University of Twente

Sound Light: photoacoustic imaging of cancer

Wiendelt Steenbergen
MIRA institute / Biomedical Photonic Imaging Group

University of Twente
The Netherlands

Biomedical Photonic Imaging group

Geography

Amsterdam

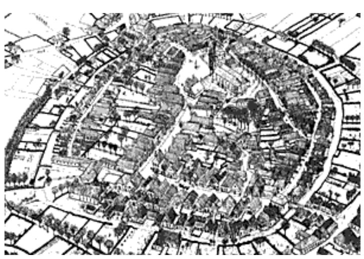
Twente

Enschede
(155000 inhabitants)

www.lib.utexas.edu/maps/europe/netherlands_rel87.jpg

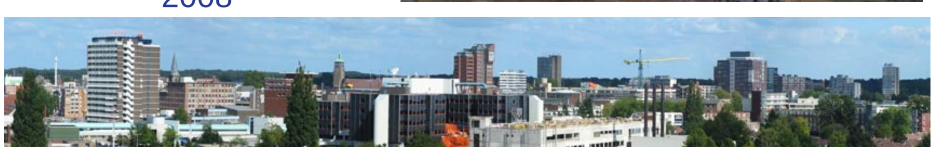
Enschede

1826



1916

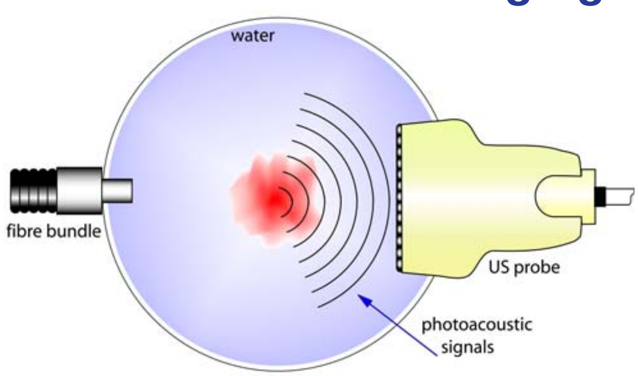
2008



http://www.enschede-stad.nl

Enschede

Photoacoustic Imaging



$$p = \Gamma \mu_a \Phi(x, y, z)$$

Absorption → Temperature rise → Thermal expansion → Stress → Sound

Overview of tumor imaging studies

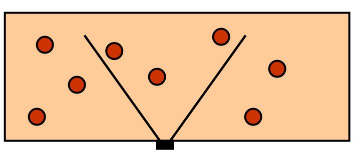
Animals:

- Vascularisation during tumor growth

Humans:

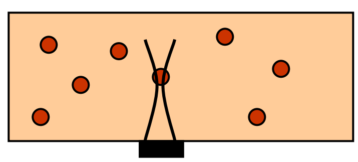
- PA Mammography

Detection geometries



Wide angle detection

- Reconstruction needed
+ Can be made into array



Focussed detection

+ No reconstruction needed
- Cannot be made into array

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Photoacoustic imaging of subcutaneous tumor

- Lewis rat (male, 250 g)
- 8 x 10^6 pancreas tumor cells injected subcutaneously in hind limb
- Measurements on day 3, 7, 8 and 10 (tumor injected on day 1)
- Wavelength 1064 nm
- Pulse duration 14 ns
- Pulse energy 2 mJ
- Focussed and unfocussed detector

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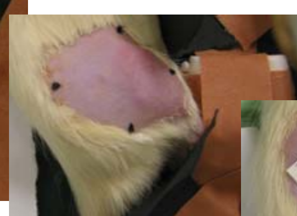
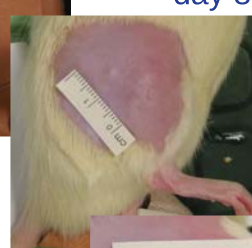
day 3

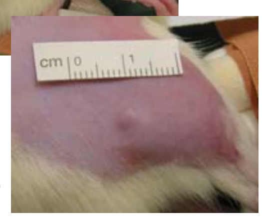


day 7

day 8



- Lewis rat (male, 250 g)
- Subcutaneous pancreas tumor
- Wavelength 1064 nm
- Focused detector



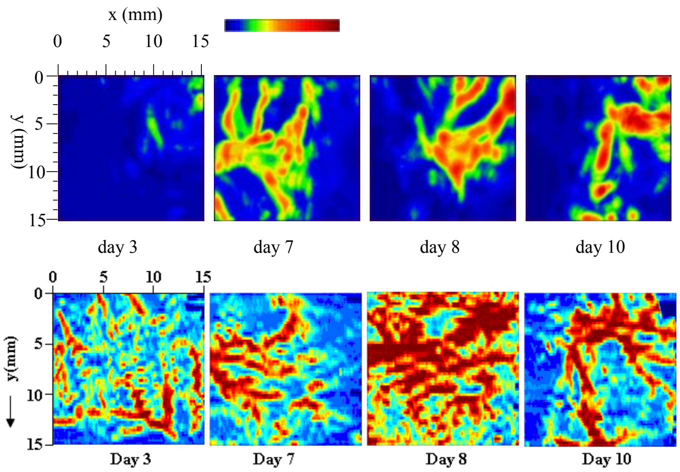
day 10

Erasmus Universiteit Rotterdam

Maximum intensity projections

unfocussed sensor

focussed sensor



Thumma *et al.*, Optics Express (2005)

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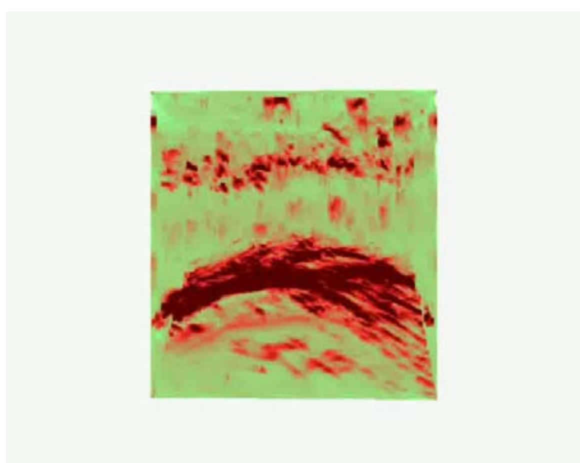

Overview of tumor studies

Animals:

- Vascularisation during tumor growth

Humans:

- PA Mammography

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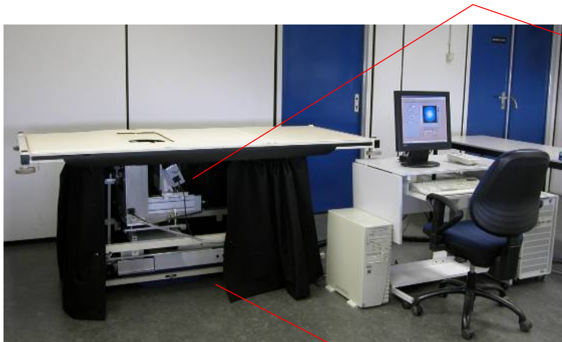
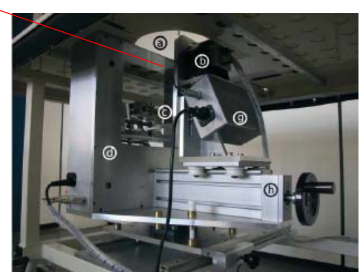
The Photoacoustic Mammoscope 1 (PAM1)

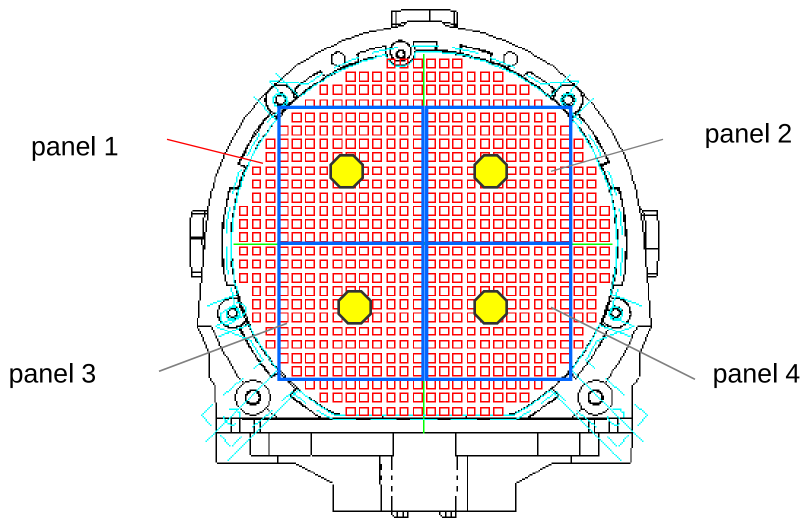
ultrasound detection array, 1 MHz





ND-YAG laser, 1064 nm, pulse energy 60 mJ

Phys. Med. Biol. (2005)



Photoacoustic mammography

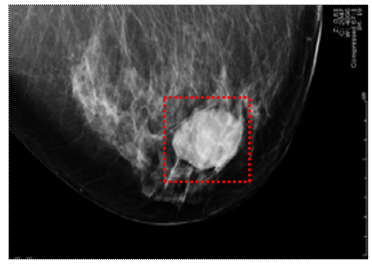
pilot study

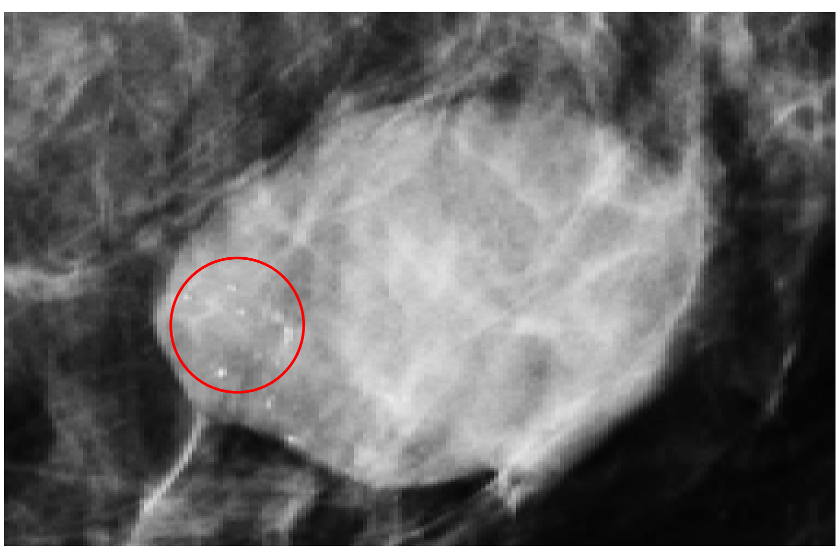
- Inclusion criteria
  - Palpable lump
  - X-ray and US: high suspicion for malignancy
  - Pre-selected by clinician for high probability of detection
  - Subjects in good general health (45 minutes exam)
  - Of legal age; fully competent to give informed consent etc
- Exclusion criteria
  - Patients with history of surgical biopsies

Manohar *et al.*, *Optics Express* (2007)

Case

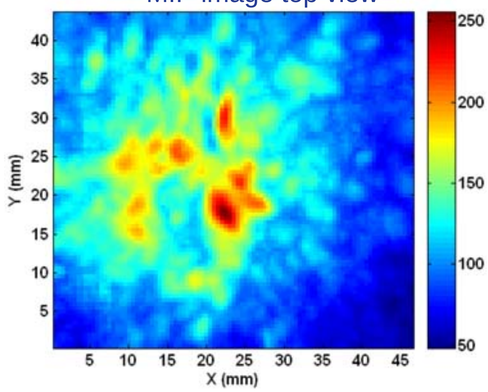
- 57 year, Caucasian
- Palpable lump central in right breast
- Carcinoma with neuroendocrine differentiation
- ROI photoacoustic scan: 43x46 mm
- Breast thickness in scanner: 59.5 mm

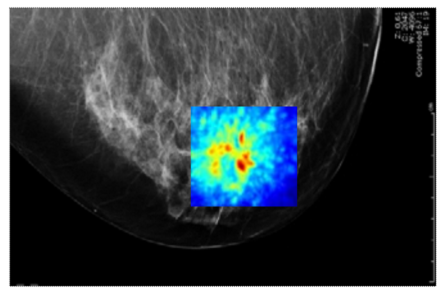




Optics Express (2007)

MIP image top view

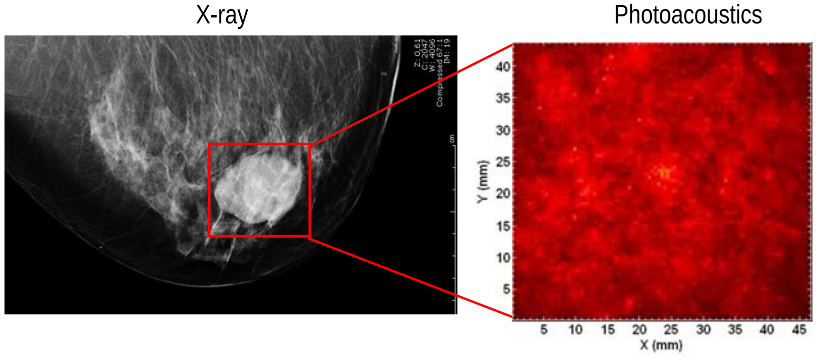




Carcinoma
Pathology: tumor size = 26 mm
Photoacoustics: tumor size = 25 x 32 mm

X-ray

Photoacoustics



Steps of ¼ mm,
from 20 to 5 mm depth

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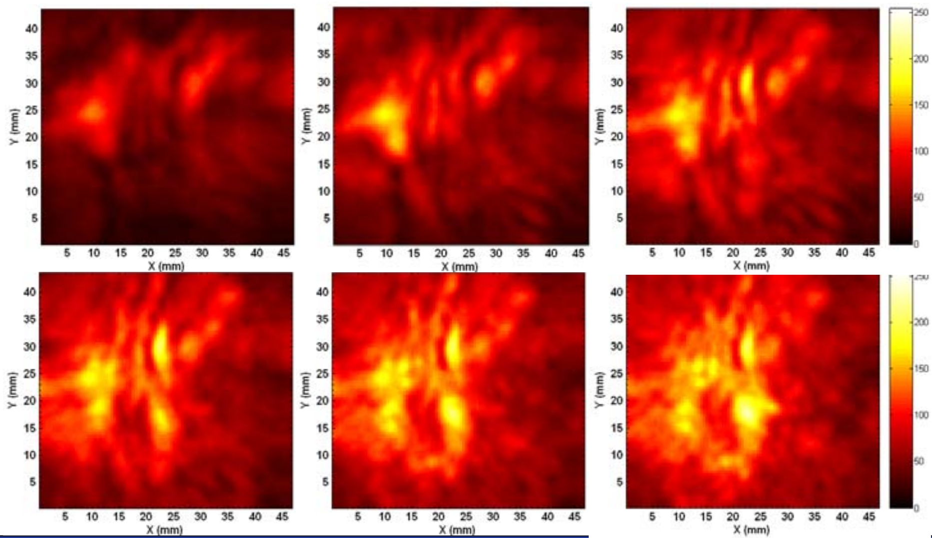
Slices starting at 7 mm in steps of 1 mm



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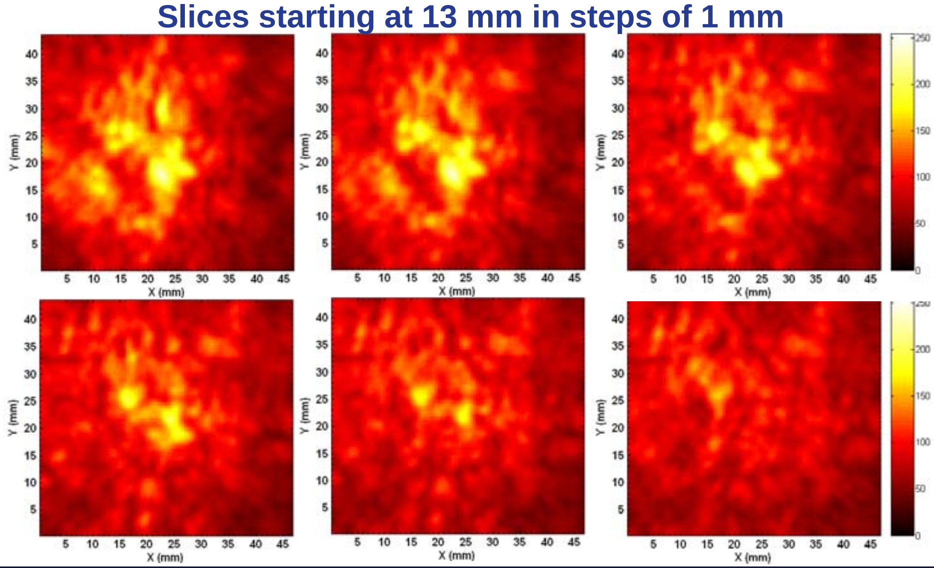
Slices starting at 13 mm in steps of 1 mm



Photoacoustics, current status

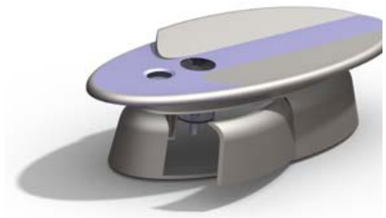
Capabilities of PA shown *in vivo* for

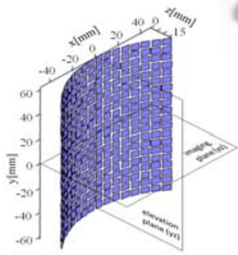
- Imaging of implanted subcutaneous tumors
  - Resolution: 100-150 μm
  - Measurement depth: 5 mm
- Breast imaging
  - Instrumental resolution 3 mm
  - Measurement depth 15-20 mm (128 averages)

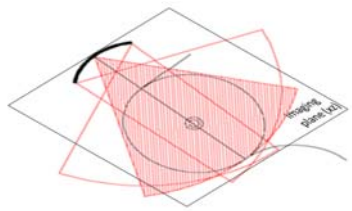
Needs for better photoacoustics

- faster imaging
  - Parallel signal acquisition (money)
- more quantitative imaging
  - More signals for better image reconstruction
  - Cope with acoustic tissue inhomogeneities
  - Measure absolute concentration of substances

PAM2: from flat plate to tomography







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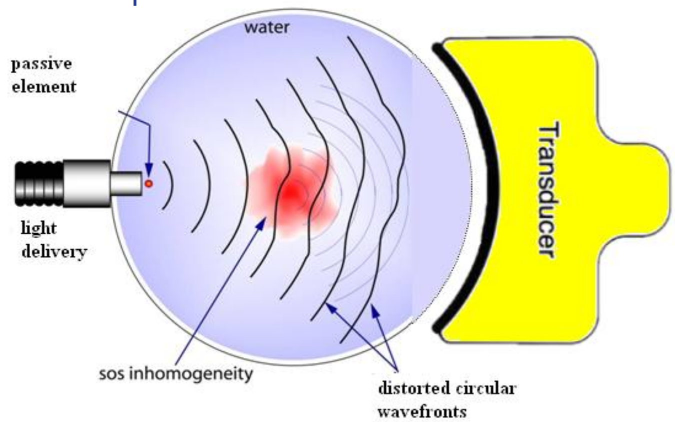
Imaging of acoustic parameters

Speed of sound and attenuation



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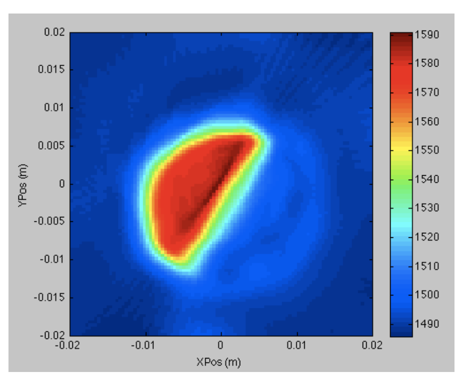
PVA inclusion in an agar phantom



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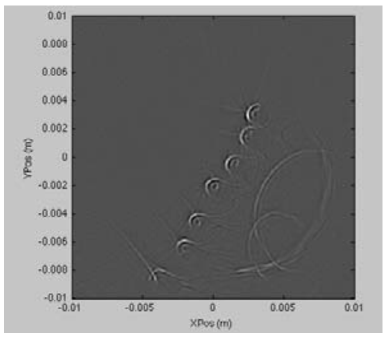
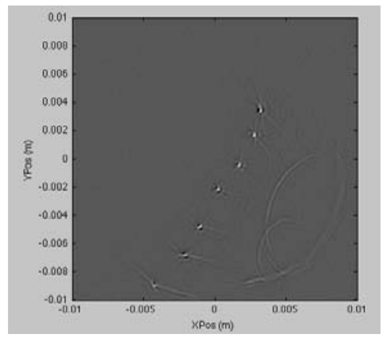
Effect of assumed speed of sound on PA image

Assumed SOS=1490 m/s



Using measured SoS map



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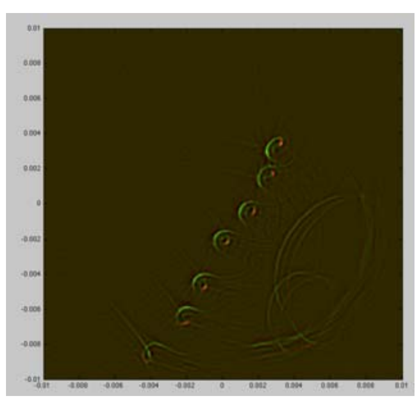
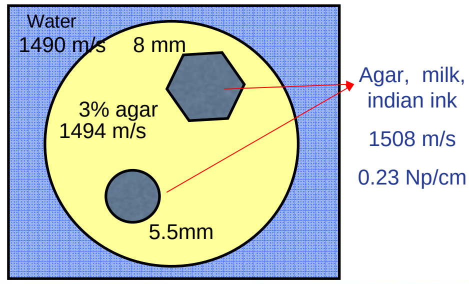
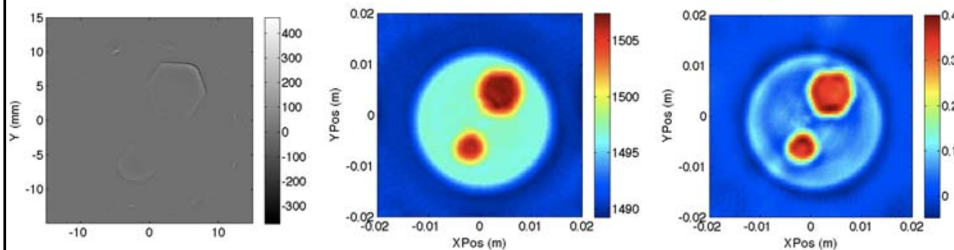
Effect of assumed speed of sound on PA image







PA Image SOS Attenuation

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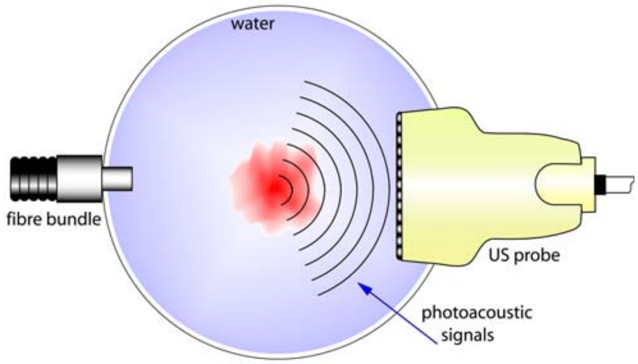
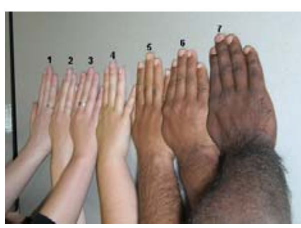
Photoacoustic Imaging



$$p = \Gamma \mu_a \Phi(x, y, z)$$

Absorption → Temperature rise → Thermal expansion → Stress → Sound

Tissue is a pinball machine



BSc thesis H.E. van Herpt

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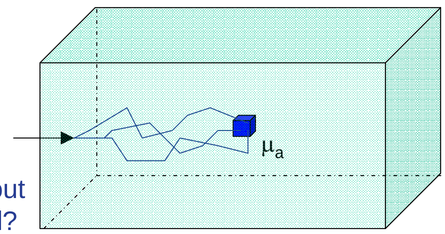
The quantification problem of photoacoustics

Initial pressure in absorbing volume after laser pulse:

$$P_0 = \Gamma \mu_a \boxed{\Phi(x,y,z)} ?$$

Γ: Grueneisen coefficient
Φ(x,y,z): Fluence

Can we estimate absolute absorption coefficients without using a light transport model?



Yes

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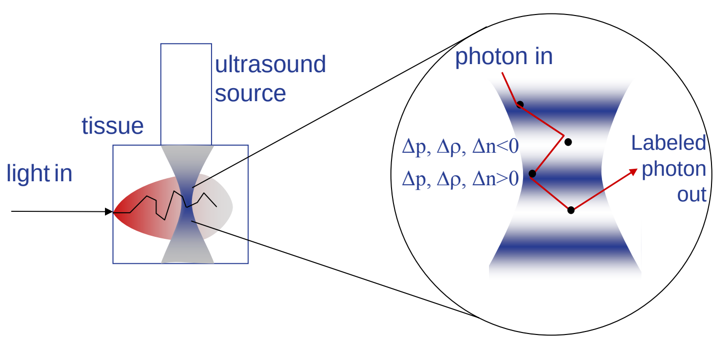
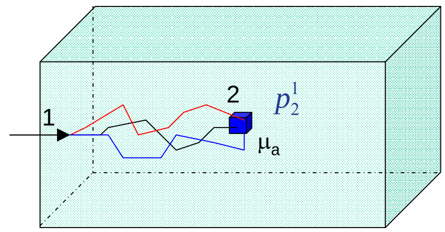
Principle 2: labeling of light

acousto-optic modulation

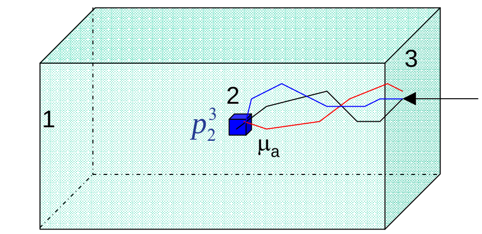


Step 1: PA excitation in point 1 and 3



$$p_2^1 = \Gamma \mu_a \Phi_2^1$$

$$\Phi_2^1 = fluence$$



$$p_2^3 = \Gamma \mu_a \Phi_2^3$$

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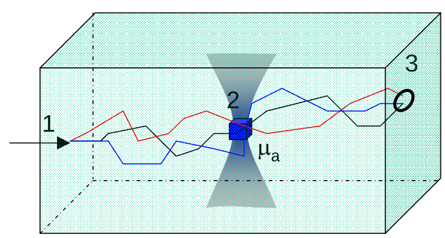
Step 2: label the light

inject in 1, label in 2, detect in 3



p_L^{13}

Amount of labeled light detected in 3:

$$p_L^{13} \propto \Pr(1,2,3) \propto \Pr(1,2)\Pr(2,3) \propto \Pr(1,2)\Pr(3,2) \propto \Phi_2^1 \Phi_2^3$$

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Step 3: combining measurements

$$p_2^1 = \Gamma \mu_a \Phi_2^1$$
$$p_2^3 = \Gamma \mu_a \Phi_2^3$$
$$p_L^{13} \propto \Phi_2^1 \Phi_2^3$$

3 equations, 3 unknowns

$$\mu_a = c\sqrt{\frac{p_1 p_3}{p_L^{13}}}$$

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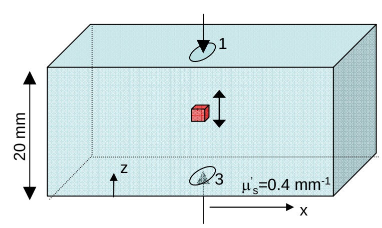
Verification with Monte Carlo

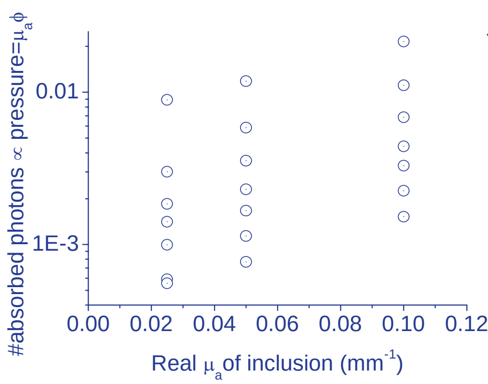


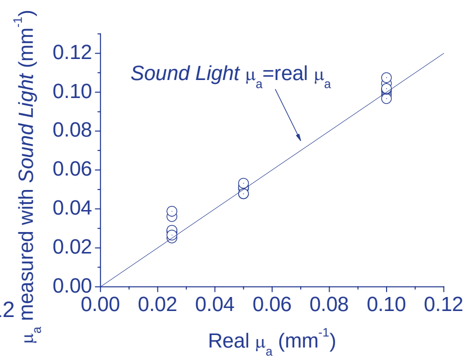
- 2D slab, thickness 20 mm
- Single absorbing inclusion: μ_a=0.025 , 0.05 and 0.1 mm^{-1}

Position variations for the absorbing inclusion:
At fixed x=y=0: 4<z<16 mm

Verification with Monte Carlo

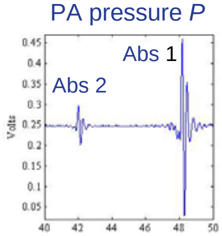
$P_0 = \Gamma \mu_a \Phi(x, y, z)$ varying z-position



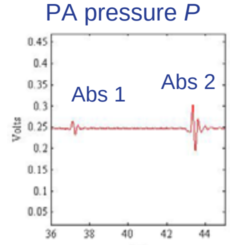


SOUND LIGHT: PRELIMINARY EXPERIMENTAL RESULTS

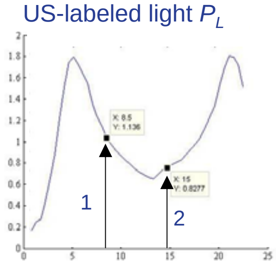
PA pressure *P*



PA pressure *P*



US-labeled light P_L



$$\mu_{a1} \propto \sqrt{\frac{P_{a1}^1 \times P_{a1}^2}{P_{L,a1}}} = 0.1092$$

$$\mu_{a2} \propto \sqrt{\frac{P_{a2}^1 \times P_{a2}^2}{P_{L,a2}}} = 0.1096$$

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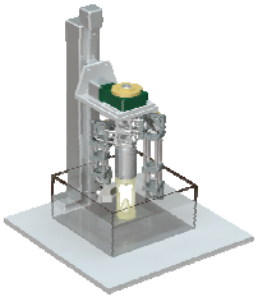
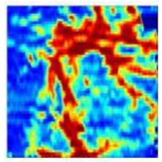
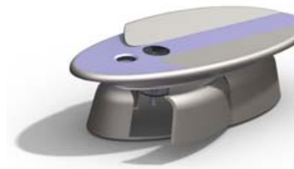
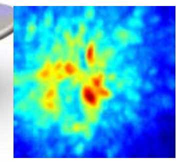
SOUND LIGHT IN ONCOLOGY





PAM2, PAM3...





Research: quantification of
- neovascularisation
- smart contrast agents
- local drug delivery
- molecular processes

Clinical: mammography
- screening
- diagnosis
- monitoring of therapy

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Han van Neck (Erasmus Medisch Centrum)
Joost Klaase (Medisch Spectrum Twente)
Frank van den Engh (Medisch Spectrum Twente)

FOM
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NWO Netherlands Organisation for Scientific Research
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