Multiwave Imaging and Elastography



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A difficult problem for radiologists : breast cancer detection

Ultrasound Images of different breast lesions

Begnin

Malign

Begnin



Fibrotic

Lesion

Carcinoma V Grade II

Viscous cyst



Good sensitivity but bad specificity

How to improve specificity ?

Multi-modality : superposition of two images, one morphology and one metabolic

Two examples : morphology / metabolic activity

Lung Cancer

54-year-old patient, primary lung tumor and extensive metastases.

PET scan protocol: 10.5 mCi FDG with 92 minute uptake time, 5 beds / 2 minutes per bed CT scan protocol: 130 kV, 30 mAs* Total scan time: 11 minutes





igure 4 A dedicated single-bed position study acquired after whole body acquisition allows for active intervention and optimisation of CT acquisition protocols. This is particularly helpful in regions of complex anatomy like the neck and upper abdomen. These authors use this capacity for evaluation of gastric cancers, performing studies without and with gastric distension. The images on the left represent those with the stomach collapsed whereas those on the right are following gastric distension with an oral fluid load and buscopan to minimise gastric motility.



PET/CT Scan

Multi-Modality Imaging

Superposition of 2 images each obtained with a single wave

One single wave is sensitive only to a given Contrast :)

Ultrasound to bulk compressibility,

Optical wave to **dielectric permitivity and optical absorption**,

Sonic Shear wave to shear modulus, viscosity

LF Electromagnetic wave to electrical impedance, conductivity X ray to density

Gamma ray to radio tracer distribution

Spatial Resolution depends on wave physics laws and on sensor technology.

Spatial resolution with one-wave imaging system

Spatial resolution δ ?

- z observation depth
- λ wavelength*I** transport mean free path

In strongly heterogeneous medium (**multiple scattering**), waves lost their coherence on a distance called the transport mean free path /*



Transport mean free path *I**

Distance needed for a wavefront to loose the memory of its initial direction. In all tissues **Ι*>** λ.



Optical wave in tissues /*~ 500 μm Ultrasound in tissues , 1 * > 1 m LF Electromagnetic waves, *I* * >> 1 m



Spatial resolution with one-wave imaging system

Spatial resolution δ ? 3 different regimes



Multi-Wave Imaging: A physicist approach



How to play Multiwave Imaging ?

Three potential Interactions between different waves

• The interaction of the first wave with tissues **Can generate** a second kind of wave

PhotoAcoustic Imaging ThermoAcoustic Imaging

• The first wave **IS TAGGED** locally by a second kind of wave

AcoustoOptical Imaging Electrical Impedance Imaging with Ultrasound



• A first wave travelling much faster than the second one can be used to produce *a movie* of the slow wave propagation

> Transient Elastography Shear Wave imaging (Supersonic mode)

A unique case that allows the observation of the near field of the slow wave inside the body,

I – A wave generates a second type of wave : Photo-Acoustics



Figure 3. Photoacoustic generation and detection. Black dots in the left panel represent regions of high optical absorption. When heated by a laser pulse, they launch acoustic waves, which are picked up by an ultrasound detector. The ultrasound waveform shown in the right panel is approximately proportional to the time derivative of the optical pulse.

Photo-Acoustics





Photo-(opto)-Acoustics $\Delta p - \frac{1}{c_{\star}^2} \frac{\partial^2 p}{\partial t^2} = -\frac{\beta}{c_{\star}} \frac{\partial H_{abs}}{\partial t}$ $H_{ab}(\mathbf{r},t)$: Energy absorbed per unit volume per unit time (W.m⁻³) For optical absorption: $H_{abs}(\mathbf{r},t) = \mu_a(\mathbf{r}) \times \phi(\mathbf{r},t)$ $\phi(\mathbf{r},t)$: Optical fluence (W.m²) $\mu_{\rm c}({\bf r})$: Optical absorption coefficient (W.m⁻²)

- X. Wang, Y. Pang, G. Ku, X. Xie, G. Stoica, and L.-H. Wang, "Non-invasive laserinduced photoacoustic tomography for structural and functional imaging of the brain in vivo," Nature Biotechnology 21 (7),
- 803-806 (July 2003).

II - A wave is tagged by another wave : **Tagging Photons with ultrasound**

Optical Speckle

Porteuse

Fréquence



Experimental results in vitro laser @790 nm + US bursts Imaging an absorbing inclusion

Agar Agar + Intralipid-10% + 1 inclusion 3 mm x 10 mm



L = 2.3 cm µs'=µs(1-g)= 6 cm⁻¹ US: 2.3 MHz, 4 cycles, 1 ms





More difficult to implement in-vivo because the tissue speckle has a coherence time smaller than 1 ms

« Photorefractive acousto-optic imaging in thick scattering media at 790 nm with a Sn2P2S6:Te crystal » *S.Farahi, G Montemezzani, A. Grabar, JP. Huignard, F. Ramaz Optics Letters (2010)* III - A wave produces a movie of another wave : Transient Elastography :

How to image elastic properties of tissues with millimetric resolution ?

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 Bulk Modulus (Compression) almost constant, of the order of 10^9 Pa, Fluctuations $\approx 5\%$ Quasi incompressible medium



 μ Shear Modulus, Strongly heterogeneous,
varying between 10 2 and 10 7 Pa
(A. Sarvazian)Young modulus
 $E \approx 3 \mu$

Human Body Seismology : Mechanical waves in soft tissues

 $\begin{cases} \text{Compressional Waves propagate at } c_p \approx \sqrt{\frac{K}{\rho}} & (\approx 1500 \text{ m.s}^{-1}) \\ \text{Shear waves propagates at} & c_s = \sqrt{\frac{\mu}{\rho}} & (\approx 1-10 \text{ m.s}^{-1}) \end{cases} \end{cases}$

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 : a Multiwave approach

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

$$\stackrel{1 \text{ mm}}{\frown} \stackrel{1 \text{ à 5 m.s}^{-1}}{\frown} 5.000 \text{ images.s}^{-1} !$$

• 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 :

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

1D Transient Elastography



1994

In a first step (1994) we observed transient shear waves with a single ultrasonic transducer . Then in 2000 a company ECHOSENS was created (45 persons) to develop the Fibroscan to get a global measurement of liver elasticity

M.Fink, S. Catheline, L. Sandrin

2001

From 1D Transient Elastography to SuperSonic Shear Wave Imaging











Research Work in Laboratoire Ondes et Acoustique (now Institut Langevin)

2D Transient Elastography needs an ultrafast ultrasound imaging system

How to make an ultrafast ultrasound scanner ?

: Time reversal



128 shots for one image,50 frames /second



1 shot for one image, 5000 frames/s

Transient Elastography and Ultrasonic Radiation Force



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

A. Sarvazian, J. Greenleaf, C. Nithingale, G. Trahey, M. Fink, M Tanter

Shear Wave Bandwidth generated by the Ultrasonic Radiation force ?



How to measure the displacements induced by shear waves ?

Tissues behave as random distributions of scatterers. **The speckle is moving with shear wave** One repeat ultrasonic shots at high rate (> 5000 shots/s) and create an ultrafast movie



0 ms

Moving window cross-correlation gives the axial displacements $u_z(x, z, t)$

It is possible to measure **displacements of 1** μ (λ /1000) between 2 consecutive shots



Multiwave Imaging of a hard inclusion



Movie duration 20 ms

<u>Ref:</u> Supersonic Shear Imaging: a new technique for soft tissue elasticity mapping. J. Bercoff, M. Tanter and M. Fink, IEEE Trans., April 2004

A Simple Inversion Algorithm

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

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

Compressional shear

- Assumptions:

- 1) The medium is considered as infinite, isotropic, purely elastic and locally homogeneous.
- 2) $\lambda \gg \mu \Rightarrow$ 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

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

Hard Inclusion with a liquid zone



The Evolution of Ultrafast Imaging Technology

SuperSonic Imagine was founded in September 2005 by Jacques Souquet, 120 employees, Aix en Provence and Seattle

UPERSONIC

Aixplorer ©

Time Reversal Prototype V1 HDI 1000 Prototype 1996-2002 2004-2005 2006-2007

Echographic System with Real-time and Quantitative Elastography









First SSI experiment : May 2002 45 Minutes processing



SSI Prototype 2006 some seconds processing



October 2007 0.2 seconds processing

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

Shear wavelength : typicaly 10 mm

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



Medical applications of Elasticity Multiwave Imaging

- Breast
- Tyroid
- Liver
- Kidney
- Muscle
- Vascular
- Cardiac
- Eye
- Prostate
- Monitoring therapy (RF ablation, HIFU)

Breast Imaging



Invasive ductal carcinoma

This secondary lesion is an IDC Grade III & HR+ of 15mm.

Emax > 150kPa in the center of this 3mm lesion.

Breast Imaging



IDC Grade I, partially necrotic center proved by histology.

Emax > 200kPa on surrounding tisue.

E = 70kPa in the center.

Breast Imaging



Emean < 30kPa and totally homogeneous.

Fibro-adenoma

Diagnostic impact in breast :







Shear Wave Imaging for Liver fibrosis Staging

Clinical Study on 118 patients with Hepatitis C



F ≤3 versus F ≥4





Prostate – multiwave imaging



Dynamics of Muscle 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

Shear Wave Dispersion

 Does the shear wave velocity depends of frequency ?

• Does
$$c_s = \sqrt{\frac{\mu}{\rho}}$$
 always valid ?

- Origin 1 : viscosity
- Origin 2 : guides wave

SuperSonic Shear Imaging : Liver in vivo

36 mm



2000 frames per second

26 Years old healthy volunteer

- Intercostal Exam
- Linear Probe L7-4 4-7 MHZ 128 elts.
- Mechanical Index Push 1.4 Imaging 0.7
- ISPTA Push+ Imaging
 600 mW.cm⁻²
- Less energy deposit than Color Doppler !!!

M. Tanter, G. Montaldo, T Deffieux, JL Gennisson, J Bercoff, M.Fink

Tissue Rheology with Shear wave dispersion



Can we assess viscoelastic properties of tissues using SSI ?

SuperSonic Wave Generation

Plane Wave Approximation is valid !!!

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

$$\phi(x) = \frac{\omega}{c} x$$

Shear Wave Phase Speed (m.s⁻¹) Versus Frequency



Can we assess viscoelastic properties of tissues using SSI ?



T. Deffieux, M. Tanter, G Montaldo, J. Bercoff. M. Fink

Shear Wave Spectroscopy : a broadband approach



What Viscoelastic model ?

Isotropic, homogenous, linear, viscoelastic



Wave Dispersion on arterial phantoms (agar-agar, gelatin)





Wave velocity is strongly reduced when shear wave is generated in a thin layer : guided propagation

Guided shear wave along a tube



 Guided shear wave is dispersive : phase velocity is a function of the frequency

In vivo application

- In vivo experiment on healthy volonteers
- Dispersion curves behavior is similar to phantom
- Measured shear modulus : μ^{\sim} 90 kPa





Real Time Elasticity of the carotid during one single cardiac cycle

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





Athérosclérosis, fibrodysplasia, myocardial fibrosis...

		Intra-individual	Reproducibility
N=70 Healthy Volunteers	Mean	Reproducibility (s.d)	(relative error)
local PWV (m/s)	5,45	0,68	12%
Shear wave velocity (m/s) @			
900 Hz	5 <i>,</i> 68	0,2	4%

Arterial stiffness estimation

Propagation of shear wave (Lamb wave) in the arterial wall

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Exemple of a hard plaque

MultiWave Imaging

One wave gives the contrast. The other wave gives the spatial resolution.

- Ultrasound based Shear Wave imaging
- MRI based Shear Wave imaging
- Shear Wave AcoustoOptics
- AcoustoOptics
- PhotoAcoustics
- Electric Impedance / Ultrasound Imaging
- Current Density / Ultrasound Imaging
- US Imaging of mechanical contraction due to Action potentials
- MR Imaging of Ultrasonic Radiation force
- Transient Shear Waves / OCT



Multiwave imaging and super resolution

Mathias Fink and Mickael Tanter

Interactions between different kinds of waves can yield medical images that beat the single-wave resolution limit.

Mathlas Fink is director of the Langevin institute at the Ecole Supărisure de Physique at de Chimle Industriales de la Ville de Parts in Parts. Midwail Tanter is a research professor in the institute, They, along with strothers, founded SuperSonic Imagine in 2005.

The human body supports the propagation of many lands of waves, each of which can provide an image with a specific type of information. For example, ultranome waves reveal a fastart density and how it responds to compression forces, and methanical shear waves indicate how tissues respond to shear forces. Low-frequency electromagnetic waves as sensitive to electrical conductivity: optical waves tell about optical absorption. In all those circumstances, physiolatic have servicen to obtain the best overall contant and resolution. Now, after decades of work, we are pushing against the physicallimits inference in each imaging modality. As desorfied in the box on page 36 that limit is, in many cases, set determined by wavelength.

Physiciane quickly realized that for medical imaging and diagnosis, one ways toosencome the inhearest institution of singlemode imaging is to combine different imaging modalities. Thebasic idea of positron emission homography and computed tomography – is to associate the high-resolution morphological image of a first modality (2T) to an image of the second modality (PET) that is poorly resolved but that provides a clinically interesting contrast, revealing metabolic activity in this case. A second example of multimodality imaging, used for mammography, combine ultranoad and x-ray images. However, multimodality imaging remains externely onity and coestrained by the inherent physical limits of each sepante imaging mode.

New approaches

Is there any way to improve diagnostic capabilities other than with multimodality imaging? Two scientific communities have suggested new research directions. One line of attack, called molecular imaging, was proposed by chemists and biologists. It differs from traditional imaging in that bioconsriers are used to help image particular targets or pathways. Those biomarkers interact chemically with their surroundings and thereby increase the contrast.

The other approach was proposed independently by various groups in the physics community. It consists of combining two different waves – one to provide contrast, another to provide spatial resolution – to build a new kind of image. Because of the way the waves are combined, malifwave imaging produces a single image with the best contrast and resolution properties of the two waves. Multimodality imaging, on the other hand, wiles on the analysis of two images, each limited by the contrast and resolution properties of the wave that generated it.

28 February 2010 Physics Today

Three different types of wave interaction can be exploited in multiwave imaging. In one application, the interaction of one kind of wave with fissue can generate a second kind of wave. In thermoacountic imaging, for example, absorted electromagnetic indiation causes a transient change in temperature that radiates an ultrason ic wave through thermal expansion (see the article by Stanisbar V. Emellance, Pai-Chi Li, and Matthew O'Donnell in Printic's TCDA, May 2009, page 34).



Figure 1. Conventional versus uhrefast ukrasoric imaging (a) in conventional uhrasound, a kochadan successionly fecusar 160 or more beams into a madium and processes the advocquent backsattand advocago generate a single image. (b) in ukrafast imaging, a plane wave probes the whole medium in a single shoc. Again, the backsattened echoes are processed to produce the ultrasonic image.

