Photoacoustic Imaging in Biomedicine

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JOHNS HOPKINS
MEDICINE

Interventional Photoacoustic Ultrasound

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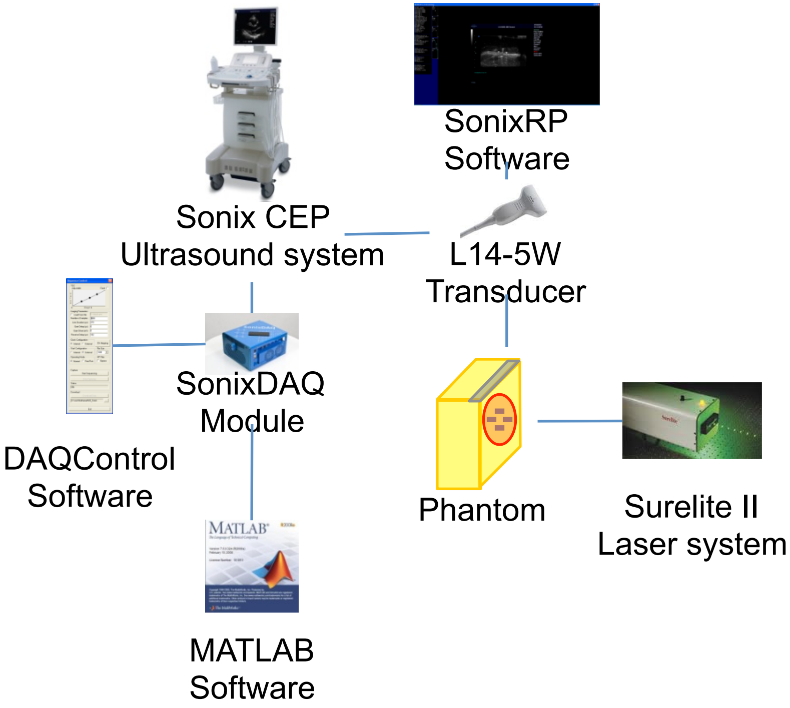
- Our project uses the principle of the photoacoustic effect to revolutionize Laparoscopic Partial Nephrectomy surgical procedures.
- Use photoacoustic imaging to obtain rigid transformations (perform registration) between ultrasound (US), camera, and laser domains.



SonixRP Software

Sonix CEP Ultrasound system

L14-5W Transducer

DAQControl Software

SonixDAQ Module

Phantom

Surelite II Laser system

MATLAB Software

Paper Selection

- This paper is a review of all modern theoretical and quantitate approaches of PA imaging.
- Thorough introduction to the quantitative approaches of Computer Tomography—most common area of application of PA imaging.
- Current state of the field including promising biomedical applications and recent experiments.
- Benefits of PA imaging (PAT) over other medical imaging technologies.

Background

- When matter is exposed to high frequency pulses of light, most of the light's energy will be absorbed by the molecules in the incident matter.
- As the energy from the light is converted to heat, the molecules become thermally excited.
- Heat waves will then radiate away from the matter causing sound waves due to pressure variations in the environment around the medium.
- These sound waves can then be detected by acoustic devices such as ultrasound.

RF/Laser Pulse

Absorption

Thermal Expansion/
Acoustic Wave
Generation

Ultrasonic Detection

Introduction

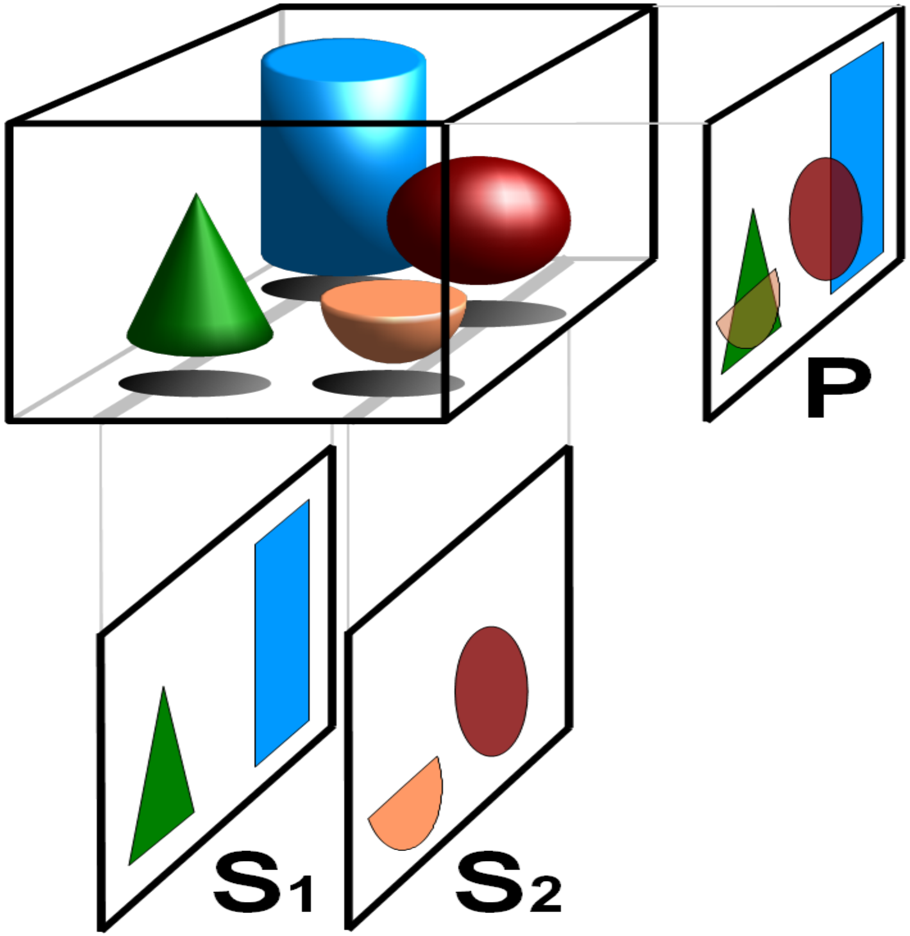
- Nonionizing waves (lasers, rf, etc) are often used to excite sound waves (PA signals) in biological tissues.
- Motivation behind PA imaging is to couple ultrasonic resolution with high contrast light due to a laser source, or rf, absorption.
- Current optical imaging technologies can only provide a maximum spatial resolution of ~1cm. PA imaging overcomes this and can provide resolution of ~0.1mm.

Optical Properties of Tissues

- Optical properties include absorption and scattering.
  - Scattering tells you architectural changes at the cellular/sub-cellular levels of the tissue.
  - Absorption properties can be used to quantify angiogenesis and hypermetabolism ("hallmarks of cancer")
- These optical properties can be used to determine light propagation in tissues by performing a Monte Carlo Simulation.
- PA imaging has a greater spatial resolution b/c ultrasound scattering is 2-3 orders of magnitude greater than optical scattering.
- As a result PA imaging that relies on optical properties can be used to deduce physiological parameters (such as O2 levels, [] of hemoglobin, etc).
  - This can be used to quantitatively identify angiogenesis and hypermetabolism, hence functioning as an early indicator for cancer.

Scanning Tomography

- More than 90% of papers that exist on PA imaging are on computational approaches and algorithms for tomography.
- Tomography is the basic idea of imaging by sections or layers of the entire image.



Laser-based microscopic imaging

- A laser system can generate pulses of 10ns durations.
- These are small enough to excite PA signals at high frequencies (100 MHz)
- Therefore PA images can be obtained in large soft-tissue areas with good SNR.
- Average laser-based PA scanning tomography can produce images with axial resolutions of 30µm.
- Ex: Imaging early stages of squamous-cell carcinoma in the oral mucous of golden hamsters *in vivo.*

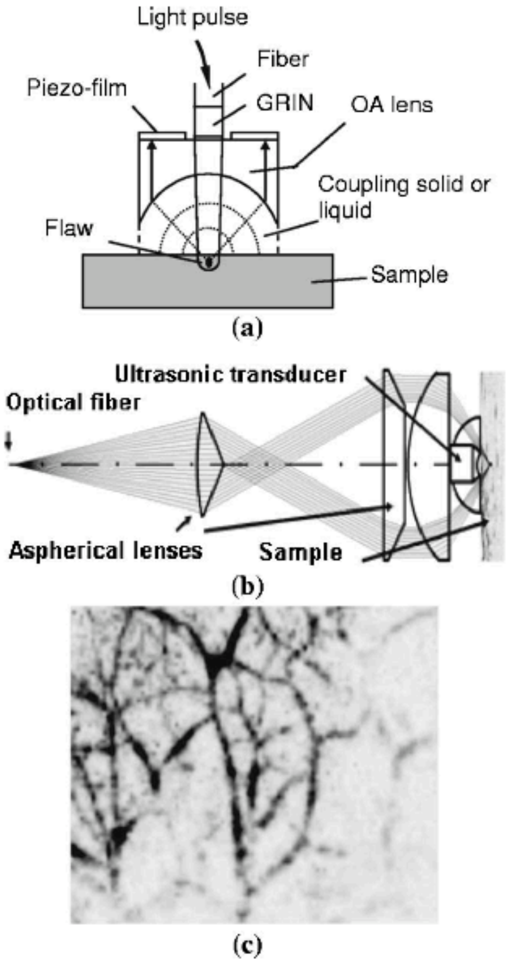


FIG. 3. (a) Diagram of a bright-field confocal photoacoustic microscope in the backward detection mode. (b) Schematic of the photoacoustic sensor of a dark-field reflection-mode photoacoustic microscope. (c) Photoacoustic image of vascular distribution in rat skin.

Computed Tomography

- >90% of modern works on PA imaging deal with PA Tomography (PAT)
- The emphasis is on reconstruction-based PAT
  - More flexible in dealing with PA signal b/c you don't have fixed lenses or transduces with limited (and fixed) imaging regions
  - Obtain temporal measurements by measuring the PA signal at various detection positions
  - Obtain a complete 3D reconstruction by combining these temporal and 2D spatial measurements.
- The Inverse Source Problem is the primary motivator of PAT reconstruction.
  - Let H(r,t) be the heat source, and p(r,t) be the pressure at position r; this obeys a linear wave equation.
  - The key to the PAT reconstruction is the difference between the initial source pressure Po(r) and the measured data Pd(r, t)
  - The following wave equation can be solved by using the free-space Green's function.

$$\nabla^2 p(\mathbf{r},t) - \frac{1}{c^2}\frac{\partial^2}{\partial t^2}p(\mathbf{r},t) = -\frac{\beta}{C_p}\frac{\partial}{\partial t}H(\mathbf{r},t), \qquad p_d(\mathbf{r}_0,t) = \frac{\partial}{\partial t}\left[\frac{t}{4\pi}\int\int_{|\mathbf{r}_0-\mathbf{r}|=ct} p_0(\mathbf{r})\,d\Omega\right],$$

$$p(\mathbf{r},t) = \frac{\beta}{4\pi C_p}\int\int\int \frac{d^3r'}{|\mathbf{r}-\mathbf{r}'|}\frac{\partial H(\mathbf{r}',t')}{\partial t'}\bigg|_{t'=t-|\mathbf{r}-\mathbf{r}'|/c}.$$

Algorithms

- Radon transform (Energy Deposition Function) – Provides a “decent” reconstruction of an object located near the center of a spherical detection geometry.
- Main idea is to represent projections on the detector as integrals over a spherical shell geometry.
- Fails when the source is not located near the center of the spherical geometry (often the case).

$$F(\mathbf{r}_0,t) = \frac{4\pi}{t}\int_0^t p_d(\mathbf{r}_0,t)dt = \int\int_{|\mathbf{r}_0-\mathbf{r}|=ct} p_0(\mathbf{r})d\Omega.$$

$$p_0(\mathbf{r}) \approx -\frac{1}{2\pi}\int_{S_0}\int \frac{dS_0}{r_0^2}\left[t\frac{\partial p_d(\mathbf{r}_0,t)}{\partial t} + 2p_d(\mathbf{r}_0,t)\right]_{t=|\mathbf{r}-\mathbf{r}_0|/c},$$

- Back Projection – A time domain “delay-and-sum” focus beam is used to locate PA sources in spherical, cylindrical and planar geometries.
- Mathematically says that the 3D reconstruction, back projection quantity, is related to the first derivative of the acoustic pressure (vs. the acoustic pressure directly)
  - This makes it more general than the Radon Transform formula.

$$p_0(\mathbf{r}) \approx -\frac{1}{2\pi}\int_{S_0}\int \frac{dS_0}{|\mathbf{r}-\mathbf{r}_0|^2}[\mathbf{n}_0^s(-\mathbf{n}_0)] \times\left[t\frac{\partial p_d(\mathbf{r}_0,t)}{\partial t}\right]_{t=|\mathbf{r}-\mathbf{r}_0|/c},$$

Fourier Domain Algorithms

- Xu and Wang borrowed mathematical techniques from ultrasonic reflectivity imaging to derive the Fourier domain representation of the spherical geometry.
- They also derived the corresponding Fourier relationships for the planar, and cylindrical geometries.

Spherical Geometries (Reconstruction Process)

- Started with the same definitions from before for the reconstruction.
  - First Step was to obtain the FT with respect to t (=*ct*)
  - Rewrite the equation in terms of frequency components
  - Represent in terms of Polar Coordinates (use a spherical bessel function)
  - Expand the first two spherical harmonics in terms of a spherical Hankel function, and a Legendre Transformation

$$\tilde{p}_d(\mathbf{r}_0,k)=\int_{-\infty}^{+\infty} p_d(\mathbf{r}_0,\bar{t})\exp(ik\bar{t})d\bar{t},$$

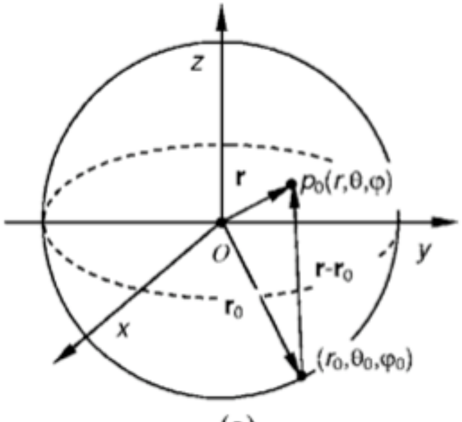
$$\tilde{p}_d(\theta_0,\varphi_0,k)=\sum_{l=0}^{+\infty}\sum_{m=-l}^{+l}\tilde{q}_l^m(k)Y_l^{m*}(\theta_0,\varphi_0),$$

$$\tilde{p}_d(\mathbf{r}_0,k)=-ik\int\int\int d^3r\,p_0(\mathbf{r})\tilde{G}_k(\mathbf{r}_0,\mathbf{r})$$

$$\tilde{p}_{0l}^m(k)=\frac{(+i)^l 4\pi\tilde{q}_l^m(k)}{k^2 h_l^{(1)}(kr_0)}$$

$$p_0(\mathbf{r})=\frac{1}{2\pi^2}\int\int_{\Omega_0}d\Omega_0\int_0^{\infty}dk\,\tilde{p}_d(\mathbf{r}_0,k)$$

$$\times\sum_{i=0}^{\infty}\frac{(2l+1)j_l(kr)}{h_l^{(1)}(kr_0)}P_l(\mathbf{n}_0\cdot\mathbf{n}),$$



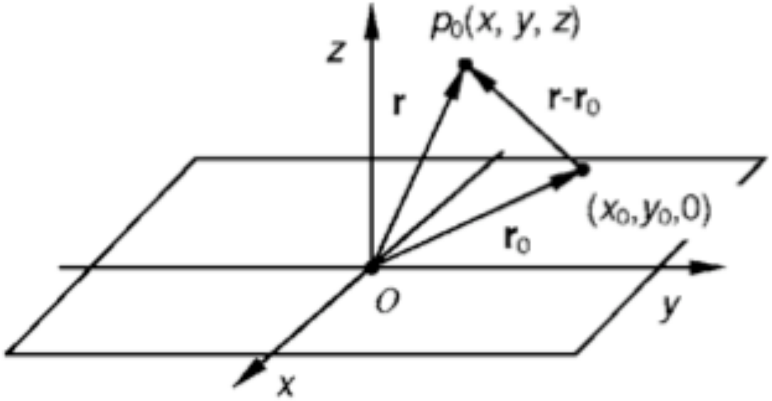
(a)

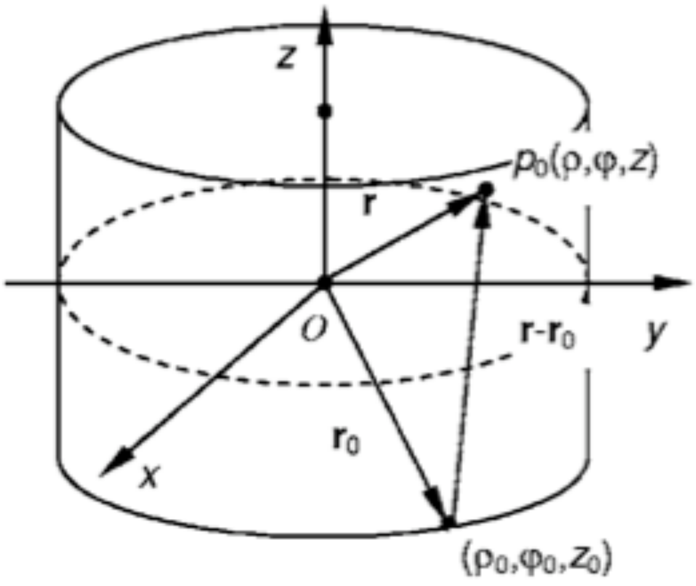
Planar and Cylindrical Geometries (Reconstruction Process)

1. Take the 2D FFT of P_d to find the Fourier decompositions, q, as a function of k.
2. Compute P_o from q
3. Take the inverse FFT of P_o

$$\tilde{p}_{0n}(\mu,\gamma) = \frac{4(+i)^n \tilde{q}_n(\gamma, \sqrt{\mu^2+\gamma^2})}{\sqrt{\mu^2+\gamma^2}\, H_n^{(1)}(\mu\rho_0)}.$$

$$\tilde{p}_0(u,v,w) = \frac{2w\,\mathrm{sgn}(w)}{\sqrt{u^2+v^2+w^2}}\, \tilde{q}(u,v,\mathrm{sgn}(w)\sqrt{u^2+v^2+w^2}).$$





Spatial Resolution

- One of the most important parameters in Imaging (especially interventional medical imaging)
- PAT imaging is limited by the following factors
  - Homogeneous sound speed (else blurring will occur)
  - Full-angle view (limited FOV affects spatial resolution)
  - Impulse excitation (diffusion effect on PA signal)
  - Wideband detection
  - Point detector measurement (finite sensing aperture)
  - Continuous Sampling (Discretized samples -> LPF)

Breast Imaging and Cancer Detection

- Breast Cancer is the leading cause of death among women all around the world.
- X-Ray mammography is still the Gold Standard for cancer detection
  - It may miss up to 20% of existing lesions
  - Additionally provide number of false positives
- Advantages of PAT
  - Nonionizing radiation is not harmful to humans (unlike x-ray mammography)
  - Better at early cancer detection b/c light absorption is very sensitive to tissue abnormality
  - Provide sub millimeter spatial resolution
  - No breast compression necessary (compression is painful)
  - Coupled with a US detection array it can be applied *in vivo* for real-time imaging
  - Physiologically well adapted to be used with human tissues (Propagation speed needed for human tissue is perfectly right).
  - Much Cheaper!

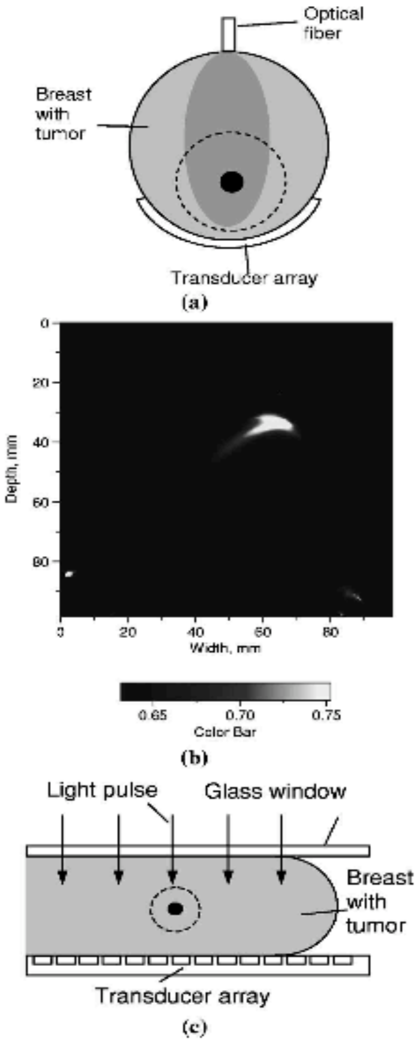
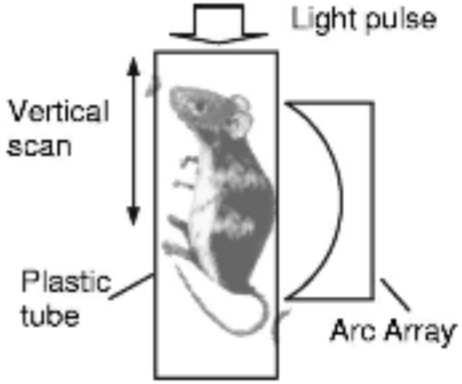
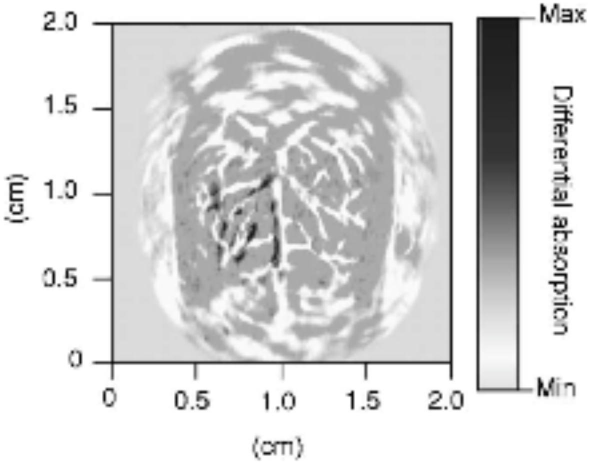


FIG. 12. (a) Side view schematic of optoacoustic imaging of a breast using an arc array. (b) Noninvasive optoacoustic image of a human breast containing a tumor. (c) Diagram of the photoacoustic mammoscope.

PAT Benefits in Small Animal Imaging

- PAT is a non-invasive imaging technology of choice b/c it doesn’t require ionizing radiation like PET, CT, SPECT, etc.
- Doesn’t rely on mechanical properties such as proton spins (MRI), and provides high contrast due to light/rf absorption.
- PAT can achieve sub millimeter spatial resolutions
- Its really quick to obtain the fully 3D constructed images (minutes to hours rather than days)





Cerebral Cortex of Rats

Summary

- PAT offers fantastic acoustic resolution with optical and rf absorption contrast (50µm in soft tissues)
- Suited for biological tissues with inhomogeneous absorption of light/rf
- PA signals are excited internally through EM absorption so only one way propagation of waves (rather than round-trip pulse echo methods of ultrasound imaging)
- Used to image animal or human organs where angiogenesis networks, blood vessels, and blood perfusion can be measured.
- PAT can be applied *in vivo* for real-time imaging

- PAT has its shortcomings in hard tissues and brain imaging, as the skull can produce strong ultrasonic wave-front aberrations.
- No large clinical trials have been done using PAT as of 2007.

Bibliography

Photoacoustic Imaging in Bioscience, Minghua Xu and Lihong V. Wang, Optical Imaging Laboratory, Department of Biomedical Engineering, Texas A&M University, 3120 TAMU College Station, Texas 77843-3120. Review of Scientific Instruments 77, 041101 (2006).

THANK YOU!
QUESTIONS?