
# Photothermal tomography as a non-invasive technology in breast cancer imaging

**Centro de Ciencias Aplicadas y Desarrollo Tecnológico**
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**Universidad Nacional Autónoma de México**
**(UNAM)**



## Objetives

1. To develop and set-up the technological platform on photothermal tomography for breast cancer imaging.

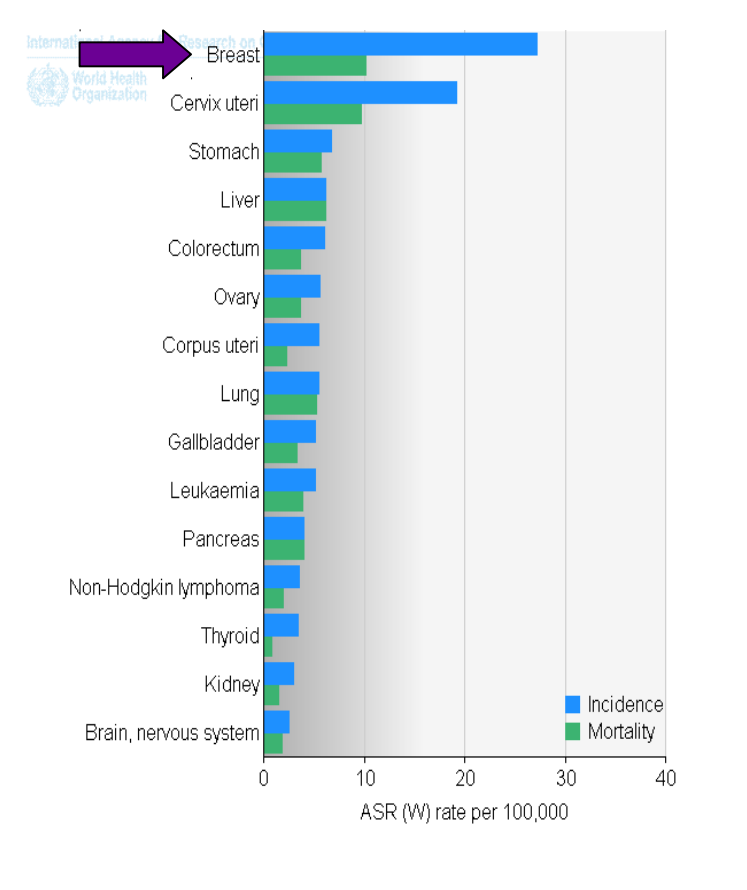
1. R&D of 2D-sensor arrays as basis of proprietary tomography technology.

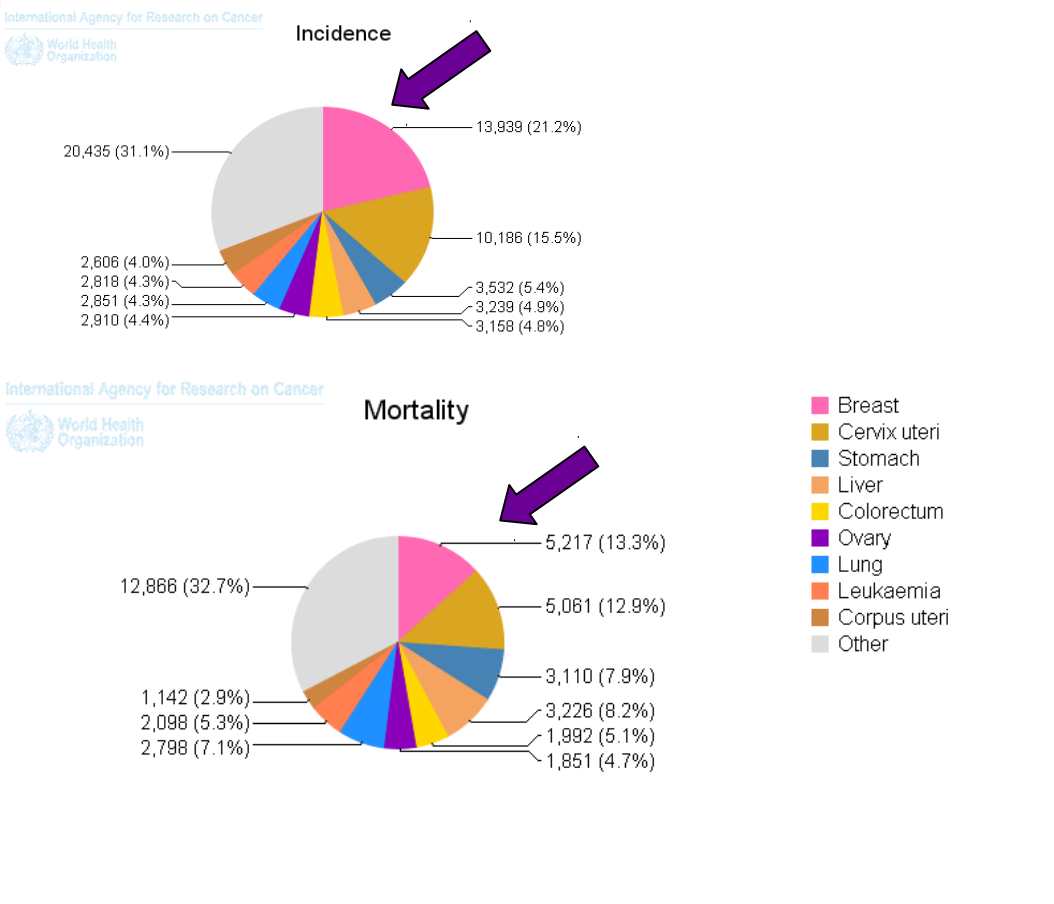
1. R&D on signal detection, storage and interpretation, focused on tomography image reconstruction.

1. Bringing up specialized human resources.

1. To achieve proprietary technology and proprietary specialized knowledge.

# Cancer statistics for Mexico: women



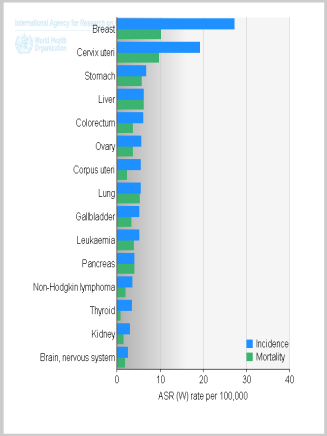

**All data taken from: www.globocan.com**
**Figures are updated up to 2008.**

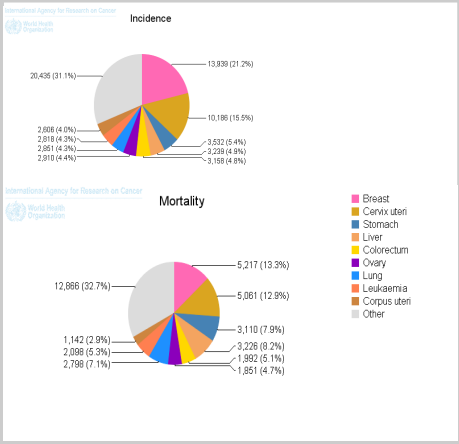
# Cancer statistics for Mexico: women

| Cancer | Incidence Number | Incidence ASR (W) | Mortality Number | Mortality ASR (W) |
|---|---|---|---|---|
| Lip, oral cavity | 932 | 1.8 | 281 | 0.5 |
| Nasopharynx | 40 | 0.1 | 23 | 0 |
| Other pharynx | 176 | 0.3 | 105 | 0.2 |
| Oesophagus | 385 | 0.7 | 304 | 0.6 |
| Stomach | 3532 | 6.7 | 3110 | 5.8 |
| Colorectum | 3158 | 6.1 | 1992 | 3.7 |
| Liver | 3239 | 6.2 | 3226 | 6.1 |
| Gallbladder | 2605 | 5.2 | 1688 | 3.3 |
| Pancreas | 2115 | 4 | 2074 | 4 |
| Larynx | 249 | 0.5 | 156 | 0.3 |
| Lung | 2851 | 5.4 | 2798 | 5.3 |
| Melanoma of skin | 645 | 1.2 | 236 | 0.4 |
| Breast | 13939 | 27.2 | 5217 | 10.1 |
| Cervix uteri | 10186 | 19.2 | 5061 | 9.7 |
| Corpus uteri | 2606 | 5.4 | 1142 | 2.3 |
| Ovary | 2910 | 5.6 | 1851 | 3.6 |
| Kidney | 1478 | 3 | 736 | 1.5 |
| Bladder | 593 | 1.1 | 316 | 0.6 |
| Brain, nervous system | 1292 | 2.5 | 972 | 1.9 |
| Thyroid | 1844 | 3.4 | 408 | 0.8 |
| Hodgkin lymphoma | 481 | 0.9 | 210 | 0.4 |
| Non-Hodgkin lymphoma | 1891 | 3.6 | 1047 | 2 |
| Multiple myeloma | 475 | 1 | 425 | 0.9 |
| Leukaemia | 2818 | 5.2 | 2098 | 3.9 |
| All cancers excl. non-melanoma skin cancer | 65674 | 126.2 | 39361 | 75 |

ASR (age-standardised rate)

The ASR is a weighted mean of the age-specific rates
the weights are taken from population distribution of the standard population.

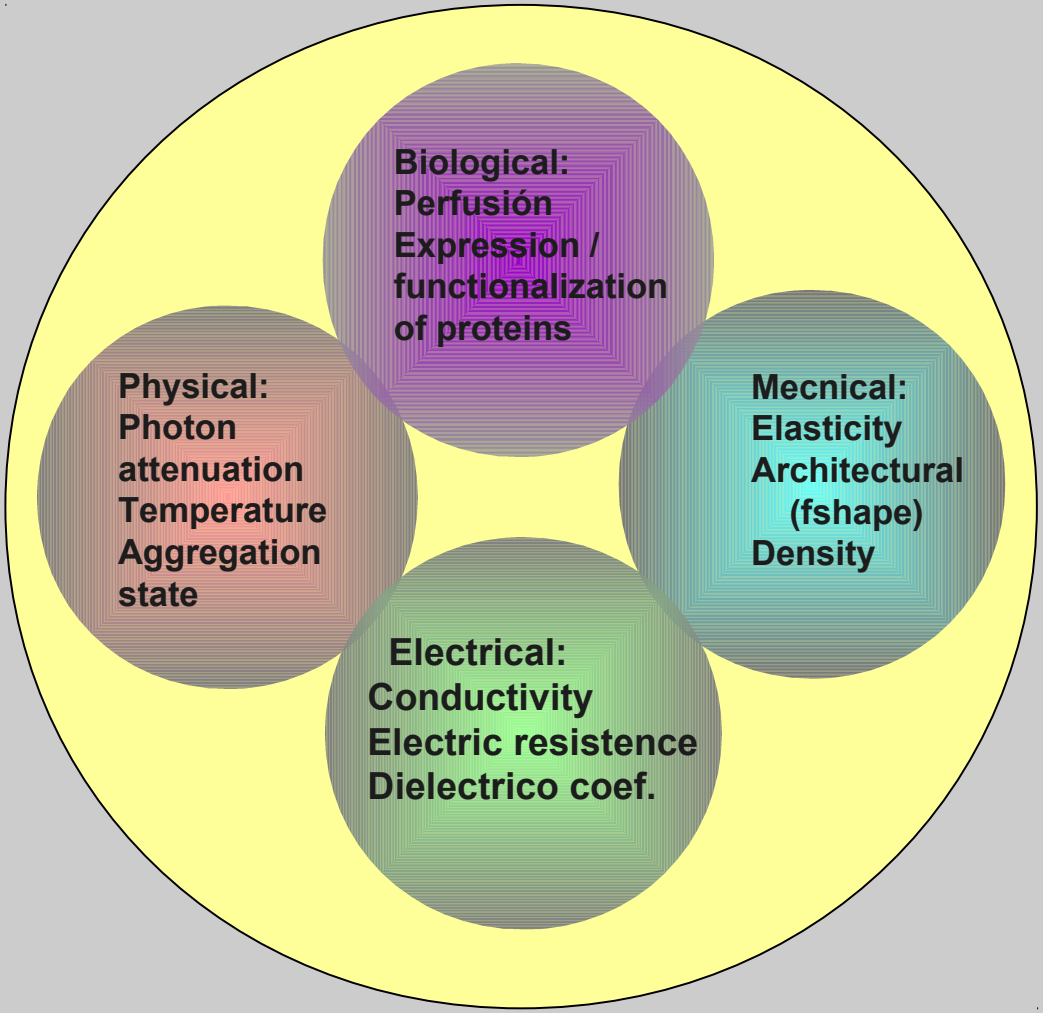


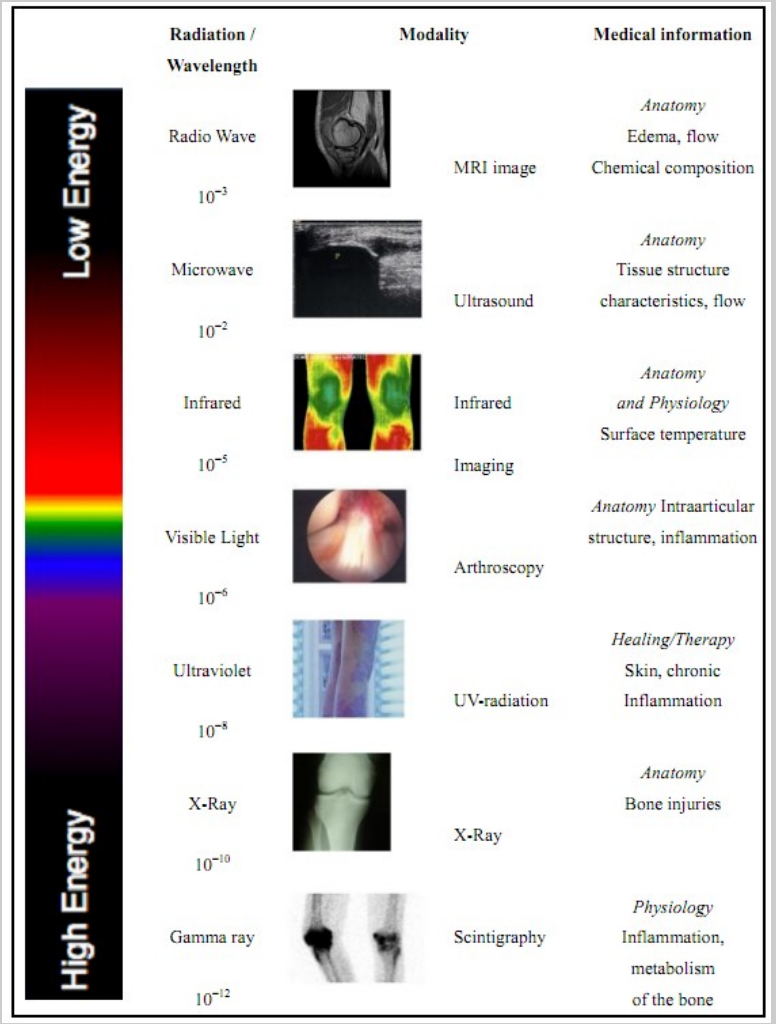




**Incidence rate = (New cancers / Population) × 100,000 (Mortality)**

All data taken from: www.globocan.com

# Imagenology techniques apply depending on Phys-Bio-Chem specific properties



# Summary of mamography technology up to 2001

**Mamography and Beyond: Developing Technologies for the Early Detection of Breast Cancer: www.nap.edu/catalog/10030.html**



| Technology | Image | Diagnosis | FDA aproval |
|---|---|---|---|
| Mamografia de imagen en plícula (FSM) | +++ | +++ | Sí |
| Mamografía Digital de Campo Completo (FFDM) | ++ | ++ | Sí |
| Detección Asistida por Computadora (CAD) | ++ | O | Sí |
| Ultrasonido (US) | + | +++ | Sí |
| Métodos de US novedosos (compuesto, 3D, Doppler, Armónicos) | O | O | No |
| Elastography (Resonancia Magnética --MR-- y US) | O | O | No |
| Imagenes por Resonancia Magnética (IMR) | + | ++ | Sí |
| Espectroscopia por Resonancia Magnética (MRS) | --/O a | --/O a | No |
| Scintimamografía | O | + | Sí |
| Tomografía por Emisión de Positrones (PET) | O | O | Sí |
| Imágenes Ópticas (OI) | O | + | No |
| Espectroscopia Óptica (OS) | -- | O | No |
| Termografía | O | + | Sí |
| Mediciones del Potencial Eléctrico | O | + | No |
| Imagenes por Impedancia Eléctrica (EII) | O | + | Sí |
| Palpitación Eelectrónica (EP) | O | NA | No |
| Tomografía Computacional por Termoacústica (TCT) | | | |
| Imagenes de Microondas (MI), Efecto Hall (HEI) | | | |
| Magnetomamografía | NA | NA | No |

**La tabla es un intento por clasificar muy diversas tecnologías en continuo cambio, por lo que la clasificación no es fija**

**a: Material de biopsia ex-vivo / para RMS es in-vivo**

**Tabla explicativa de la simbología:**

**--** La tecnología no es apta para esta aplicación
**NA** No hay datos disponibles respecto a esta aplicación
**O** Los datos pre-clínicos sugieren que la técnica puede ser útil para la detección de cáncer mamario. Sin embargo los datos clínicos aun son pobres, no hay conclusión final.
**+** Los datos clínicos sugieren que esta tecnología podría llegar a ser útil e importante. Requiere de mas investigación.
**++** Ésta técnica podría ser útil en situaciones específicas, ya que complementa (o es equivalemnte a tecnologías existentes. Su uso rutinario aun no es recomendable.
**+++** Ésta tecnología es de uso rutinario para hacer desiciones clínicas en este tipo de aplicación.

# Photothermal tomography: an existing system

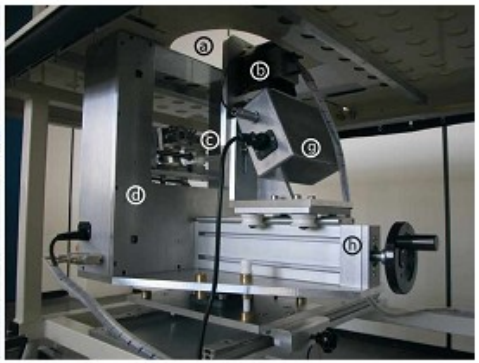
**The Twente Photoacoustic Mammoscope: system overview and performance**

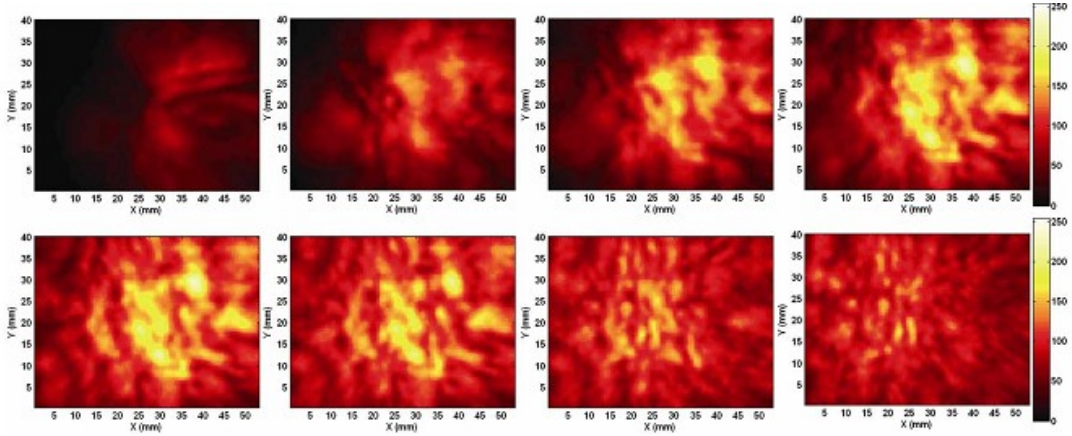
Phys. Med. Biol. **50** (2005) 2543–2557

Srirang Manohar[1], Alexei Kharine[1], Johan C G van Hespen, Wiendelt Steenbergen and Ton G van Leeuwen

**Initial results of *in vivo* non-invasive cancer imaging in the human breast using near-infrared photoacoustics**

Srirang Manohar[1*], Susanne E. Vaartjes[1], Johan C. G. van Hespen[1], Joost M. Klaase[2], Frank M. van den Engh[3], Wiendelt Steenbergen[1], and Ton G. van Leeuwen[1,4]

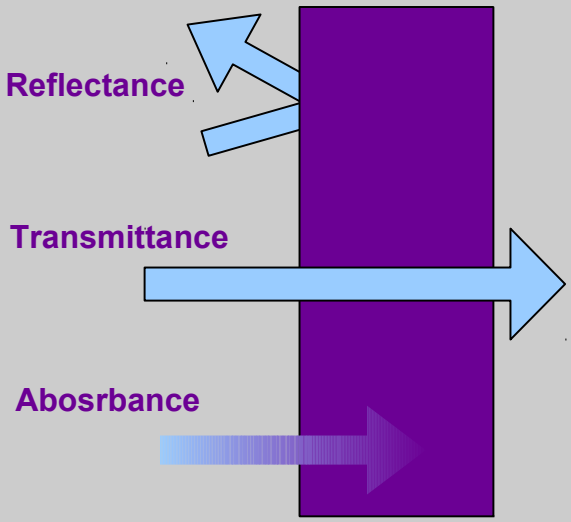




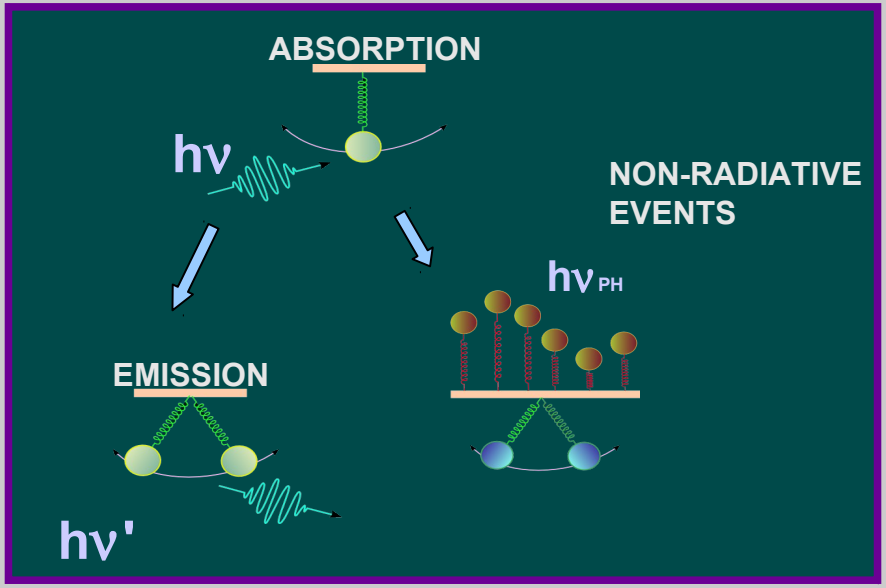
'Slices' having .5 mm separation .

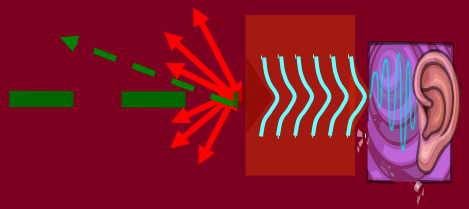
Scanned range:
6.5 mm to 17 mm depth, starting at the laser light illuminated surface

# Fenómeno Fototérmico




The Interaction Radiation Matter



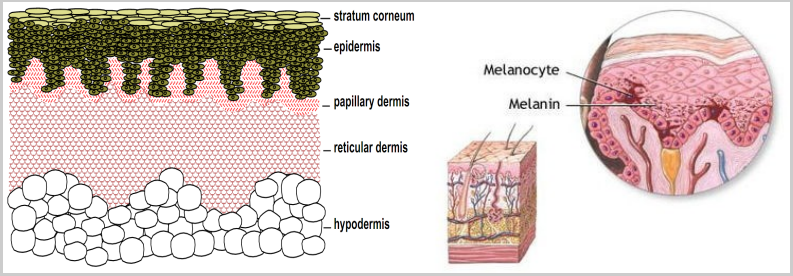



Non-radiative processes induces thermal and mechanical perturbations similar to waves

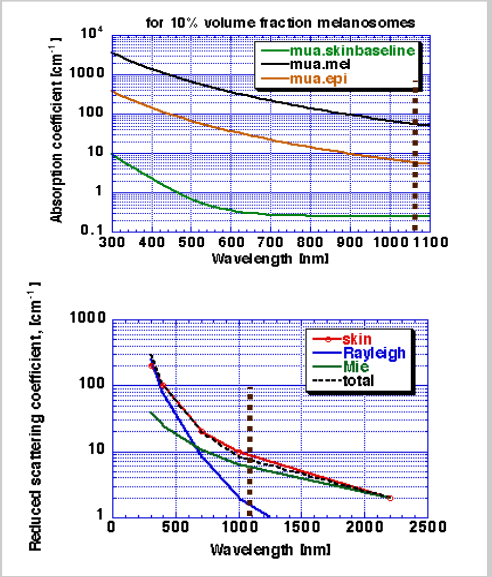
**Energy balance (conservation of the energy)**

$$R + T + A = 1$$

# SKIN OPTICAL PROPERTIES




Schematic cross-section of human skin tissues and the subcutaneous fat tissue (hypodermis)




## Optical absorption coefficients

Skin optical baseline

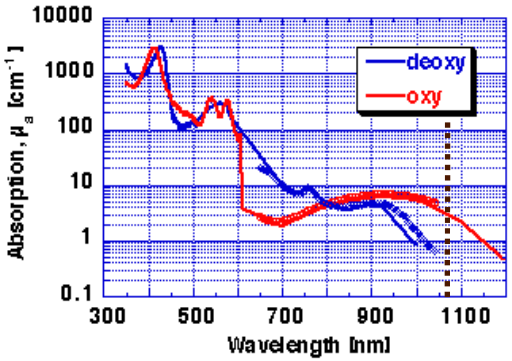
$$skinbaseline = 0.244 + 85.3\,e^{-\frac{\lambda - 154}{662}} \quad [cm^{-1}]$$

Melanine absorption coefficient

$$mel = 6.6\text{x}10^{11}\ \lambda^{-3.33} \quad [cm^{-1}]$$

Epidermal absorption coefficient

$$epi = f * mua + (1 - f) * skinbaseline$$



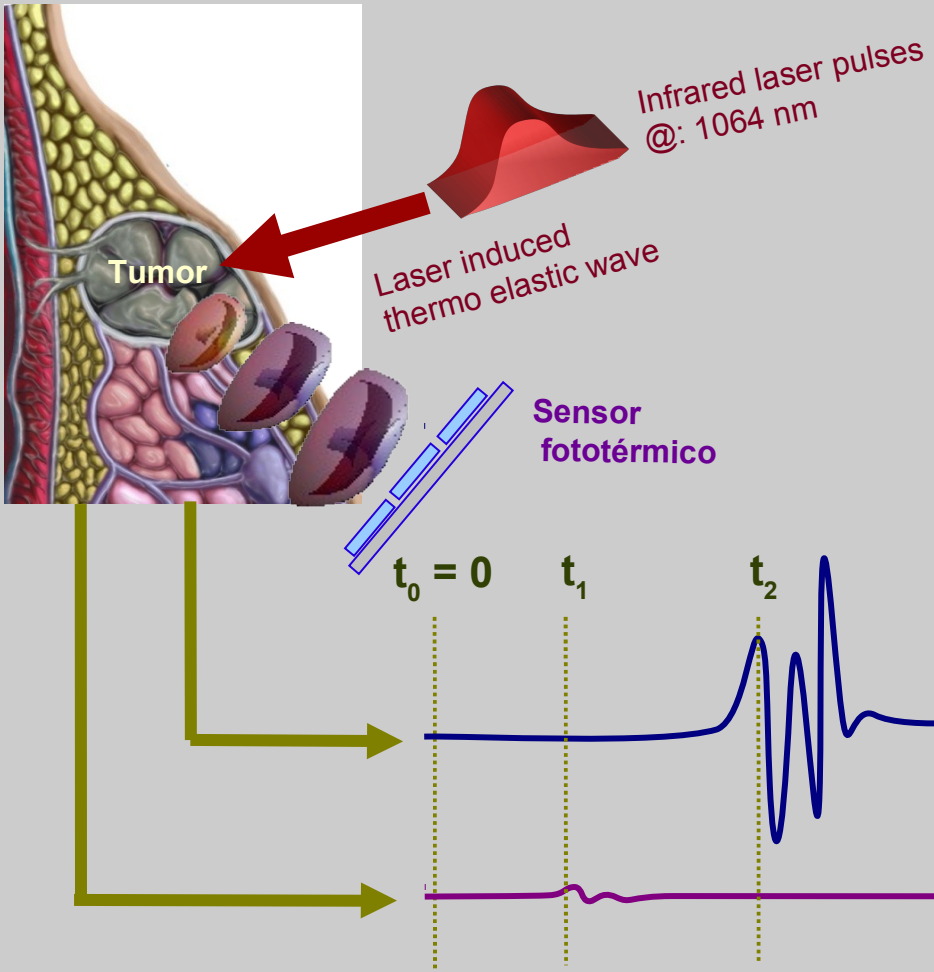

f : melanosomes fraction

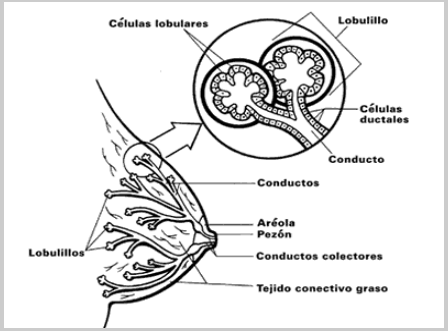
- light-skinned adults 1.3 – 6.3 %
- moderately pigmented adults 11 – 16 %
- darkly pigmented adults 18 – 43 %

**All data taken from: http://omlc.ogi.edu/news/jan98/skinoptics.html**

# Photothermal breast cancer tomography concept

## Concept Schematics




**For purposes of concept the skin optical response is neglected**

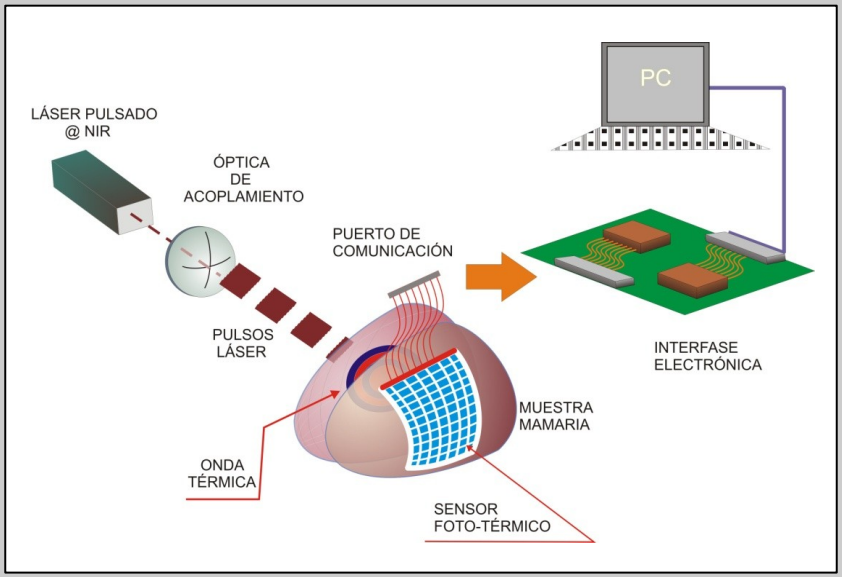
Cureves are cartoo-representation of the aimed copncept

# CCADET's Photothermal Tomiography concept

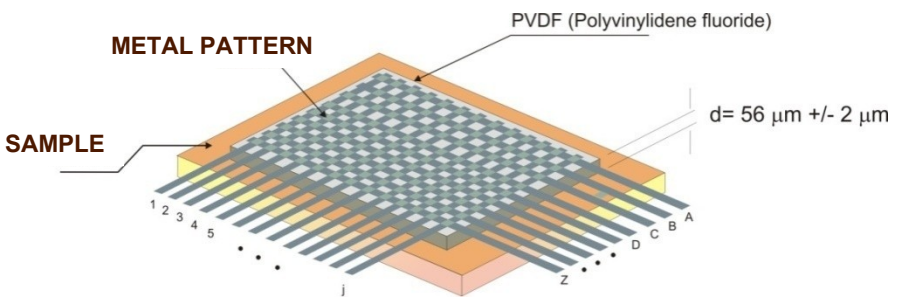
## Methodology

1. Manufacture of testing phantoms
2. 2D-sensors array development
3. Testings
4. Development of signal amplification and data storage.
5. Data processing and image formation
6. Development of theroetical models

**Note: the whole protocole dealth with lab testings without get involbed with the use of biological samples.**




**EARLY SKETCH OF 2D SENSOR ARRAY**

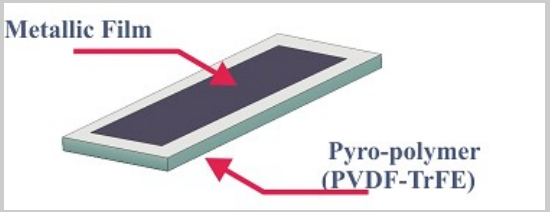



**Initial main target:**

**To develop conditions to simulate related aspects of breast tissue and thus achieve lab testings of the developed technology**

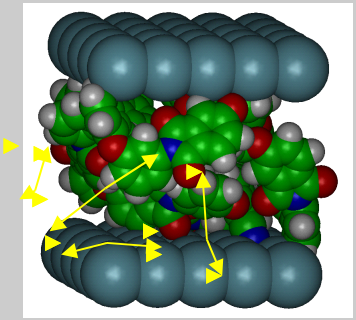
# Pyroelectric sensors

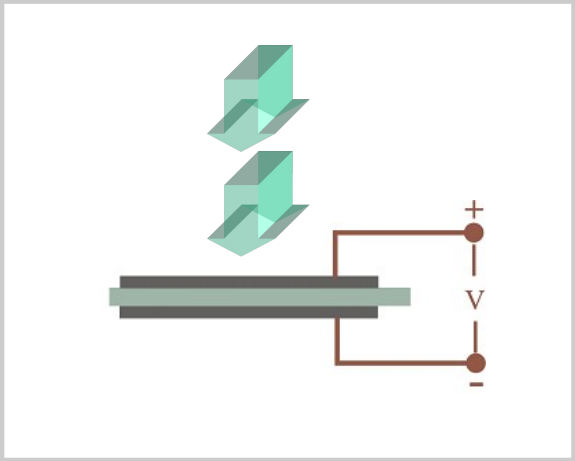
Pyroelectricty: Caused in specific material, where a temperature or stress gradient prompts a sudden potential difference Voltage) or electric current

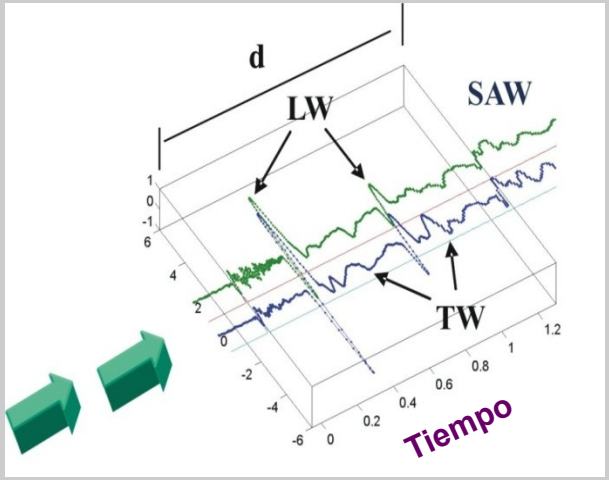



PVDF (Polyvinylidene Fluoride): KYNAR-500® ).

Rango de respuesta: 0.01 Hz – 2 GHz

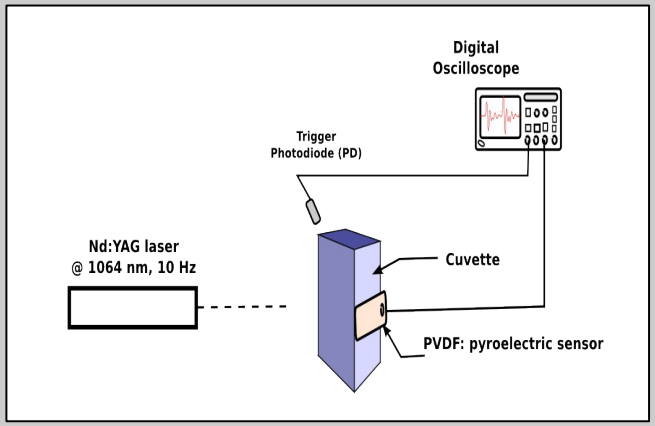




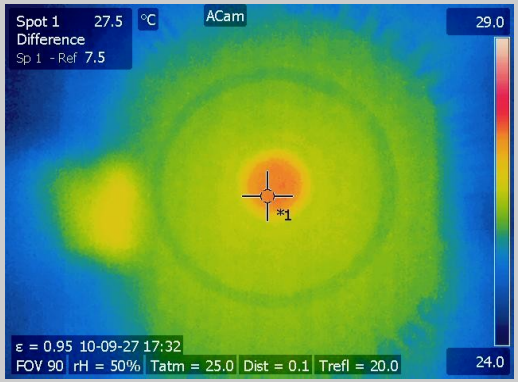



# Finding the right nanoparticles

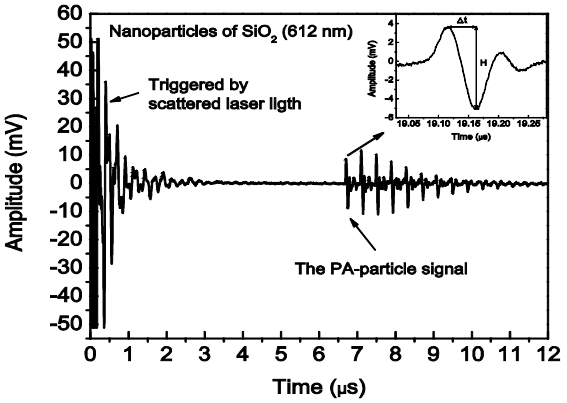
## Experimental set-up

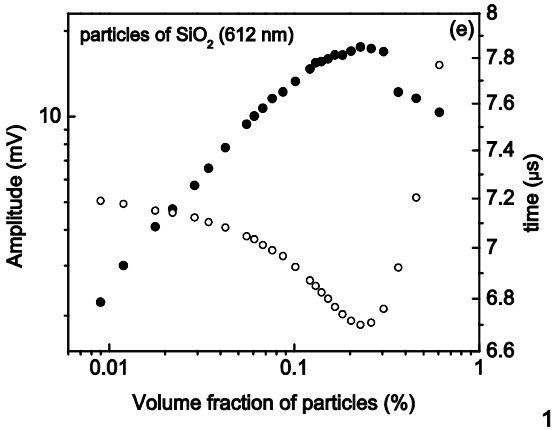


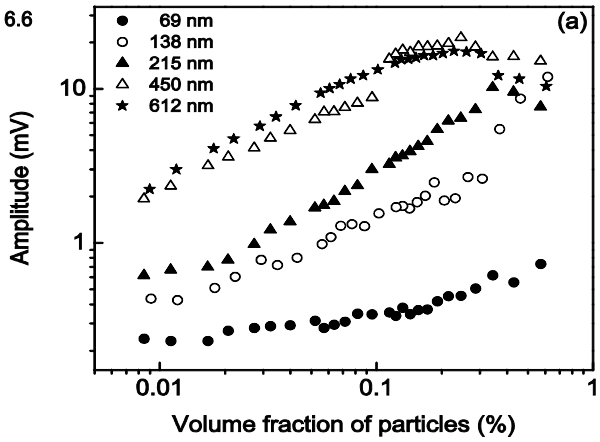

## Thermography of nano-particles estimulated with CW laser light




## Photo-thermal response of nano-particles diluted in water and stimulated with laser pulses

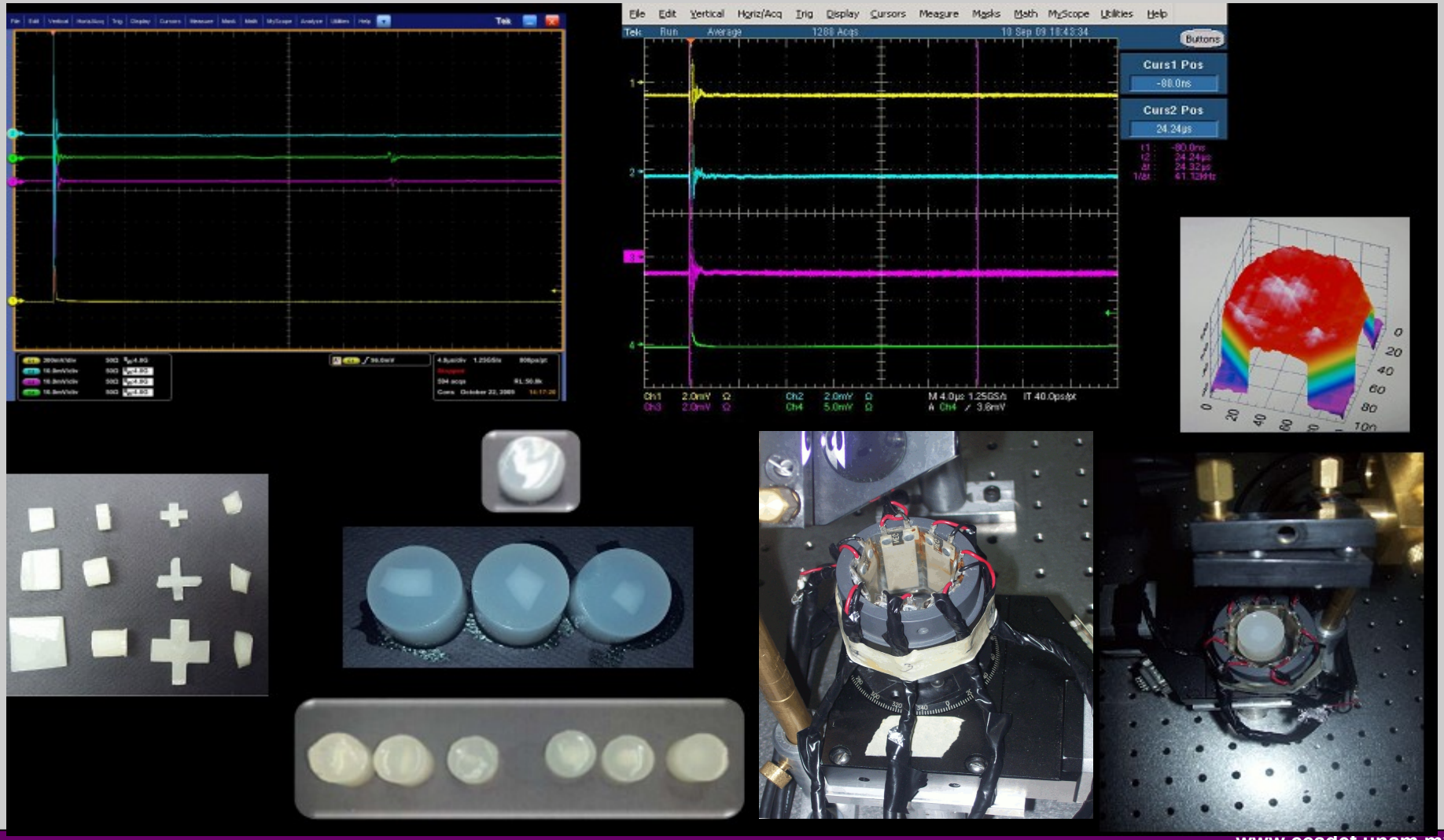


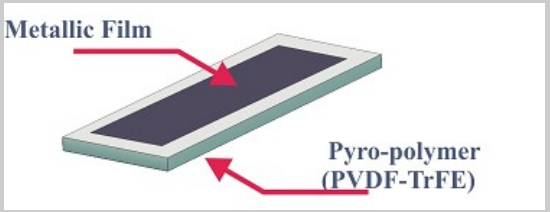



# Early phantom manufacture and signal detection

## Phantoms based on Agar + nano-particles

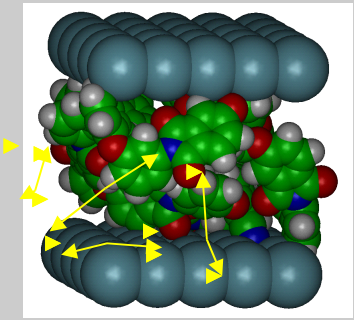


# Manufacture of 2D-array sensors

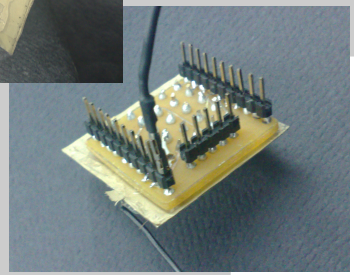


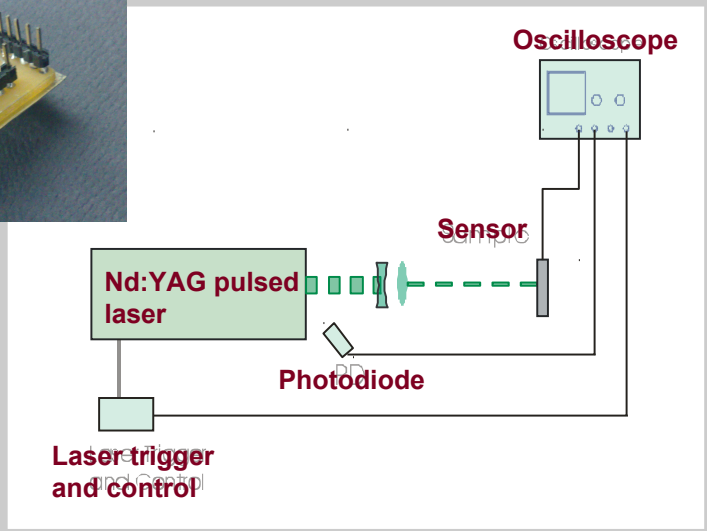

PVDF (Polyvinylidene Fluoride): KYNAR-500® ).

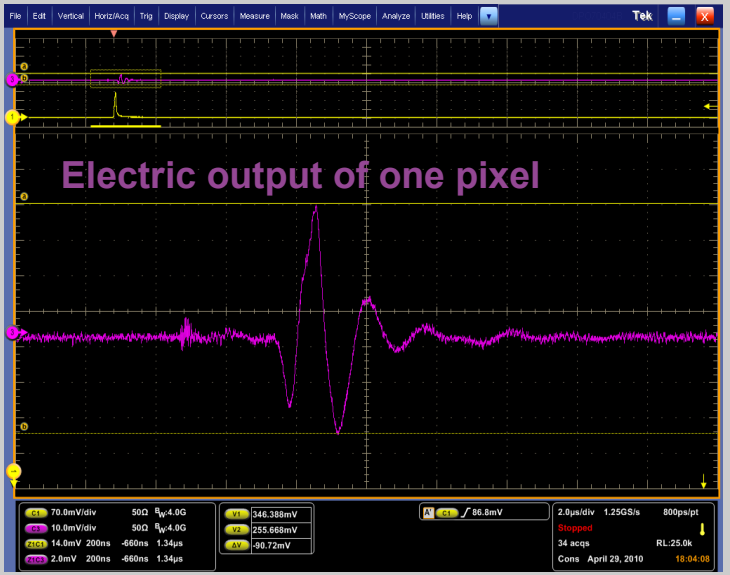
Rango de respuesta: 0.01 Hz – 2 GHz



## Front and back side view of sensor





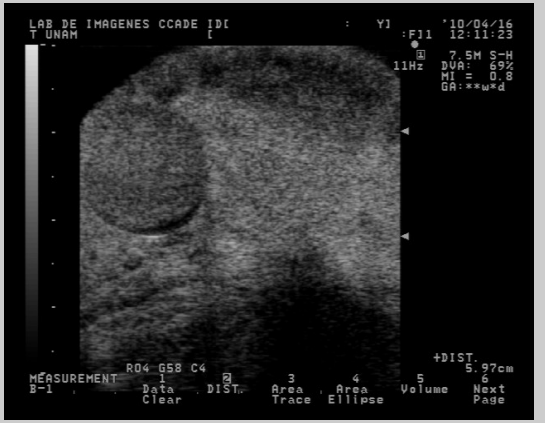



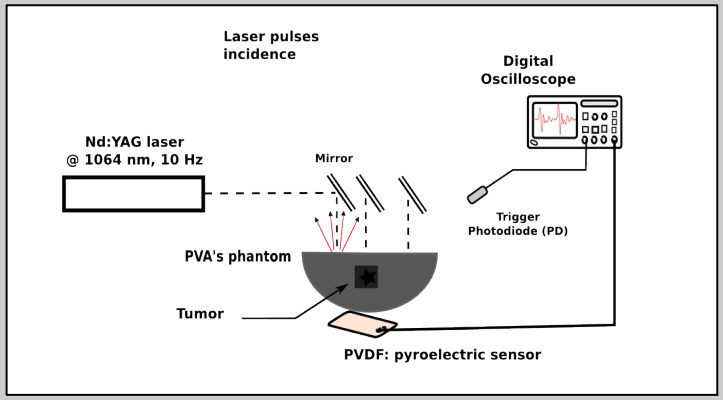
# Advanced Phantom

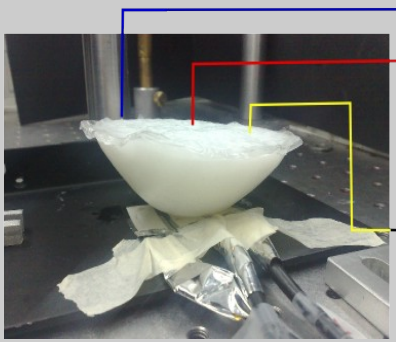
## Laser testing of a phantom with dummy lesion inserted

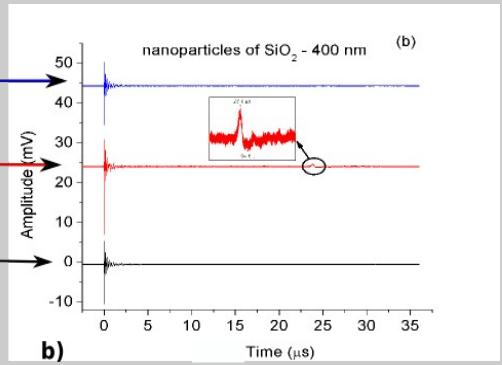
## Phantoms based on polyvinyle alcohol (PVA) and nano-particles of different kinds

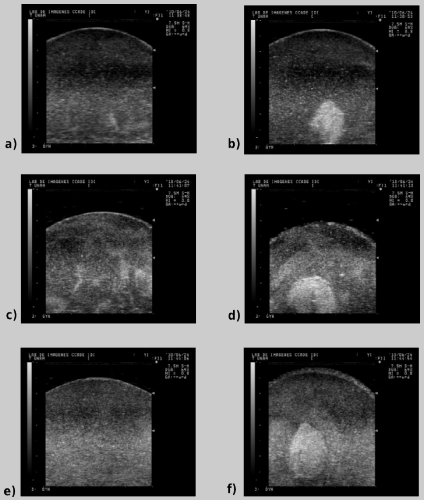
## Ultrasound image testing of a phantom



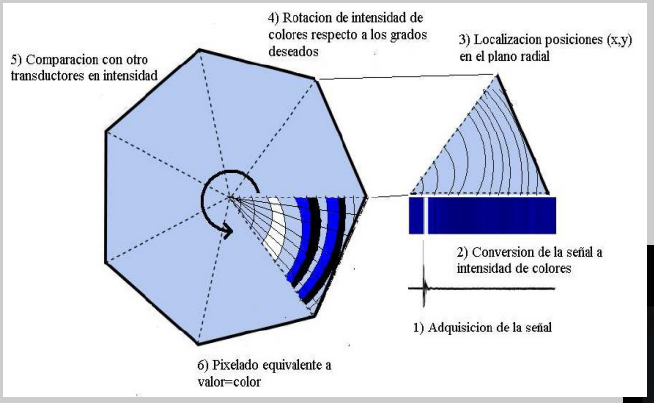



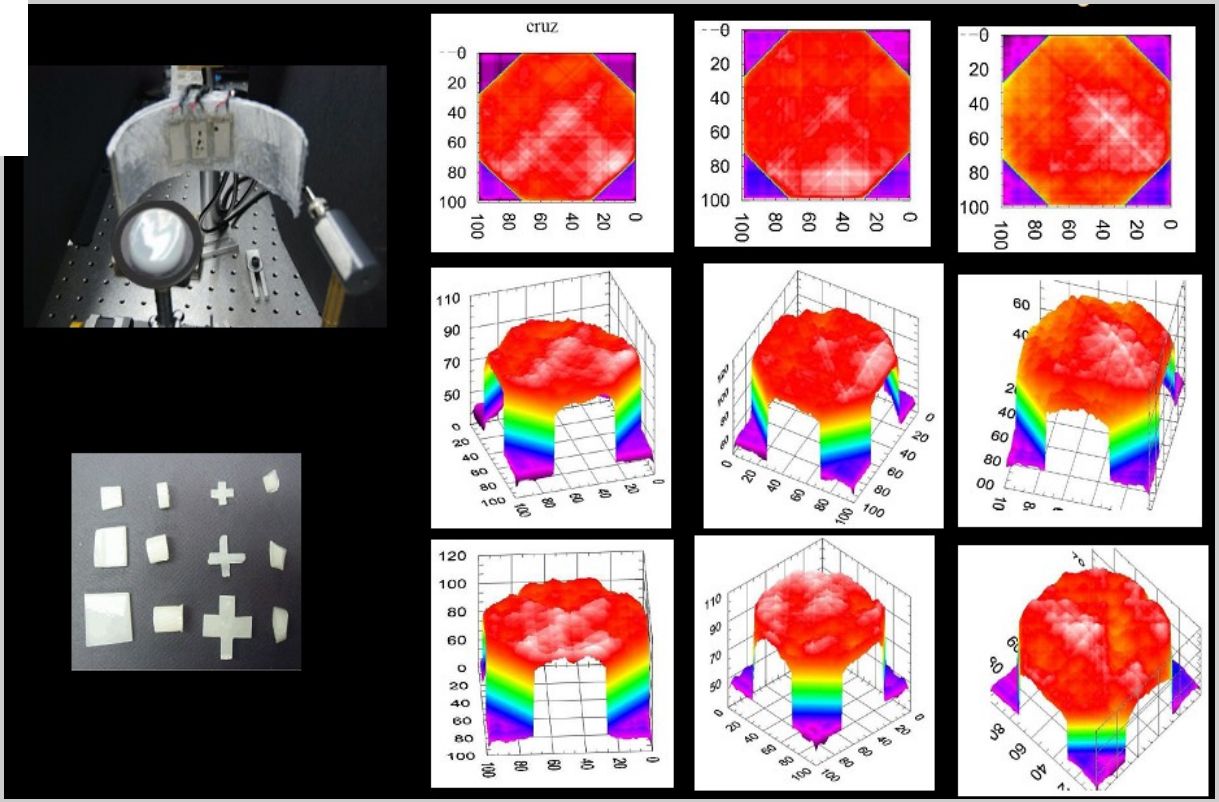




With the support of lab facilites from Dra. Yolanda López Vidal and Dr. Gonzalo Castillo Rojas (Fac. med-UNAM)

# Image generation scanning obejcts with one sensor




Data processing and Image formation via Radon transform




**This piece of work was carried on by students at U. de Gto supervised by Dr. Gerardo Gutierréz Júarez and Dr. C. García Segundo**

# Bottomline in developing breast cancer tomography

The Imagenology technology alone will not eliminate breast cancer.

There is no imagenology technique that produces definitive breast cancer diagnosis.

The tomographic image interpretation is still largely depending on human subjective interpretation.

Ideally, early detection (diagnosis) is desirable.

Early diagnosis is a relative term: It depends on tumor growth rate.

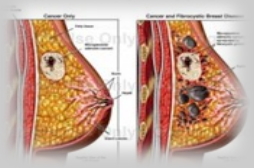


Diagram for marking the image test output.

| Image test outcome \ Prognosis | + | - |
|---|---|---|
| + | TRUE POSITIVE (TP) | FALSE POSITIVE (FP) |
| - | TRUE NEGATIVE (TN) | FALSE NEGATIVE (FN) |

# Base of Technology is there,
# How come this tuns out to be out of the science lab ?

Now days cost - effectiveness ratio is the cornerstone:
early detection?

Early detection largely depends from research and
novel advancements in science and technology

Several kinds of approvals are required:

- Industry and medical community
- Government
- End user cost (patient)
- End user perception

ISSUES BEFORE REACHING THE END-PRODUCT DEVICE

- Medical counterpart
- Testings
- Set up the safety conditions
- Verify we have definitive and reproducible results
- Cost-effectiveness analysis can be done once points above are answered.
- Reduction and /or elimination of collateral effects = research

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