Photoacoustic Ultrasound (PAUS)

Introduction / Background:
Photoacoustic Ultrasound (PAUS) is an ultrasound technique that relies on short duration laser pulses to produce the signal to be read by the transducer. These short duration laser pulses create an acoustic wave from the imaged object which can be read out by a transducer. This ultrasound method exploits the strong optical contrast of tissues, allowing it to image anatomy unable to be seen by other modalities. This potential for high contrast is perhaps the most intriguing advantage of this technique. It is hoped that this non-invasive imaging technique can be used to visualize the internal structures and functions of soft tissues. Some applications may include screening for breast cancer, assessing vascular disease, and imaging skin abnormalities.

Theory:
When electromagnetic radiation interacts with matter, sound waves can be generated. This process is known as the optoacoustic, or photoacoustic effect. Photoacoustic sound waves are generated through the thermoelastic effect when short laser pulses are absorbed by a medium. When the laser pulse interacts with the medium, a fraction of the energy is absorbed and converted into heat. The subsequent thermal expansion will produce a pressure wave that will propagate from the medium, as diagramed in the following illustration.

![Acoustic Wave Diagram](image)

Figure 1: A sphere of radius $R$ expands to radius $R + \Delta R$ in time $\Delta t$, creating an acoustic pressure wave.

Electromagnetic Radiation
The electromagnetic pulses generally have wavelengths ranging from the visible and infrared into the microwave region of the spectrum. In this range, it has been found that different biologic tissues exhibit significantly different interactions to the radiation, leading to a strong optical contrast. The strong contrast resulting from photoacoustic ultrasound allows for good imaging of the blood vessels, whereas the contrast of conventional ultrasound tends to be limited by the poor echogenicity of the vessels. An advantage of the better contrast from the PAUS technique is the opportunity to detect changes in the surrounding vasculature through angiogenesis, which could lead to the detection of cancerous lesions.

Contrast Sources
A natural source for this strong contrast is hemoglobin and its various oxygenated states. The strong contrast provided by hemoglobin makes this technique well suited to the imaging of microvasculature. The relationship between the optical absorption and blood oxygenation could also be used to map the distribution of oxygen saturation in the microvasculature. Other
examples of natural contrast materials include chromophores, melanin, beta-carotene, and lipids. There is also some scattering based contrast that can result from the presence of fibrous tissue, collagen, increased cellularity, and calcification.2

Wave Production (Thermoelastic Effect) / Image Production

The imaging regions that absorb these laser pulses thermally expand, which in turn creates a mechanical disturbance. This disturbance will then propagate into the surrounding medium in the form of a photoacoustic (sound) wave. The waves can then be recorded at the surface with the aid of broadband (~30 MHz) ultrasound transducers, allowing us to derive information about the optical properties, location, and structures of the absorbing objects within the measured sample.5,10 This process is similar to conventional pulse-echo ultrasound.

Photoacoustic Ultrasound Transducers

In order to properly record the photoacoustic ultrasound signals, a wideband transducer is required. The photoacoustic pulse is expected to be narrower than that produced with a medical ultrasonic transducer, requiring a wider bandwidth to be imaged.6

While conventional piezoelectric transducer arrays have been used in photoacoustic ultrasound, there are some associated limitations. In high resolution applications having acoustic frequency components of several tens of MHz and an element size and inter-element spacing on the order of 50 μm with wideband detection sensitivities of approximately 1 kPa, this performance is difficult to achieve using piezoelectric transducers.2,4

One possible solution for these limitations is an alternative transducer array, which has been studied by Beard and his colleagues at the University College London.1-4 With this transducer array, the acoustic field distribution is mapped onto an optical field. The prospect of having this 'transparent' sensor head would allow one to transfer the 'spatial discretisation' of the detection process from the acoustic detection plane to a remotely located array of optical detectors. This would, in effect, create the possibility of a smaller effective element size and inter-element spacing from a piezoelectric array.3,4 The following diagrams depict the experimental sensor head and the polymer film, along with the schematic for the experimental setup.

As seen from Figure 2, the proposed ultrasound sensor head incorporates a Fabry Perot (FP) polymer film interferometer. The transduction mechanism of this transducer comprises two processes. The first process linearly relates the external acoustic pressure to a change in the optical thickness of the film. The second process converts the resulting optical shift into an intensity modulation through a function in the interferometer. This process is not strictly linear, but through tuning, small phase shifts will be detected with acceptable linearity.3,4
One negative aspect of the Fabry Perot sensing interferometers is the large variation in sensitivity across the sensor head, resulting from changes in the phase bias due to changes in the optical thickness. To account for this, the system adjusts the angle of the incident beam, and therefore the optical path length, allowing the phase bias to be controlled. In testing, it has been found that this sensor head results in a uniform wideband frequency response to 20 MHz, with effective element sizes of <35 µm, and kPa acoustic pressure resolutions. These figures show excellent potential for this transducer array to be used in photoacoustic imaging.

**Image Reconstruction**

To perform reconstruction, an equation resembling a 3-D Radon transform of the heat source is used, but integration is carried out over spherical surfaces rather than planes. If we assume a short pulse, the basic relationship between a photoacoustic ultrasound signal and a heterogeneous distribution of absorbed energy is given by the following equation:

\[ S(r,t) = \int \int \rho(r')dr' \]

where \( S(r,t) = \frac{4\pi C}{\lambda I_o} \int_0^t p(r,t')dt' \)

If the irradiated volume is then restricted to a thin slice, or the detector were predominantly sensitive to acoustic signals originating from within a pre-selected plane, then the following equation can be used:

\[ S(r,t) = \frac{4\pi C}{\lambda I_o} \int_0^t p(r,t')dt' \int_0^\infty \rho(r')dr' \]

where \( z \) is the 'slice' thickness and \( r \) and \( r' \) are two-dimensional vectors within the plane. These equations include terms representing the heat source, a wave equation, and excess pressure. Planar reconstruction can then be performed using data found along a circular orbit. For this particular equation, the 'projections' would correspond to line integrals over arcs. Reconstruction would therefore consist of temporal integration, backprojecting over the arcs, summing those backprojections, and filtering the result using a 2-D apodized ramp in the Fourier domain.

This reconstruction technique ignores the effects of acoustic attenuation, diffraction, and refraction; acoustic attenuation being the most troublesome. The diffraction and refraction affect the delay time, introducing a spatial blurring of about 0.1 mm, and limiting the spatial resolution by about the same amount. These limitations do not appear to be that severe. It is thought that by localizing the photoacoustic pulses resulting from the absorption of the electromagnetic energy, the negative effects of both scatter and diffraction can be limited.

**Experimental Setups**

The following diagram, Figure 3, illustrates an example of an experimental setup used for the study of photoacoustic ultrasound used by Beard and his associates. The phantoms used in the laboratory studies incorporated either a 0.5% solution of Liposyn® or an Intralipid® scattering solution, which were used to simulate the scattering properties of biologic tissues.

In the studies performed by Kruger and his associates, a 3 mm diameter black latex sphere immersed in the Liposyn® solution, was irradiated using 10 ns pulses from a Nd:YAG laser. The laser beam diameter was about 30 mm and operated at 1.064 µm, with 420 ml/pulse at a width <10 ns. The transducer had a nominal focal length of 75 mm, a diameter of 37.5 mm, and a peak frequency response at 2.25 MHz. The output was amplified by a pulser-receiver with a nominal bandwidth of 10 MHz.
In the studies performed by Beard and his associates, plastic sheets and an India ink tube were irradiated in a phantom filled with an Intralipid® solution. The phantom was irradiated using 7 ns pulses from a Q switched Nd:YAG laser operated at 1.06 μm with 30 mJ/pulse\(^1\).

**Photoacoustic Ultrasound Results / Statistics**

It has been found that penetration depths of several centimeters with a sub-mm spatial resolution can be obtained when using laser pulses in the near infrared wavelength portion of the electromagnetic spectrum. It is possible to achieve an even higher resolution (approximately 50 μm) if shorter penetration depths, on the order of a few mm, are used\(^10\).

In the studies performed by Kruger and his associates, it was found that the photoacoustic signals could easily be measured to a depth of 60 mm for \(\text{eff} \approx 0.1 \text{ mm}\). It was also found that both near and far sides of the 3 mm sphere were visible, which implies an axial spatial resolution of \(\sim 1 \text{ mm}\). It is hoped that better figures for depths and resolution will be obtained when the detectors and techniques are optimized.

The studies performed by Beard and his associates have found that 'depths of several cm with mm spatial resolution' have been reported for microwave and near infrared laser wavelengths for applications such as breast imaging. Spatial resolutions < 100 μm have been demonstrated with sub-cm depths for applications such as skin imaging and superficial vessels\(^2\). A lateral resolution of a few hundred microns is limited by the aperture of the detector\(^1\).

**Research / Applications:**

In a recent laboratory investigation, the journal of *Anesthesiology* reports on an in vivo study on optoacoustic, noninvasive, real-time, continuous monitoring of cerebral blood oxygenation in sheep. In this laboratory investigation, it was found that the induced optoacoustic signals demonstrated a linear correlation with the oxyhemoglobin saturation in the superior sagittal sinus.
of sheep. This data demonstrates the feasibility of monitoring the oxyhemoglobin saturation noninvasively using an optoacoustic (photoacoustic) technique.

This trial, however, is still not without its limitations. Measurements were made using a single wavelength, only allowing for a correlation between the oxyhemoglobin saturation and the optoacoustic signals. It is thought that multiple wavelengths will allow for the quantification of these signals. Improvements in the ultrasound probes and reconstruction algorithms can also improve the results of this experiment, and eventually the clinical trials. While there are still some limitations with this technique, these results merit the further study of photoacoustic ultrasound, hoping to eventually culminate in the practical use for human imaging.

Conclusion:

Photoacoustic ultrasound seems to be a technique that, while not perfect, will be beneficial for certain imaging applications. The ability to image biologic tissues, such as vasculature, in a non-invasive, and non-ionizing, manner will improve upon traditional ultrasound techniques and possibly decrease the need for x-rays in certain applications. There also exists potential to use photoacoustic ultrasound for portable screening purposes. Continued experimentation and development of photoacoustic ultrasound systems should only increase the viability and effectiveness of this technique.
References:
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