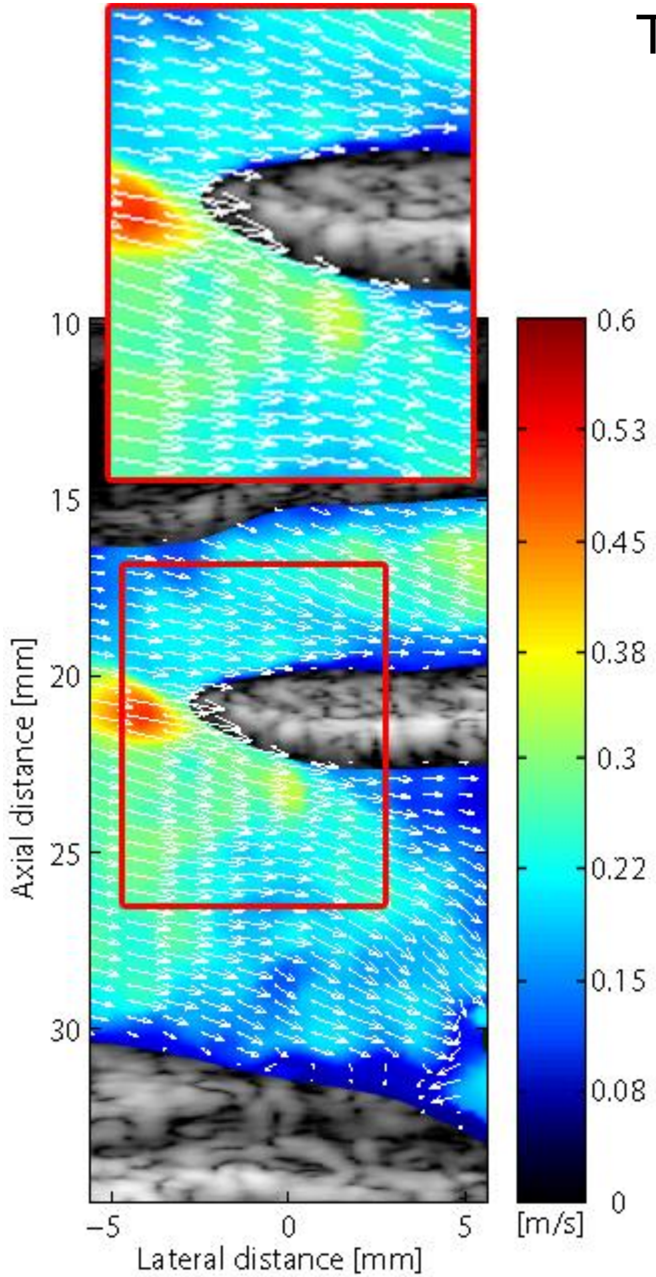



From Hansen et al: *In-vivo Examples of Flow Patterns With The Fast Vector Velocity Ultrasound Method*' Ultraschall in der Medizin, vol 30, no. 5, pp. 471-477, 2009

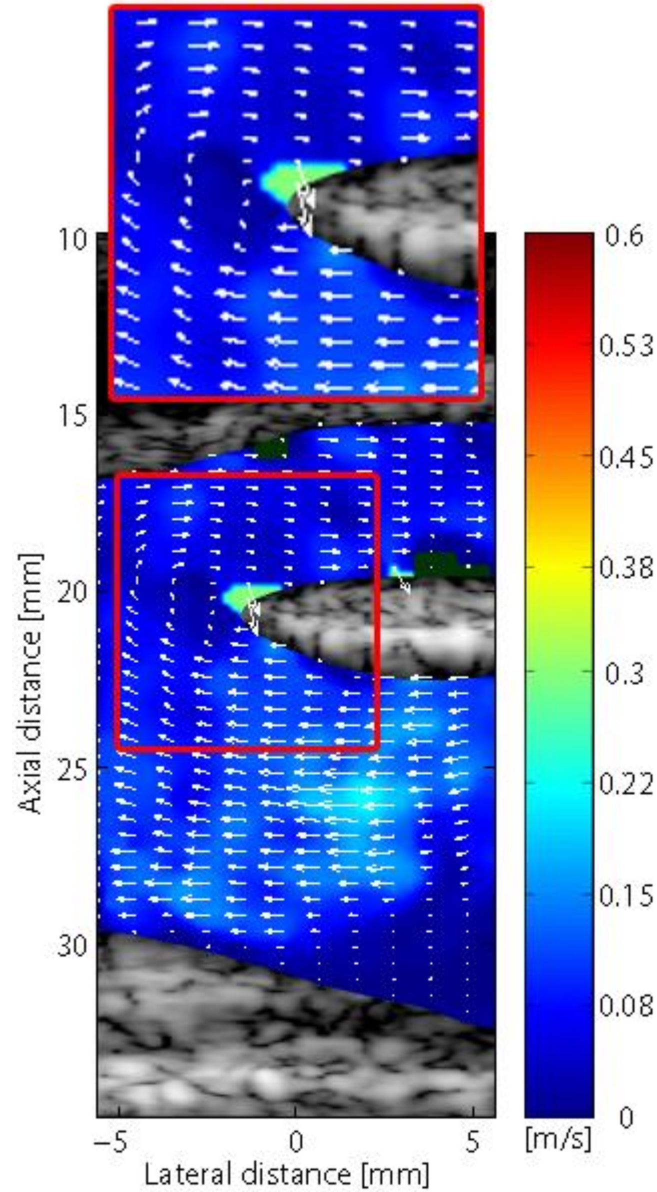



Truncus brachiocephalica, a. subclavia and
a. carotis com.

# Truncus brachiocephalica

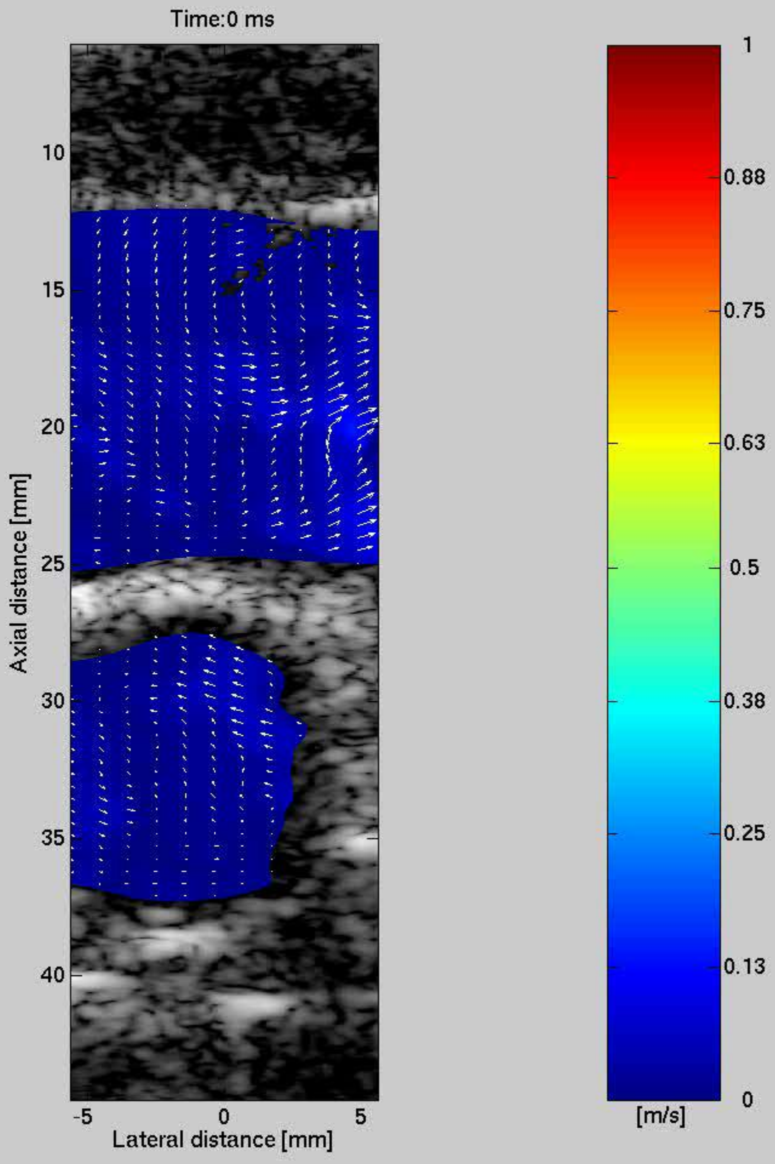



Center for Fast Ultrasound Imaging
Technical University of Denmark




Carnegie Mellon University
Next Generation Medical Imaging

From Hansen et al: *In-vivo Examples of Flow Patterns With The Fast Vector Velocity Ultrasound Method'* Ultraschall in der Medizin, vol 30, no. 5, pp. 471-477, 2009

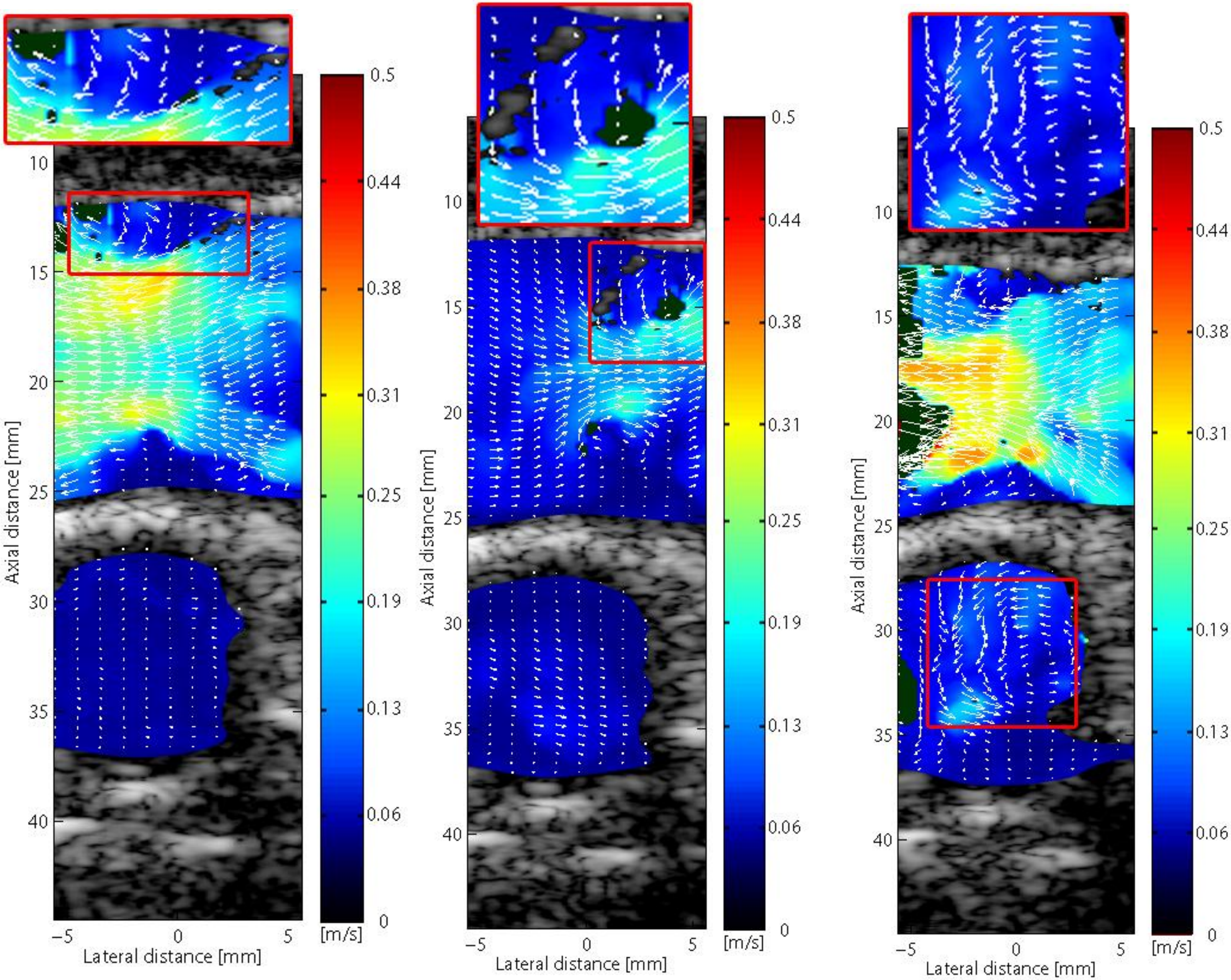



The jugular vein and carotid artery

Center for Fast Ultrasound Imaging
Technical University of Denmark

Carnegie Mellon University
Next Generation Medical Imaging

From Hansen et al: *In-vivo Examples of Flow Patterns With The Fast Vector Velocity Ultrasound Method'* Ultraschall in der Medizin, vol 30, no. 5, pp. 471-477, 2009



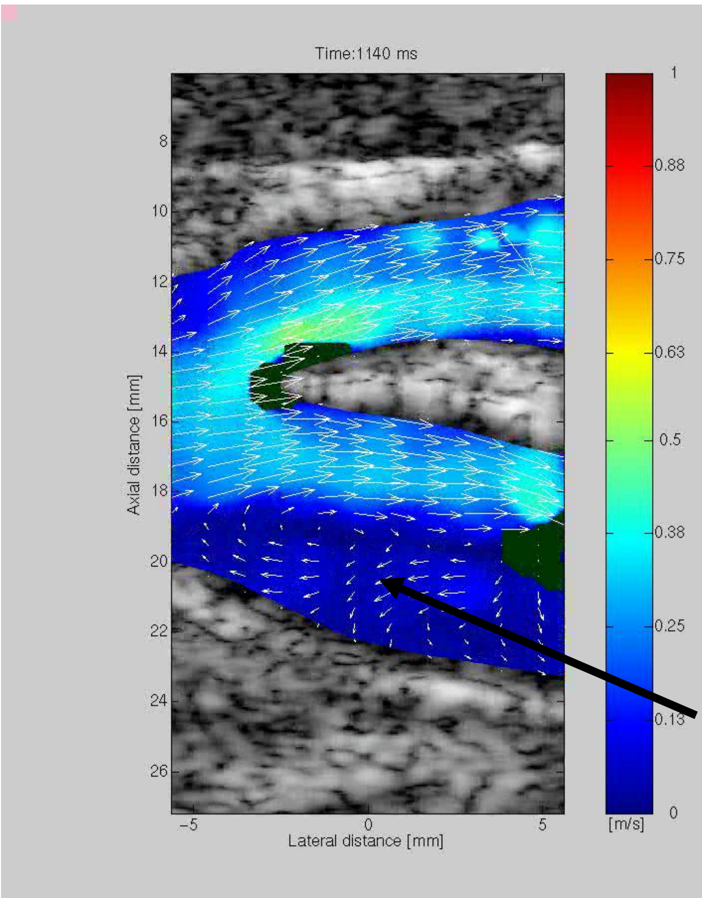

The jugular vein and carotid artery

Center for Fast Ultrasound Imaging
Technical University of Denmark

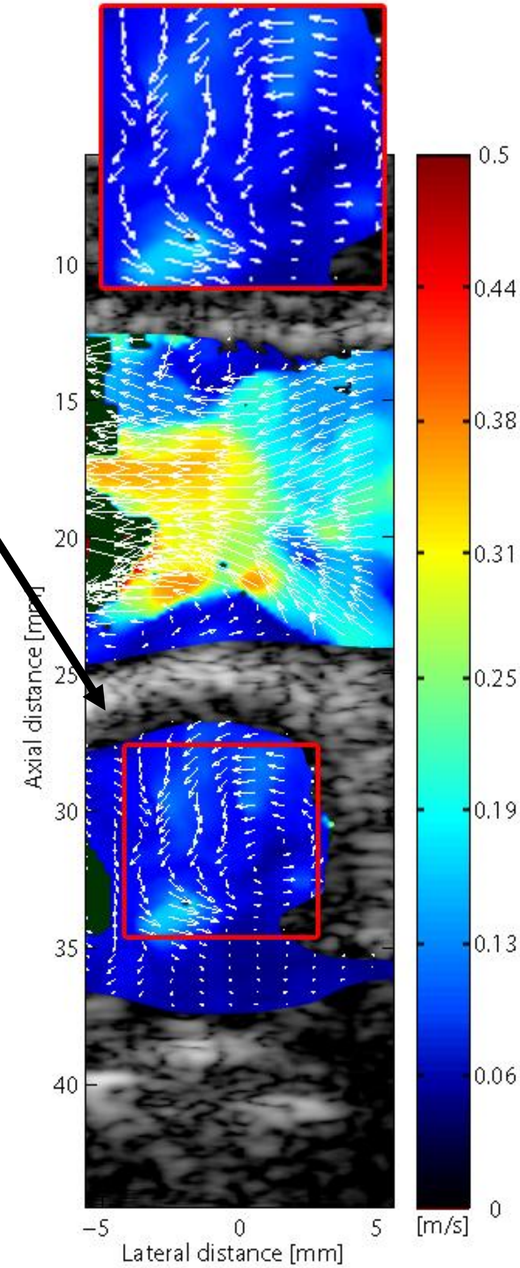
Carnegie Mellon University
Next Generation Medical Imaging

# 3D flow

Rotational flow
in the carotid artery




Vortices after
peak systole
in carotid
bifurcation




Center for Fast Ultrasound Imaging
Technical University of Denmark

Carnegie Mellon University
Next Generation Medical Imaging

# A more complex case : the Myocardium

# Ultrafast Doppler Imaging
# of small flows
# in a fast moving organ ?

Ultrafast Doppler imaging of blood flow dynamics in the myocardium.
Osmanski BF, Pernot M, Montaldo G, Bel A, Messas E, Tanter M, IEEE Trans Med Imaging. 2012

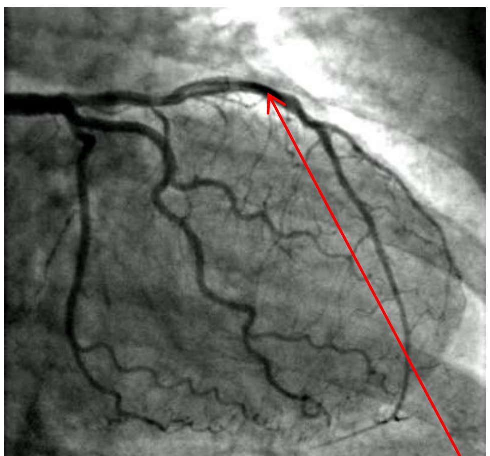
# Myocardial Blood Flow Dynamics

Intramyocardial Blood Flow Dynamics

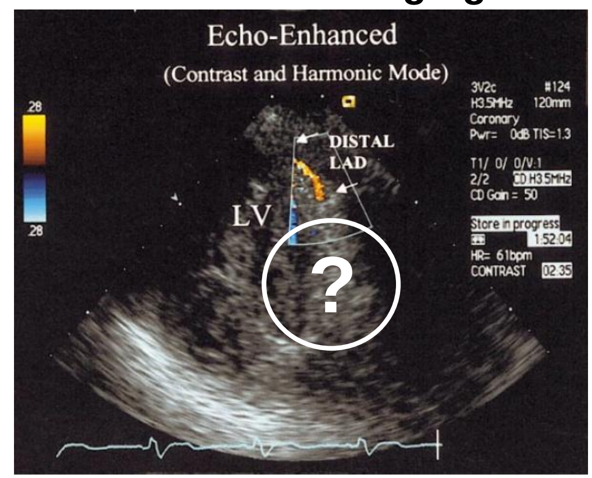
-> Early diagnosis of cardio-vascular diseases

## State of the Art

**X ray coronarography**



**Ultrasound imaging**

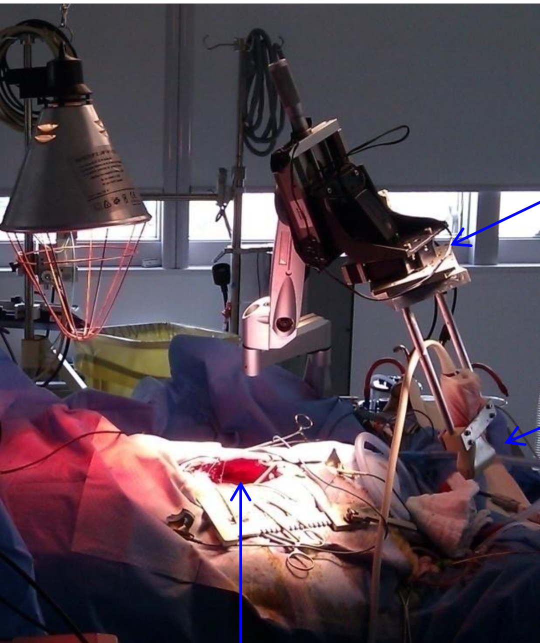



**Left Anterior Descending Coronary Artery (LAD)**

**C. Caiati, Circulation (1999)**

# Ultrafast Imaging of the myocardium : Experimental Set-Up

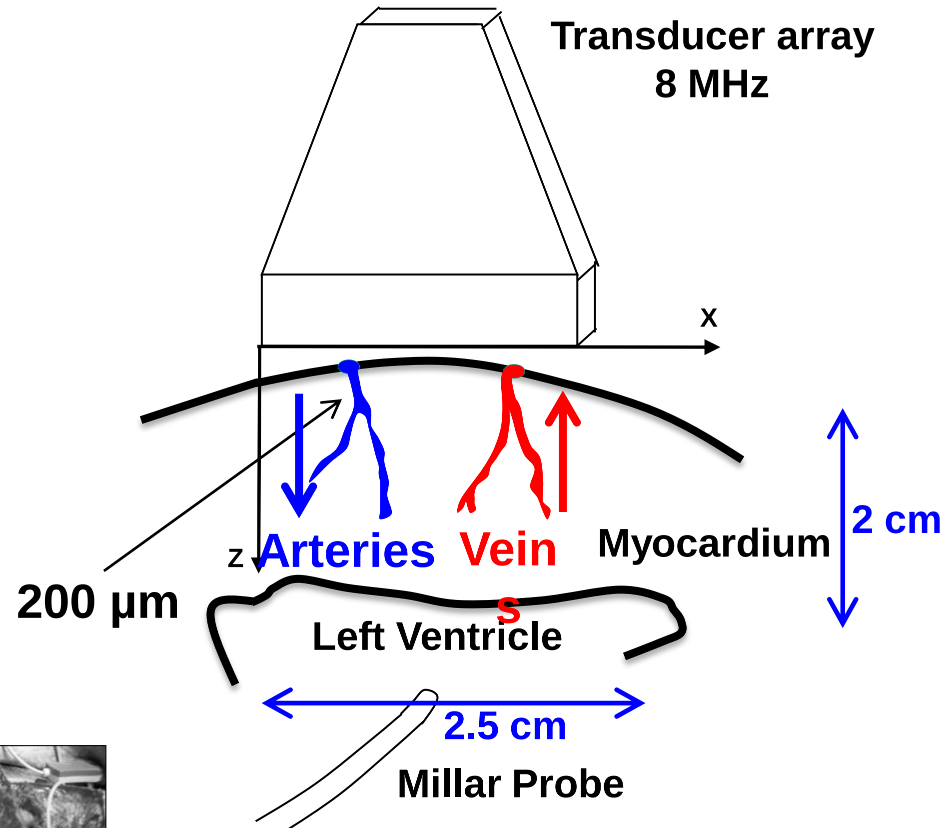
**Results obtained on 5 sheeps**



**Metallic Arm**

**Acoustic probe**

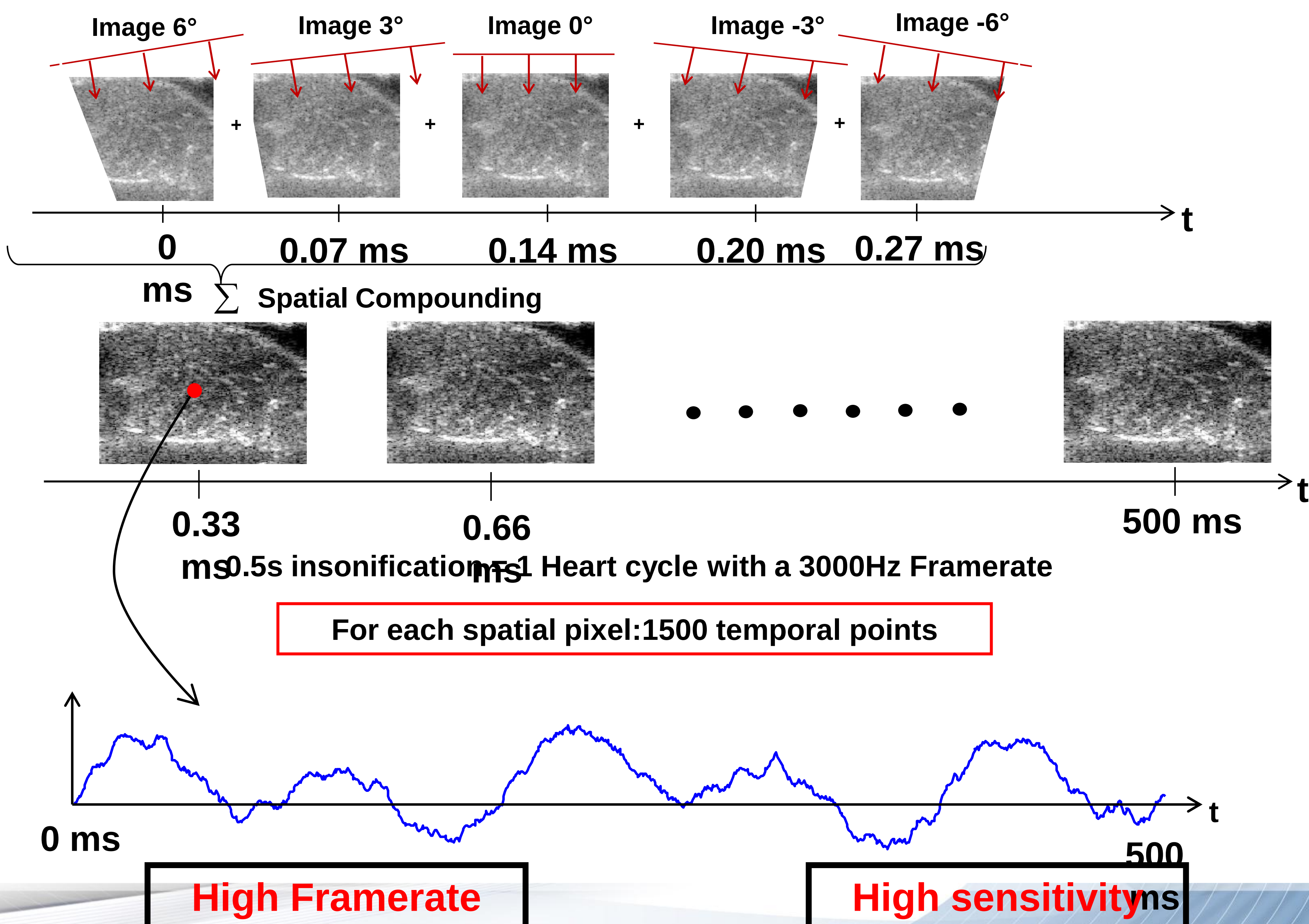
**Chest Cavity**



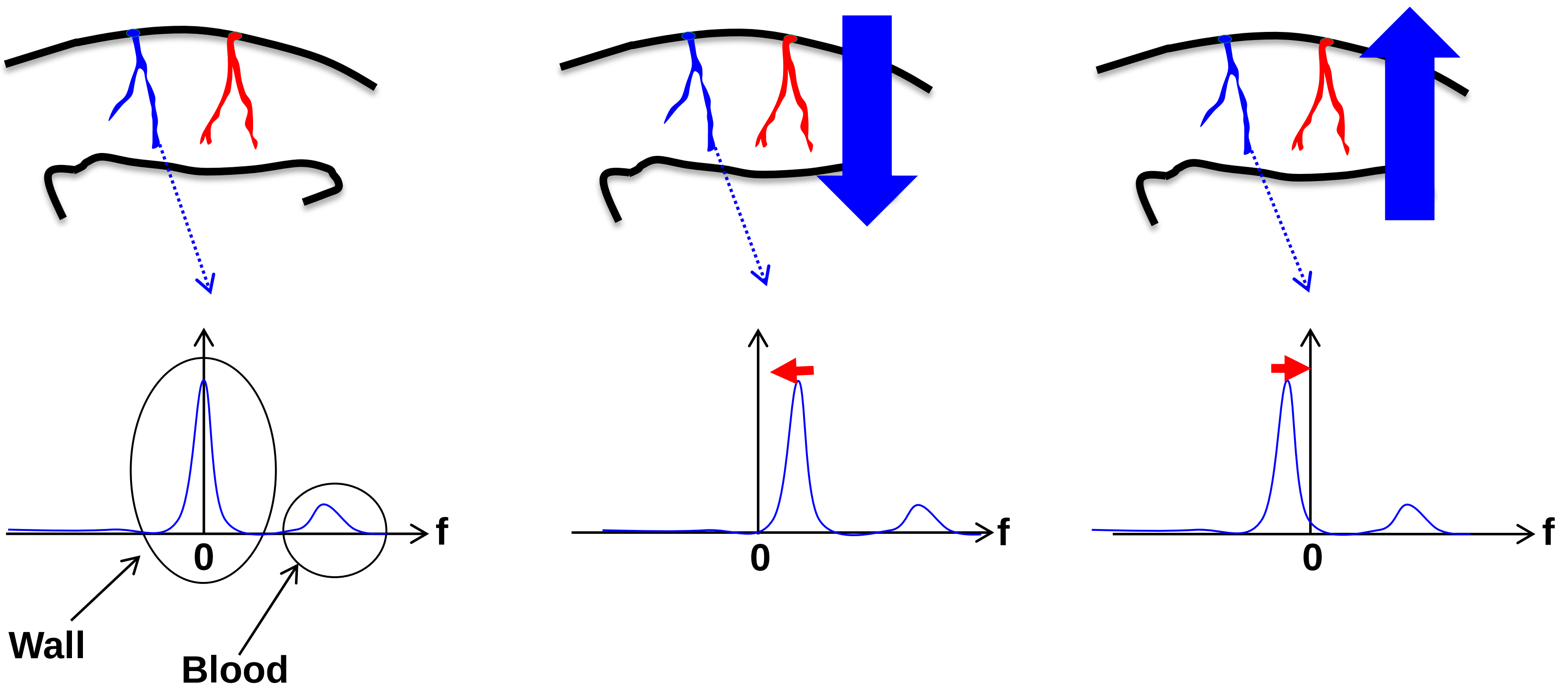

$V_{Tissue}$ ~ cm/s

**Ultrafast Acquisition**

# Ultrafast Imaging of the myocardium : acquisition sequence



# Fast tissue Motion = additional Frequency Modulation




**Solution = Frequency Demodulation**

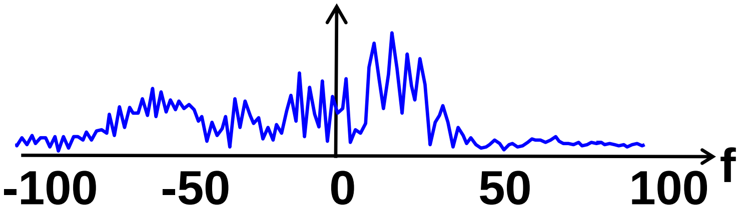
Ultrafast Doppler imaging of blood flow dynamics in the myocardium.
Osmanski BF, Pernot M, Montaldo G, Bel A, Messas E, Tanter M, IEEE Trans Med Imaging. 2012

# Ultrafast Imaging of the myocardium : demodulation process

**In-Phase Quadrature Data**
**Temporal signal of a spatial pixel**

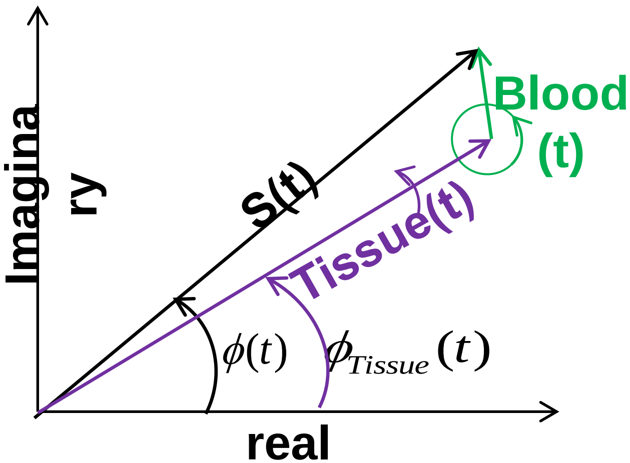
$$s(t) = A(t)e^{j\phi(t)}$$

$$FFT\{s(t)\} = FFT\{A(t)\} \otimes FFT\{e^{j\varphi(t)}\}$$




$$Arg\{s(t)\} = \phi(t) \longrightarrow s_{dem}(t) = s(t)e^{-j\phi(t)} = A(t)$$

$$s_{dem}(t) = s(t)e^{-j\phi_{Tissue}(t)}$$




$$\phi(t) = \phi_{Tissue}(t) + \phi_{HF}(t)$$

**Tissue and blood signal**

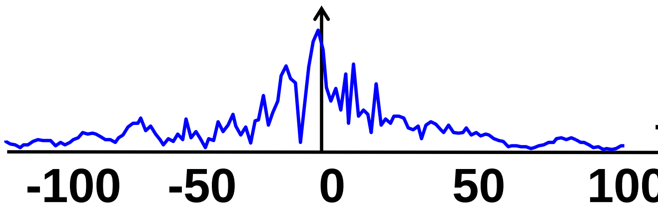
↓

$\phi(t)$

↓ **Low pass filter**

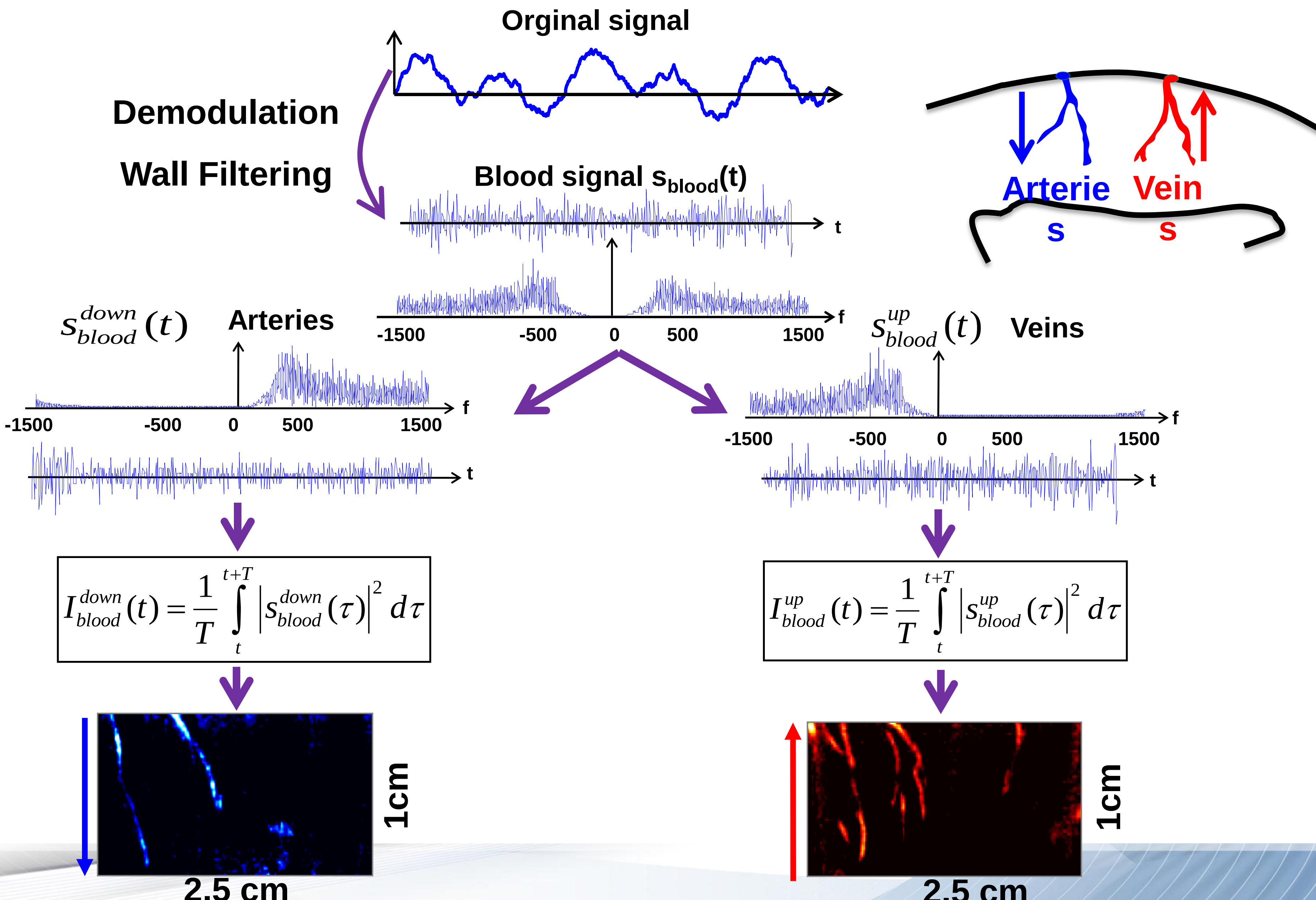
$\phi_{Tissue}(t)$

$$FFT\{s_{dem}(t)\}$$

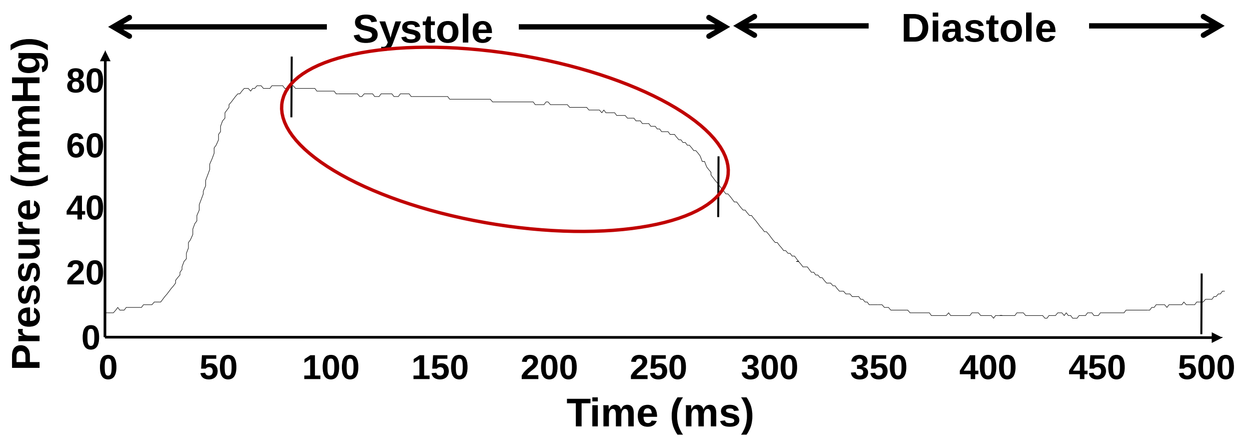



**Ultrafast Doppler imaging of blood flow dynamics in the myocardium.**
**Osmanski BF, Pernot M, Montaldo G, Bel A, Messas E, Tanter M, IEEE Trans Med Imaging. 2012**

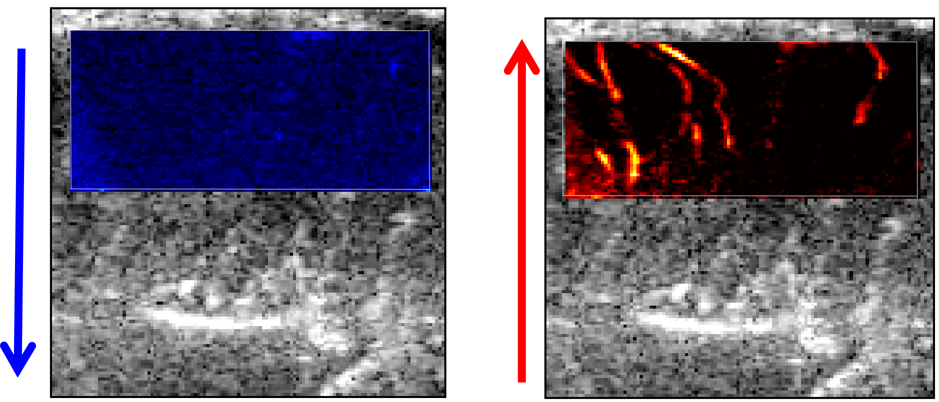
# Signed Power Doppler: discriminate arteries and Veins



# Ultrafast Imaging of the myocardium : systole ejection

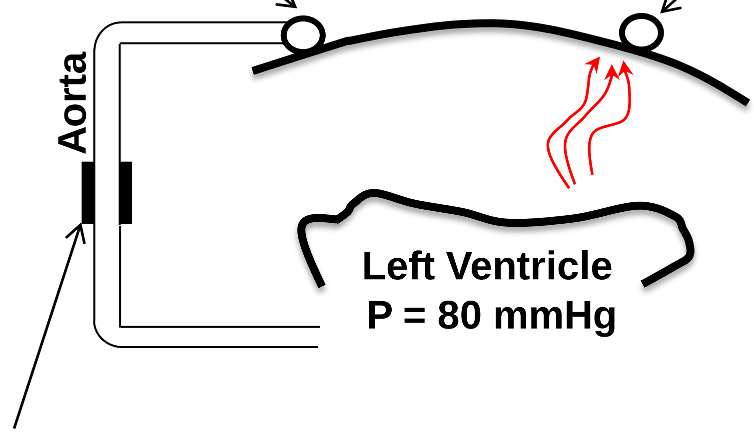



Signed Power Doppler



Arteries

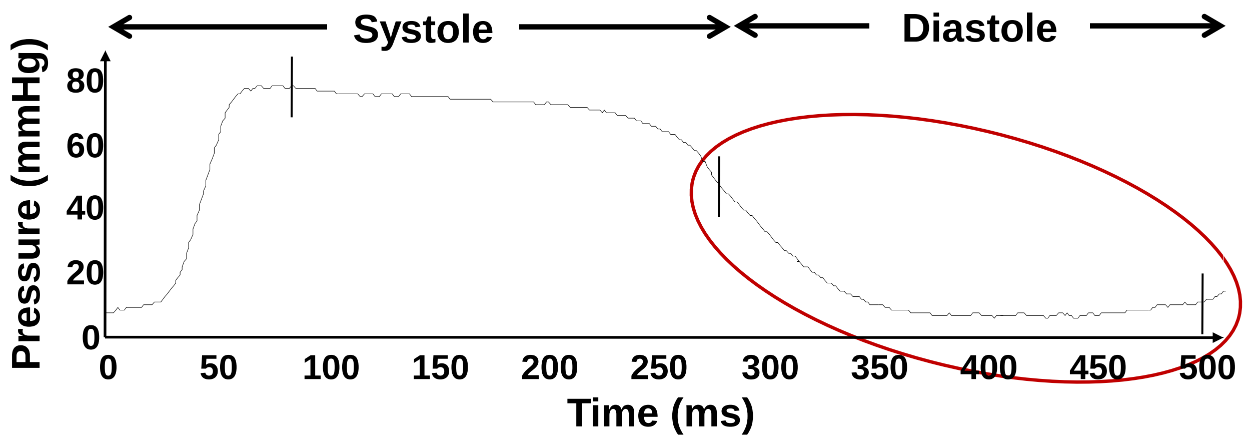
Veins



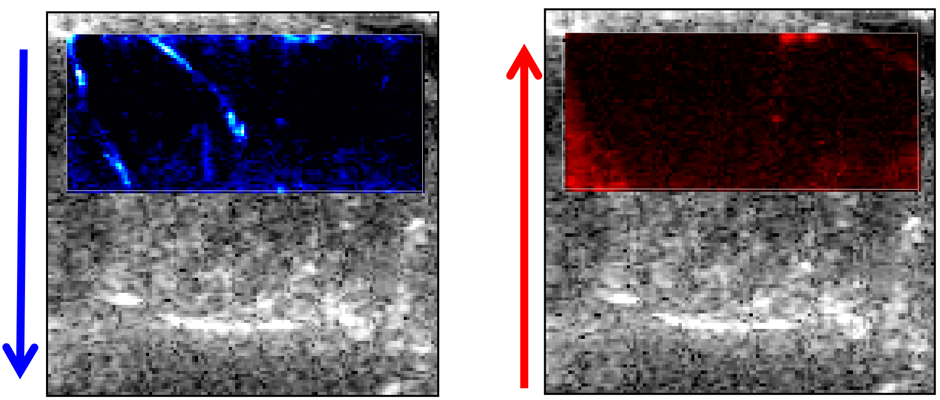

Aortic Valve opened

Ultrafast Doppler imaging of blood flow dynamics in the myocardium.
Osmanski BF, Pernot M, Montaldo G, Bel A, Messas E, Tanter M, IEEE Trans Med Imaging. 2012

# Ultrafast Imaging of the myocardium : Diastole

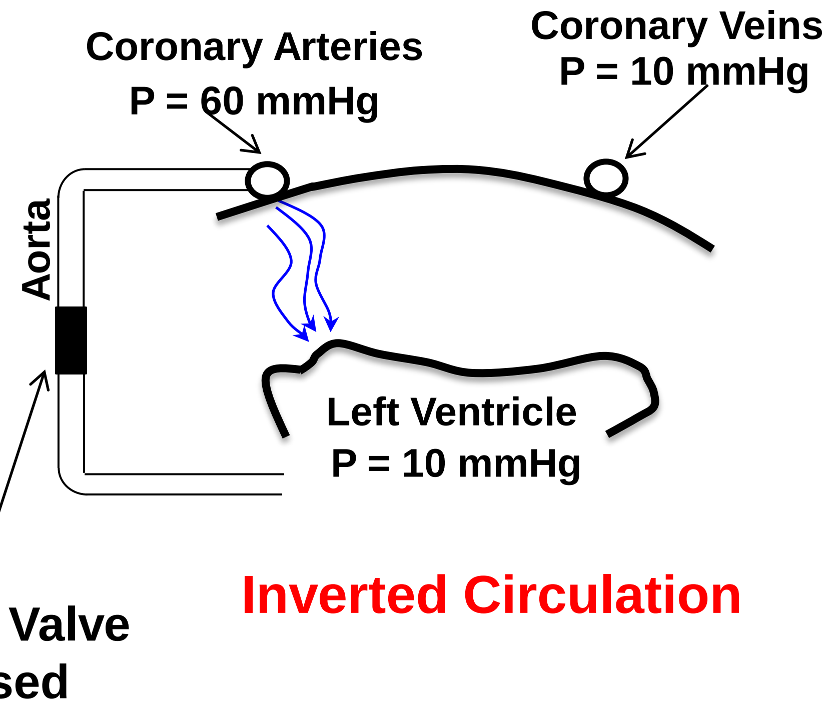



Signed Power Doppler



Arteries

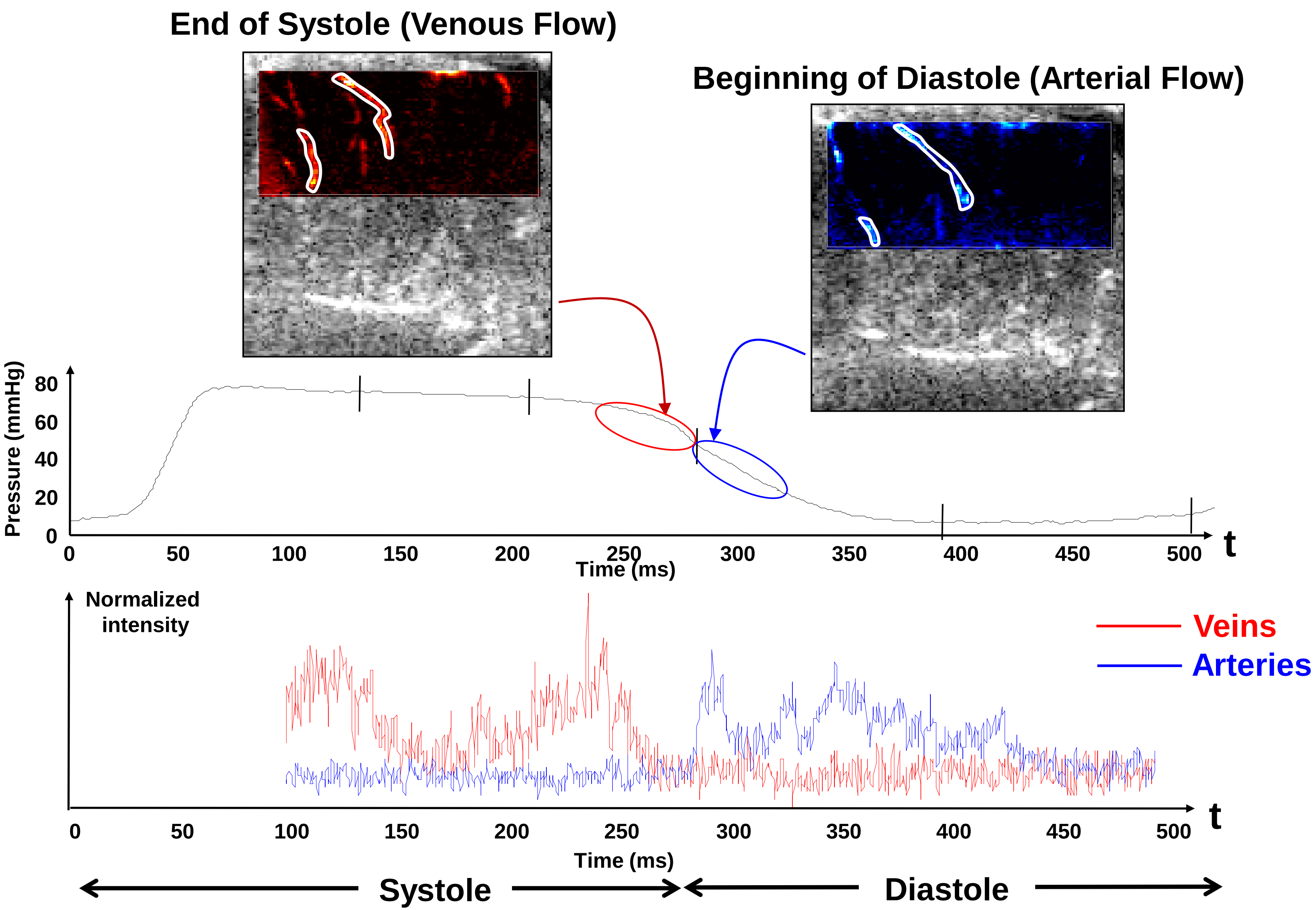
Veins




**Inverted Circulation**

Ultrafast Doppler imaging of blood flow dynamics in the myocardium.
Osmanski BF, Pernot M, Montaldo G, Bel A, Messas E, Tanter M, IEEE Trans Med Imaging. 2012

# Transition between Arterial and Venous Flow




**Phase Opposition Waveform**

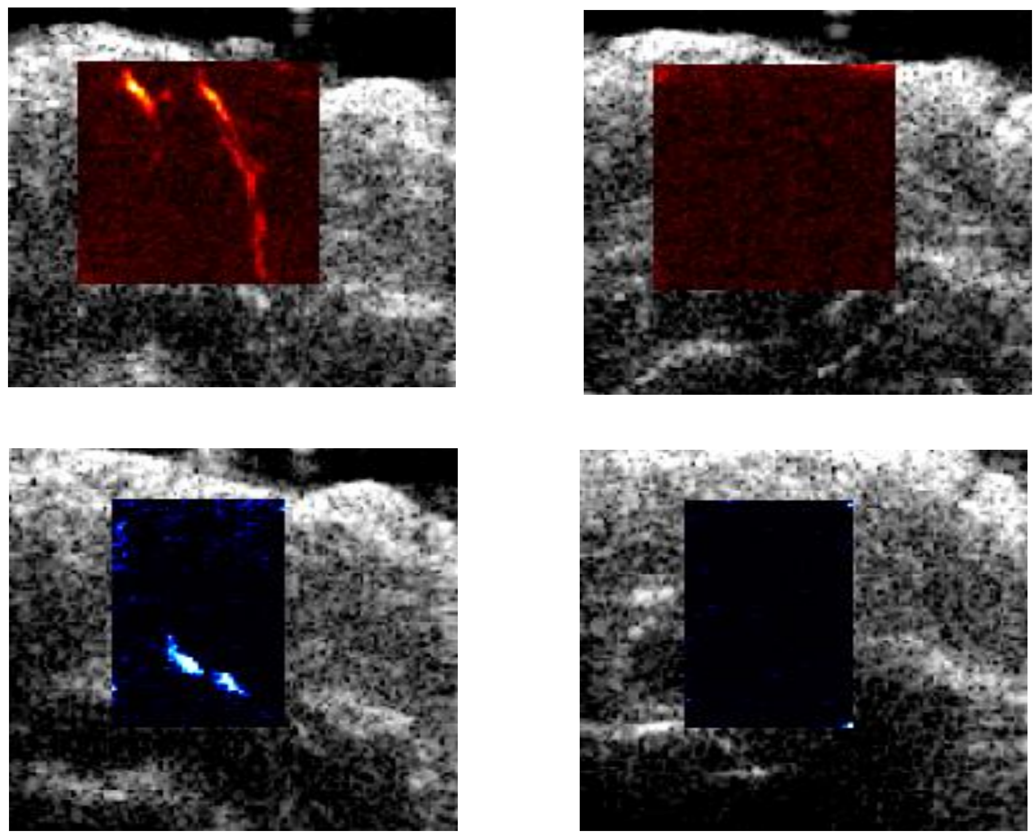
# Ultrafast Imaging of the myocardium : ischemia

Occlusion of two main epicardial coronary arteries upstream the imaging plane

**Before Ischemia** | **After Ischemia**

**Systole (Venous Flow)**

**Diastole (Arterial Flow)**



**Ultrafast Doppler imaging of blood flow dynamics in the myocardium.**
**Osmanski BF, Pernot M, Montaldo G, Bel A, Messas E, Tanter M, IEEE Trans Med Imaging. 2012**

# Ultrafast Doppler for *fUltrasound* :

# Functional Ultrasound Imaging of brain Activity

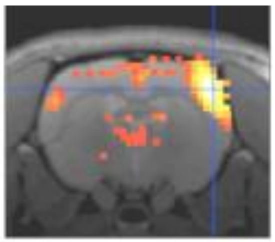
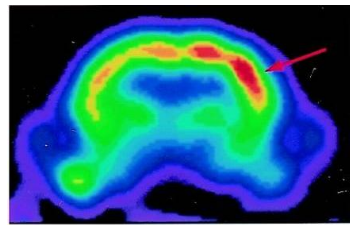
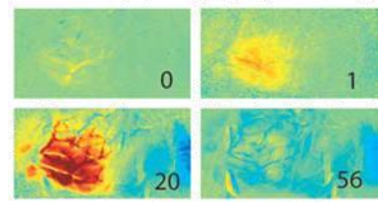
# How to image the brain in action?

**Neurovascular coupling**

**↗ Neuronal activity** ➜ **↗ Blood $O_2$ ↗ Blood flow ↗ Blood volume**

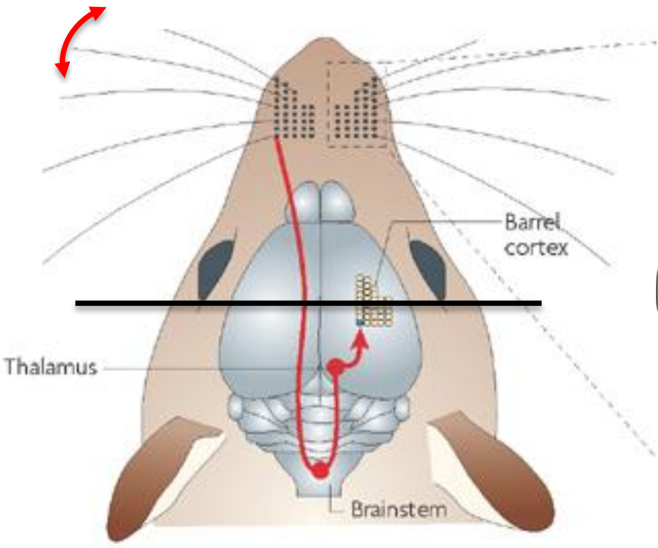
**Blood changes → Indirect image of brain activation**

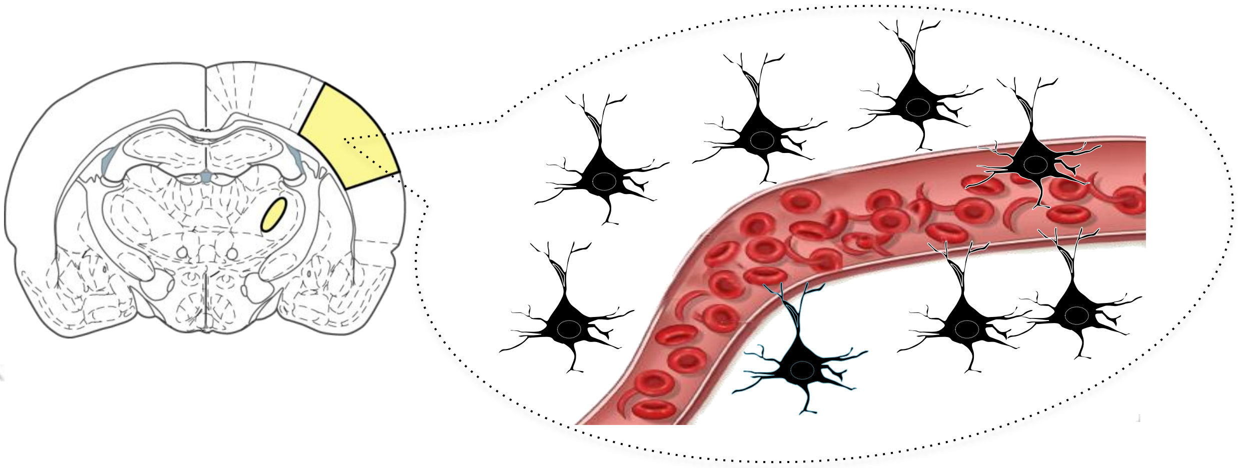
# Functional imaging techniques

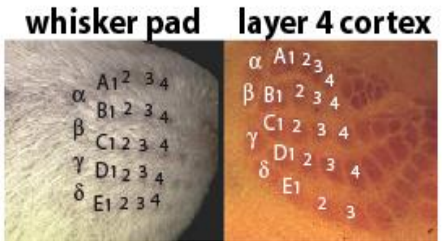
| | fMRI | PET | Optical imaging | Doppler ultrasound |
|---|---|---|---|---|
| |  |  |  | ? |
| Penetration | ✔✔ | ✔✔ | ✖ | |
| Spatial resolution | ✔ | ✖ | ✔✔ | |
| Temporal resolution | ✖ | ✖ | ✔✔ | |
| Sensitivity (SNR) | ✖ | ✔ | ✔ | |

**Functional ultrasound (fUS) overcomes the poor sensitivity of Doppler ultrasound**

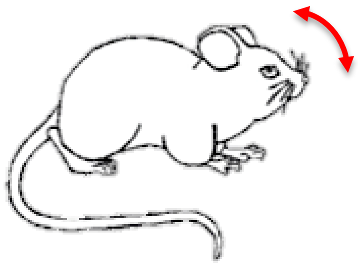
# A classical model of brain activation: whisker stimulation





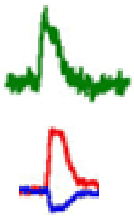

**Stimulus**



**Neurons**

**electrical potential**

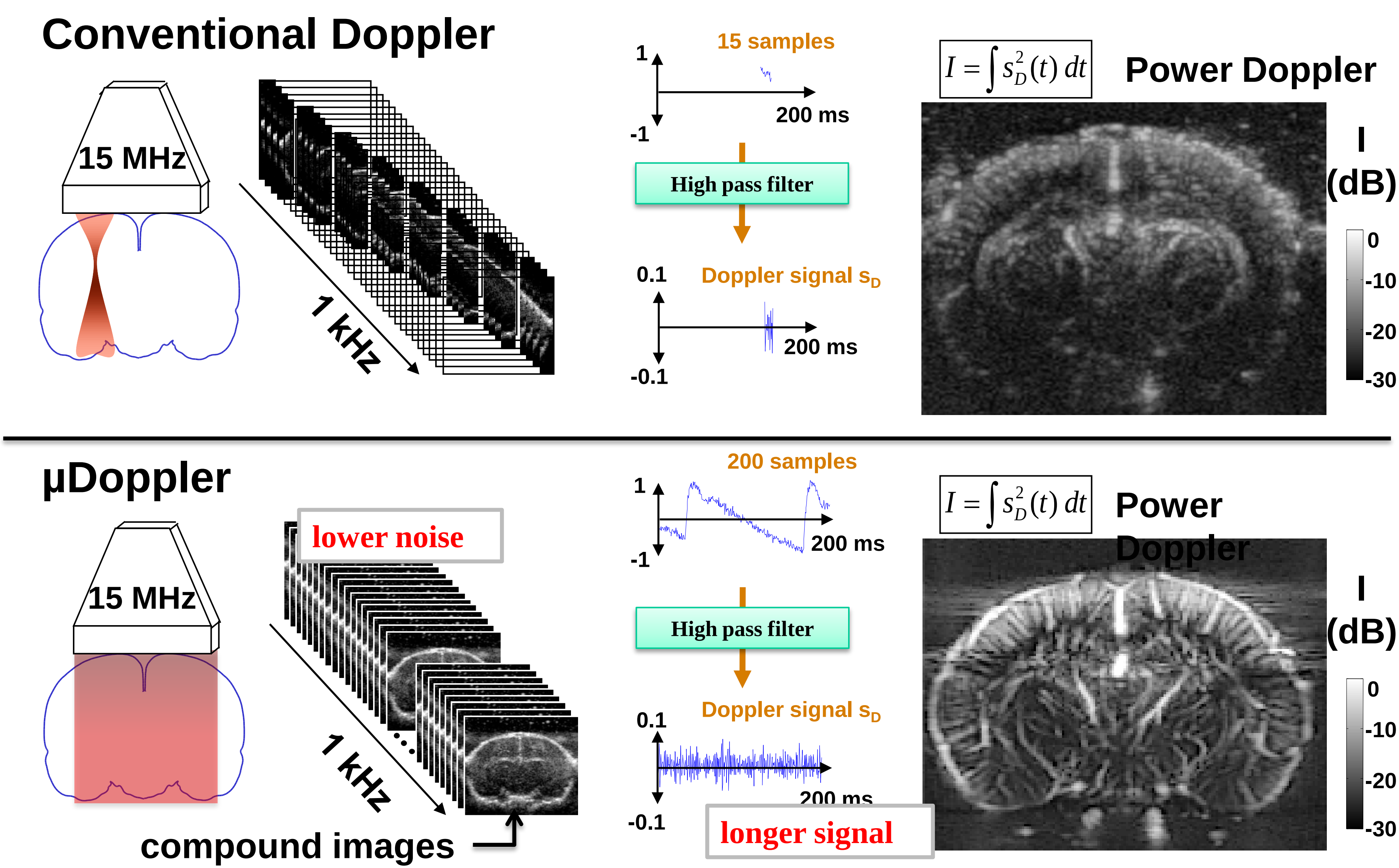
**Microvessels**



**blood flow and volume**

**blood $O_2$**

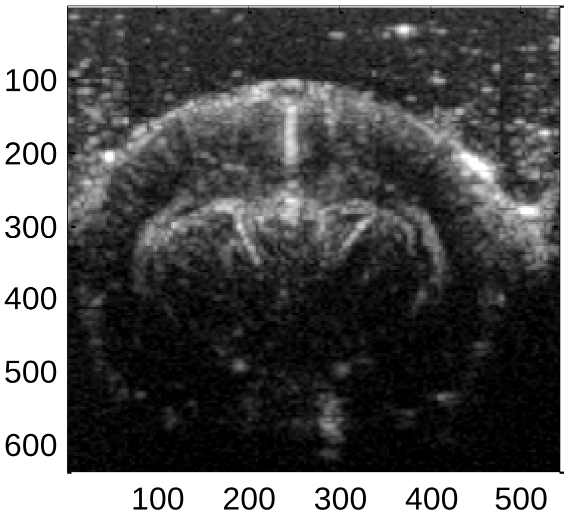
# The concept of µDoppler based on Ultrafast Imaging



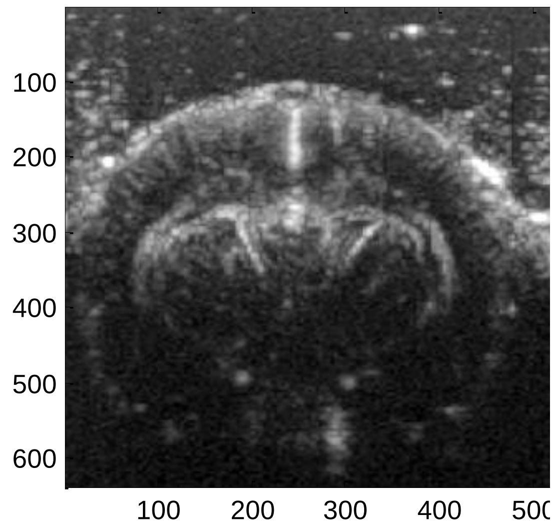

E. Macé, G. Montaldo, I. Cohen, M. Baulac, M. Fink, M. Tanter
Functional Ultrasonic Imaging of Brain Activity, *Nature Methods*, July 2011

# Impact of the number of time samples on Ultrafast Doppler sensitivity

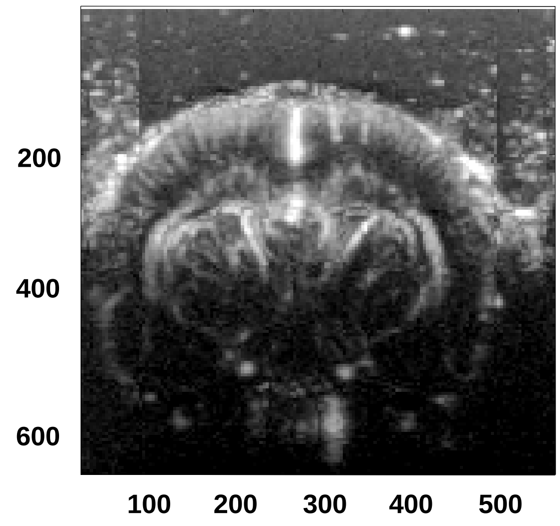
**15 focused**



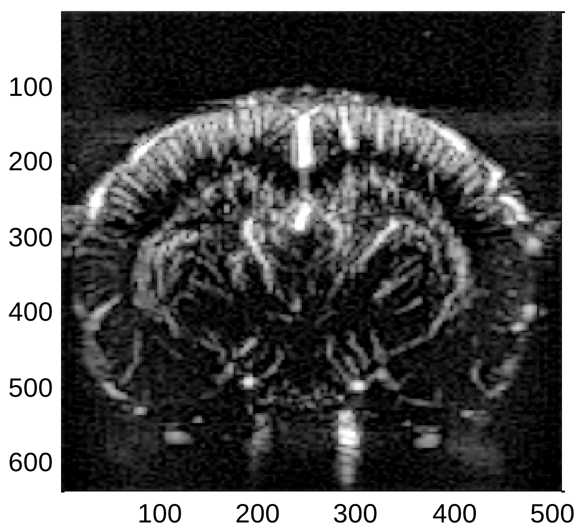

**20 focused**



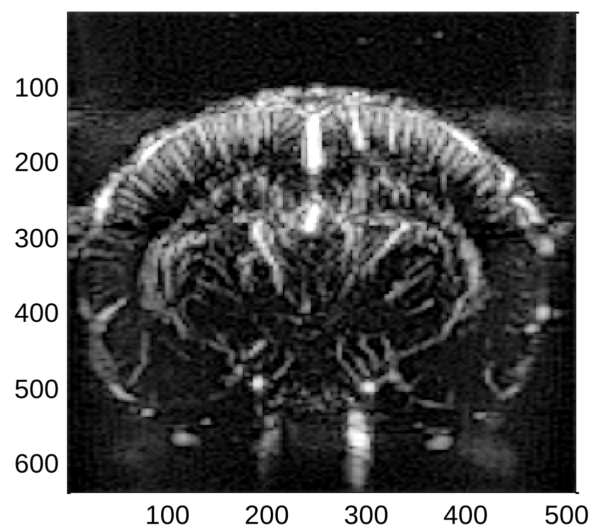

**53 focused**




**200 compound**




**400 compound**



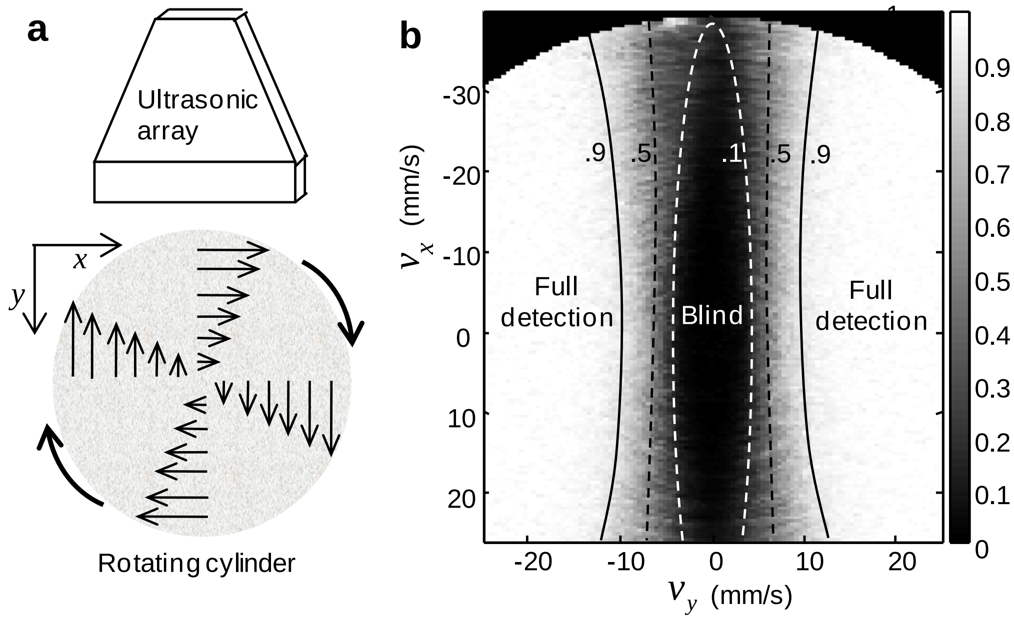
# What is really measured by I ?

**1/ I is proportional to the number of scatterers (red blood cells) in the voxel**

**2/ Only a range of velocity is detected**

- **Doppler frequencies > cutoff frequency (70 Hz)**

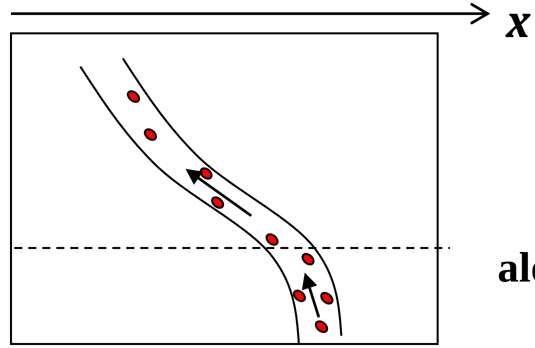
**3/ The effect of the vessel angle can be neglected**




**I measures the volume of blood flowing at a velocity higher than 4 mm/s (vessels >30 µm) in the voxel**

# What is the sensitivity of Power Doppler Imaging?

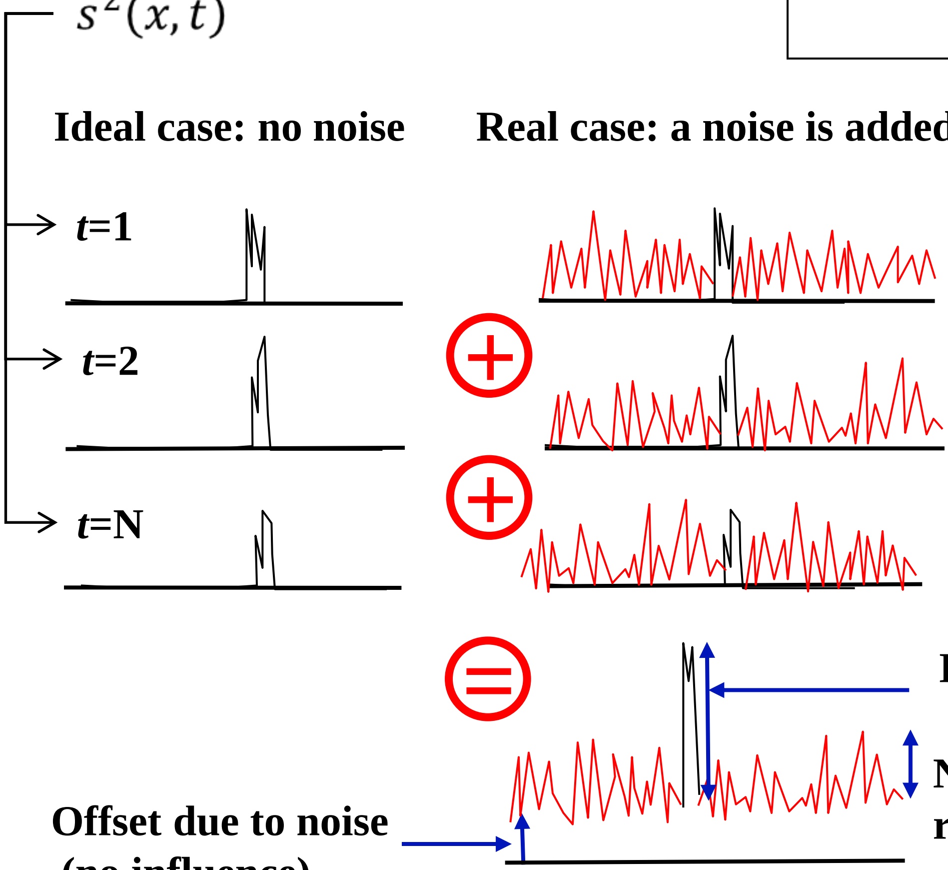
$$I_{Doppler} = \int s^2(t)\,dt$$




$I_{Doppler}$ along a line ?

$s^2(x,t)$

**Ideal case: no noise** | **Real case: a noise is added**




**Offset due to noise (no influence)**

**Blood intensity**

**Noise variance reduced by the number of frames**

$$I_{min} = \frac{I_{noise}}{\sqrt{\frac{N_{Frames}}{2} - 1}}$$

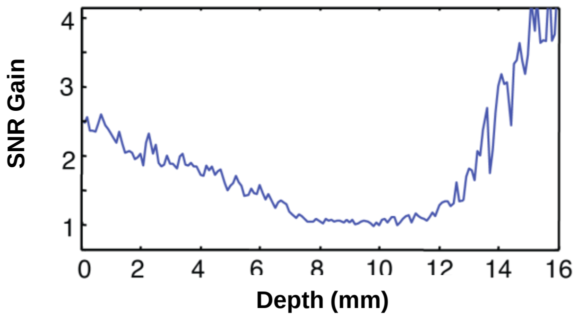
**Detectability condition**

**Blood intensity > noise variance**

# Theoretical Sensitivity Gain : Conventional/ Ultrafast Doppler

**Sensitivity Gain**

$$\frac{S_{\mu Doppler}}{S_{focalisé}}$$




$$\frac{SNR^{compound}(z_{foc}, n_{angles})}{SNR^{focalisé}(z_{foc})} = \frac{\sqrt{n_{angles}\, z_{foc}\, \lambda}}{D}$$

J. Bercoff, G. Montaldo, T. Loupas,D. Savery, F. Meziere, M. Fink, M. Tanter 'Ultrafast Compound Doppler Imaging', *Ieee UFFC* , 58(1), 134—147, 2011

$$\frac{S_{\mu Doppler}}{S_{focalisé}} = \frac{I_{\eta}^{focalisé}}{I_{\eta}^{\mu Doppler}} \frac{\left(\sqrt{n_{eff}^{\mu Doppler}/2} - 1\right)}{\left(\sqrt{n_{eff}^{focalisé}/2} - 1\right)}$$

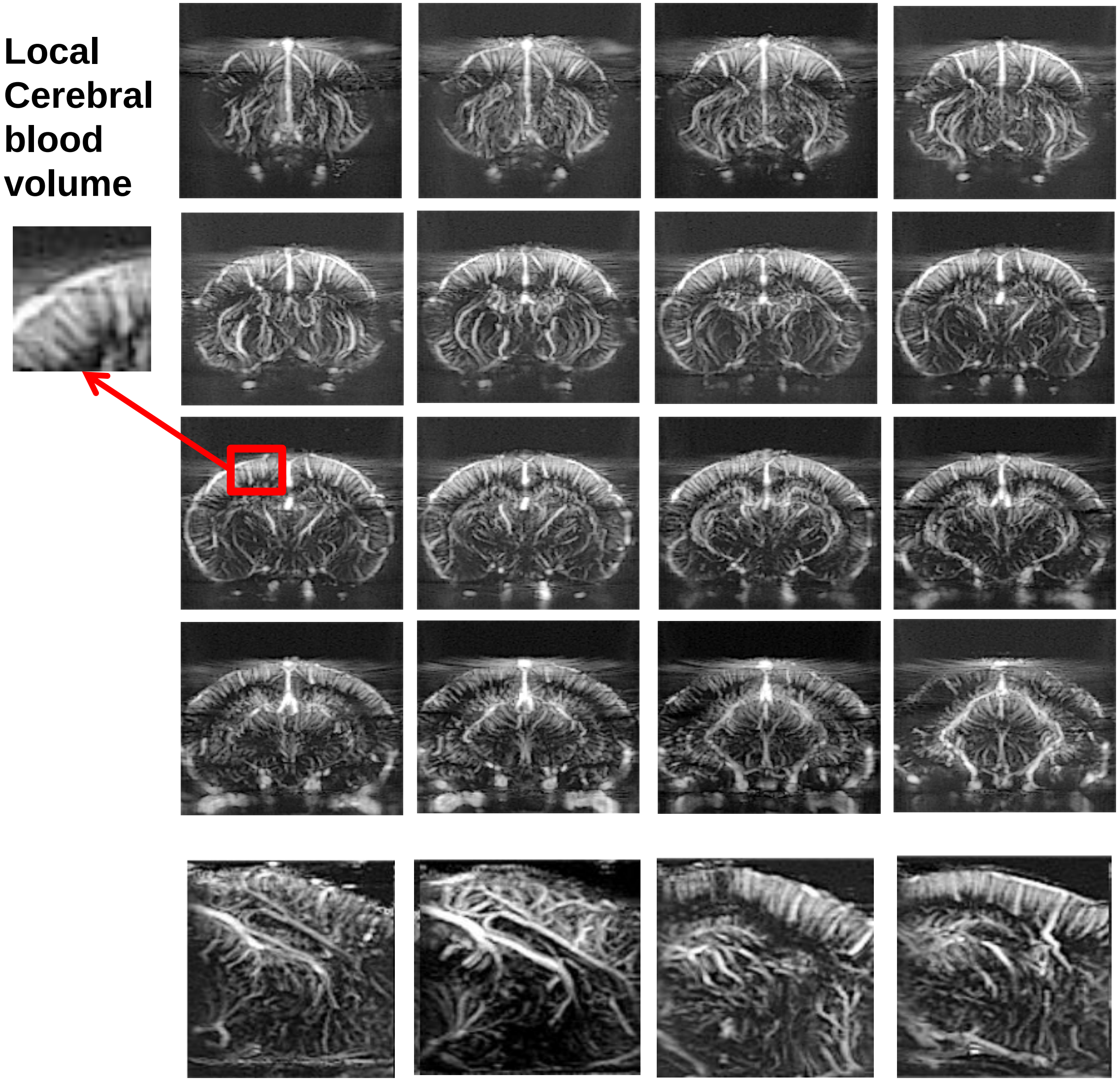
E. Macé, G. Montaldo, I. Cohen, M. Baulac, M. Fink, M. Tanter Functional Ultrasonic Imaging of Brain Activity, *Nature Methods*, July 2011

$$\frac{S_{\mu Doppler}}{S_{focalisé}}(z) \sim N_{angles} \sqrt{\frac{n_{eff}^{\mu Doppler}}{n_{eff}^{focused}}}$$

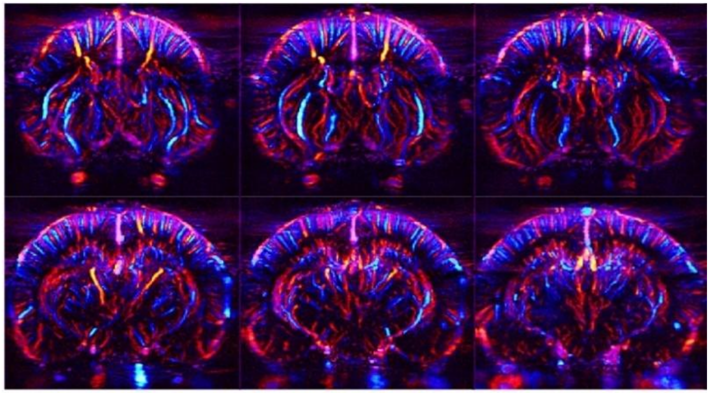
**Functional ultrasound imaging of the brain: theory and basic principles.**
**E. Mace, G. Montaldo, B.-F. Osmanski, I. Cohen, M. Fink, M. Tanter, IEEE UFFC, *under review***

# 3D µDoppler Scan of rat Cerebral Blood Flow

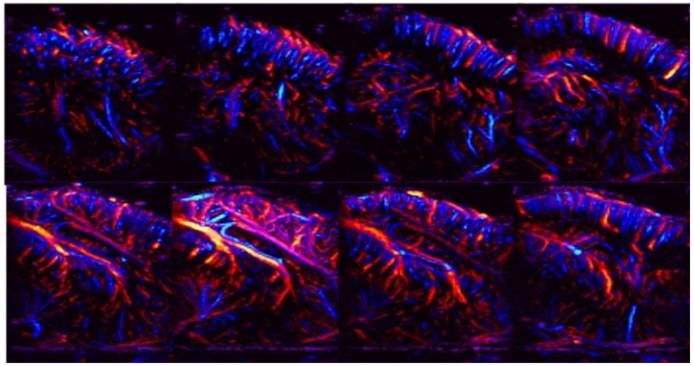
Local Cerebral blood volume



Coronal

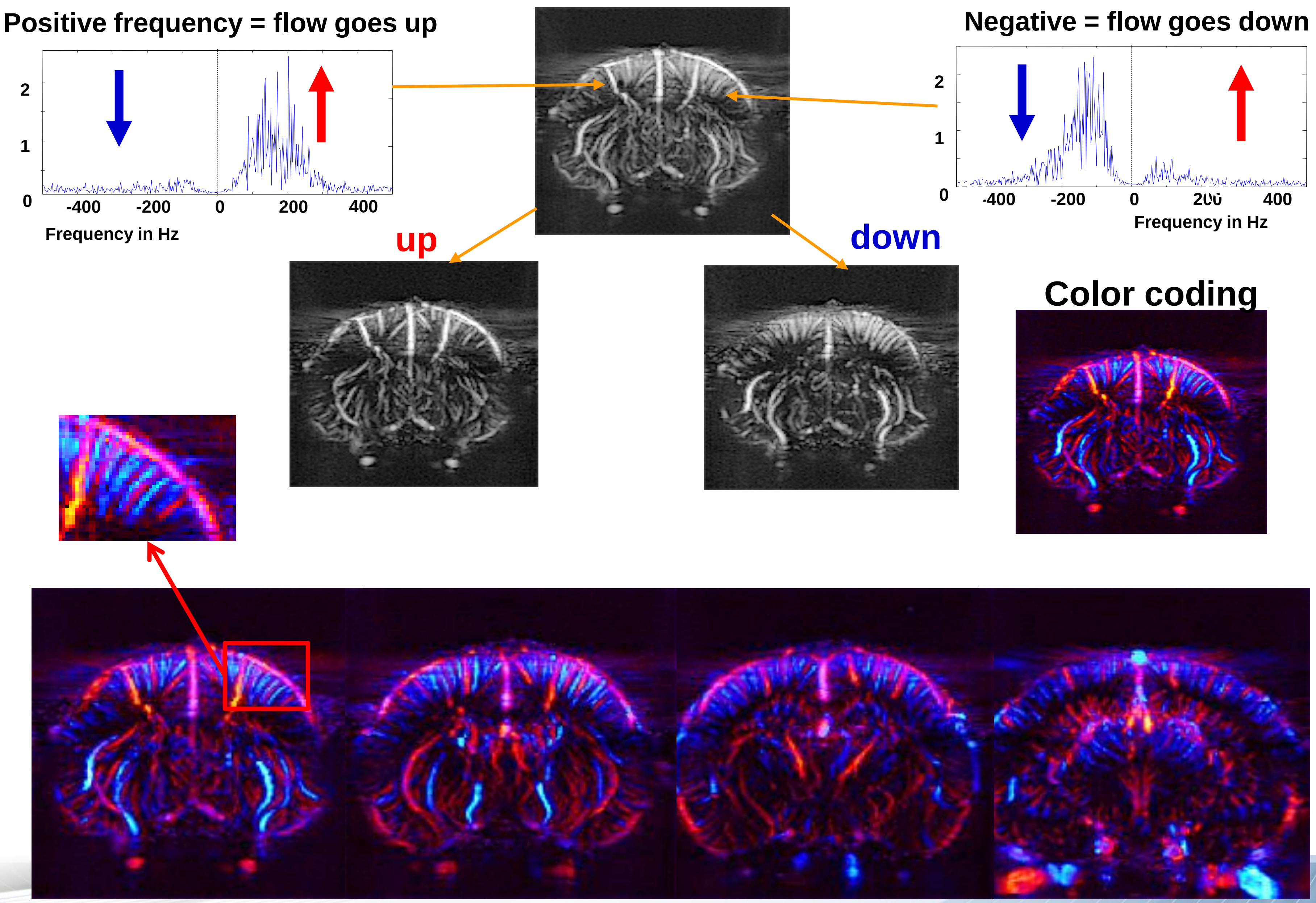


Sagittal

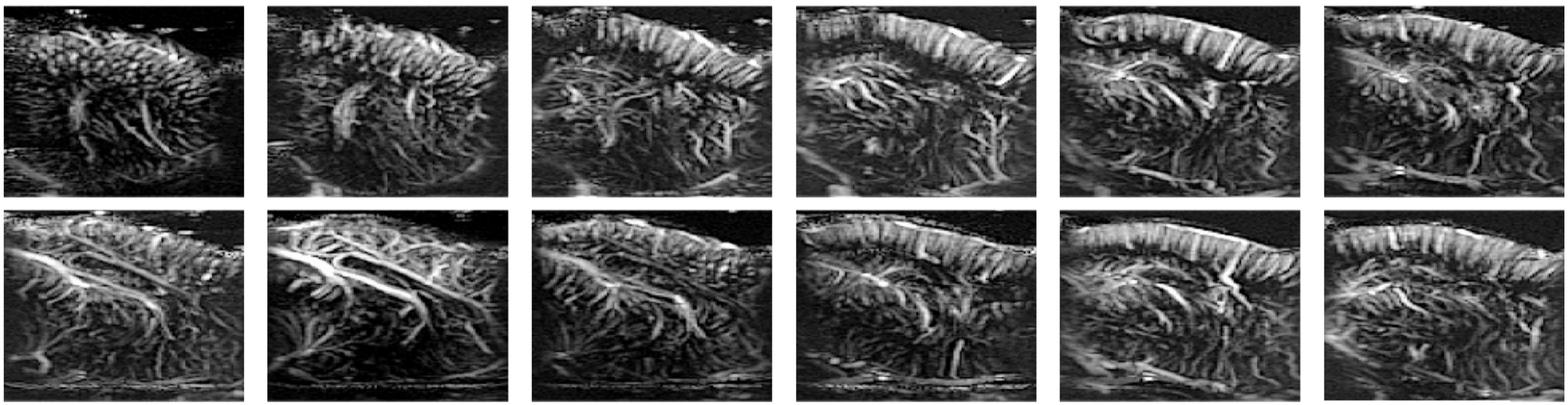


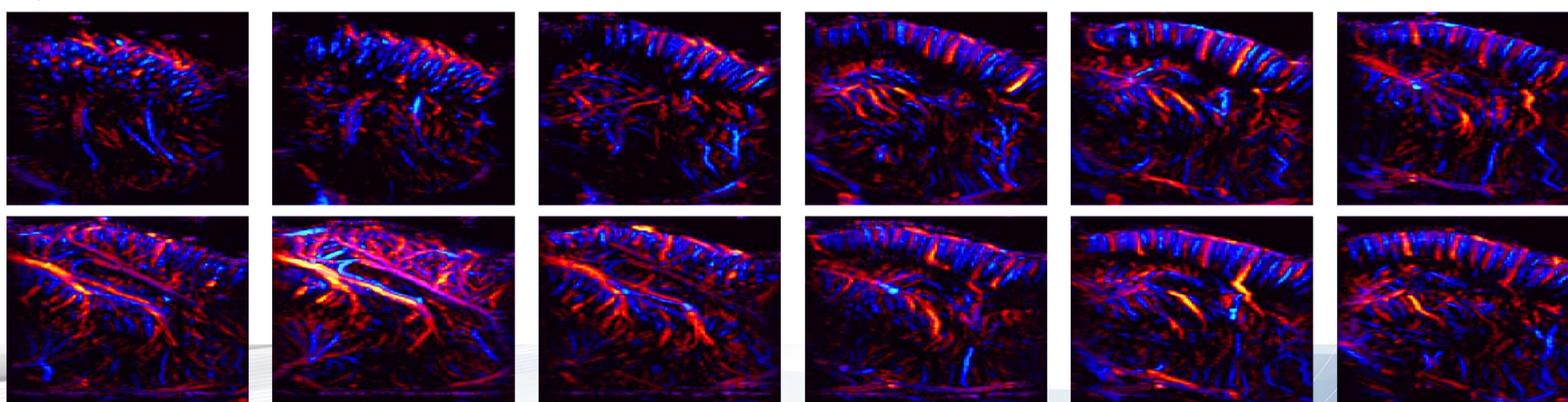
E. Macé, G. Montaldo, I. Cohen, M. Baulac, M. Fink, M. Tanter
Functional Ultrasonic Imaging of Brain Activity, *Nature Methods*, July 2011

# Mapping the direction of the flow

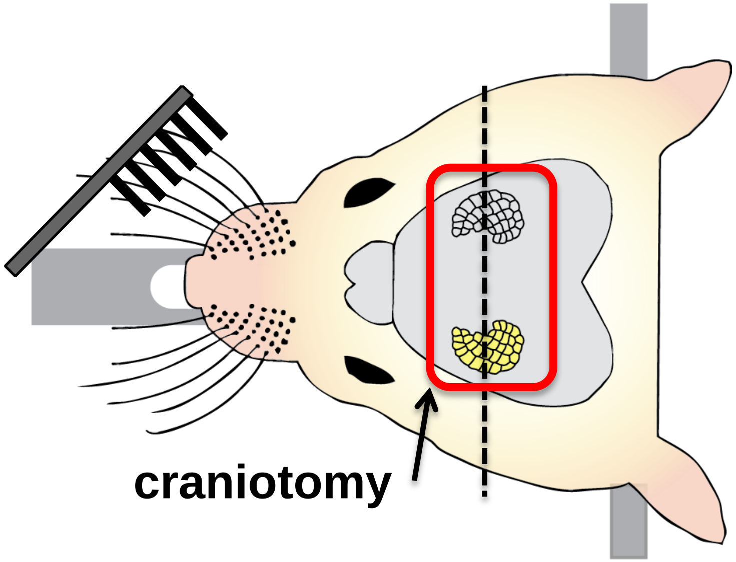


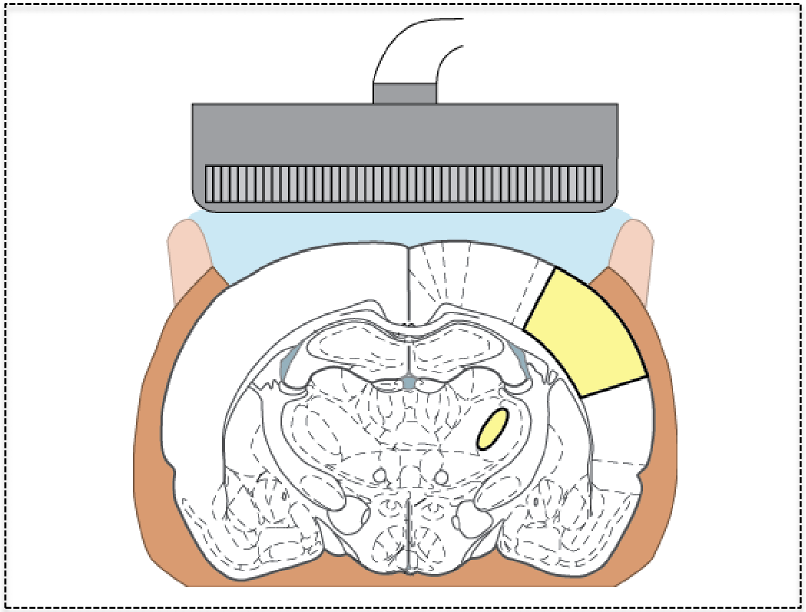
# 3D µDoppler Scan of rat CBV : Sagittal orientation

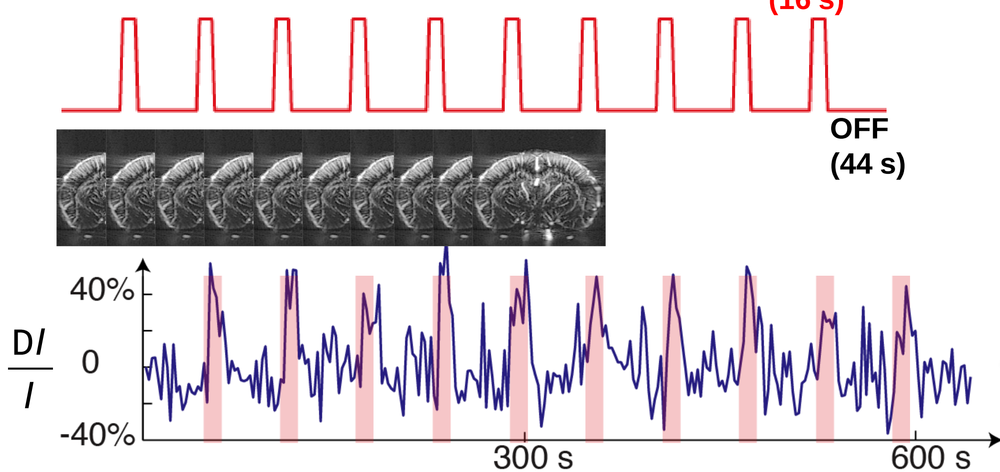


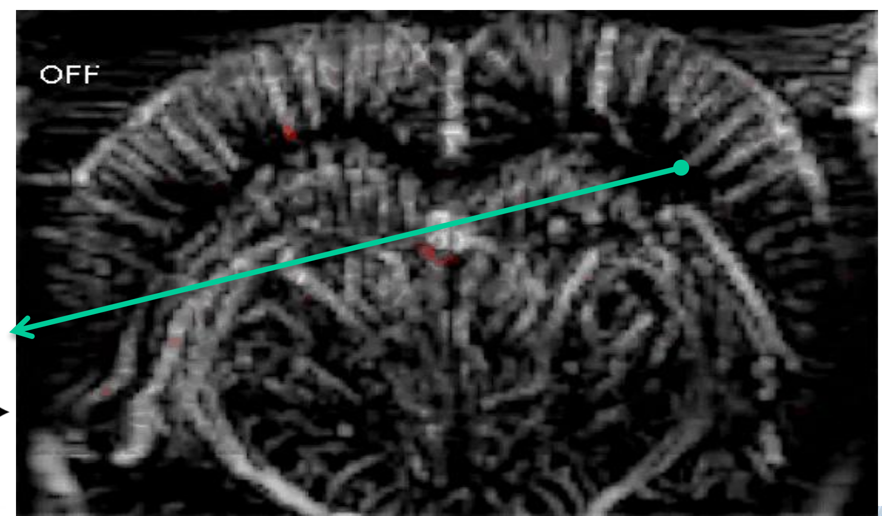
# *in-vivo* validation



**Stimulus pattern**



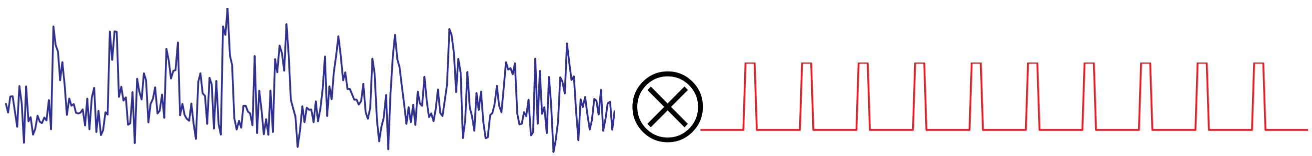

# Increased CBV during stimuli

E. Macé, G. Montaldo, I. Cohen, M. Baulac, M. Fink, M. Tanter, *Nature Methods*, July 2011

# Brain activation maps

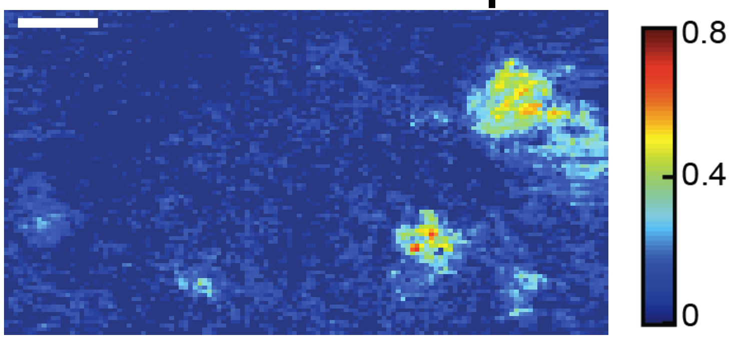
**Correlation coefficient *r* for each pixel**

**CBV(*t*)**

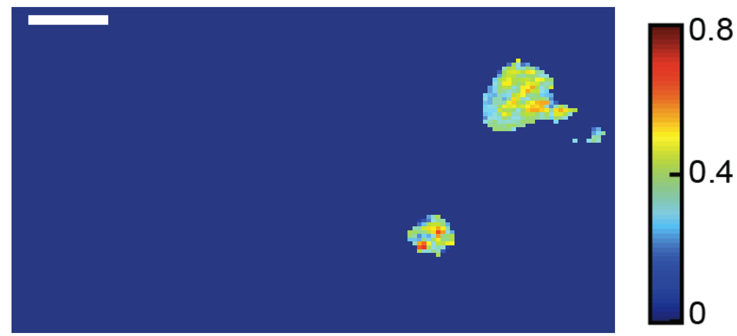


**Stim(*t*)**

**Correlation map**

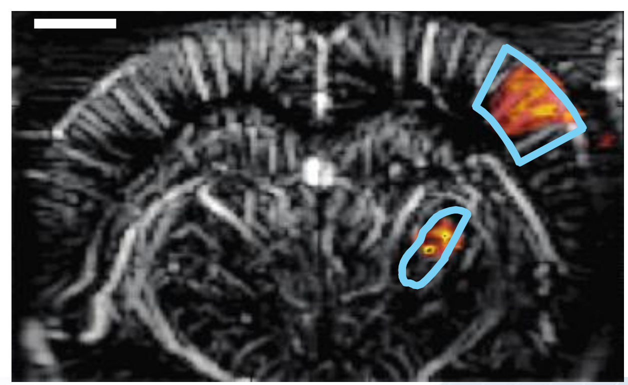



**Activated pixels (t-test, p>0.001)**



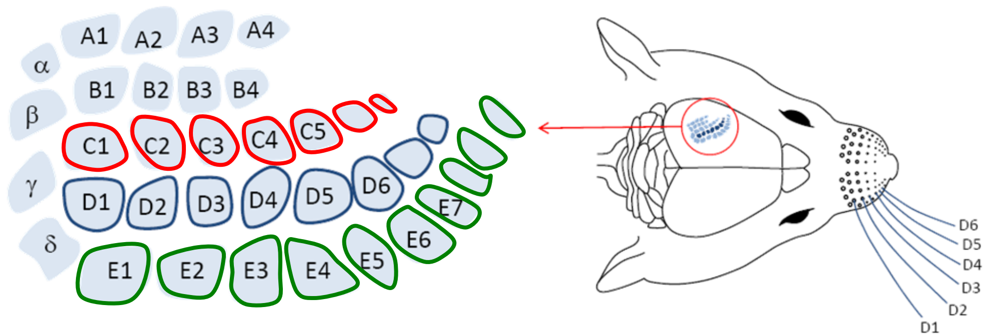

**Superposition**

**Identification**



E. Macé , *G. Montaldo, I. Cohen, M. Baulac, M. Fink and M. Tanter. Nature Methods*, 8, 662-664 (2011)

# Can we detect smaller activated areas?

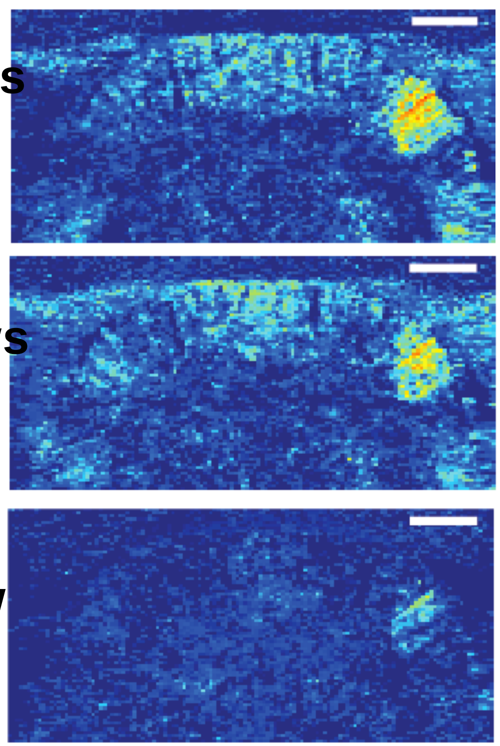


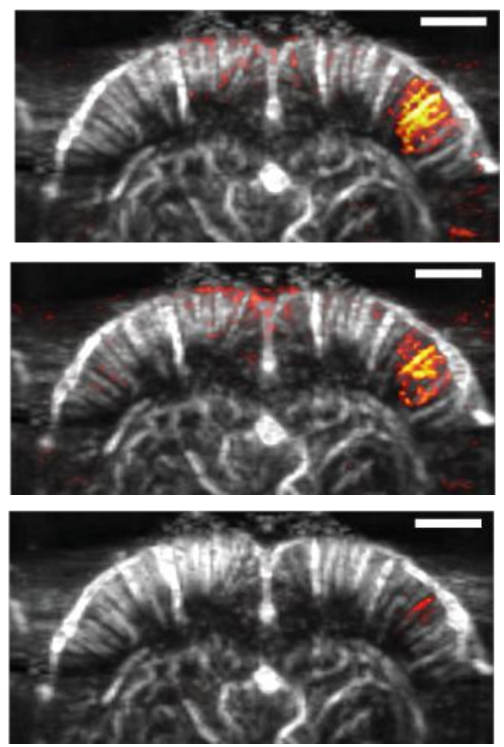

**Correlation maps** **Activation maps**

**Rows CDE**

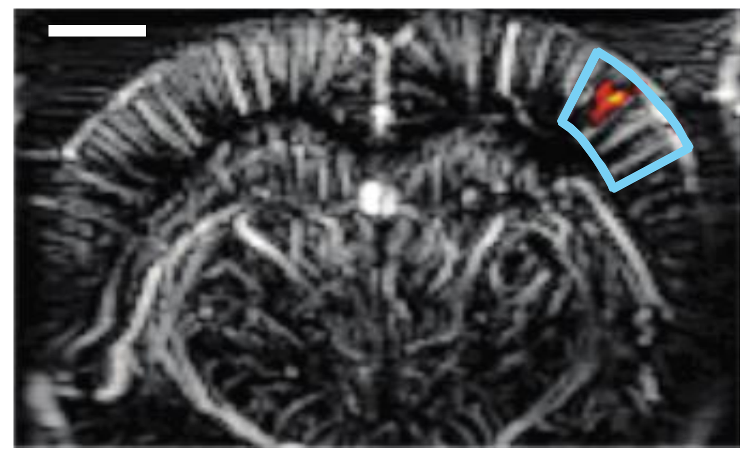
**Rows CD**

**Row D**

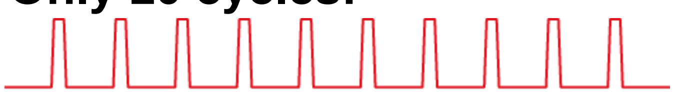




**One whisker (D2)**



**Only 10 cycles!**



**Less invasive?**

**Other areas?**

E. Macé , *G. Montaldo, I. Cohen, M. Baulac, M. Fink and M. Tanter. Nature Methods,* 8, 662-664 (2011)

# Epilepsy: A Challenge for neuroimaging techniques

**SEIZURE**

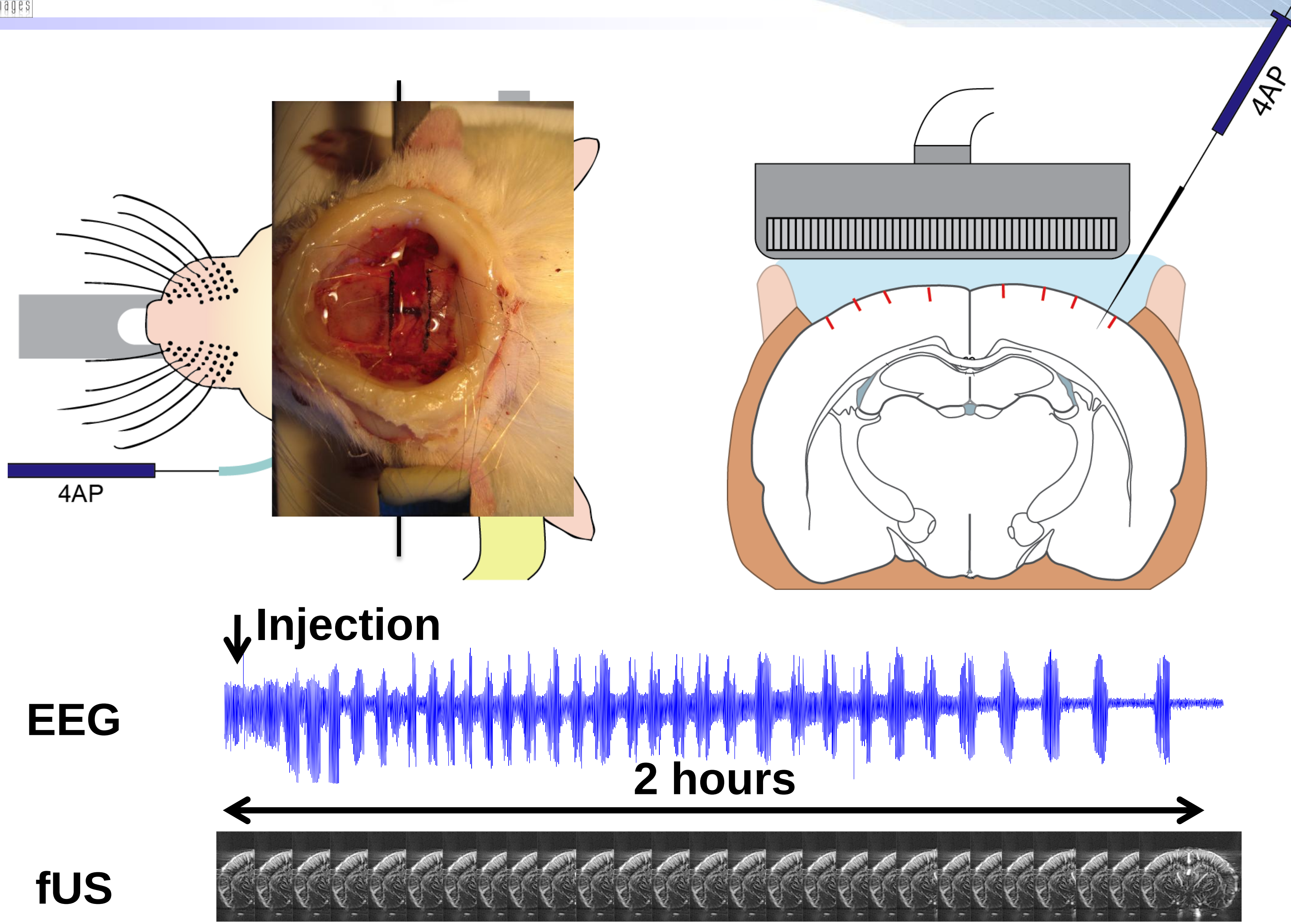
- Whole brain
- Complex spatiotemporal dynamics
- Not reproducible

**IMAGING MODALITY**

- Penetration
- Large field of view
- High spatiotemporal resolution
- High sensitivity

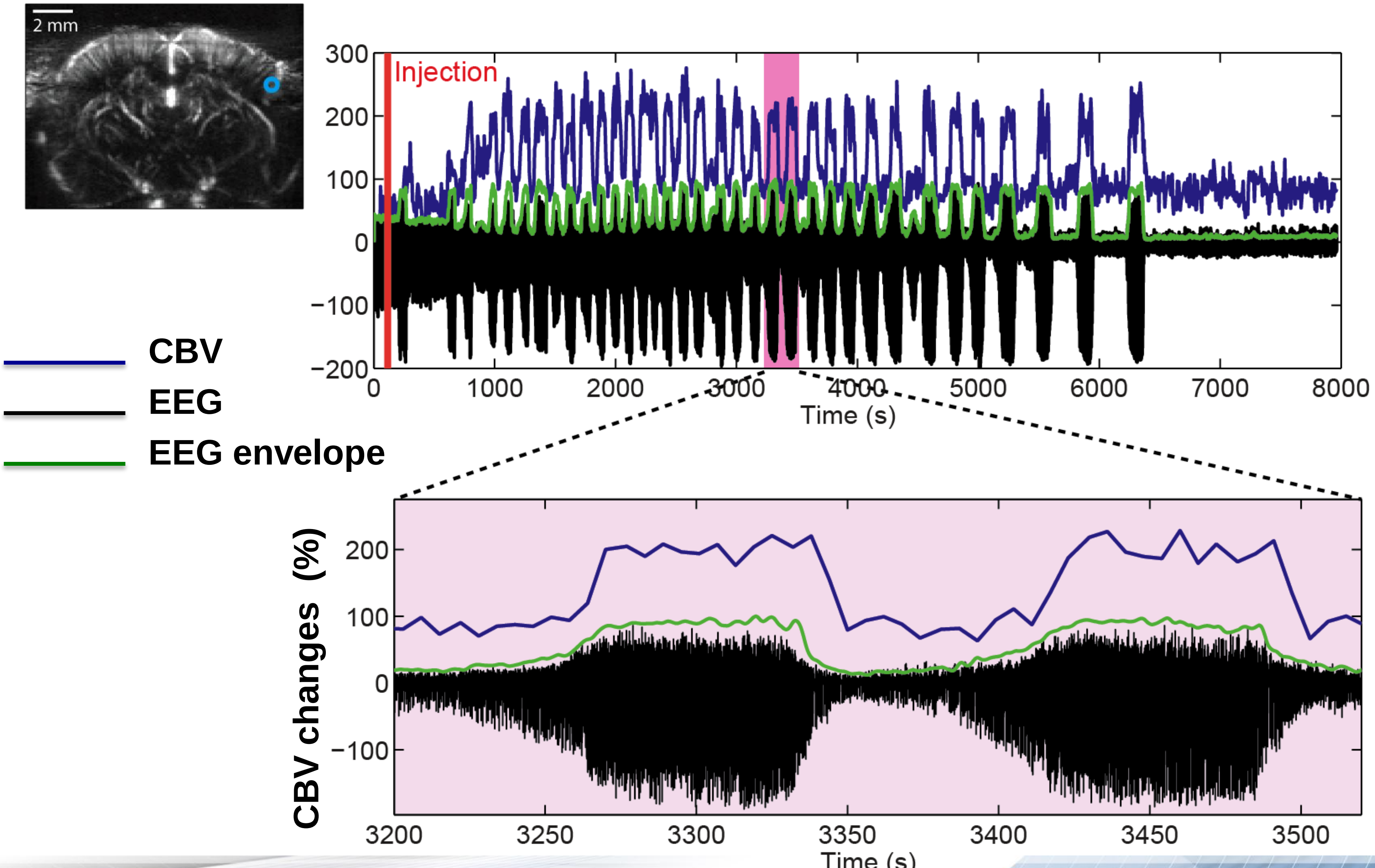
| | EEG | fMRI | PET | Optics |
|---|---|---|---|---|
| Penetration/field of view | ✖ | ✔ | ✔ | ✖ |
| Spatial resolution | only few points | ✔ | ✖ | ✔ |
| Temporal resolution | ✔ | ✖ | ✖ | ✔ |
| Sensitivity (SNR) | ✔ | ✖ | ✔ | ✔ |

# Experimental procedure



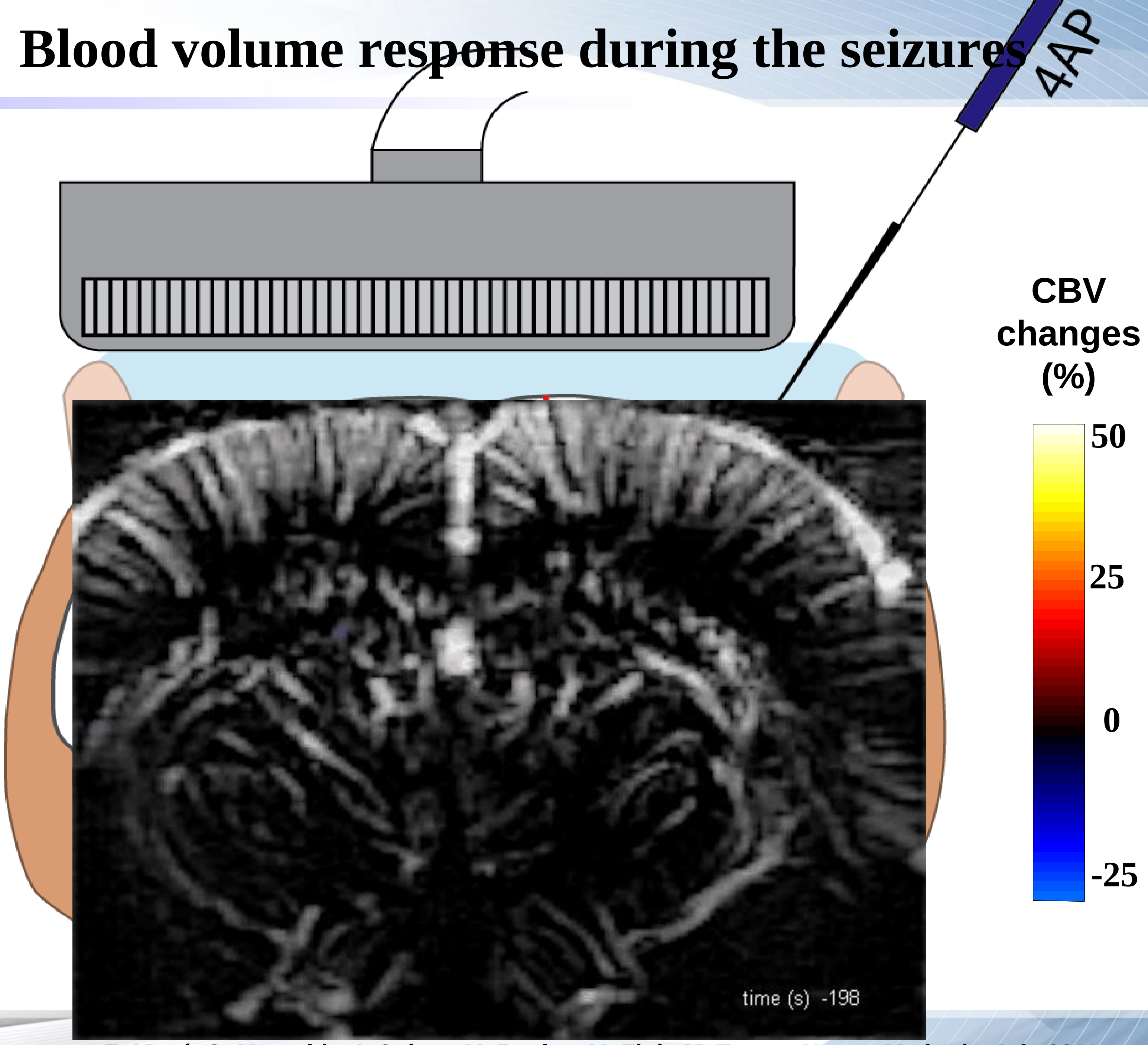

E. Macé, G. Montaldo, I. Cohen, M. Baulac, M. Fink, M. Tanter, *Nature Methods*, July 2011

# Correlated with neuronal activity?



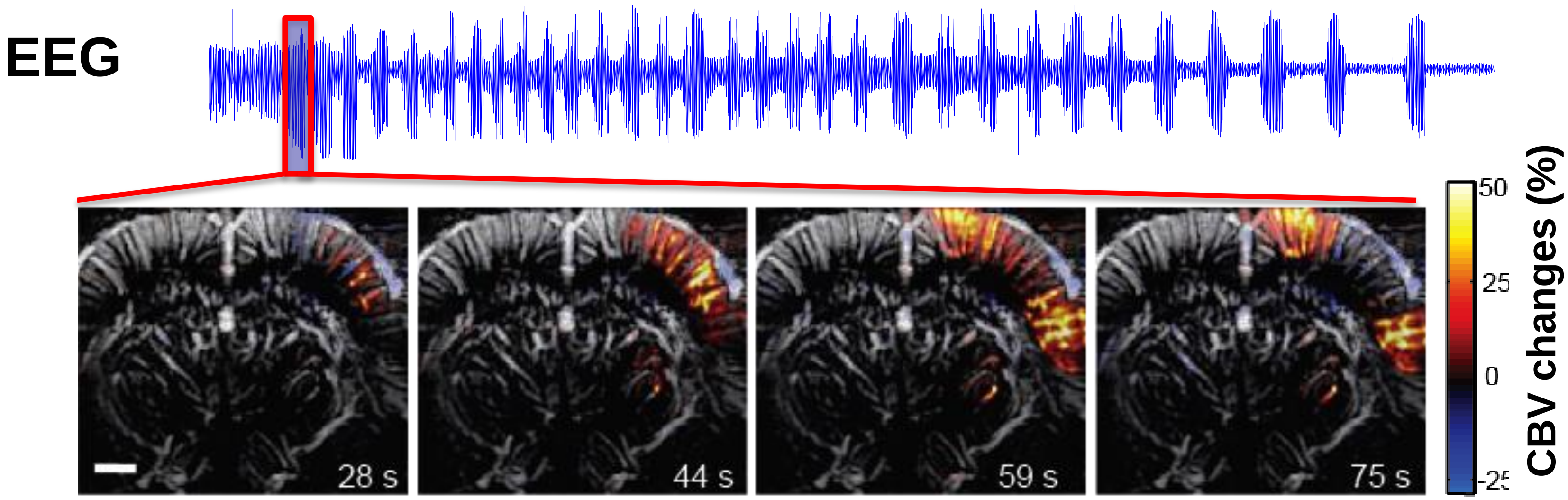

E. Macé , *G. Montaldo, I. Cohen, M. Baulac, M. Fink and M. Tanter. Nature Methods,* 8, 662-664 (2011)

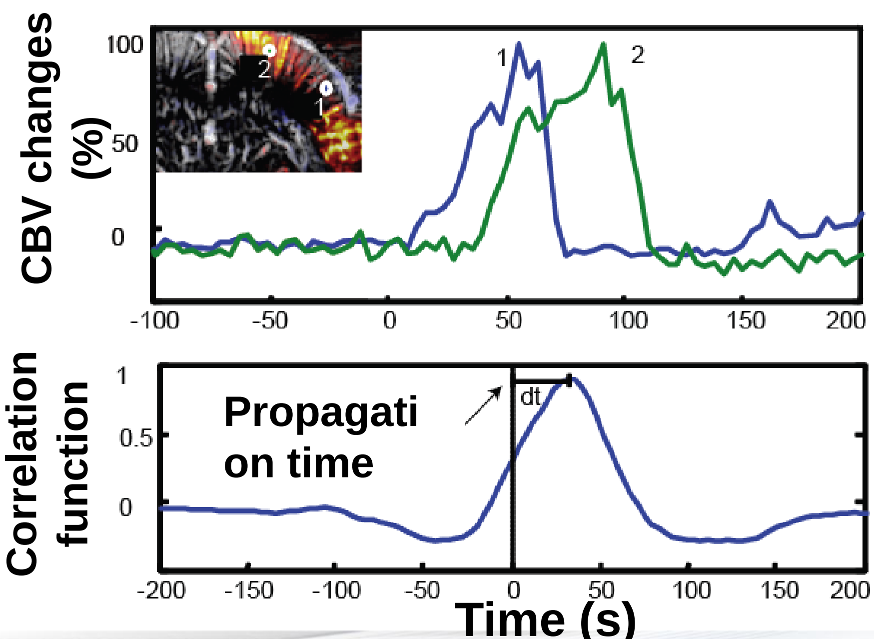
# Blood volume response during the seizures

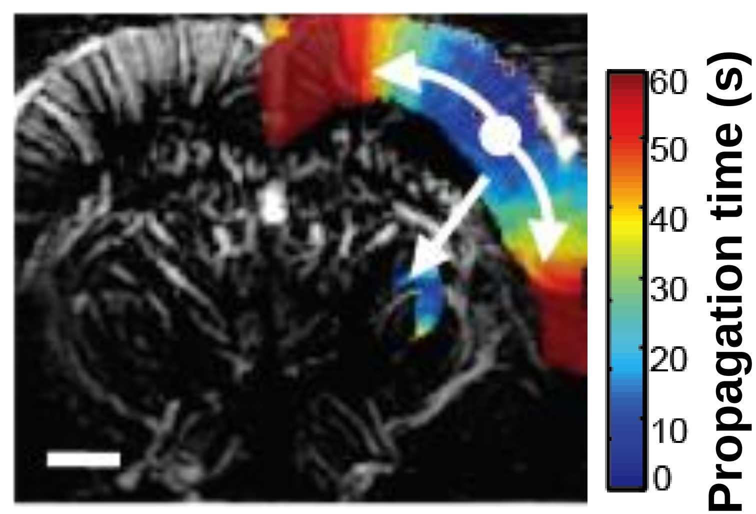



E. Macé, G. Montaldo, I. Cohen, M. Baulac, M. Fink, M. Tanter, *Nature Methods*, July 2011

# Propagation speed of epileptic seizures



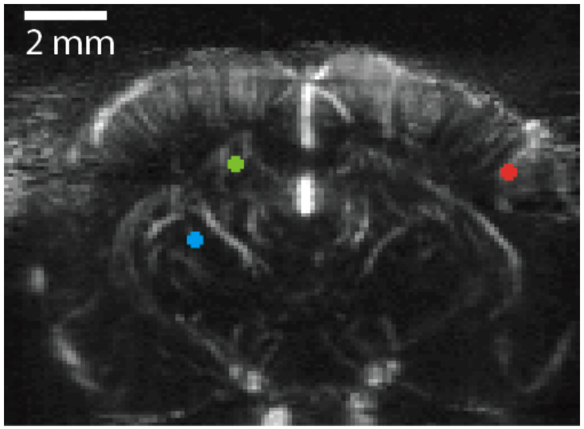




Cortical “wave” speed
3.2 +- 0.3 mm/min

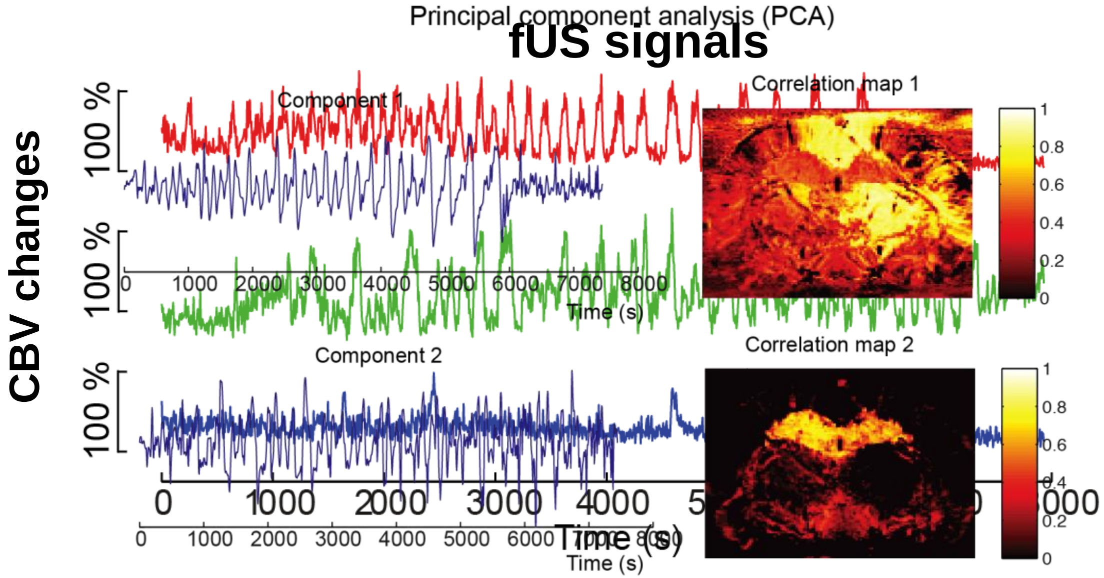
E. Macé , *G. Montaldo, I. Cohen, M. Baulac, M. Fink and M.* 664 (2011)

# Spatial extension of synchronous activity

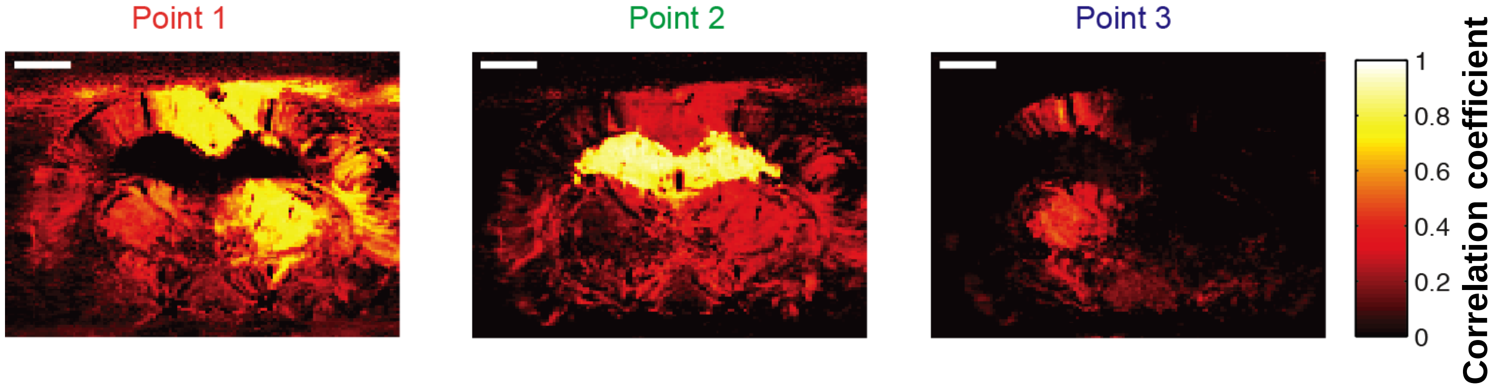
## Reference points




## fUS signals

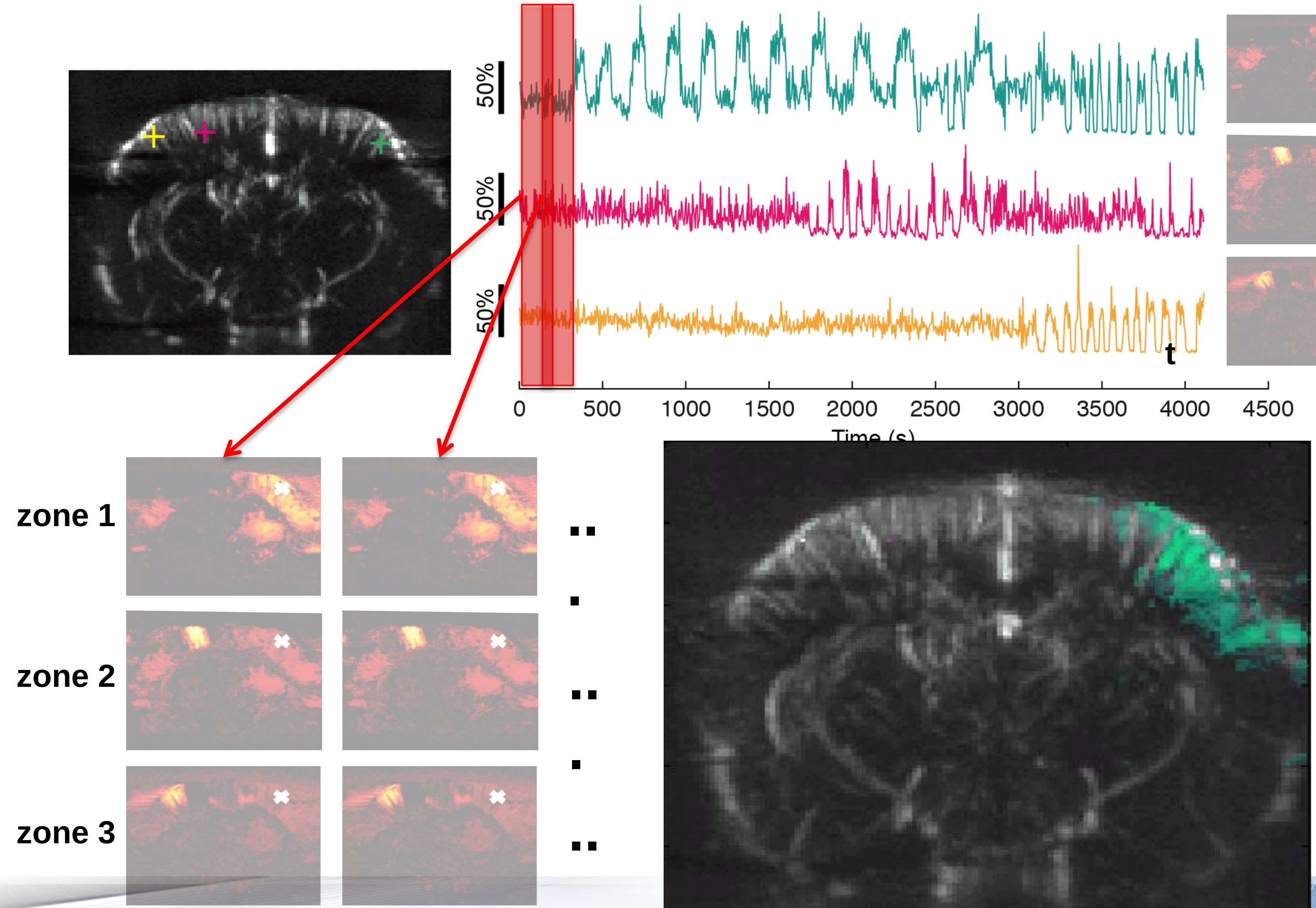



## Correlation maps

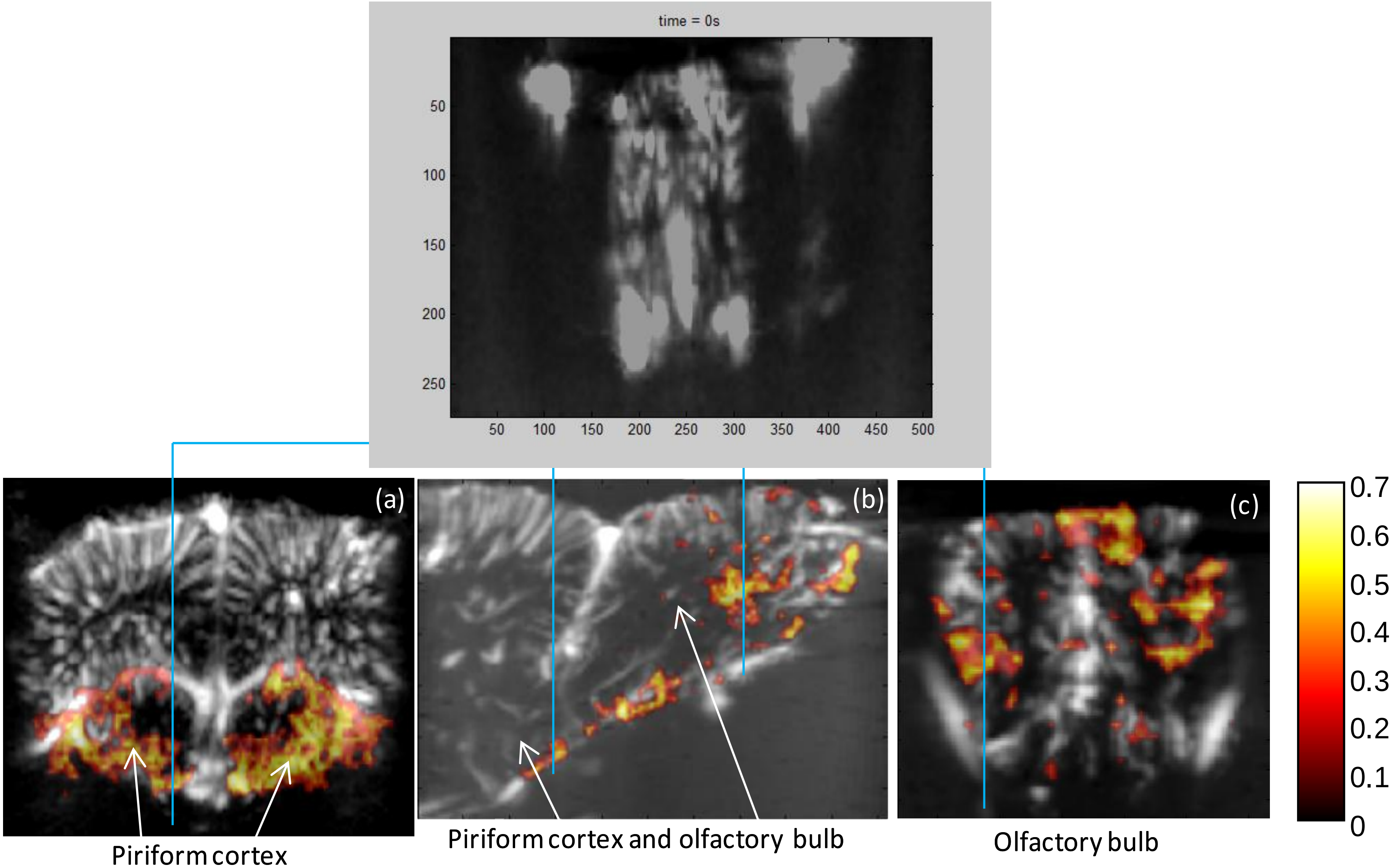



- **Large synchronous areas matching with anatomical features**
- **Areas of independent seizing patterns**

# Secondary foci



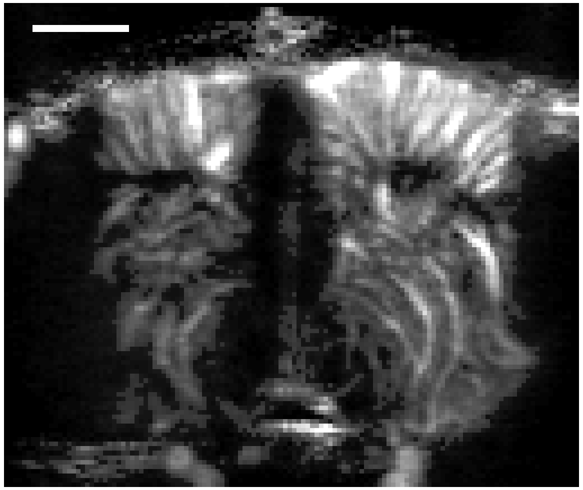
# Other functional sensorial activity : following the olfactory track



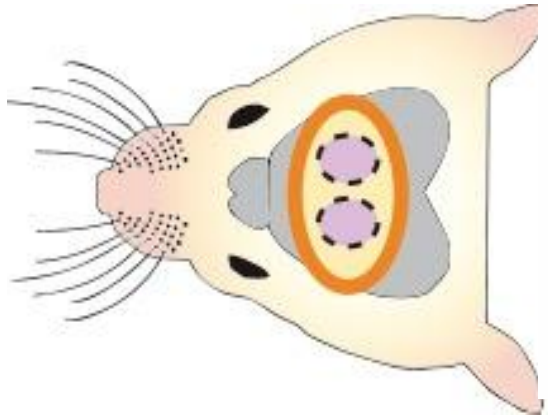

B. Osmanski, H. Gurden, G.Montaldo, F. Pain, M. Fink, M. Tanter

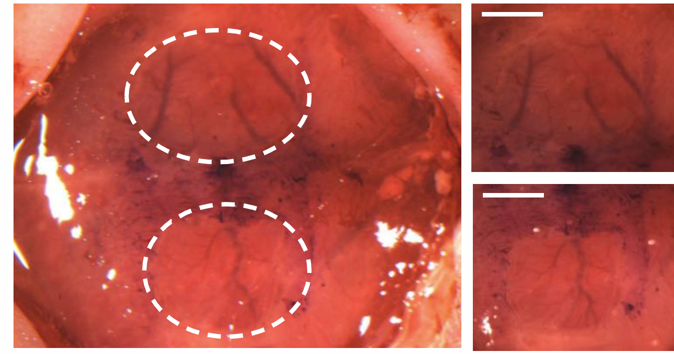
# Ongoing work (II) : Development of Chronic and awake fUltrasound

**Thinned-skull surgical procedure**



Thinned-skull Craniotomy

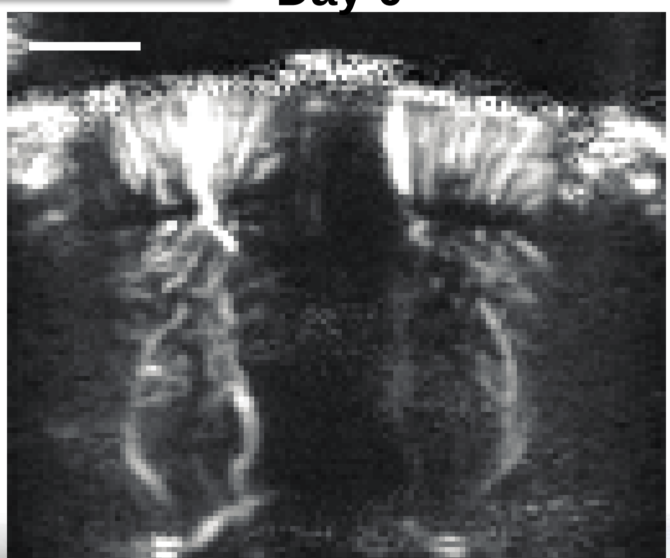




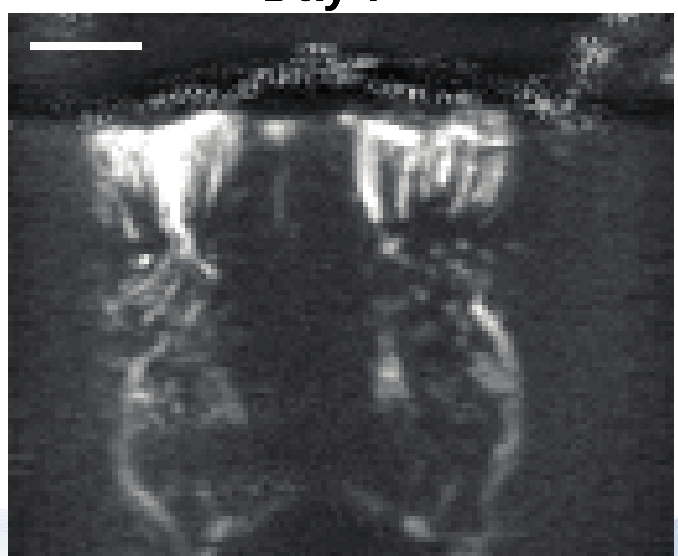
Thinned skull ≈ 50 µm

**µDoppler**

Day 0



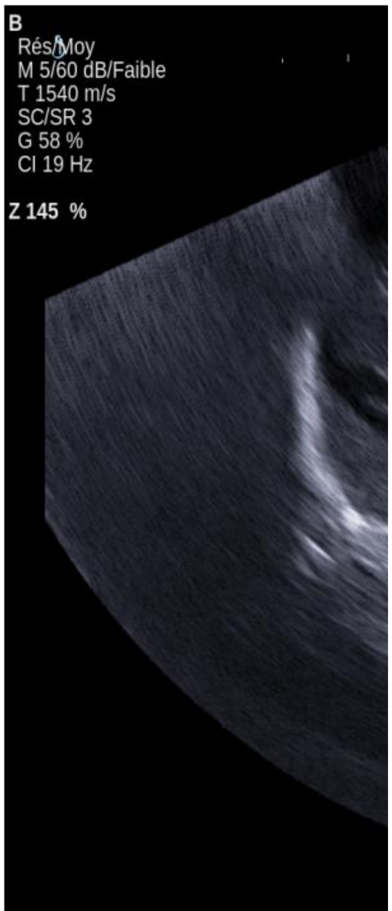
Day 7



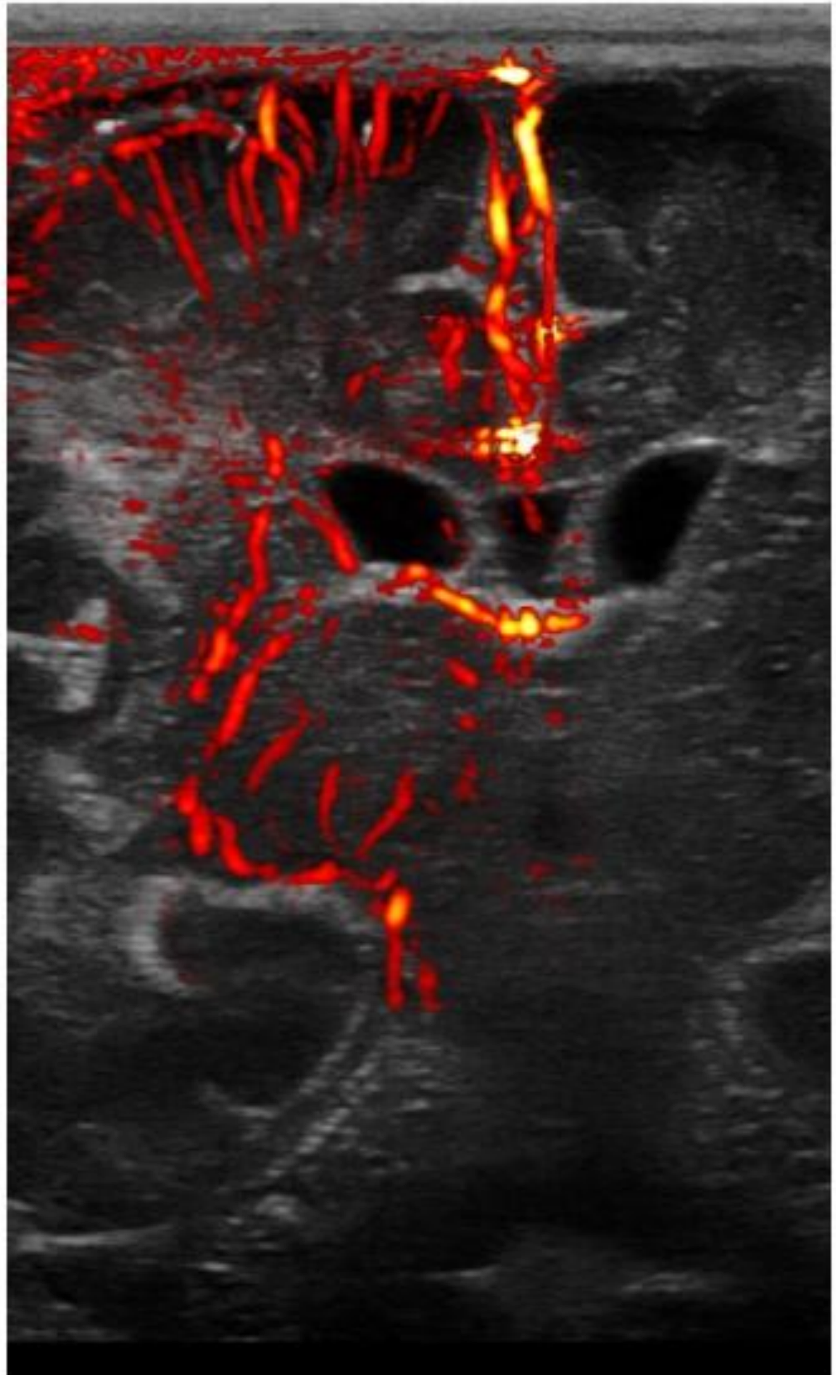
- ✔ Minimally invasive
- ✔ Quick recovery
- ✔ No sign of bone regrowth
- ✔ Low attenuation
- ! Smaller field of view

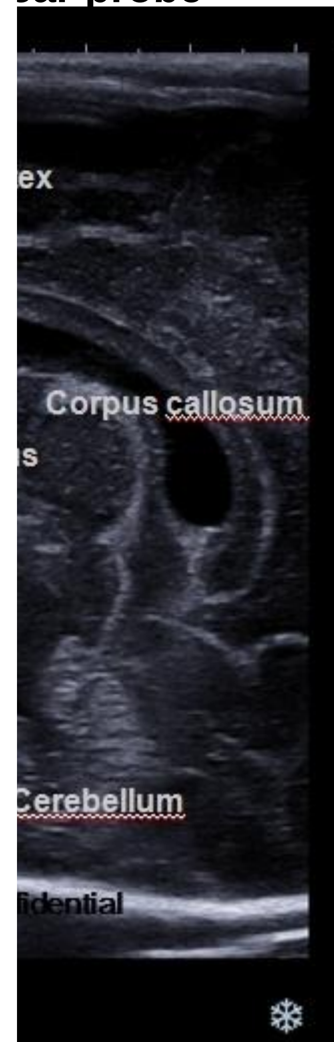
# Ongoing US

- Implementatio
- First clinical st ear probe



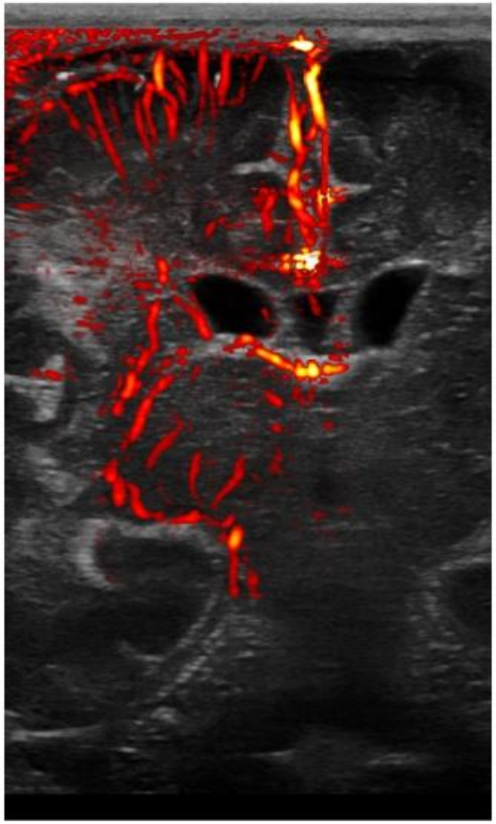

Typical Bmode

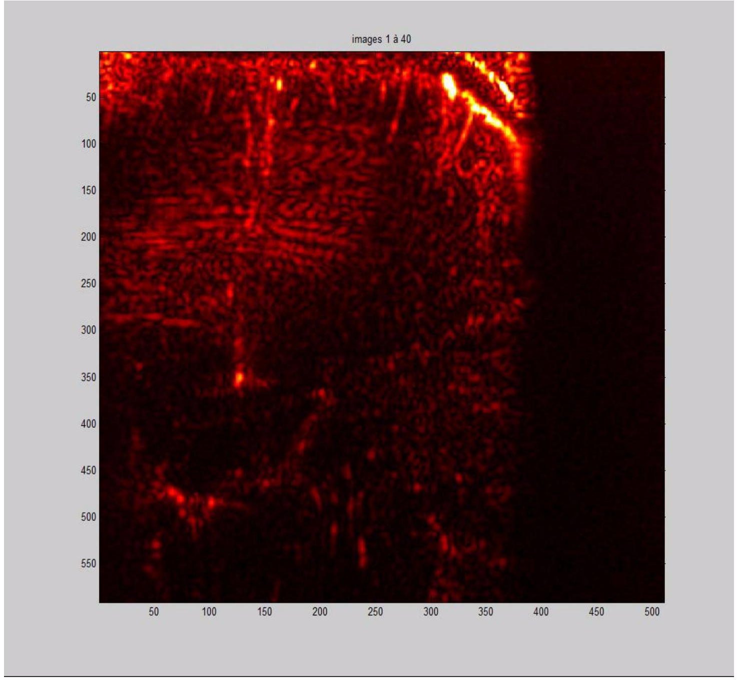




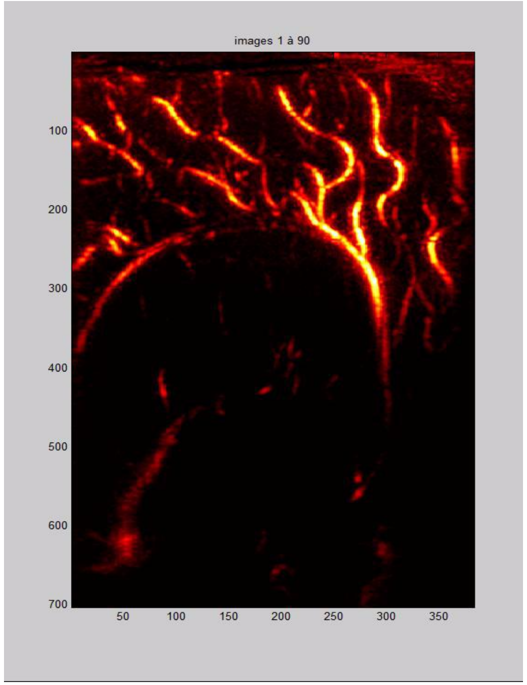
# Ongoing work (III) : Proof of concept of clinical fUS

## First in vivo data on preterm infants (transfontanel imaging)






Coronal view




Sagittal view

**Pulsatility on one single cardiac cycle**

**R Debré Hospital**
**C. Demene, M. Pernot, V. Biran, M. Alison, O. Baud, M. Fink, M. Tanter**

# Summary

- Ultrafast ultrasound imaging is linked to the concept of Holography in Optics
- Ultrafast imaging using the concept of plane or circular waves paves the way to tremendous applications for medical ultrasound
- Ultrafast plane wave imaging was initially introduced for Transient Elastography
- Ultrafast imaging is the key for quantitative and real time Elastography
- Ultrafast imaging technology has emerged thanks to video game industry
- Supersonic Shear Wave Elastography was the first clinical application of ultrafast imaging and led to the first ultrafast imaging commercial device
- Beyond Elastography, new modalities are already emerging today :
  - Ultrafast Doppler for complex flows or small vessels imaging
  - Conventional Bmode will be replaced by Coherent plane wave compounding
  - Ultrafast Cavitation Imaging
  - Ultrafast Contrast imaging
  - fUltrasound : functional ultrasound imaging of brain activation

# Thank You very much !



**Join us !**

**PhD and PostDocs positions  available**

**At Institute Langevin, Paris**