Ultrasound : more than just a non ionizing imaging modality

esi European Scientific Institute
esipap...

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Professor @ the University of Lyon

CREATIS

Outline

- Ultrasound basic physical principle
- Conventional clinical application of medical ultrasound imaging
- Ultrasound to guide radiation therapy
- From photo-acoustics to X-acoustics
- Ultrasound a competitor to radiation for cancer therapy?

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- **Ultrasound basic physical principle**
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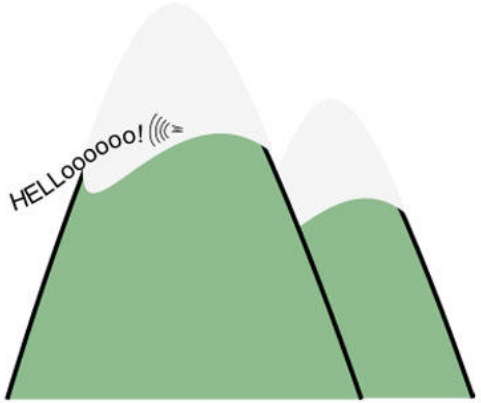
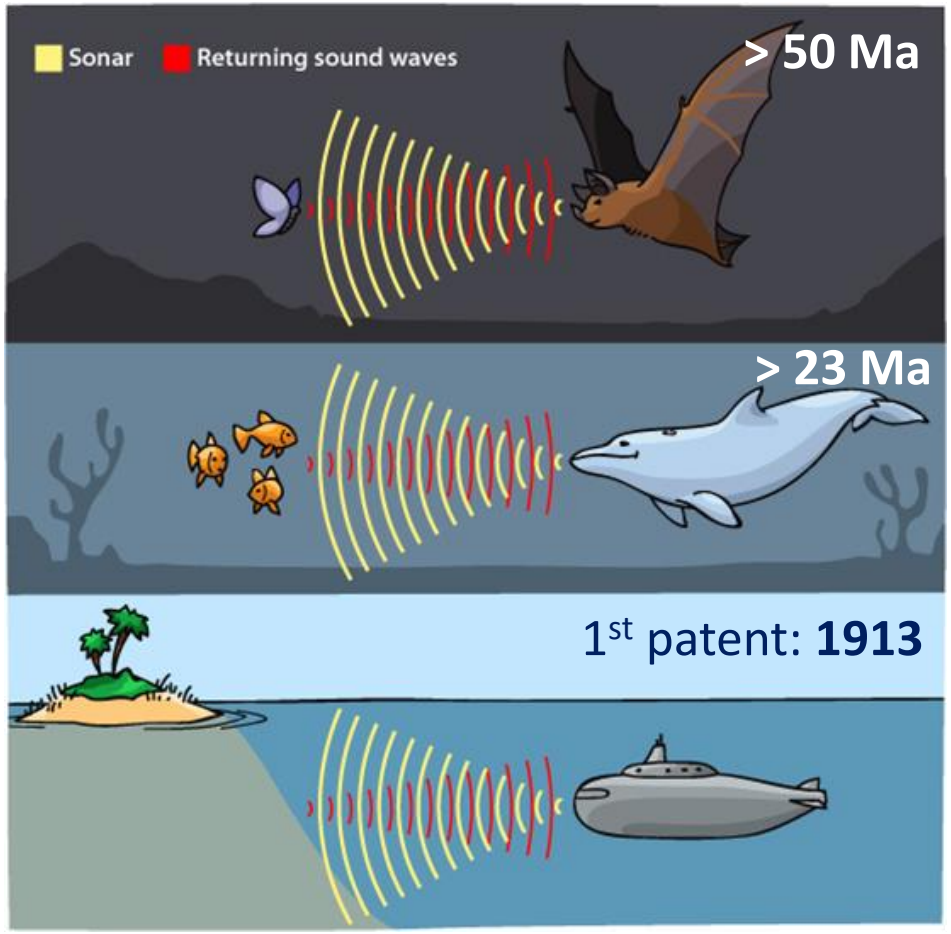
Echography: imaging based on the collection of echoes



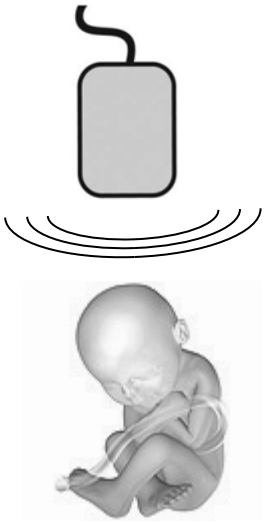
https://www.youtube.com/watch?v=TAliq8lXCZE
https://www.youtube.com/watch?v=p8GcHoSIPDg

Sens the environment with sound waves: a natural phenomenon

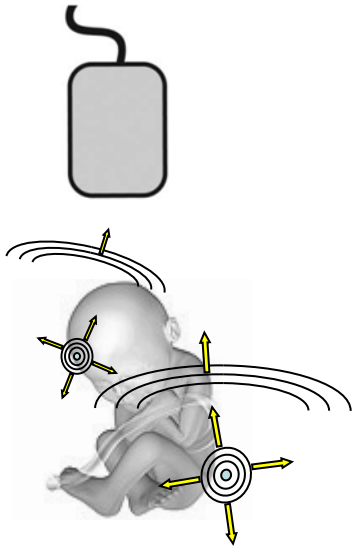


- **Medical ultrasound imaging**
  - 1st use in 1956 in Glasgow
  - becomes popular in the 70s

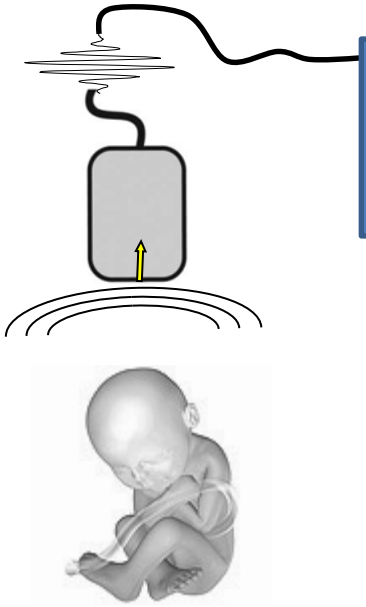
Get an image in 3 steps



Step 1:
US generation



Step 2:
Wave tissue interaction



US system with a lot of signal processing

Step 3:
Echoes collection and signal processing

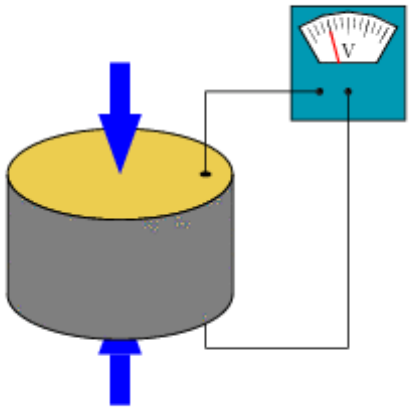
Images from wikipedia

Probes to produce and collect ultrasound waves

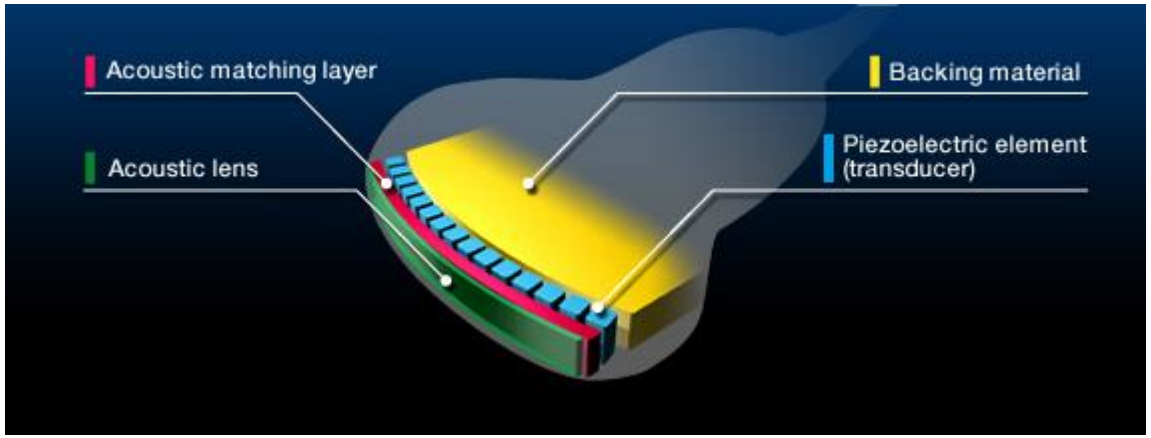
The probe is the sensing part of the system

It is used in transmit and receive
- in tx: electrical energy is transformed into acoustical energy
- in rx : acoustical energy is transformed into electrical energy

The probe material is typically a piezoelectric material

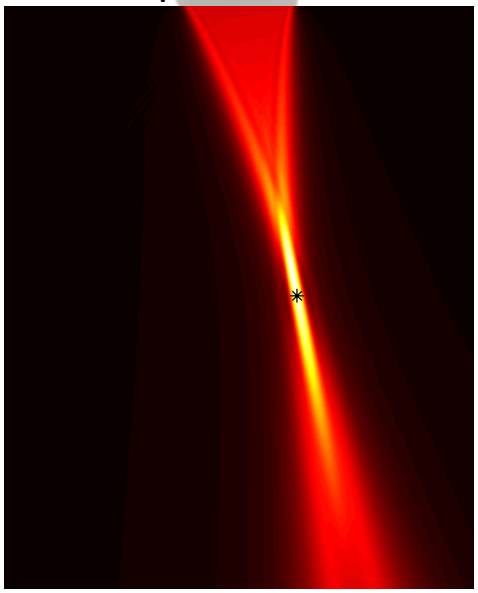


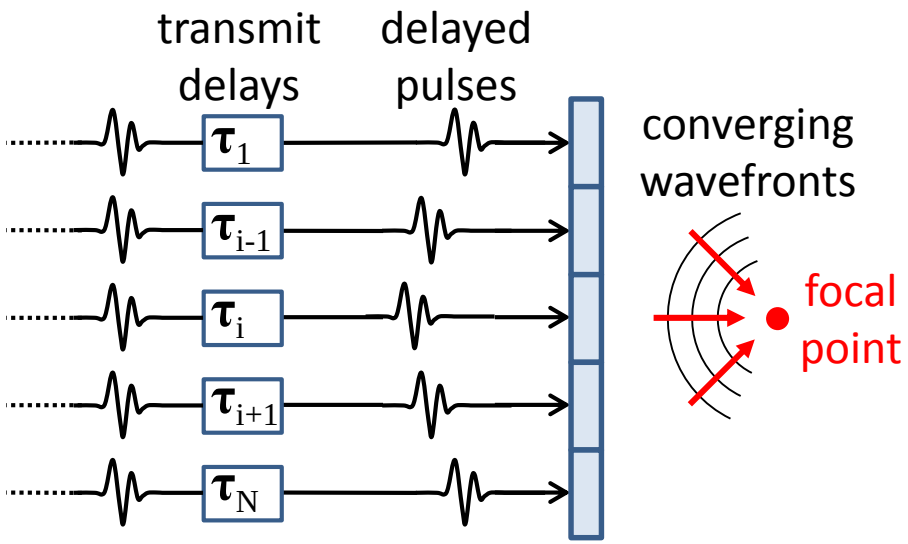
www.wikipedia.fr



sources: www.ndk.com/en/sensor/ultrasonic/basic02.html
www.youtube.com/watch?v=cI7ULKNhVcw

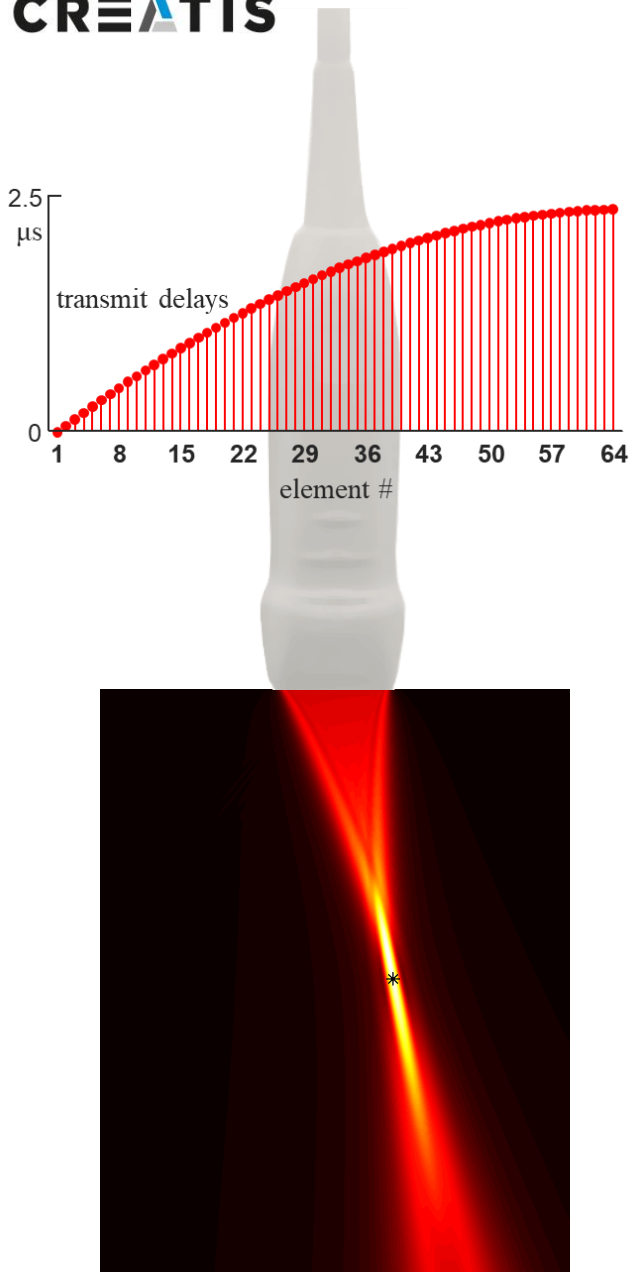
RMS pressure field

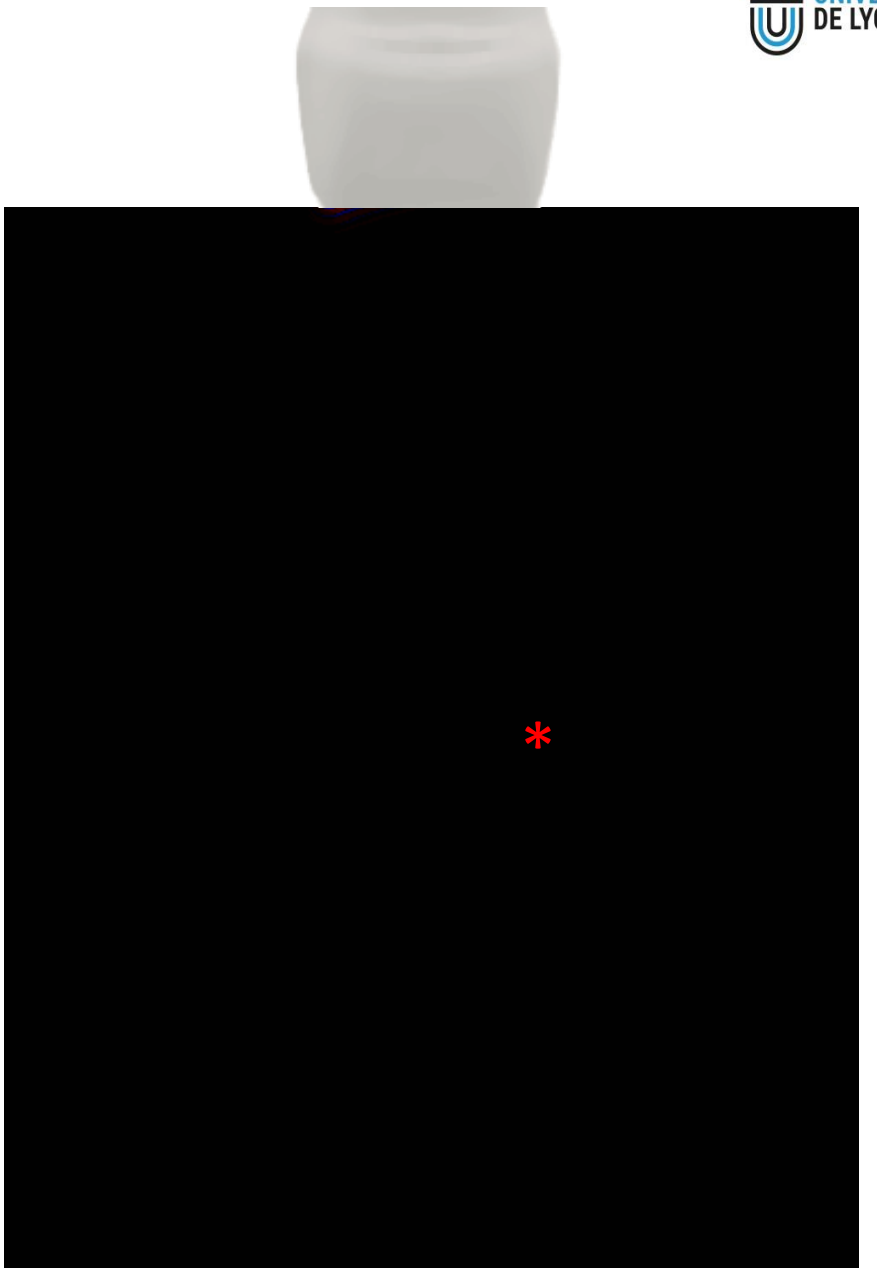




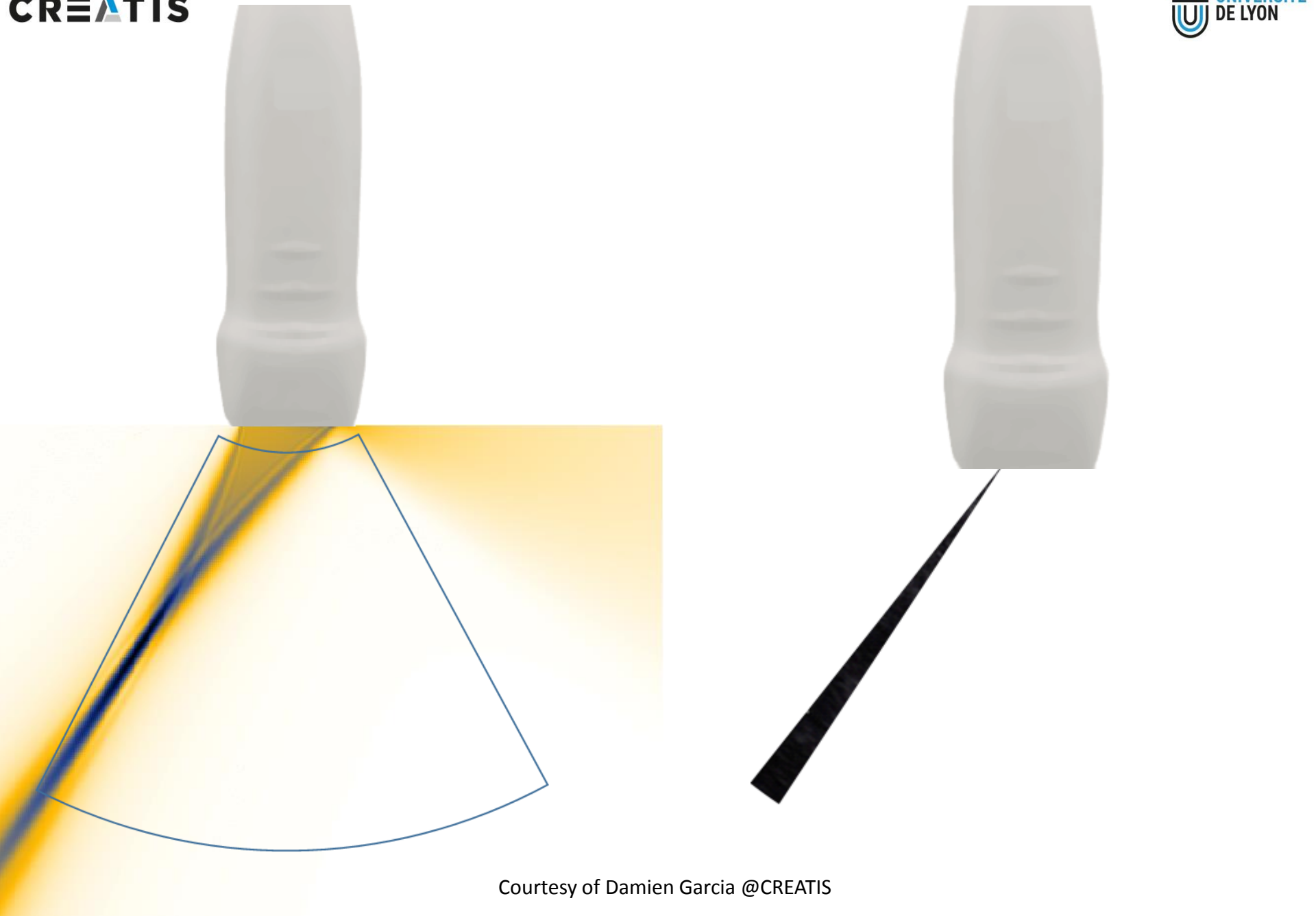
Courtesy of Damien Garcia @CREATIS

keywords
- transmit delays
- focal point



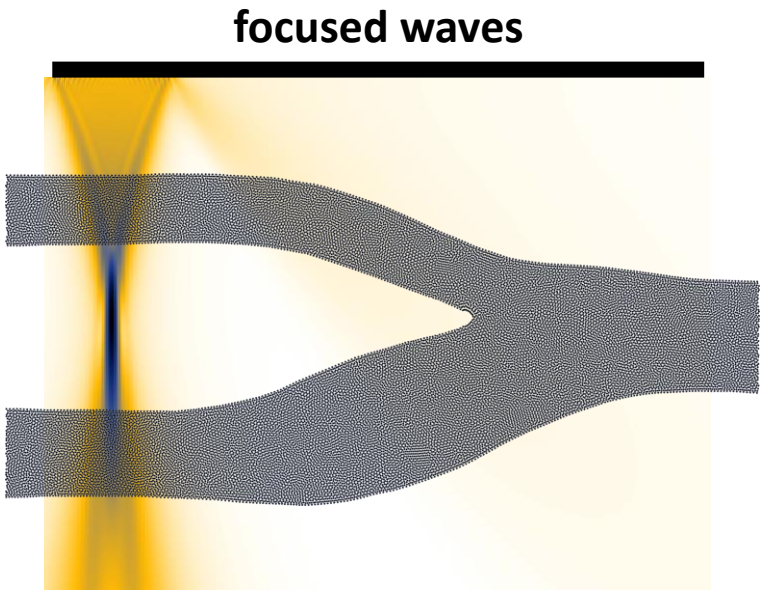


Courtesy of Damien Garcia @CREATIS



Courtesy of Damien Garcia @CREATIS

Courtesy of Damien Garcia @CREATIS



Courtesy of Damien Garcia @CREATIS and Trush et al

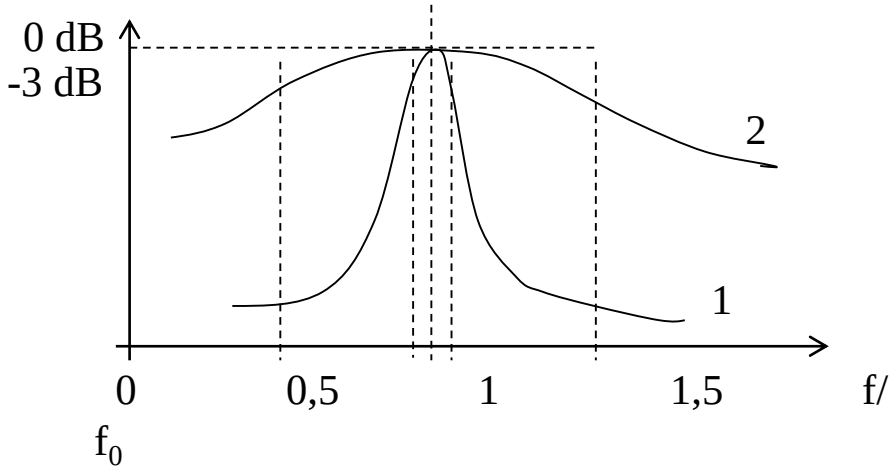
Important frequency caracteristics

Central frequency f0 and **Bandwidth** BW

Frequency response = Fourier transform of the impulse response

(1) narrow band

(2) large band



Fractional bandwidth = BW / f0 in %)

☝ **Frequency ↗ ⇨ Resolution ↗ but Penetration depth ↘**
Larger bandwidth could permit more generic probes

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Medical application: fetal growth monitoring

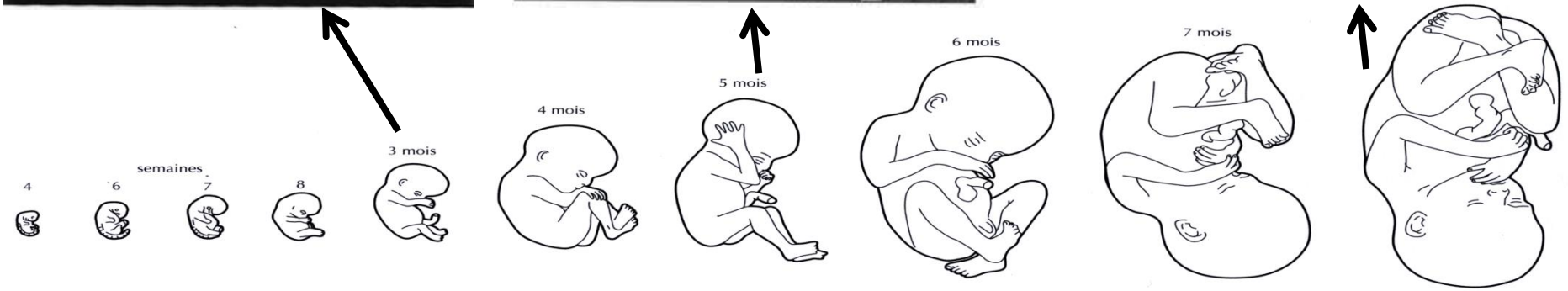
In France: 3 exams during pregnancy

- between 9 and 14 weeks
- between 20 and 22 weeks
- between 32 and 34 weeks

11 weeks

20 weeks

31 weeks



Abdominal

- Requisites:
  - Deep penetration
  - Wide field of view
  - Moderate footprint
- Solution:
  - Low frequency (a few MHZ)
  - Convex probe

Medical application: fetal growth monitoring

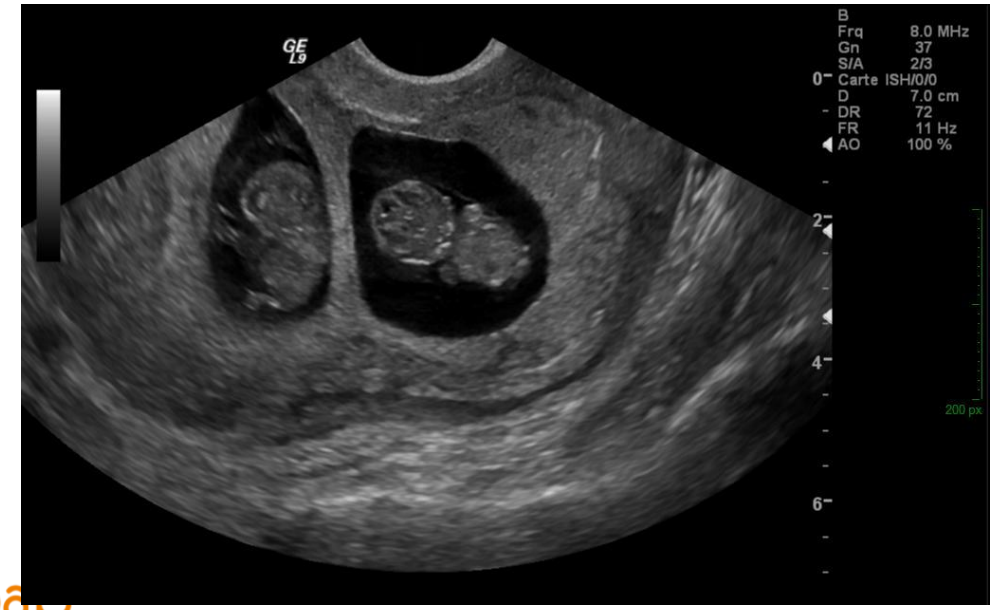
Echo 1: Goal

determine age of the pregnancy

establish the normal ongoing of the pregnancy and growing of the baby

determine if there is a multiple pregnancy

The type of the probe: depends if the exam is done intra vaginal or externally (depends on the size of the fetus)

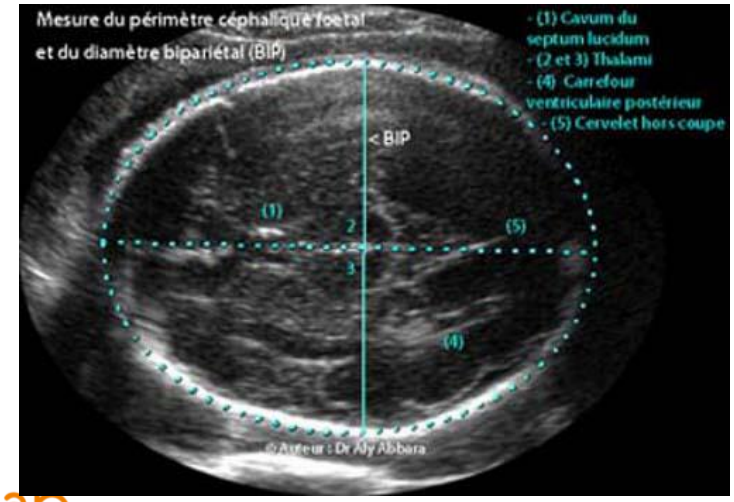


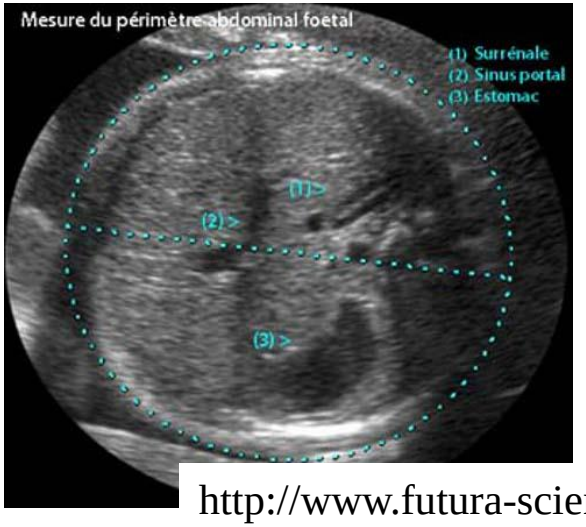
Surprise we are two ☺

www.mamo.fr

Measurement of the neck clarity
Thickness of the skin at the neck
Marker of the risk of trisomy
Markers are positioned in the image and the distance is calculated automatically

Measurement of the abdomen and cranium size ➔ age of pregnancy
Manual positioning of markers and automatic size calculation





http://www.futura-sciences.com

Medical application: fetal growth monitoring

Echo 2: Goal

Complete morphological exam. All organs are verified and measured. The exam necessitated a high concentration by the practitioner

The vitality of the fetus is evaluated (cardiac activity and motion of the fetus)
Evaluation of the placenta

Evaluation of the quantity of amniotic liquid

Important (or not) for parents : gender of the future baby

Girl or boy?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- -
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HDD:95% Free
CINE REVIEW
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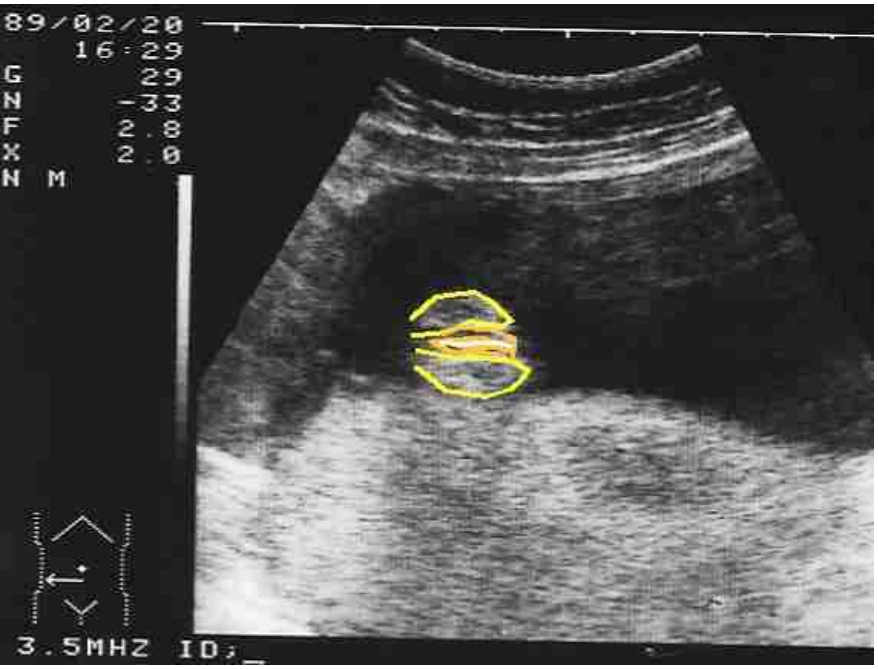
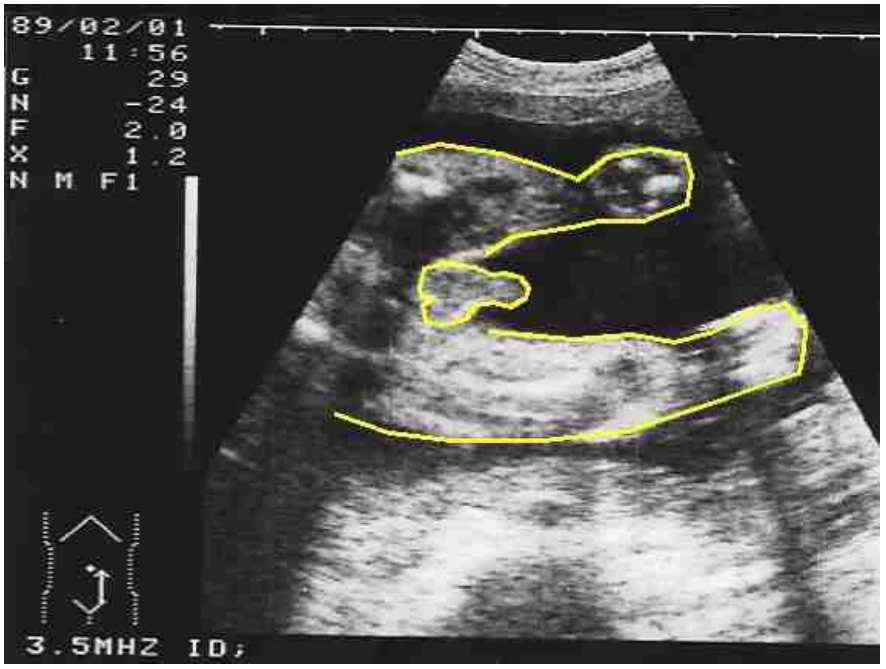
www.mamo.fr

Is it easier with some help;)





http://www.ac-grenoble.fr/

Medical application: fetal growth monitoring

Echo 3: Goal

Ensure everything is OK

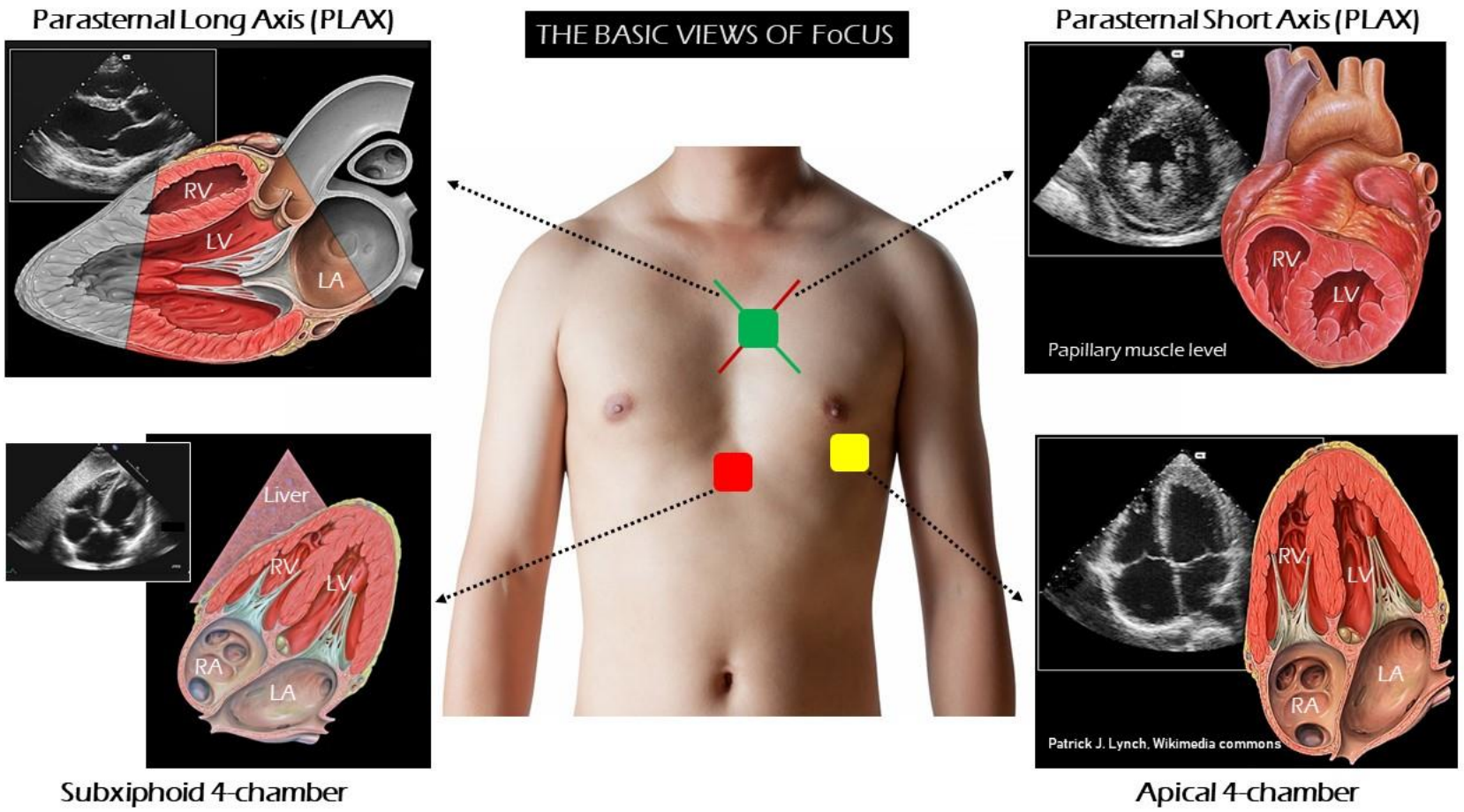
Again some measurements (for instance one verifies that abdomen and cranium increase proportionally)

The overall situation is evaluated (amniotic liquid, position of the fetus)

Last souvenir in 3D

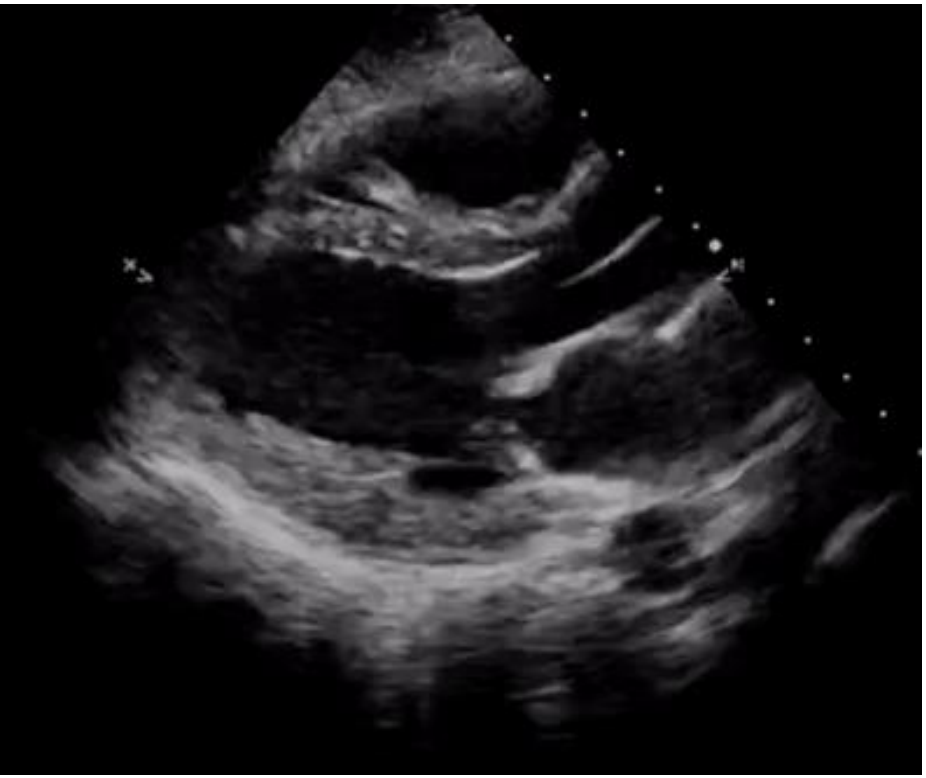
Cardiac ultrasound
(echocardiography)

- Requisites:
  - Large organ
    - Good penetration
    - Wide field of view
  - Very small footprint (few cm)
- Solution:
  - Low frequency (few MHz)
  - Phased array probe

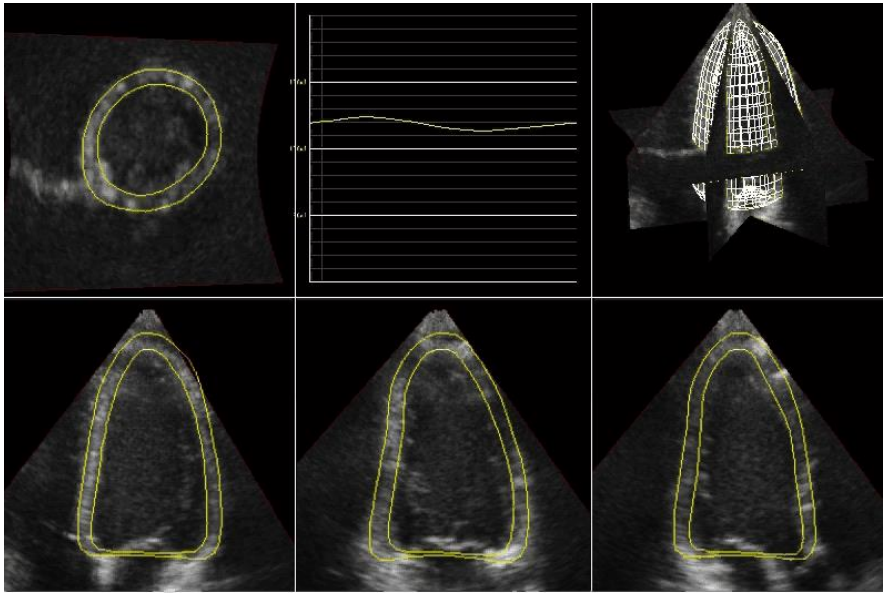


www.renalfellow.org

Examples



Parasternal long axis view
of a healthy subject
www.renalfellow.org



Left ventricle functional assessment
From 3D US (courtesy L. Lovstakken)

Advanced example: flow in a Ventricular septal defect

- Perimembranous ventricular septal defect (significant shunt)
- 36 days old, 4259 gr.

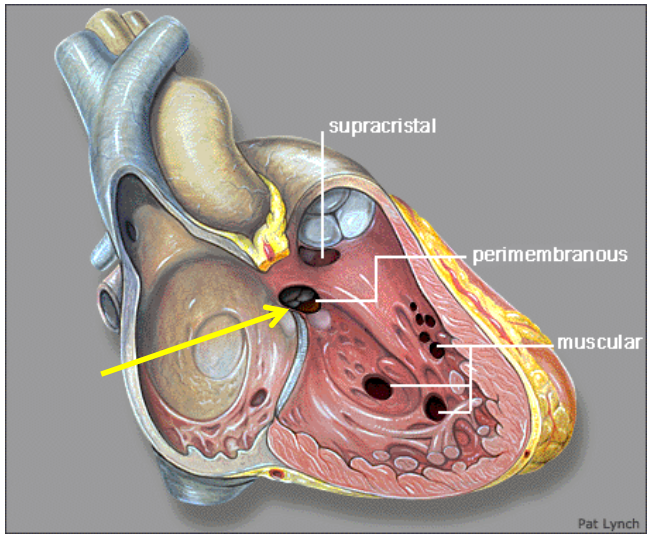
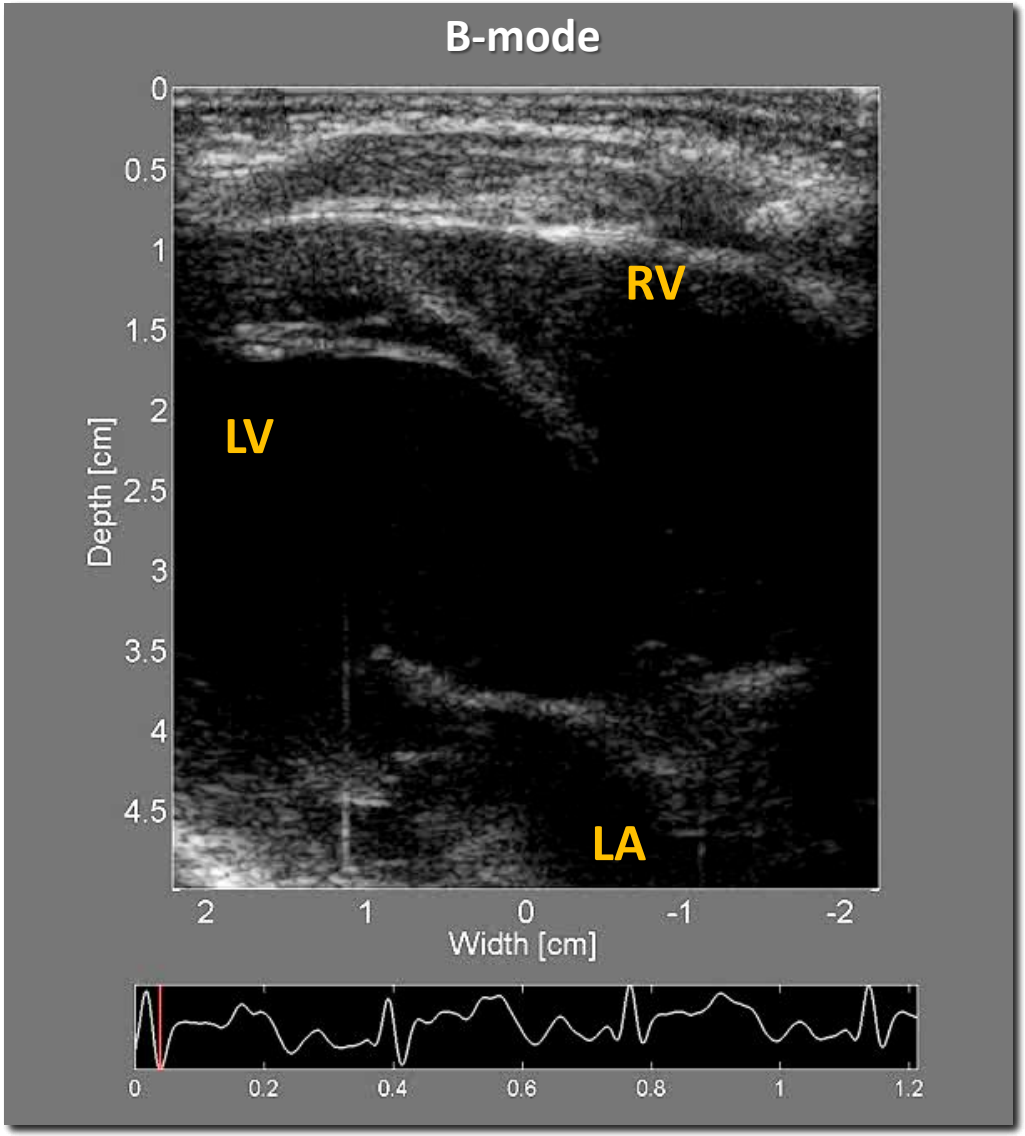


Image source: *Wikipedia, Pat Lynch*

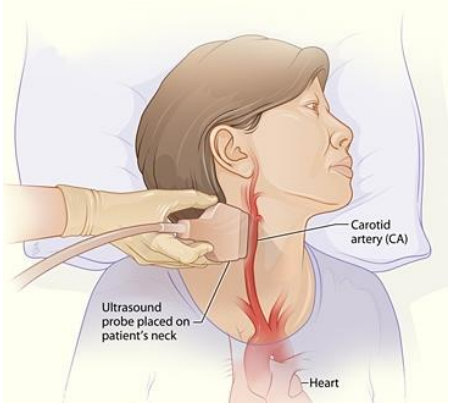


Courtesy Lasse Lovstakken

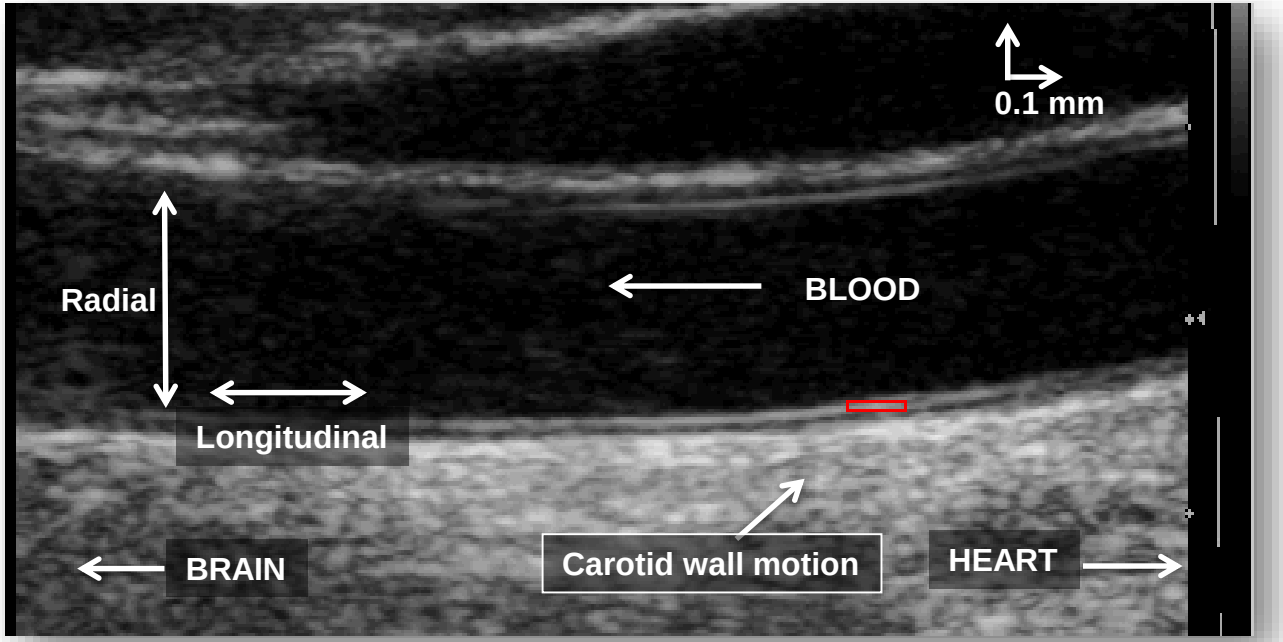
Vascular

- Requisites:
  - Fine details
    - Good resolution
  - ROI close to the skin
    - Moderate penetration (few cm)
  - Doppler flow imaging
- Solution:
  - Medium frequency
  - Linear probe

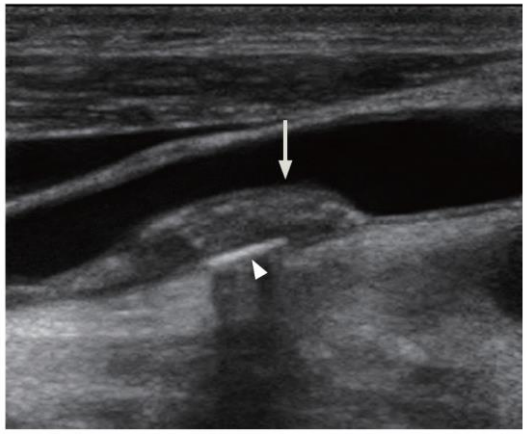
An example of US imaging in an artery



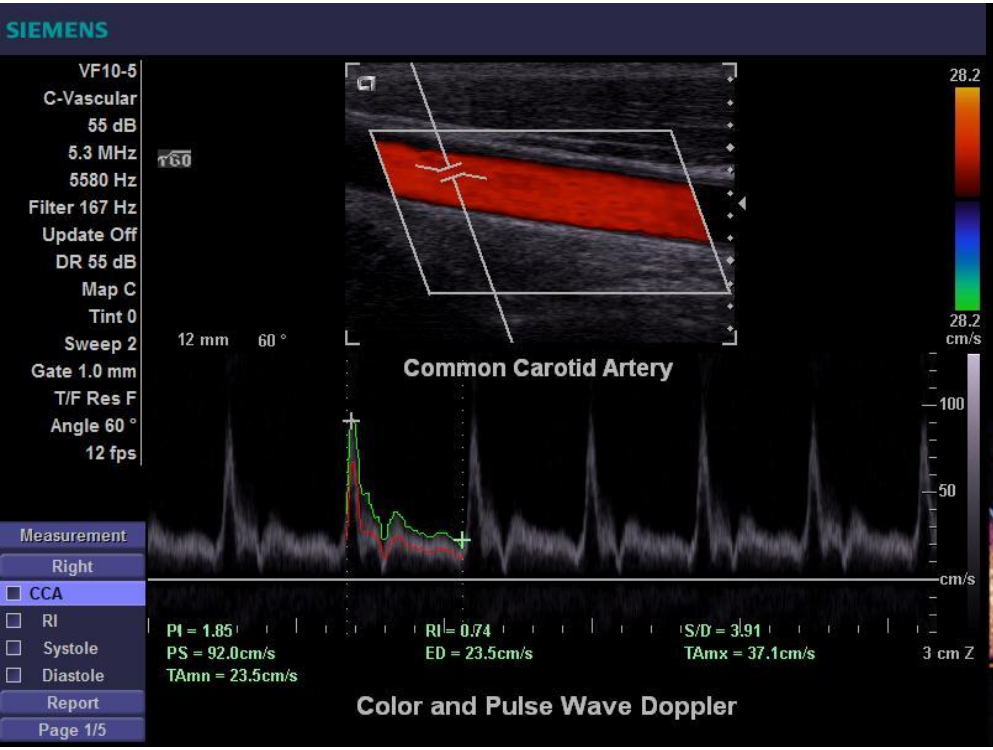
Healthy exam

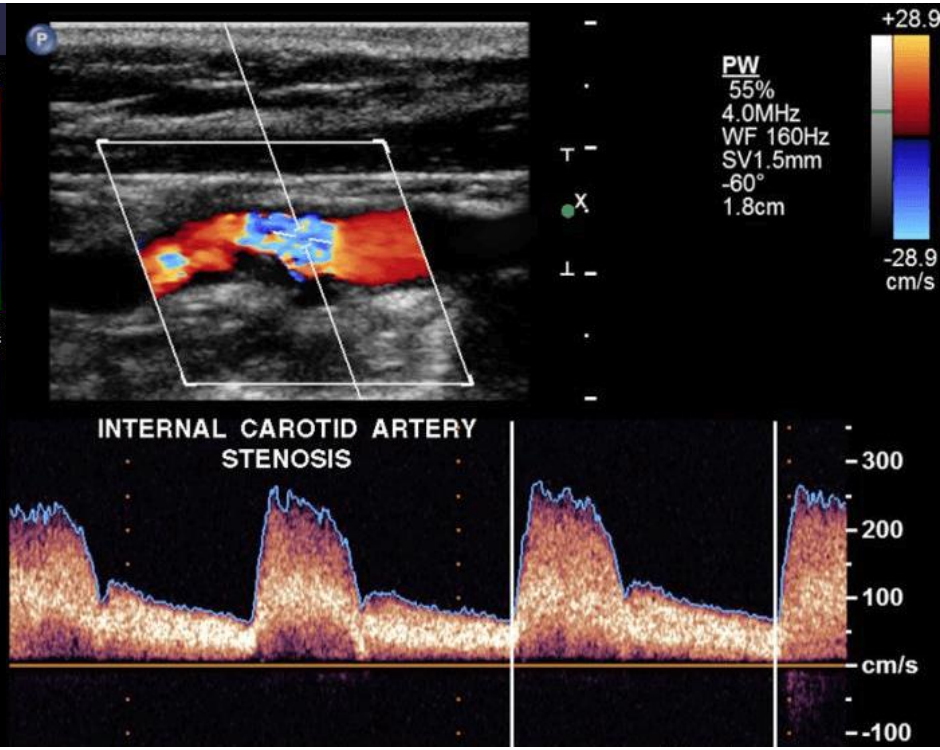


Plaque



Additionaly colour Doppler or spectral Doppler

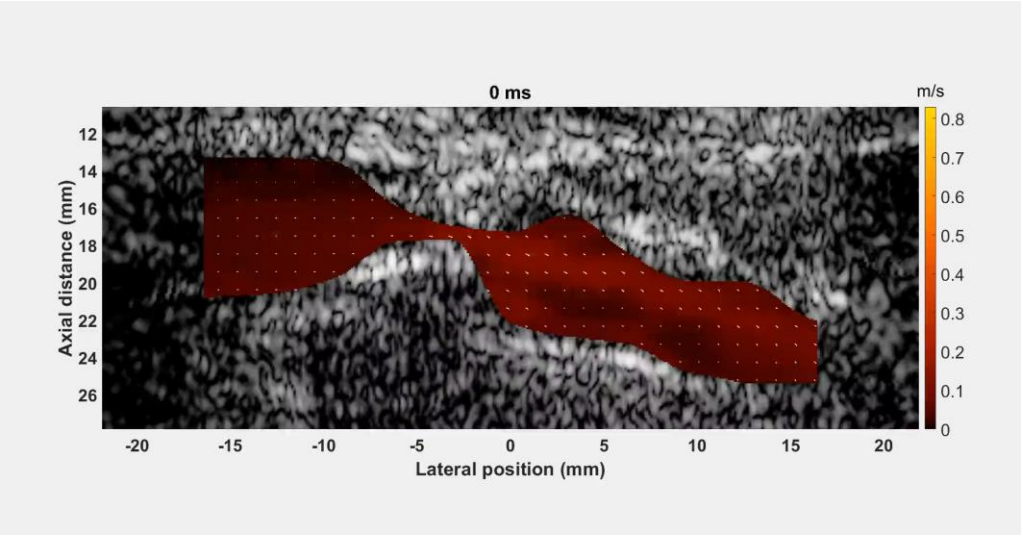


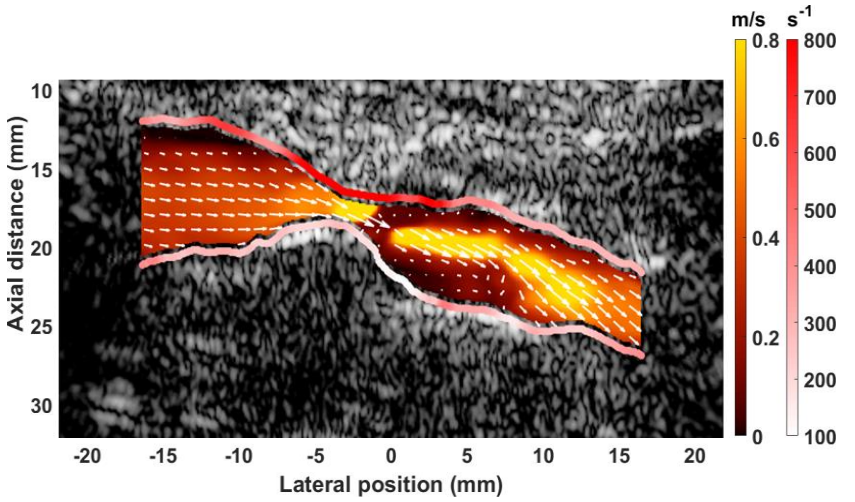


Healthy exam

Plaque

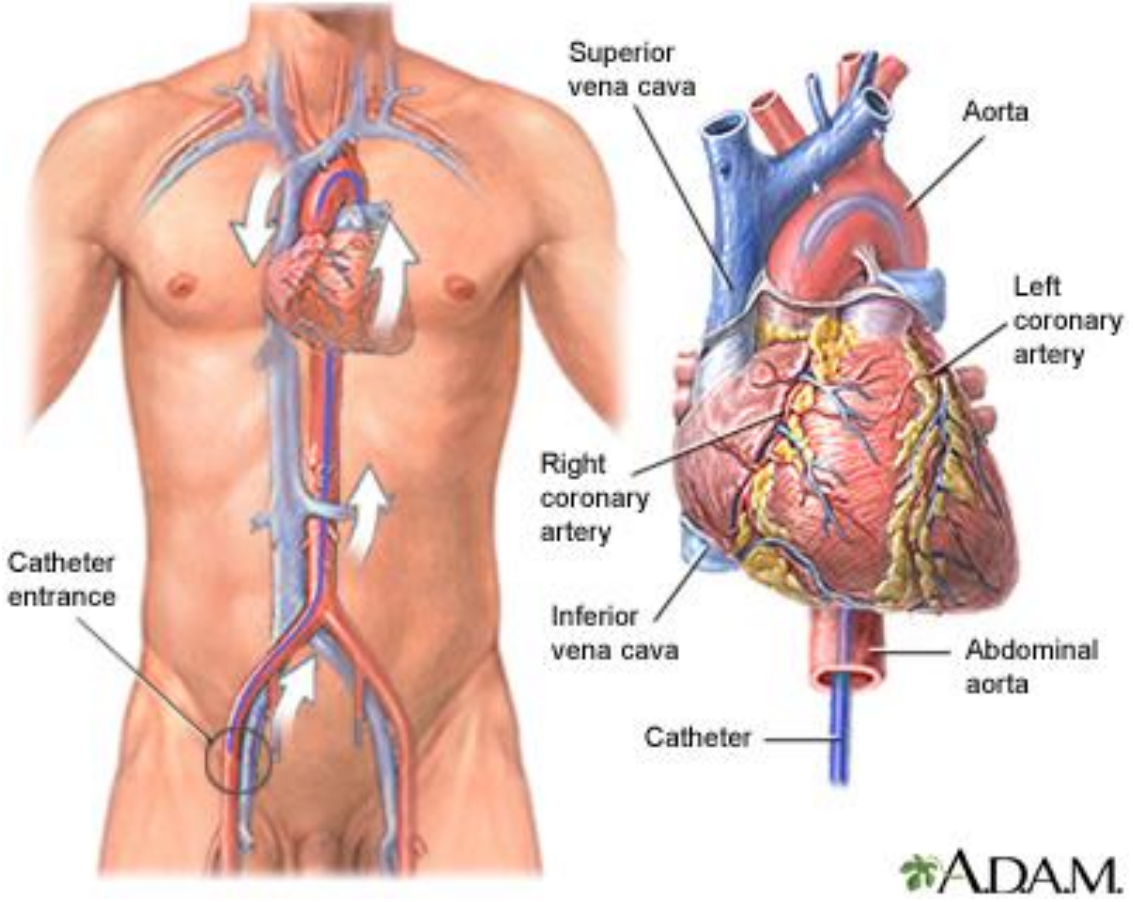
Flow and max wall shear rate during the sequence





From V. Perrot, Univ. of Lyon CREATIS, collaboration NTNU Trondheim

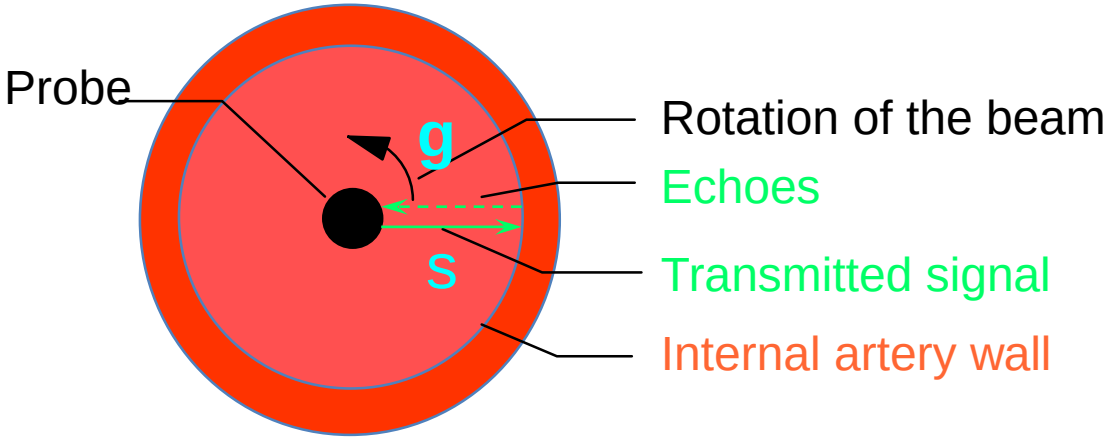
Intravascular ultrasound (IVUS): insertion of a catheter for the studies of the coronary arteries



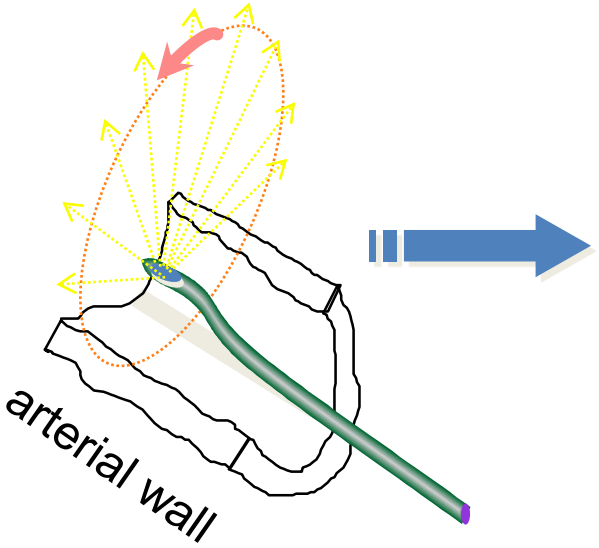
http://keckmedicine.adam.com/

Intravascular ultrasound: IVUS

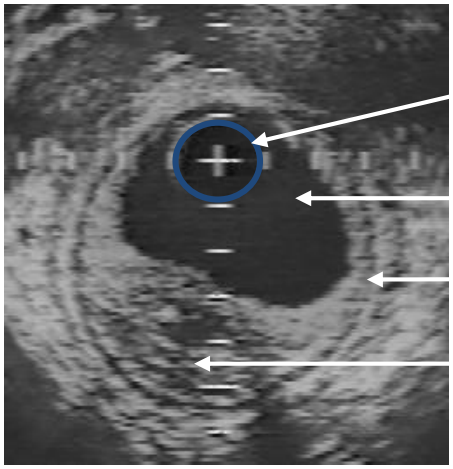
f = 30 MHz
Diameter = 1mm



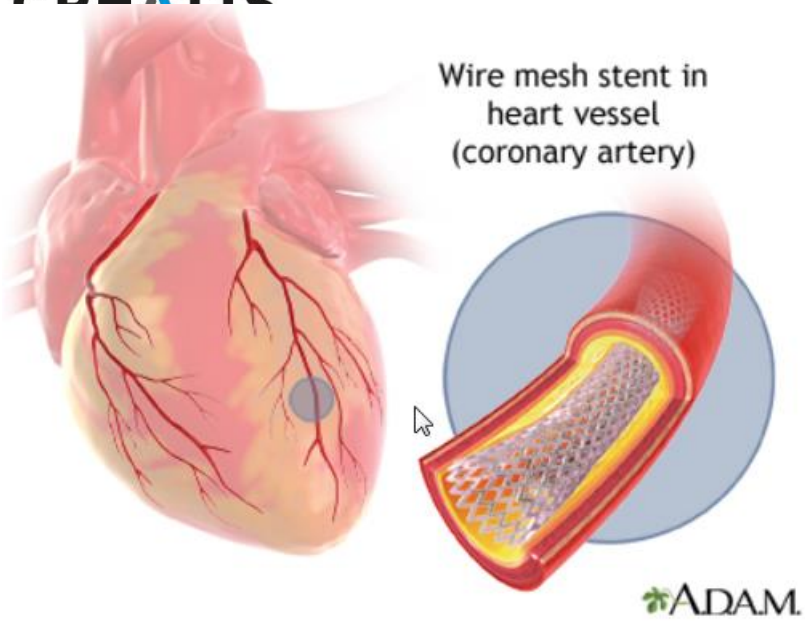
ultrasound beam

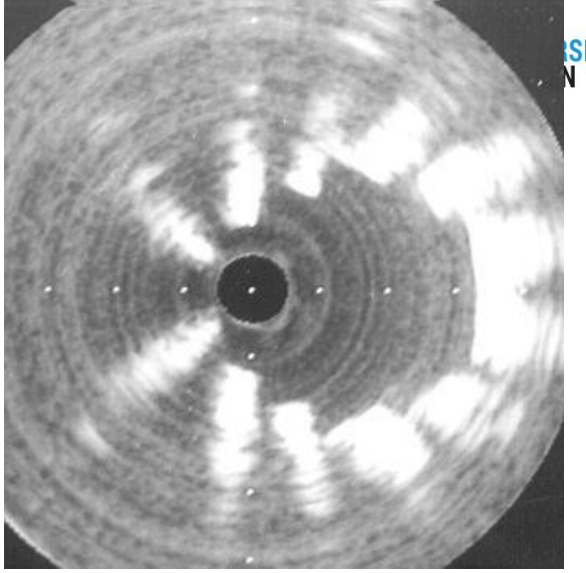


IVUS image

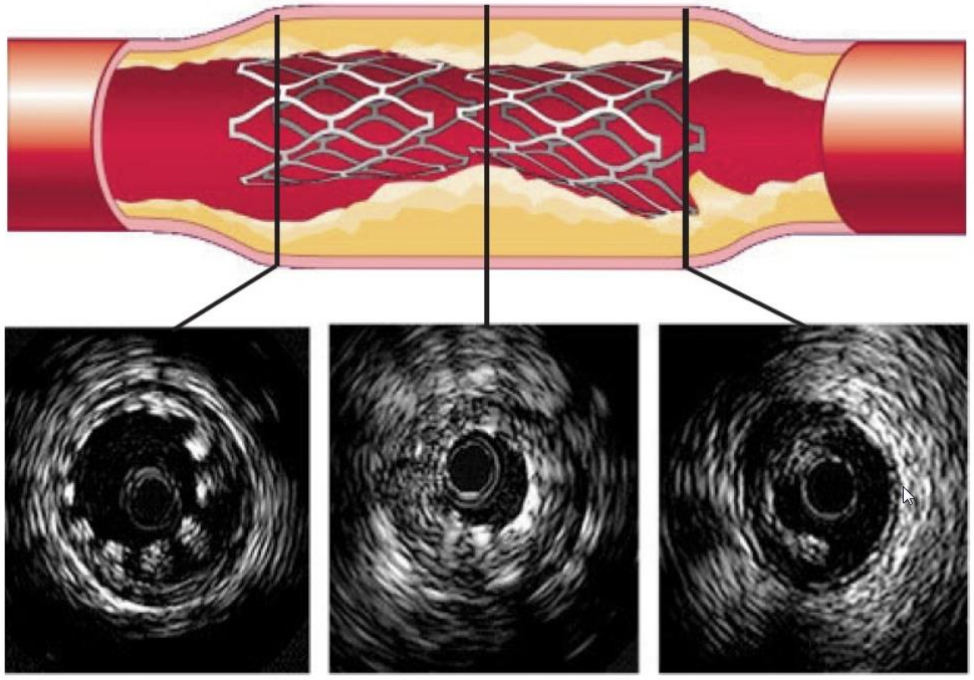


Courtesy of Christian Cachard (CREATIS Lyon)



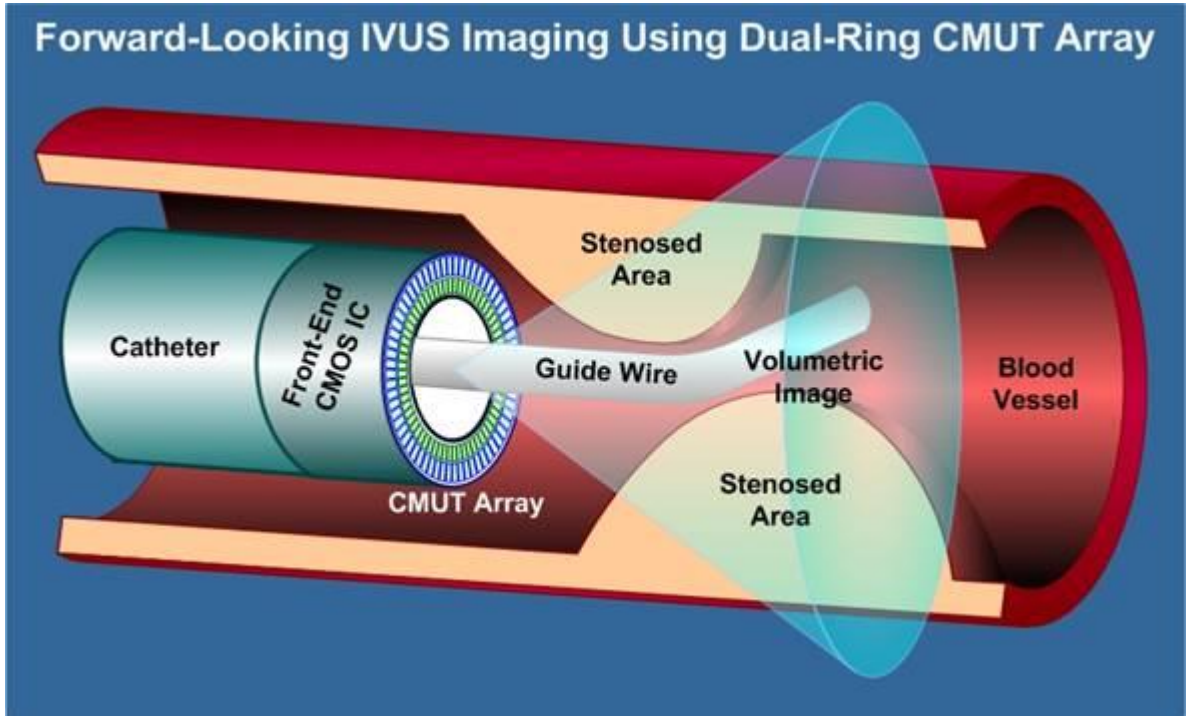


Stent in water(CREATIS) illustration of geometrical artefacts



Stent in a vessel with stenosis (www.vasculardisease management.com)

3D IVUS



http://www2.isikun.edu.tr

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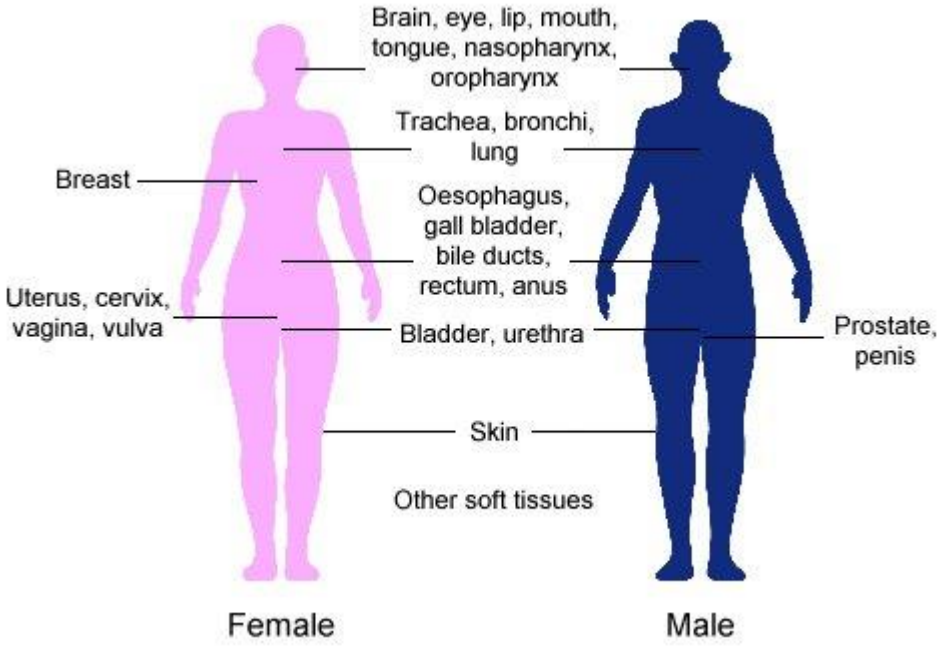
- Ultrasound basic physical principle
- Conventional clinical application of medical ultrasound imaging
- **Ultrasound to “guide” radiation therapy**
- From photo-acoustics to X-acoustics
- Ultrasound a competitor to radiation for cancer therapy?

Example 1 brachytherapy

Definition: brachitherapy is a radiotherapy technique developed at the Curie institute where the sealed source of radioactivity is placed internal or close to the zone to be treated

Radioactive seeds

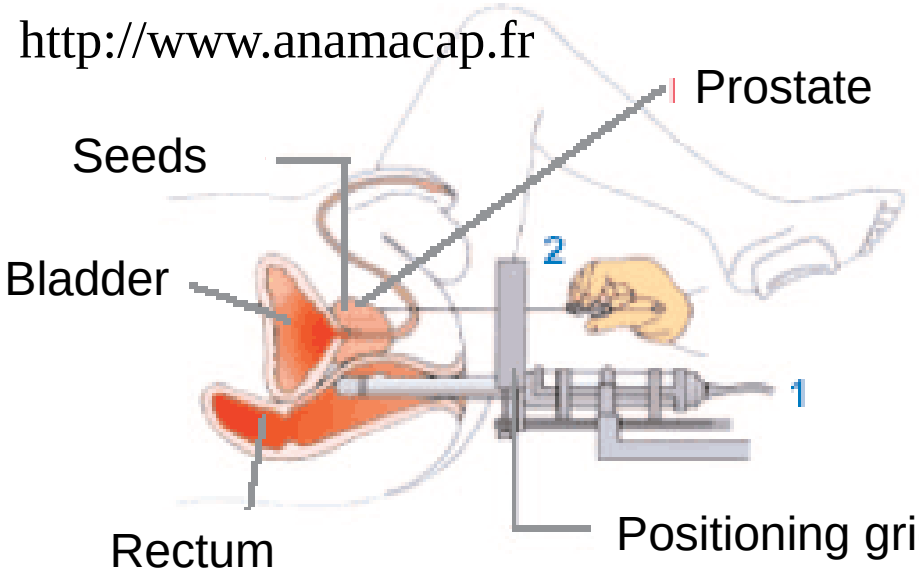
Organs for which it can be used



www.wikipedia

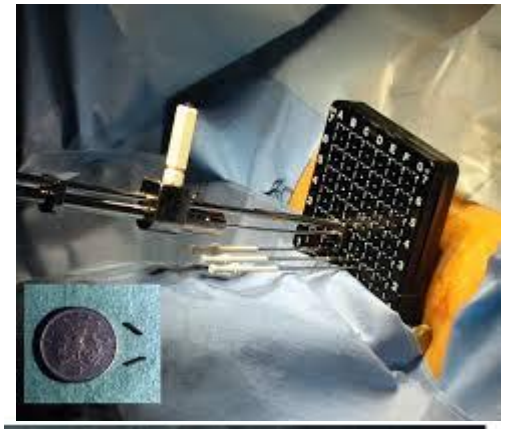
Prostate brachytherapy, the setup

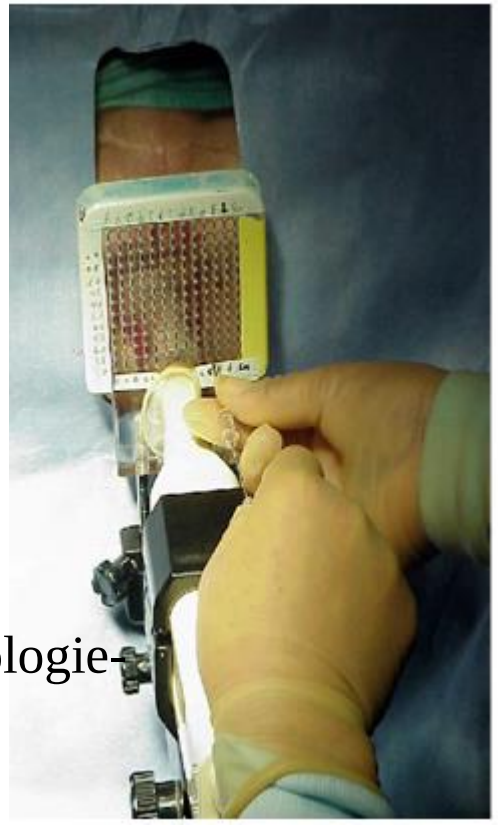
http://www.anamacap.fr



Radioactive seeds are placed using needles

www.chu-poitiers.fr



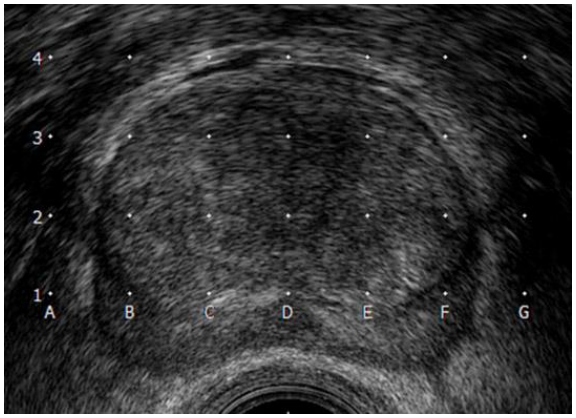


http://www.urologie-claudebernard-conti.com

http://www.urologie-valdegrace.fr

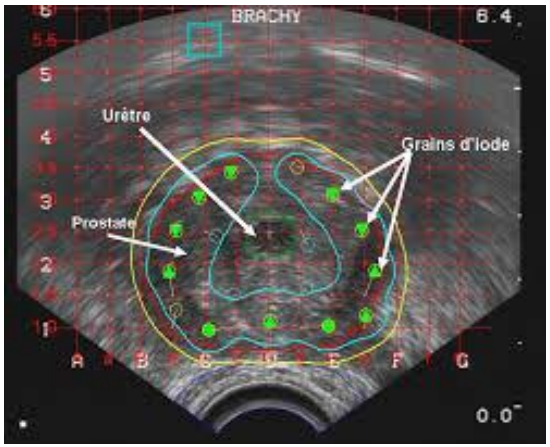
Prostate brachytherapy: imaging

Global imaging

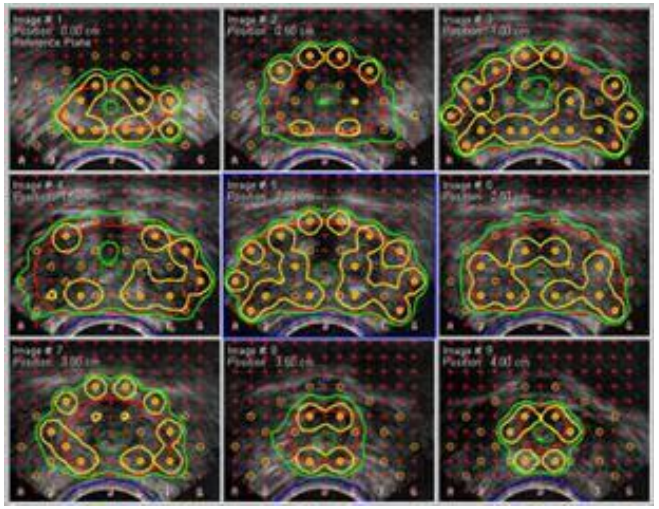


www.prostateimplant.com

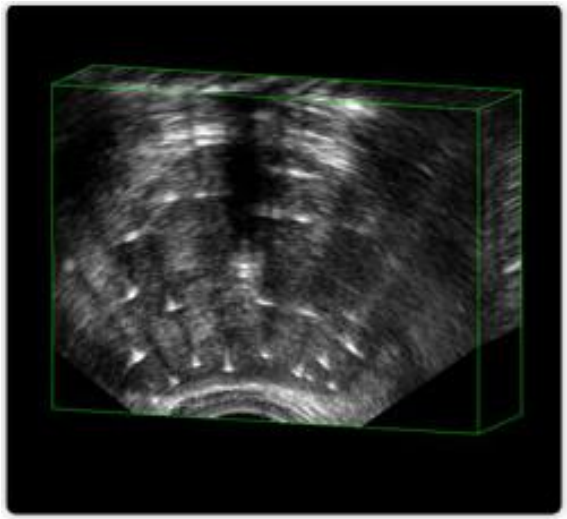
Segmentation



Planification



www.massey.vcu.edu



US image with seeds

X-ray control

Example 2 : US in external beam radiation therapy

External beam radiation therapy (EBRT) is used to treat > 60% of all cancer patients

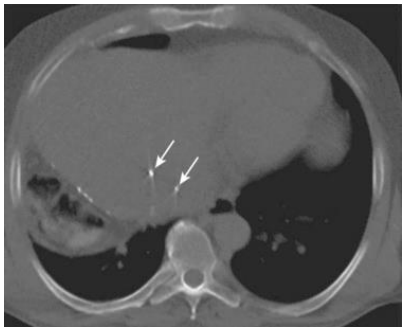
Clarity system
(accelerator and imaging)

More than planification

→ maximal dose delivered to the tumor
→ minimal margins
→ minimal toxicity for surrounding organs

Main issue: internal motion of the organs

between fractions
during fraction
gold standard X-ray imaging of implanted markers



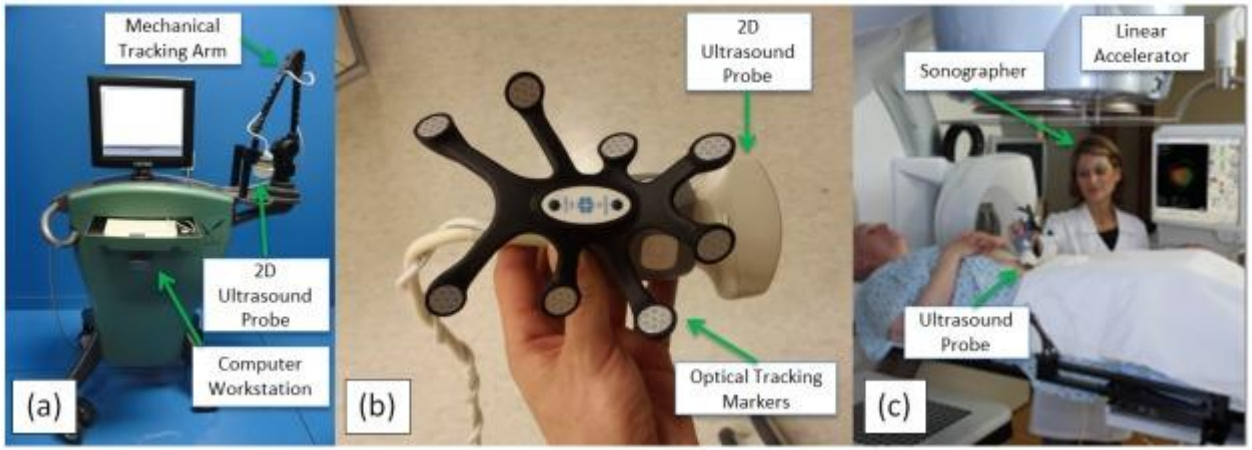
Gold fiducial markers in liver
From clinicalgate.com
Ho and Goodman

➔ Need for less invasive real-time solution : ultrasound

The images must be located in the therapy environment:

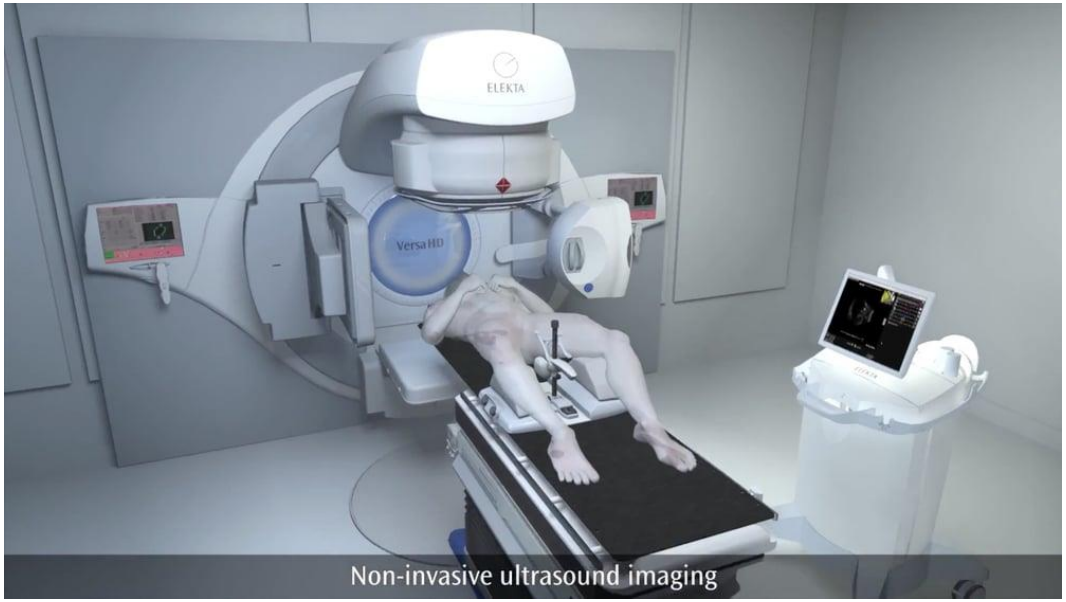
mechanical solution : probe fixed on an arm

optical markers detected with a camera

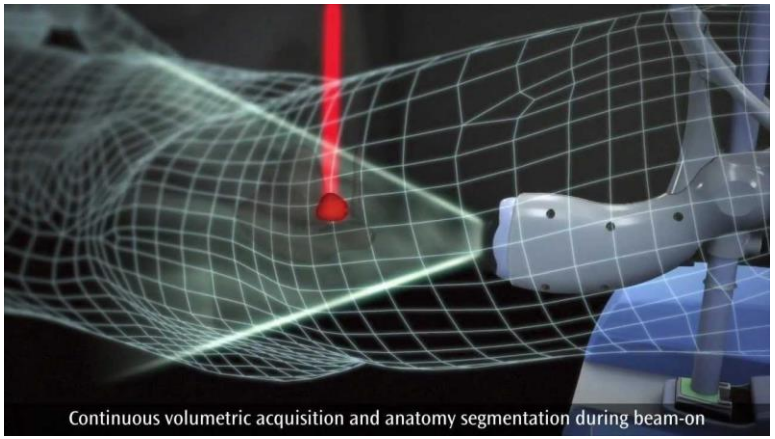


(a) NOMOS B-mode Acquisition and Targeting (BAT), courtesy of Medicka Medical LLC. (b) Elekta Clarity probe. (c) Clarity. From Western et al 2015

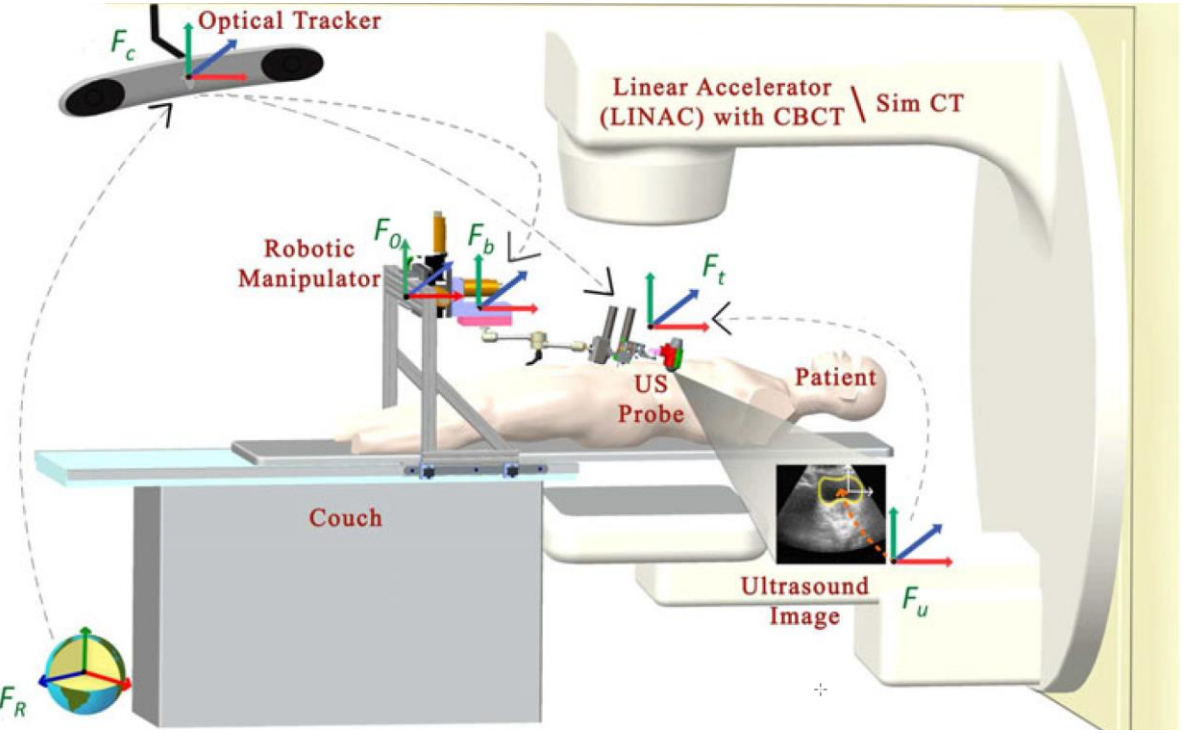
Limited to inter-fraction because the probe must be held by someone

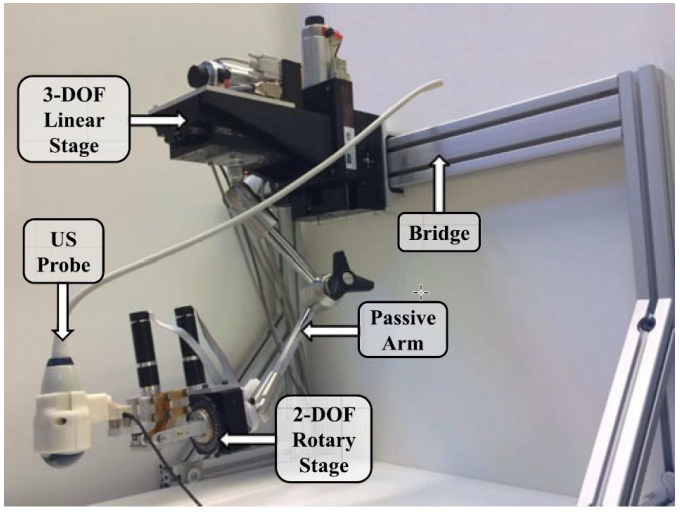


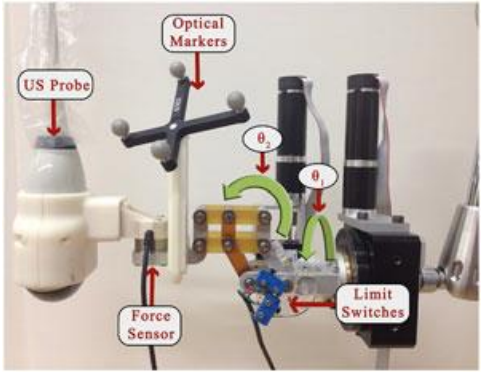
Static intra-fraction solution,
from Elekta Clarity



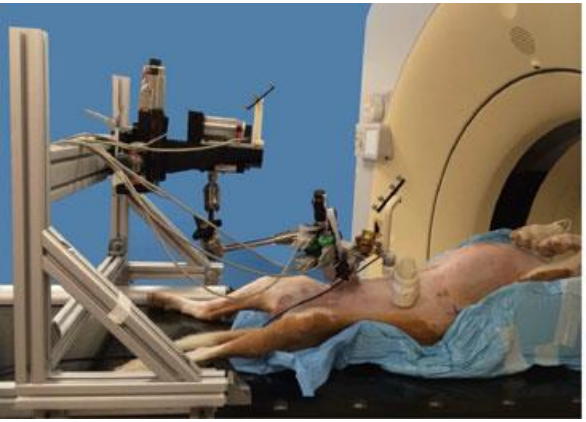
- Solution with a robot?
  - So far only academic/research work
  - No commercial solution

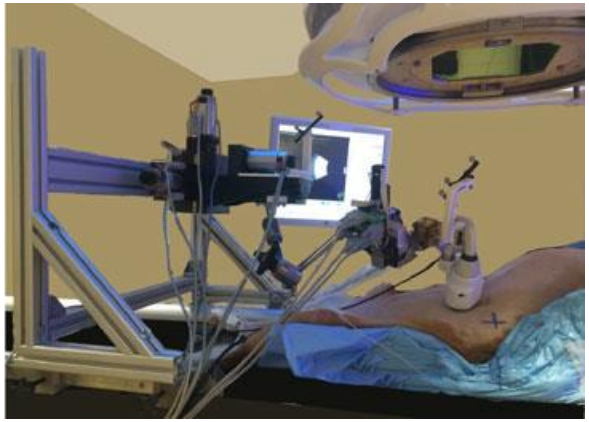






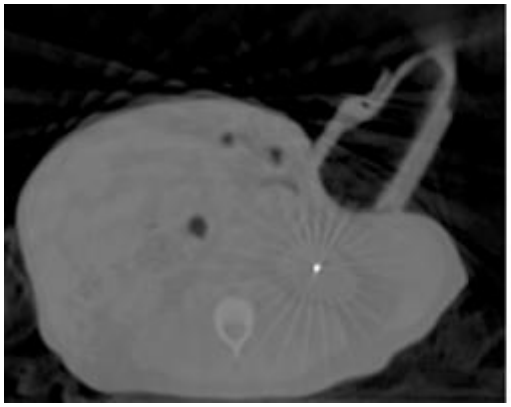
From Sen et al, John Hopkins, TBME 2017
Courtesy M.A. Lediju Bell

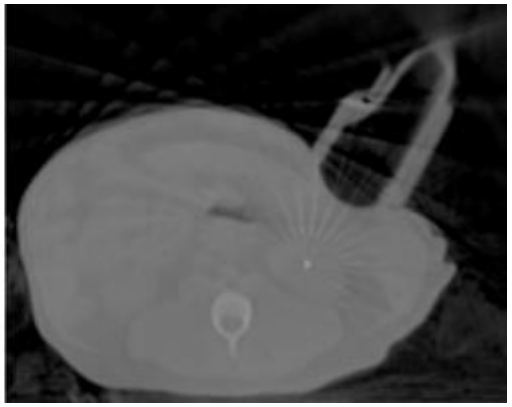


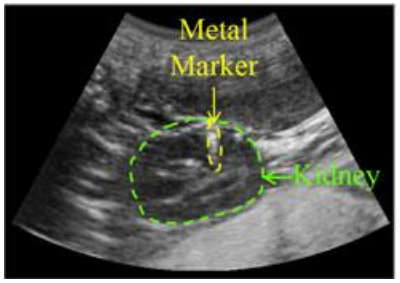


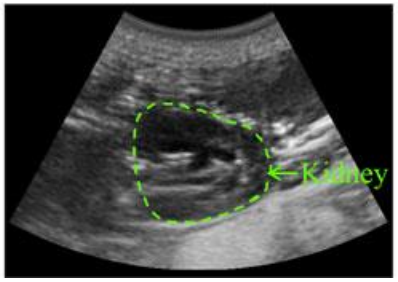
Setup for a canine model liver with a metal marker

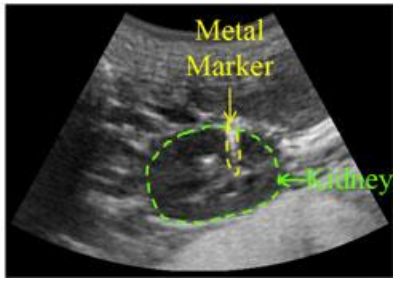
CT and US images











- Advantages beyond monitoring
  - Haptic feedback → possibility **to reproduce** exactly the same probe pressure
  - Adapt probe position/pressure to **ensure better positionning** of the target

- Difficulties
  - In this particular system → presence of a passive arm
  - **Price** of the system compared to static system

High potential

intra-fraction security possibility to detect risk and stop treatment

inter-fraction image analysis and re-planification according to real dose received

intra-fraction real-time guidance thanks to motion tracking

… but we are not there yet…

Outline

- Ultrasound basic physical principle
- Conventional clinical application of medical ultrasound imaging
- Ultrasound to guide radiation therapy
- **From photo-acoustics to X-acoustics**
- Ultrasound a competitor to radiation for cancer therapy?

WHY Photo-acoustic imaging?

Optical imaging

- Contrast
- Resolution > ~ 1 mm
- Investigation depth < ~ 5 cm
- Functional information

Ultrasound imaging

- Contrast
- Resolution > ~ 100 µm
- Investigation depth ~ 10 cm
- No Functional information

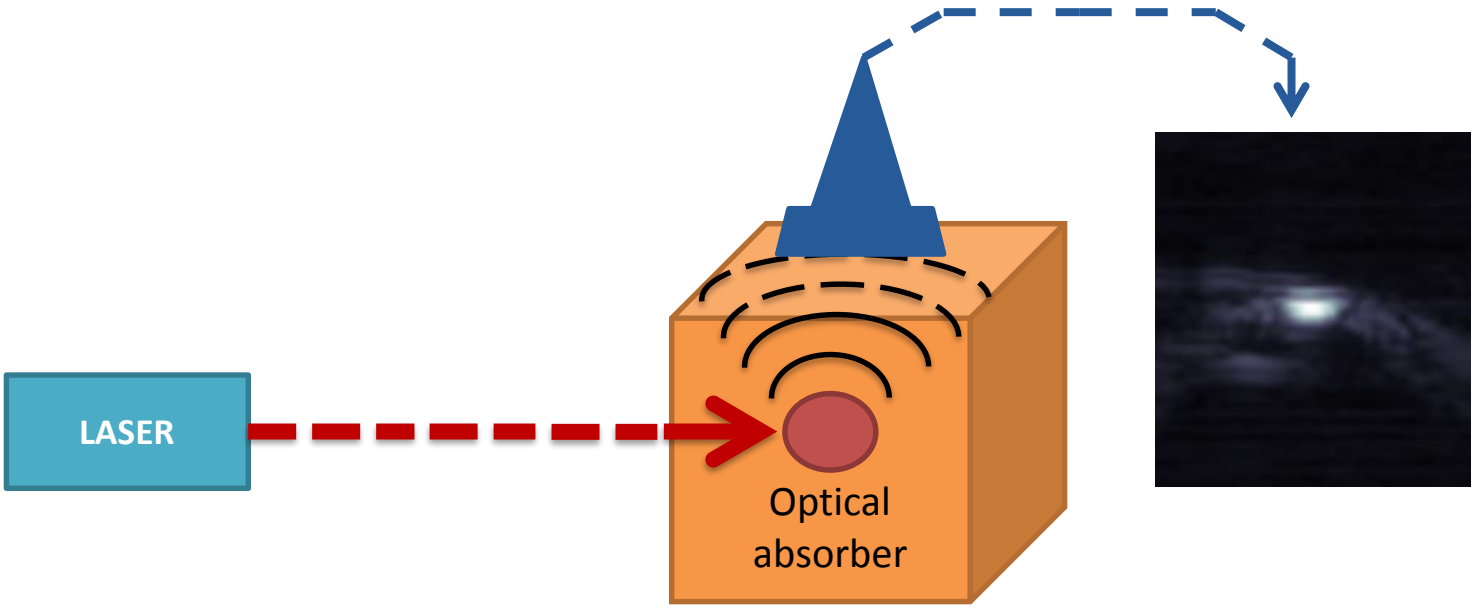
Photo-acoustic imaging

- Contrast (optical abosption)
- Resolution of Ultrasound
- Depth of investigation
- Functional information due to optical absorption
- Non invasive, non inonizing

Physical principle

Ultrasound generation with light

Laser pulse → **Local absorption by tissues** → **Thermal expansion** → **Acoustic wave**



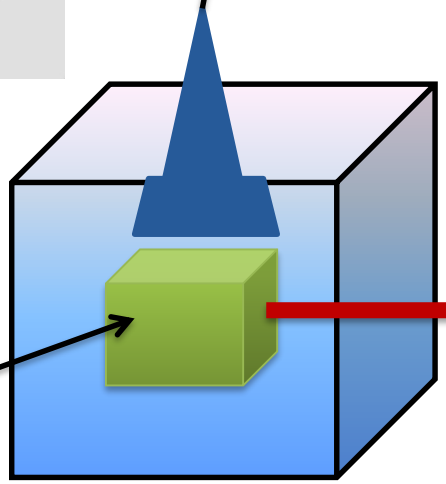
Acquisition setup (research)

All raw RF signals are collected for beamforming

Sonix DAQ

Ultrasonix RP

Phantom

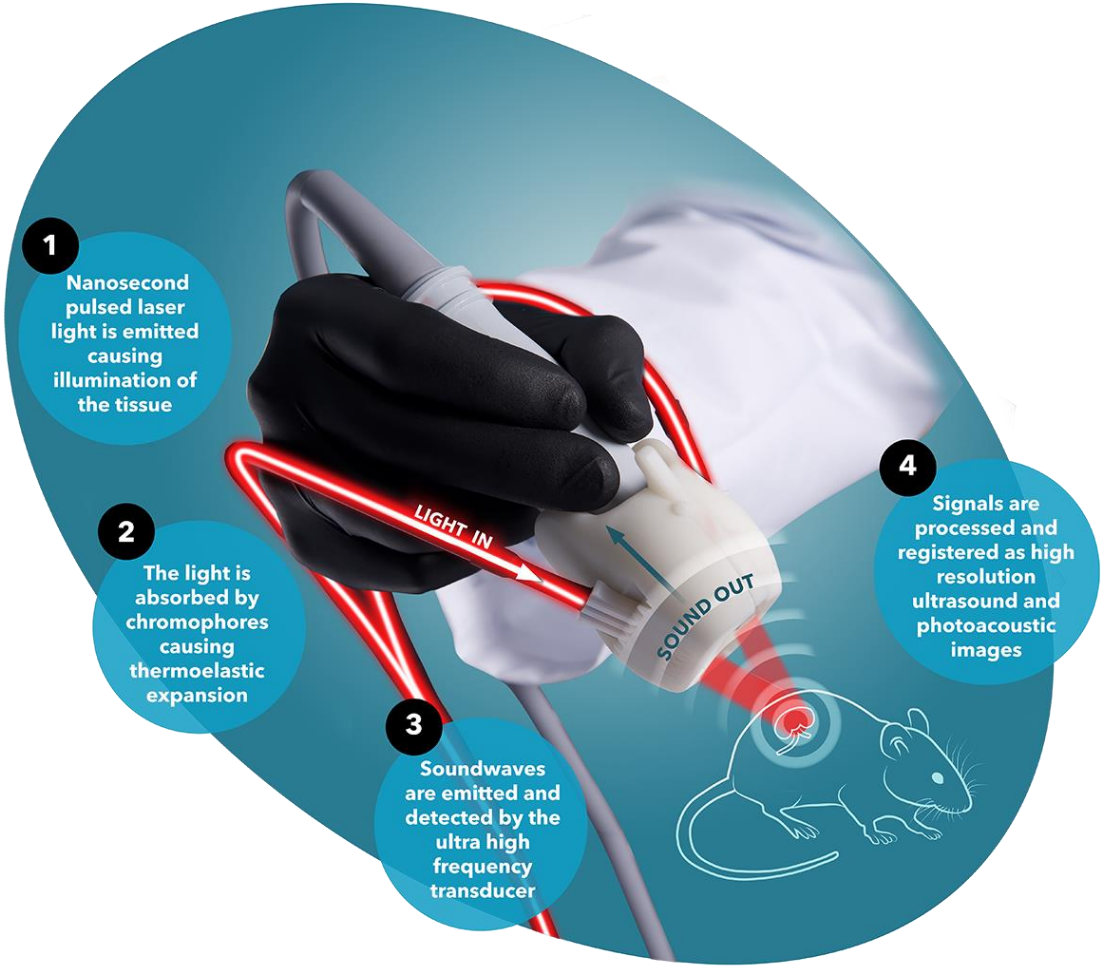


Water tank

Laser pulse

Courtesy of François Varray, CREATIS, University of Lyon

Pre-Clinical (small animal) setup

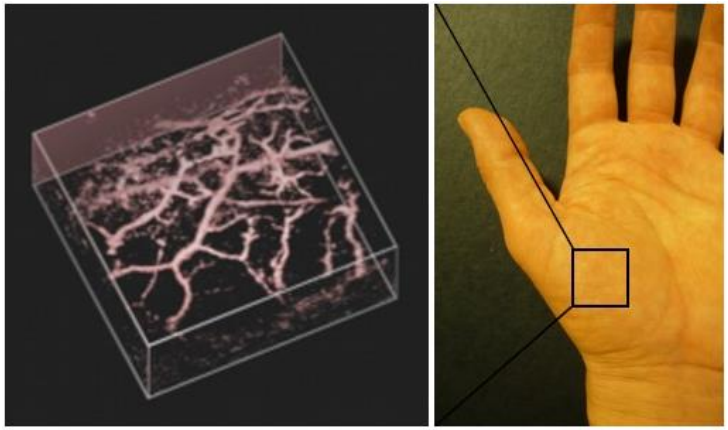


Vevo LAZR-X www.visualsonics.com

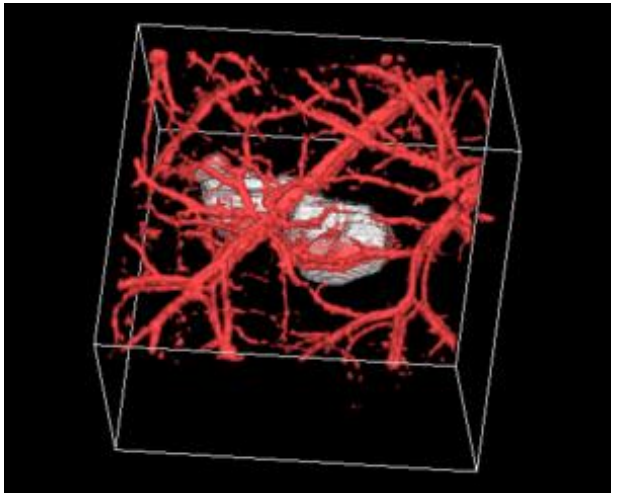
Applications

Vascularization

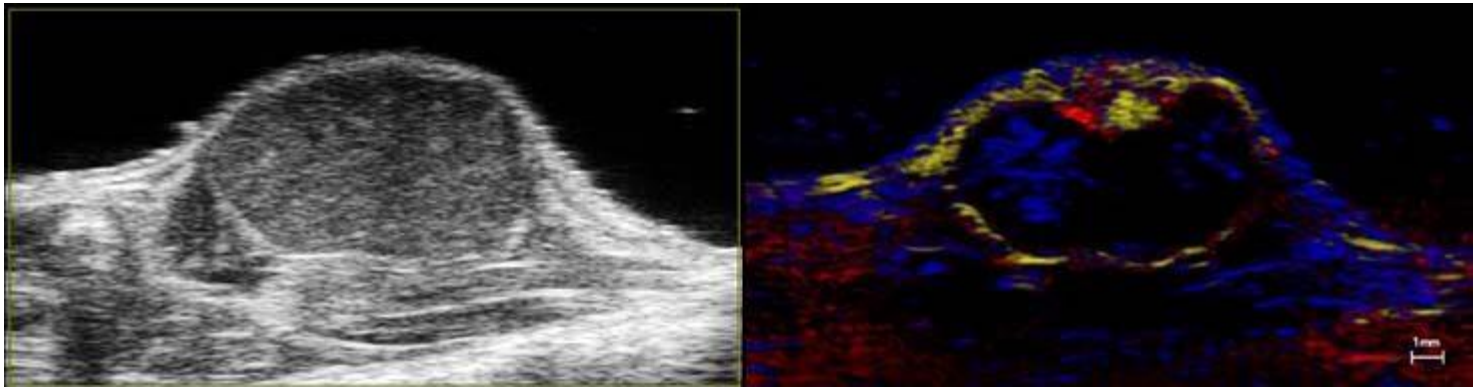
Cancer ➔ abnormal vascularization



In vivo PA image of the hand vascularization. *UCL PA Imaging Group*

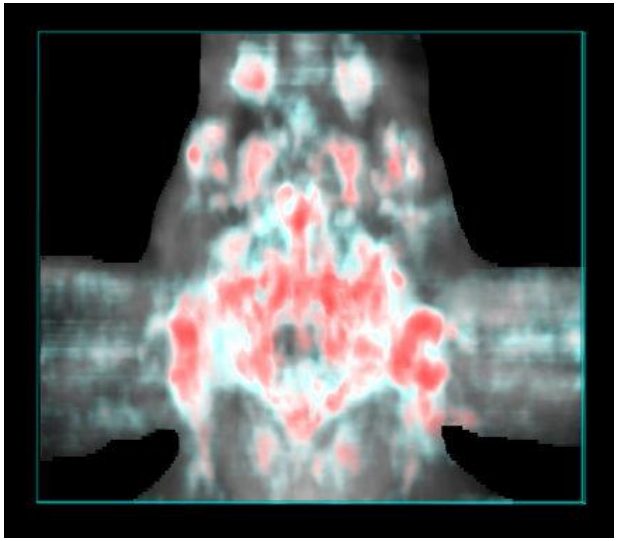


3D photoacoustic imaging of melanoma *in vivo. Zhang et.al. Nature Biotechnology 2006*

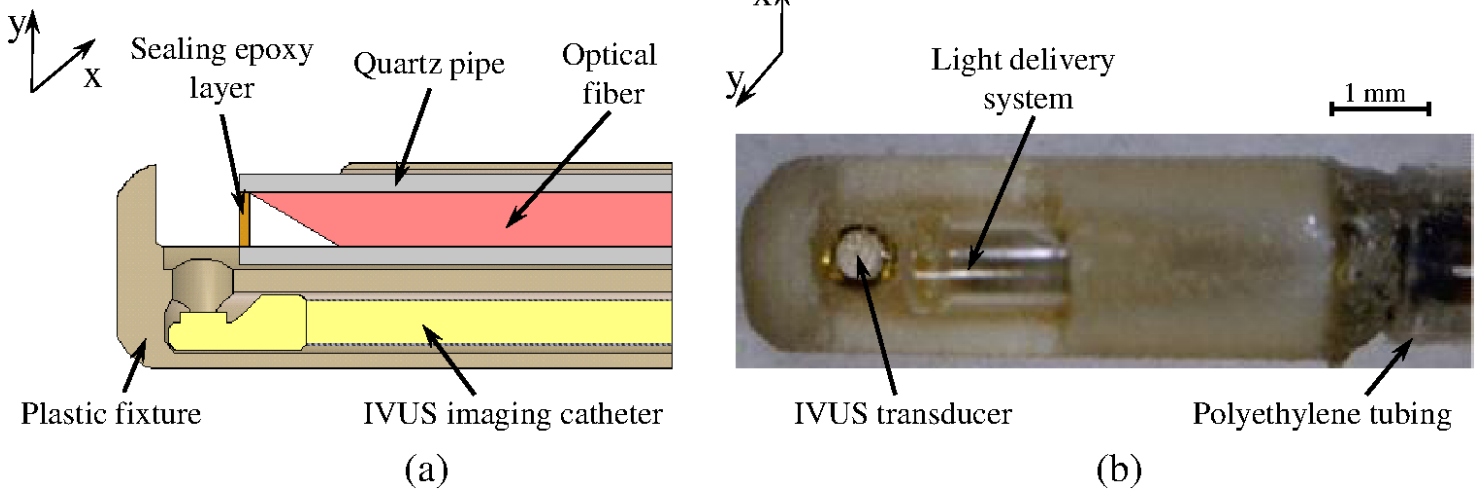


High-resolution ultrasound (left) and spectrally unmixed photoacoustic (right) image of a subcutaneous tumor showing nanoparticle distribution (yellow) as well as oxygenated (red) and deoxygenated (blue) hemoglobin signal

3D rendered coregistered ultrasound (greyscale) and photoacoustic (red, white and teal) image showing a parametric map of oxygen saturation with red signals indicating higher sO2 values



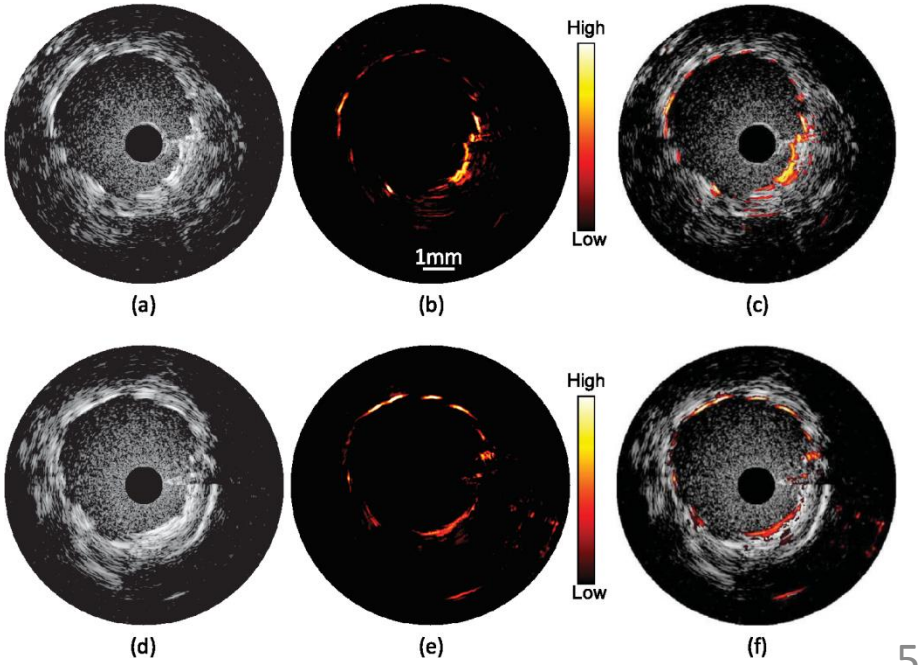
Applications



Karpiouk et.al, *J. Biomed. Opt.* 2012

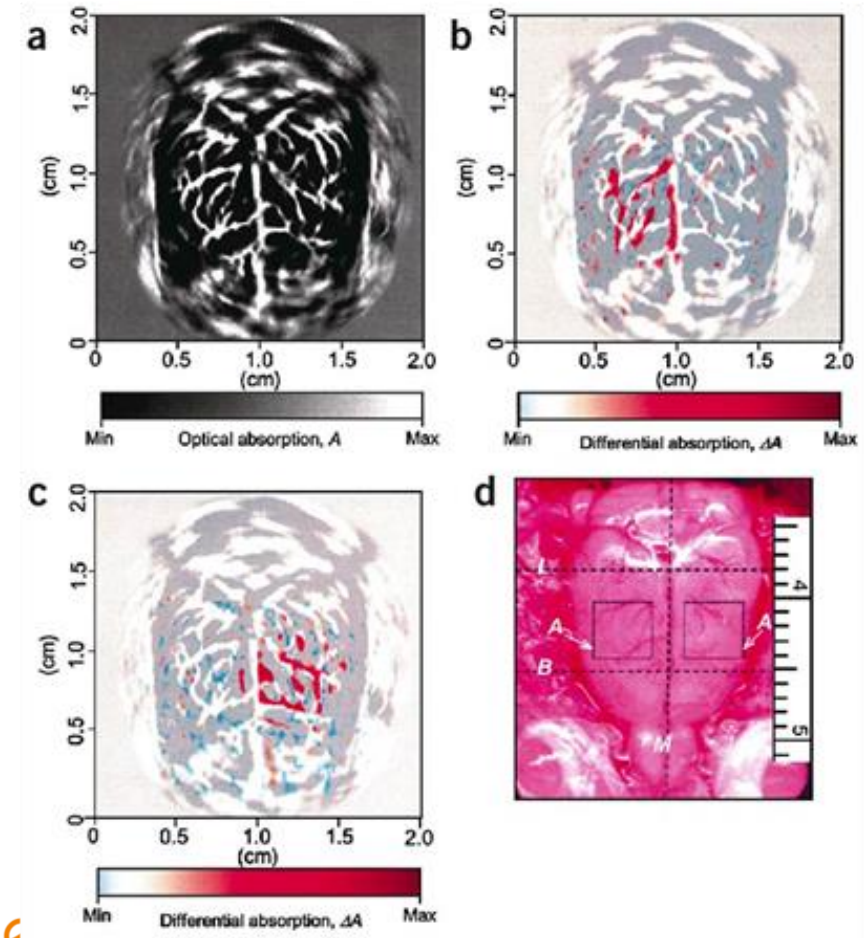
Intra-vascular photo-acoustic,

vascularization of the plaque



Applications

Functional imaging of the brain



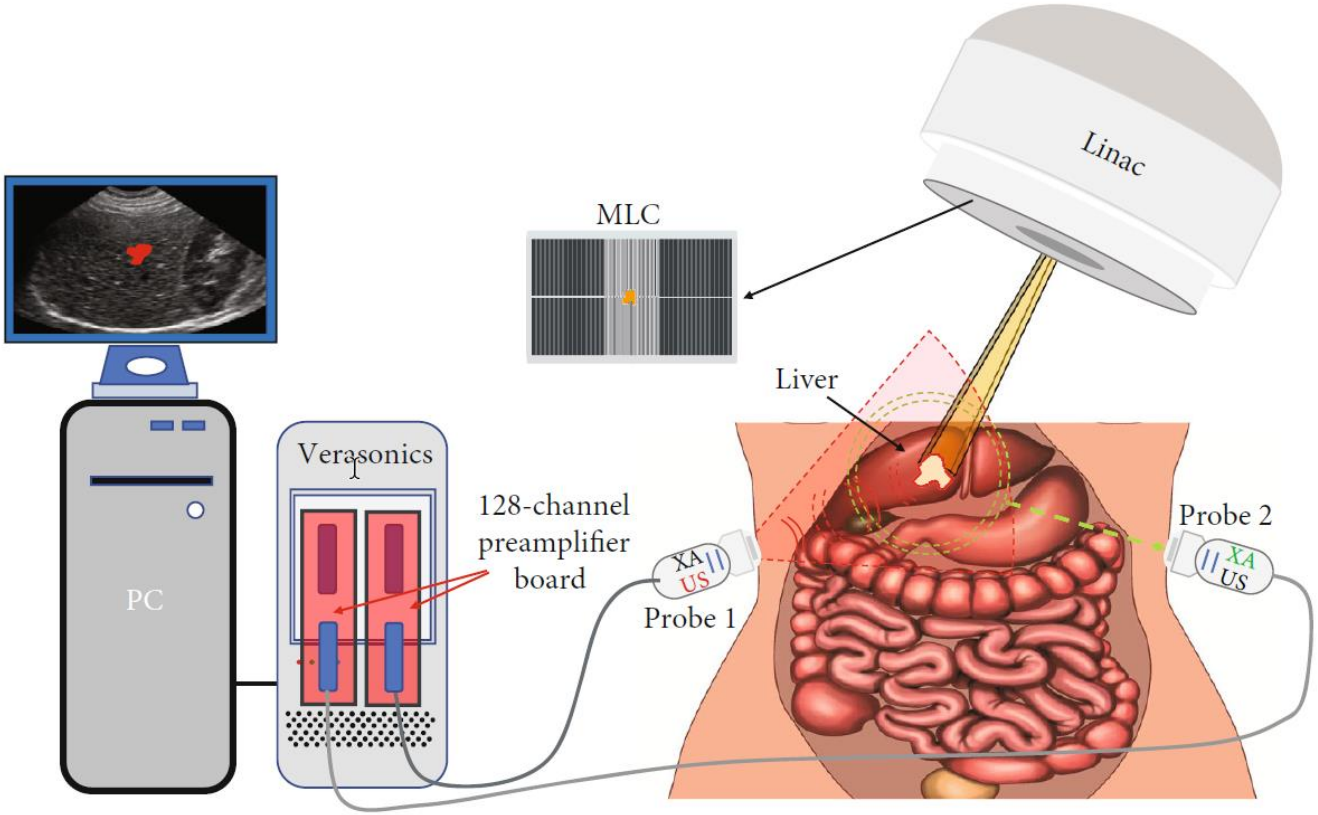
Cerebral hemodynamic changes in response to whisker stimulation, Wang et. al. *Nature Biotechnology,* 2003

X-acoustic

Laser light is an electromagnetic wave … just like X-Rays

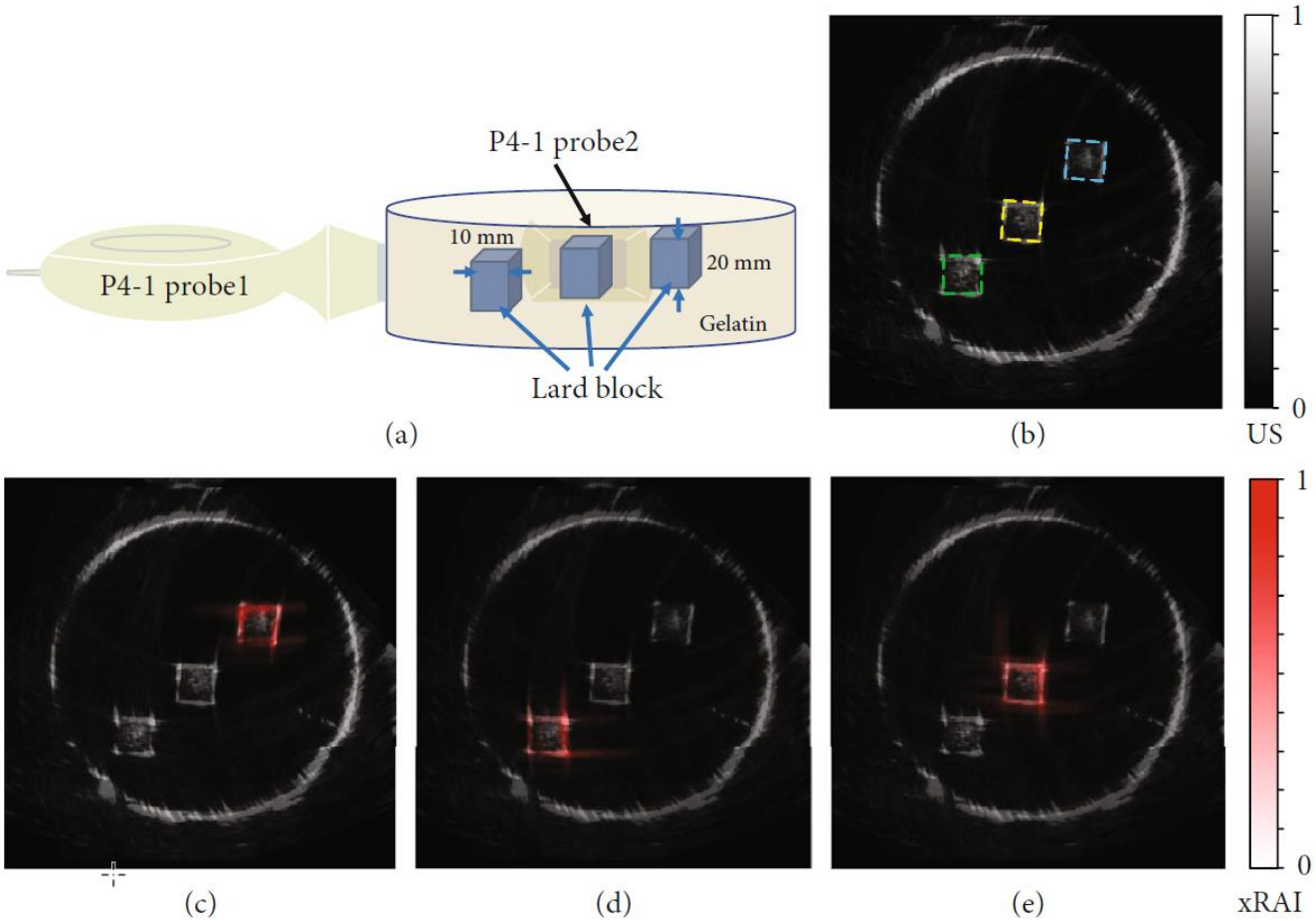
Does X-Ray produce a similar effet like acoustic?

What could it be usefull for?

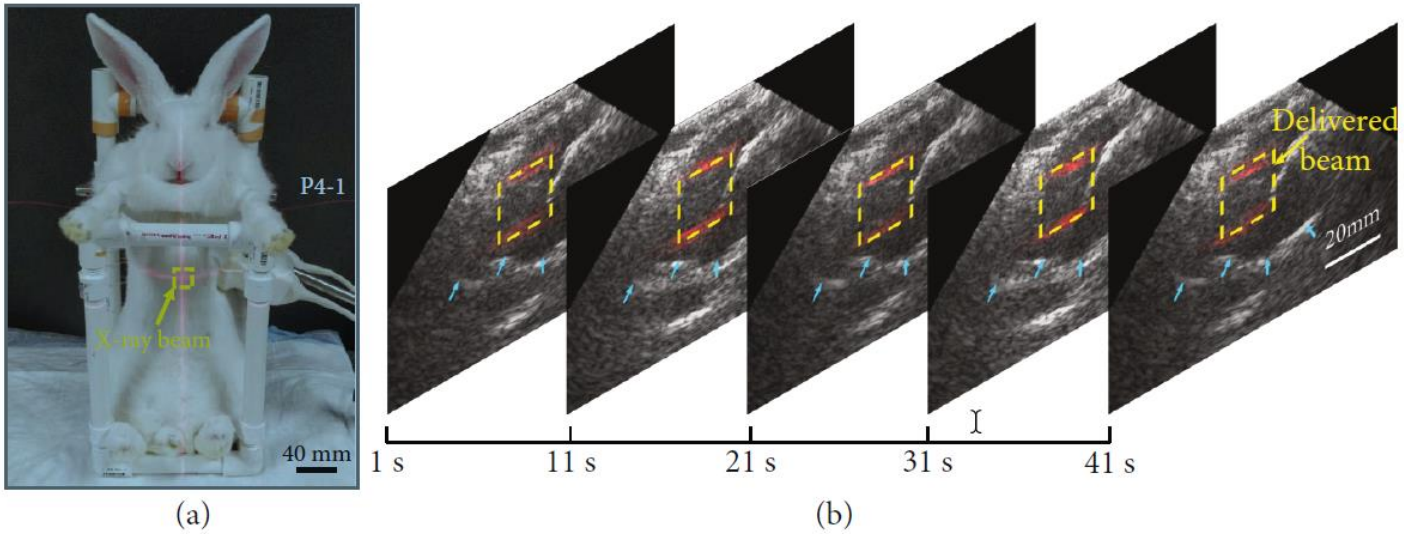


Schematic of an xRAI and US dual-modality imaging system built on a commercially available research US platform. Customdesigned 128-channel preamplifier boards are used to enlarge the XA signals acquired by the probe before sending to the US platform. MLC: multileaf collimation.

Zhang et al, BME Frontiers 2020

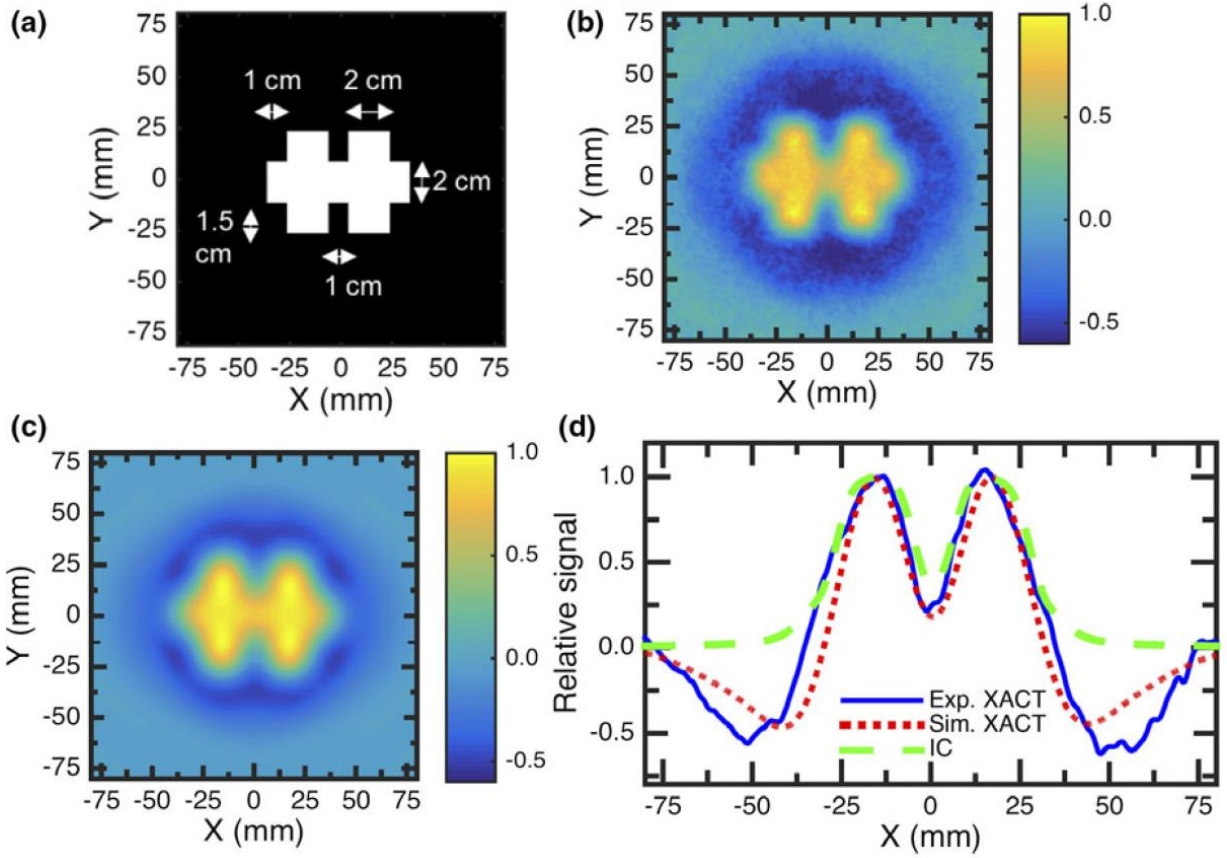


Demonstration of the feasibility for xRAI and US dual-modality imaging via imaging of lards in gel: (a) experimental setup; (b) grayscale US image showing the structure of the phantom with three lard blocks to be targeted separately by the X-ray beam; (c–e) pseudocolor xRAI images, superimposed on the grayscale B-mode image, showing in red the boundaries of the separately deposited X-ray dose in the top through bottom lard blocks, respectively.



xRAI and US real-time imaging of an in vivo rabbit liver, (a) The setup (b) The xRAI and US combined images at different time In each combined image, the xRAI image in pseudocolor presenting the location of the X-ray dose deposition (marked by the yellow dashed box) is superimposed on the US image in grayscale
showing the tissue structure.

Zhang et al, BME Frontiers 2020



(a) Block diagram of a puzzle piece shaped radiation field, where white regions represent the primary radiation beam. (b) Experimental and (c) simulated XACT images of the field. (d) Comparison of profiles extracted from experimental and simulated XACT images to ion chamber measurements along the X-axis at Y = 15 mm.

Potential use

- Like ultrasound monitor radiation therapy → motion
- Quantify dose received
  - Adapt between fraction or intrafraction the treatment
  - Verify range position in proton therapy

… probably other possibilities …

Outline

- Ultrasound basic physical principle
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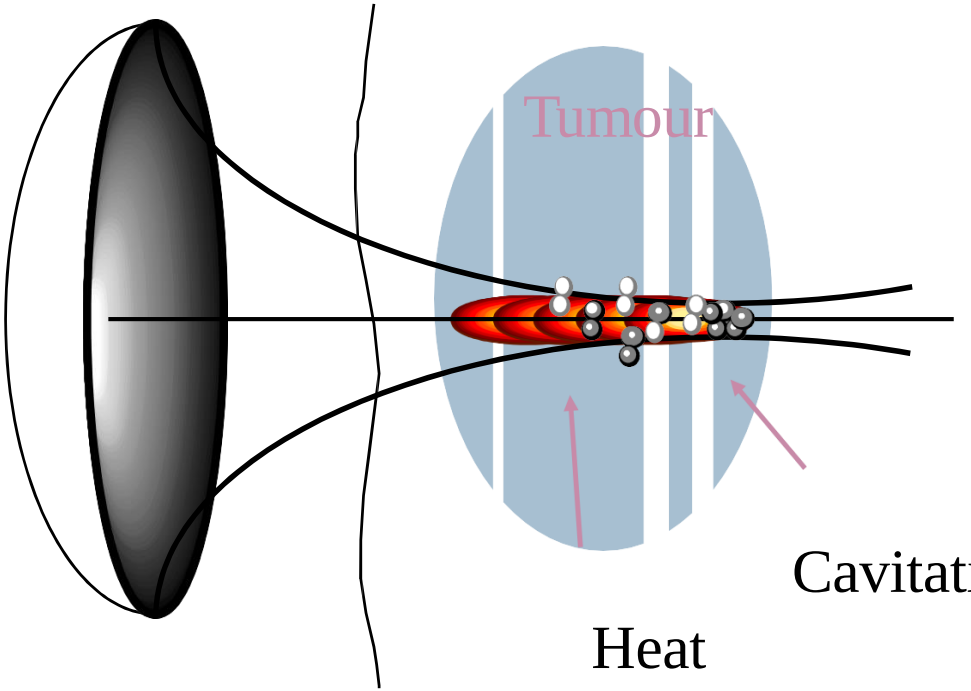
- From photo-acoustics to X-acoustics
- **Ultrasound a competitor to radiation for cancer therapy?**

Biological effects of ultrasound

- Eventhough US is reputed safe there can be an effect
- Mecanical effect → cavitation
- Thermal effect → temperature increase
- These effects are avoided in diagnostic, but could be usefull in therapy

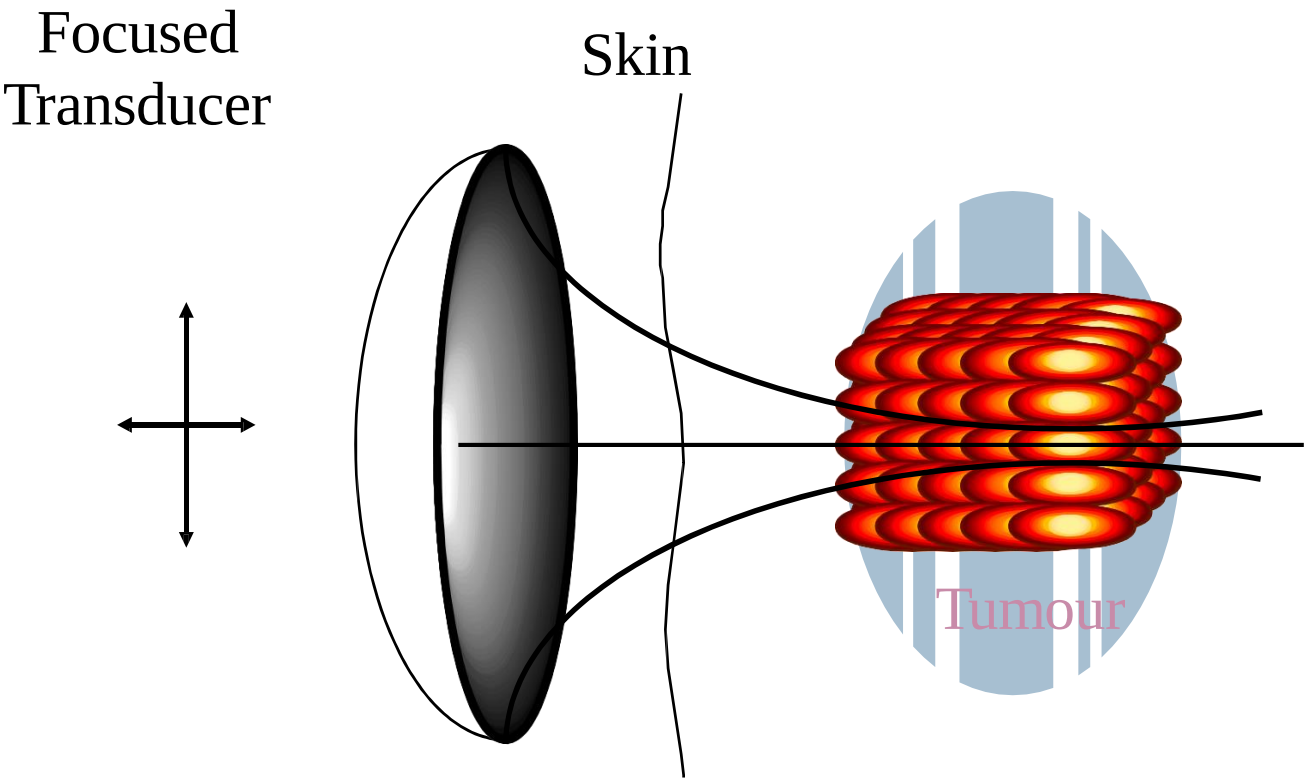
Principle of HIFU

The effect of focusing is similar to that of using a magnifying glass to focus the sun's energy on a single spot. The focused light energy does not create heat along its way. However, in the focal point , one can use the condensed energy to rapidly raise temperature in a small spot.

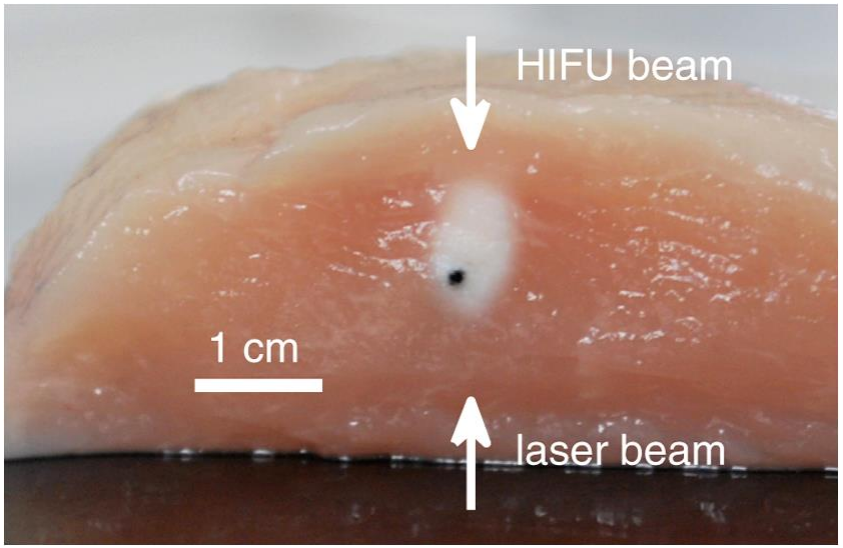


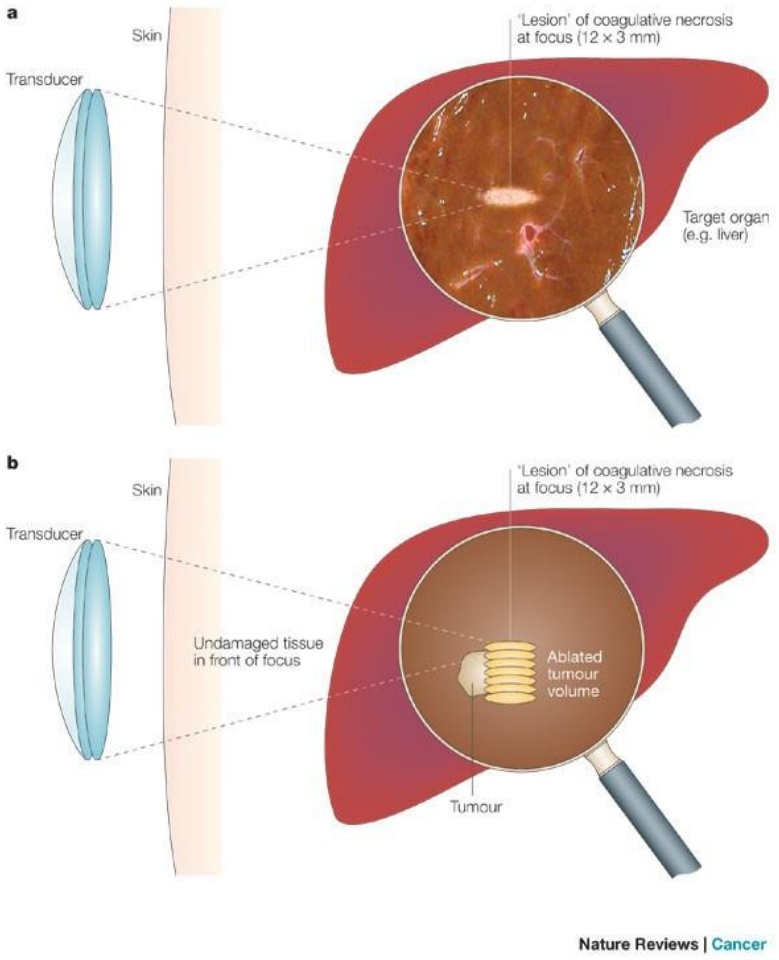
Thermal ablation of tumors
High pressure: non linearity and cavitation

Principle of HIFU



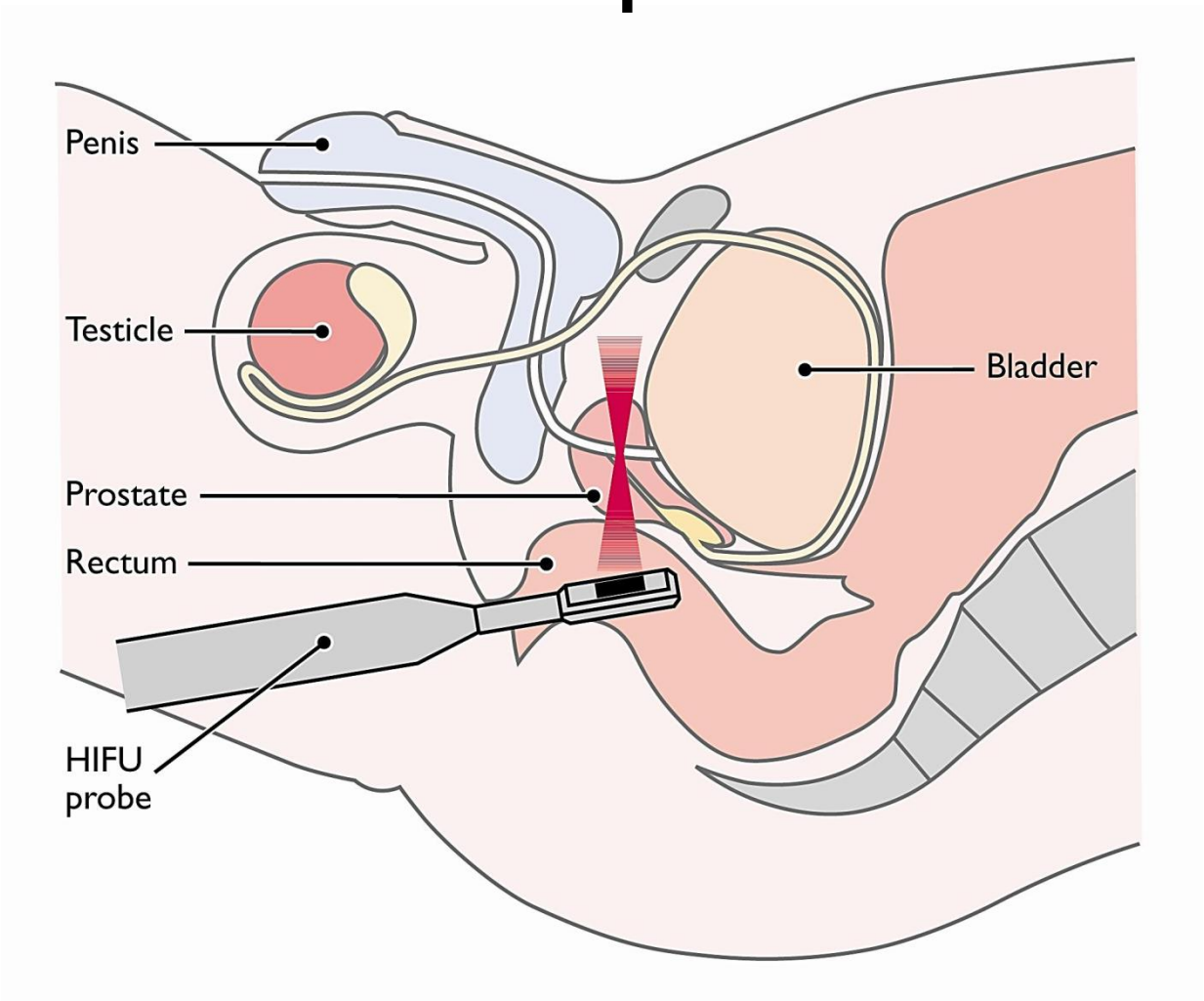
The focus is scanned over the entire volume of the tumor.





HIFU in a piece of chicken breast ……. and in a piece of liver

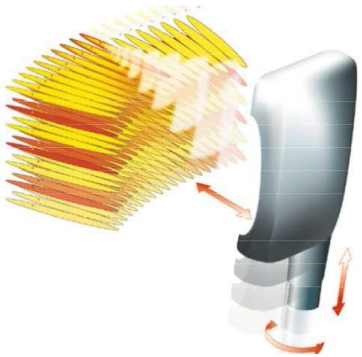
Application of HIFU to the treatment of prostate cancer



Principle of trans-rectal ultrasound for treatment of prostate cancer

- Volume to be treated defined by the urologist
  Procedure monitored by computer (ultrasound scan of the prostate, motion detection, movement of the transducer)
- Procedure performed

under epidural anesthesia



HIFU cancer therapy

- non-invasive / no anaesthesia / fewer side effects / faster treatment results

Prostate cancer

- FDA-approved for prostate
- >92% of patients cross the 10-year survival threshold after HIFU with no lasting side effects

Breast cancer

- the combination of HIFU and organ-saving surgery is effective for treatment

Bone metastases

- FDA approved
- helps relieve pain in patients with.
- less pronounced side effects and improved the quality of life

Liver cancer

- reduces the tumour in 79% of patients.
- 30% of cancer patients, the tumour is destroyed

HIFU can be an effective treatment in the last stages of liver or pancreas cancer

THANK YOU

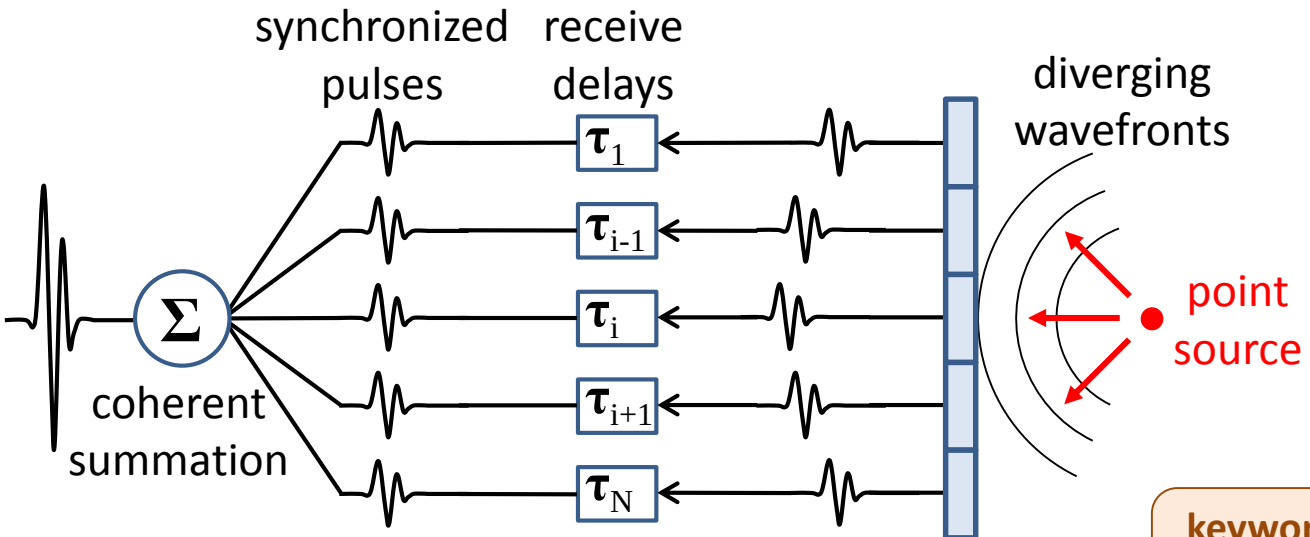
Ultrasound : more than just a non ionizing imaging modality

Hervé LIEBGOTT
Professor @ the University of Lyon
CREATIS

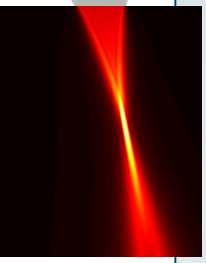
Extracorporeal applications of HIFU

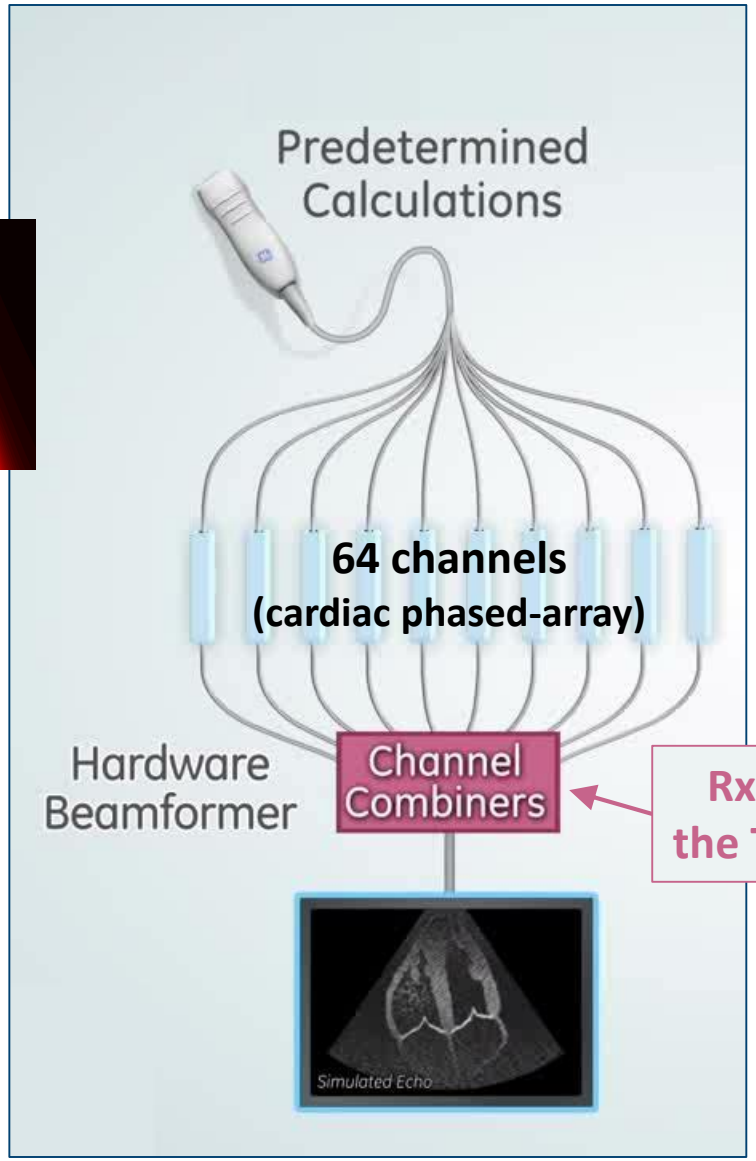
- Breast cancers
- Uterine fibroids (very large volumes)
- Liver cancers (ribcage, large volumes, very perfused organ)
- Brain tumors (phase aberration and attenuation through the skull)
- …

- **old-generation scanners**
  - receive focusing at the focal point only
  - hardware-based beamforming
- **new-generation scanners**
  - receive focusing everywhere
  - software-based beamforming

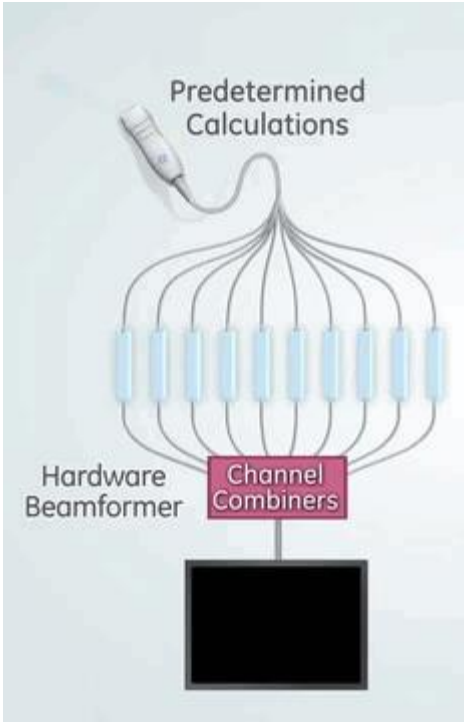


keywords
- dynamic receive focusing
- software-based beamforming





Rx focusing at the Tx focal point



source: *GE C-Sound technology in Cardiovascular ultrasound* (www.youtube.com/watch?v=__VbO5H8iH0)

“***ULTRAFAST IMAGING***”

=

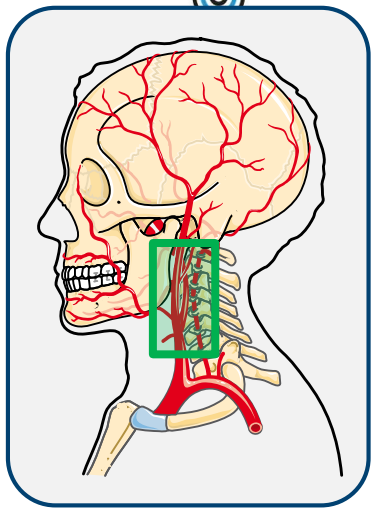
“higher frame rate than usual, for a given image quality”

- **other terms**:
  - dynamic focusing
  - dynamic beamforming
  - high-frame-rate imaging
  - plane-wave imaging
  - diverging-wave imaging
  - synthetic aperture
  - coherent imaging

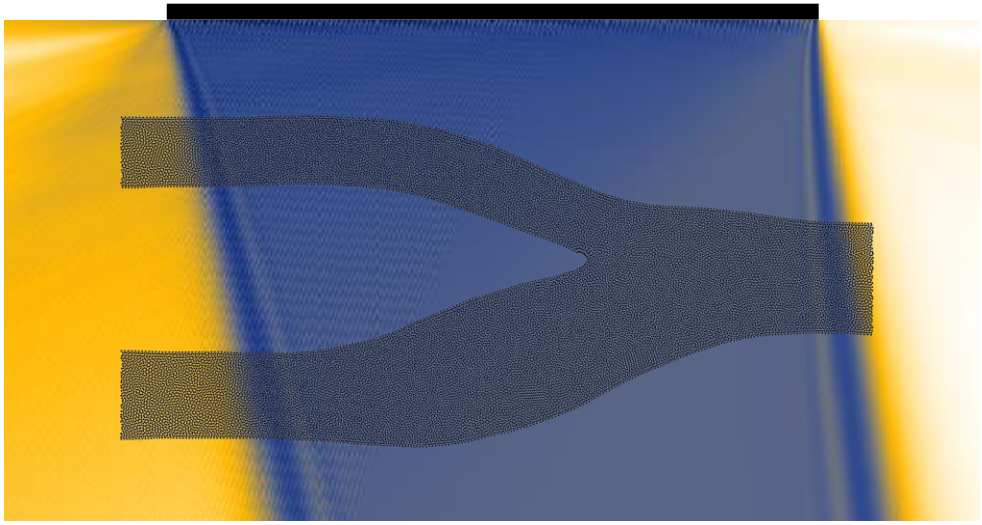
…

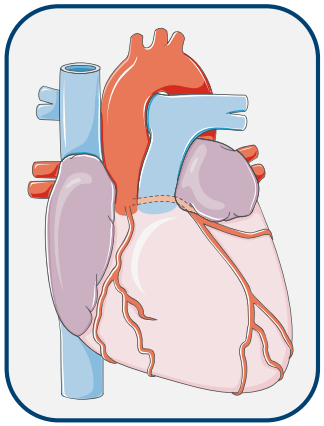
key paper

- Tanter & Fink. IEEE TUFFC 2014;61:102-119

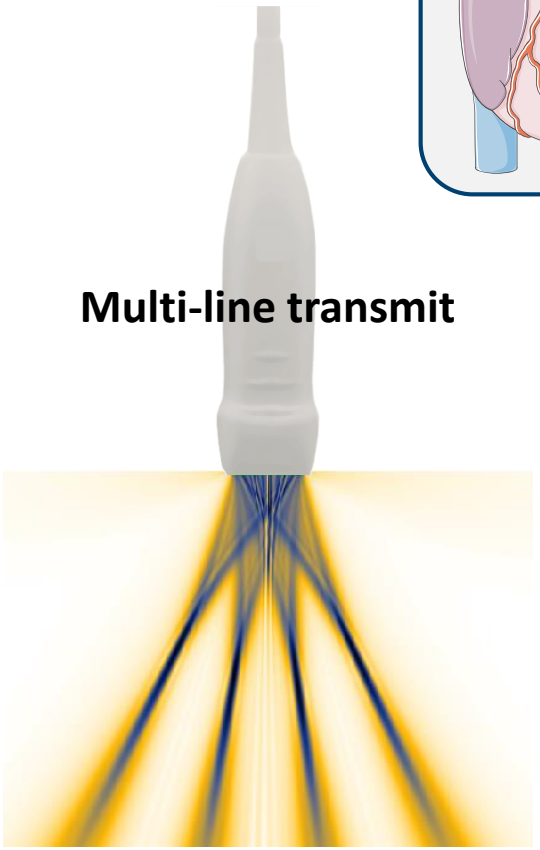


plane waves

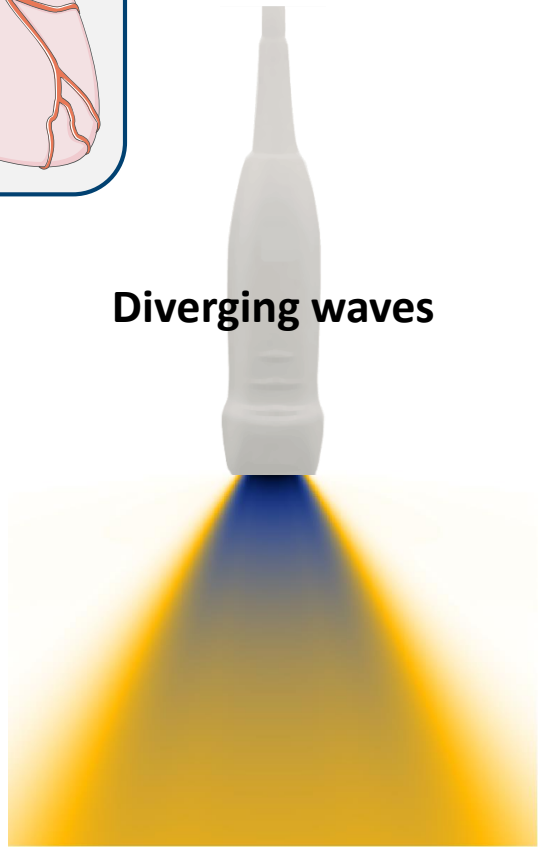




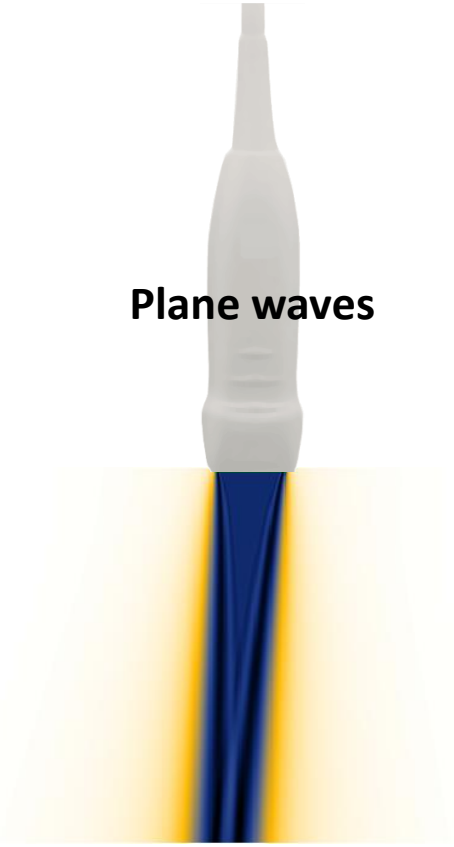
Multi-line transmit



Diverging waves



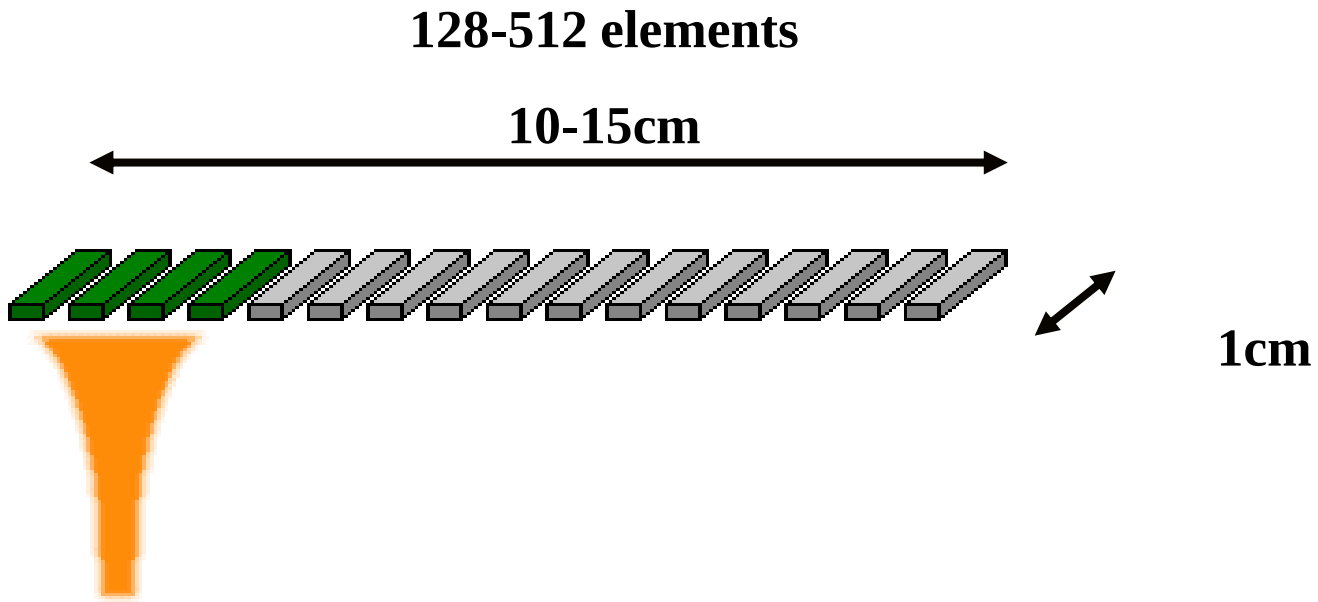
Plane waves



key paper

- Cikes *et al*. J Am Coll Cardiol Img 2014;7:812-823

A probe is an arrangement of many elements

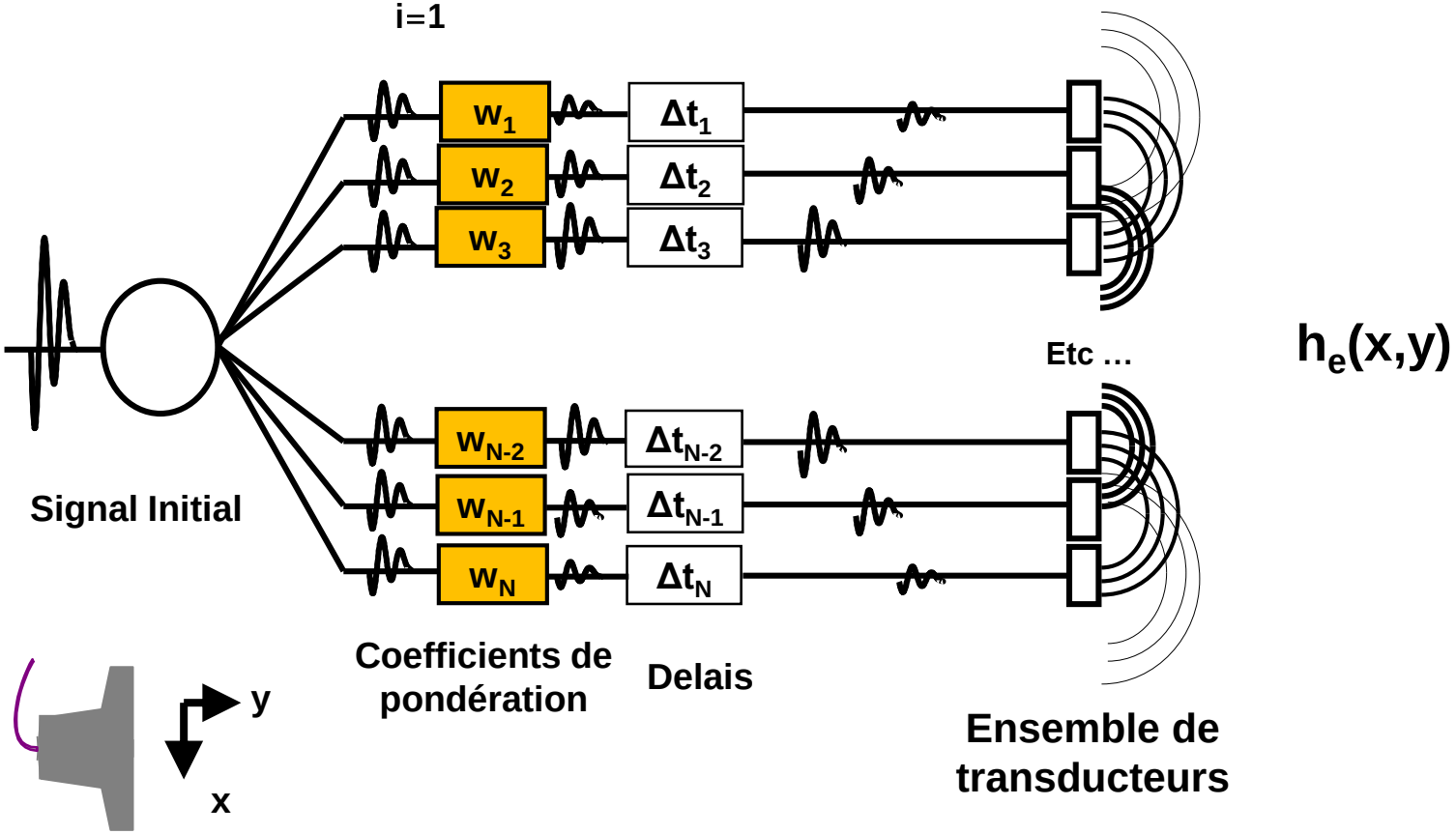


Subgroups of elements are used simultaneously to form the beam / sweep the Region of Interest

To form the beam, = change its shape

2 degrees of freedom: weithing coefficients and delays

$$h_e(x,y,t) = \sum_{i=1}^{N} w_i h_o(x - x_i, y - y_i, t - \Delta t_i)$$



Focusing : compensate for different travel times, like in optics