# Photoacoustic monitoring of changes in the blood circulation

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Photoacoustic (PA) signal generation can be used as the basis for a new medical tomographic technique. In this article, we present results, which have been obtained by applying the PA technique on animals and more specifically on Wistar rats. The primary goal was to investigate the possibility of using PA for monitoring the changes in the blood circulation. This was achieved by tracking the vessel position with one-dimensional scans and by monitoring the changes in the signal due to artificially induced changes in the blood circulation. © *2003 American Institute of Physics.*
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## I. INTRODUCTION

Photoacoustic (PA) signal generation is generally the result of photothermal heating effects. The predominant mechanism in biological tissue is the process of thermal expansion, in which the absorption of light in a restricted volume is followed by thermal relaxation. The induced temperature increase produces a stress that propagates through the sample in all directions. For short laser pulses ($<$20 ns) the pressure is linearly proportional to the absorbed energy density and the PA pulse can be calculated analytically with the assumption that the temperature distribution is Gaussian. In that case, the shape of the transient of a spherical or a cylindrical source is a bipolar signal.[1,2]

The PA technique can be used to determine tissue characteristics[3] or to construct tomographic images of biological tissue.[4] The main advantage of it, compared to the existing optical imaging techniques (transillumination, optical coherence tomography, confocal microscopy, etc.), is that it does not suffer from the strong scattering of light in turbid media such as biological tissue. As a result, the penetration depth that can be reached is in the order of centimeters by using near-infrared light. Furthermore, the light source can be tuned in different wavelengths (spectroscopy), which increases the selectivity of this technique compared to ultrasound.

The objective of the research described in this article was to explore the possibility of applying the PA technique to monitor the changes in the blood circulation. The subject chosen for this *in vivo* study was the aorta of a Wistar rat in which the blood concentration was altered artificially.

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## II. MATERIALS AND METHODS

The experimental results, which are presented in this article, have been obtained by using a disk shaped piezoelectric sensor[5] with diameter of 200 $\mu$m and PVDF film, 9 $\mu$m thickness, as the active material. For the light delivery, four fibers each with a core diameter of 600 $\mu$m, are used. The fibers are integrated in the detector head and the measurements were carried out in "backward mode."[6] As a light source, a Nd:YAG laser, frequency doubled (532 nm) with 14 ns pulses and a repetition rate of 50 Hz (LS 2139, Lotis T II) was used. The output energy of the fibers was 2.6 mJ/pulse and it was maintained below 20 mJ/cm$^2$ pulse for all the experiments, which is the maximum permissible exposure for this type of laser, according to the European regulations. The signal was collected and averaged 16 times by a 1 Gsample/s, two channel digital oscilloscope (TDS-220, Tektronix), and transferred to a computer for subsequent processing. The data acquitition time was 1.03 s per measurement. The lateral resolution of the system, is limited by the detector diameter and it is $\sim$100–200 $\mu$m. The resolution in depth depends on the duration of the laser pulse and on the data acquitition system and it is about 10–20 $\mu$m.[7] The experimental setup is shown schematically in Fig. 1.

The transients from all acoustic sources can be measured by the detector elements, in the form of time-of-flight signals. These signals contain the information for the reconstruction of the positions of the sources. For the construction of the sample 2D image, a weighted delay and sum focused beam forming algorithm[8,9] has been used. The imaging algorithm that was used for the calculation of the images has been developed by Hoelen *et al.* and has been detailed elsewhere.[10]

All the experiments were performed on Wistar rats. The animals, which weighed $\sim$300–350 g were anaesthetized by

 

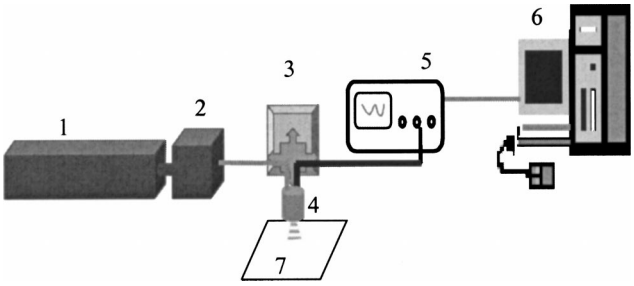


FIG. 1. Experimental setup (1) Nd:YAG laser 532 nm at 50 Hz; (2) optics box, output four fibers; 3: $X-Y$ scanning system; (4) PA detector; (5) oscilloscope (Tektronix TDS 220); (6) PC for data processing; (7) animal position.

intraperitoneal injection of urethane 12.5% (1 ml/100 g body weight) and placed in supine position on a heating blanket. A midline incision was made from the pubic bone to the xyphoid. The intestines and abdominal fatty layers were lateralized. The aorta was then meticulously isolated from the cava vein under an operating microscope using microsurgical instruments. Vessels branching off from the aorta were ligated and the vessel was placed on white gauze. The right carotid artery in the neck was also exposed and canulated under the microscope. It served as an entryway to the circulatory system (Fig. 2). All the animals were sacrificed at the end of each experiment.

The aorta was immersed in a layer of ultrasound gel (Sonogel™ transparent at 532 nm), which served as coupling medium for the sound waves. The white gauze was used in order to isolate and elevate the vessel from the surrounding tissue. And although they did not absorb light, they acted as sound reflectors, since their acoustic impedance was higher than that of the vessel walls. This may result in measurement artifacts, especially in imaging; but their use was absolutely necessary.

## III. RESULTS AND DISCUSSION

In order to find the exact position of the vessel, a one-dimensional scan, perpendicular to the aorta axis, was performed with steps of 0.1 mm. The signals were averaged 16 times and a line of a total length of 10 mm was scanned. The intensity graph, where the aorta position can be seen clearly, is shown in the Fig. 3. Taking into account the directional sensitivity of the sensor,[8,9] the signal intensity was calculated by the peak-to-peak voltage ($V_{pp}$) of the photoacoustic signal, while the depth was calculated by the time of flight.

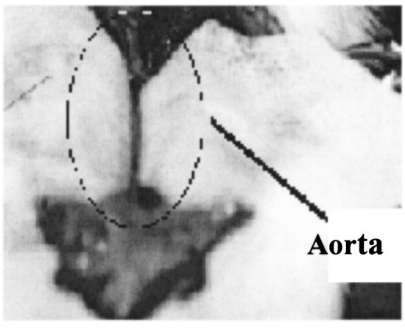


FIG. 2. Aorta isolated from the surrounding tissue by white gauzes.

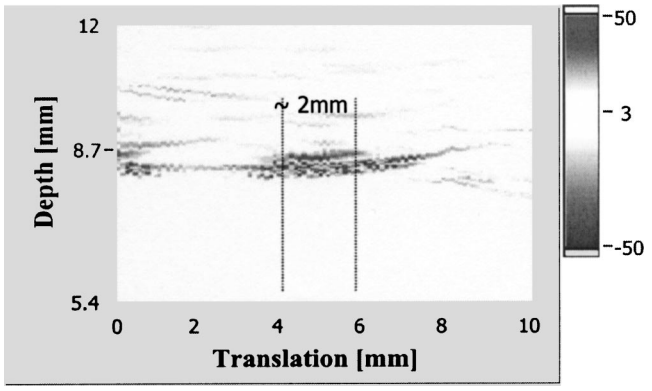


FIG. 3. One-dimensional scan over the aorta.

The aorta diameter was 1.8–2 mm and that matches the indicated dimension on the above graph. The absorption coefficient of blood at 532 nm is $\sim$30 mm$^{-1}$ and that results in a penetration depth of about 33 $\mu$m. As a consequence of that, only the upper part of the aorta can be imaged. Thus, the strong front signal, is generated by a shell, with a thickness equal to the penetration depth, while the back signal is its reflection on the gauze.

The amplitude of the acoustic transient, which is generated by the red blood cells (RBC) in the vessel, it is proportional to their concentration when the penetration depth of light is larger than the vessel diameter. In that case changes in the blood circulation can be measured by monitoring the PA signal in time. Since the penetration depth of the green light is small compared to the aorta diameter, only severe changes in the blood circulation can be measured (e.g., lack of blood). For that purpose a second set of experiments was performed.

The detector was positioned above the aorta, the optimum position found by scanning over the vessel, and saline solution injected into the rat through the right carotid artery. Approximately 40% (20 ml) of the total blood volume (estimated 50 ml) was exchanged with saline to decrease the hemoglobin content from 10.0 to 6.1 mmol/l. The PA signal was averaged 16 times and recorded for a time period of almost 110 s. The variation of the $V_{pp}$ (piezoelectric phenomenon) in time was used as a measure of the changes in the blood circulation (Fig. 4). The PA signal presented changes in the shape and in the time position (Fig. 5).

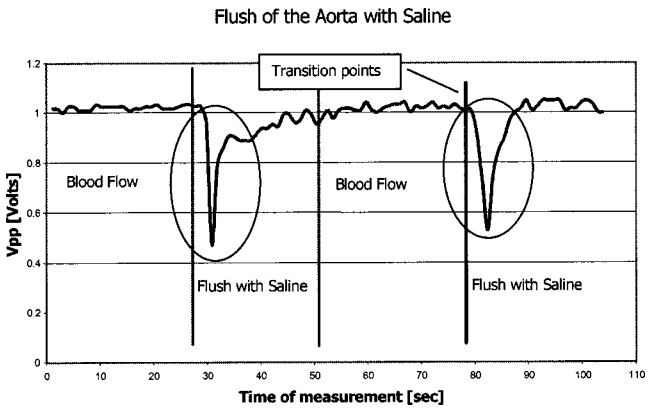


FIG. 4. Changes of the $V_{pp}$ in time due to changes in the blood circulation.

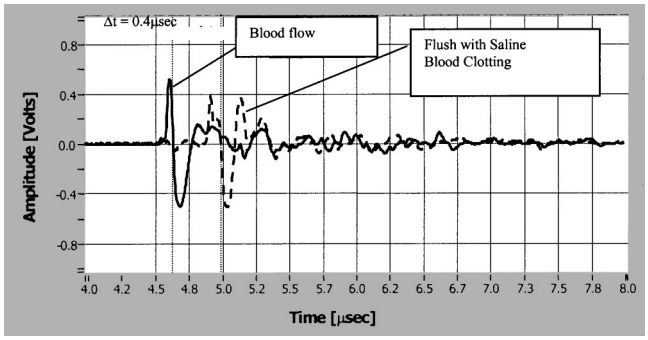


FIG. 5. Changes of the PA signal.

The saline solution was chosen to be nonheparinized, so as to prevent the death of the animal. As a result of that, the blood cells formed clots as soon as the solution was injected. These clots got attached to the aorta walls, especially in the lower part. That was found by opening the vessel at the end of the experiment. Moreover, while flushing with saline, the aorta was not completely empty because the entryway was the right carotid artery. That resulted in a dilution of blood and not in a complete replacement of it by the saline. Because of these, the signal could not be zero during the flushing.

As can be seen in Fig. 4, the $V_{pp}$ drops significantly, almost by 50%, immediately after the saline injection and returns to the initial value after the circulation has stabilized. This is the result of the blood clotting, which is formed in the lower part of the vessel and acts as an absorption volume. That is also depicted in Fig. 5 where the signal presents a backward shift in time, thus moving to greater depths in the vessel. The shift is in the order of 0.4 $\mu$s, which corresponds to a depth shift of 0.6 mm, assuming that the velocity of sound is 1500 m/s.

From the experimental results, it can be concluded that the PA technique can be used for monitoring the changes in the blood circulation. However, for measuring changes in the blood concentration, wavelengths with higher penetration depths, need to be used for accessing the vessel in its entirety.

## ACKNOWLEDGMENT

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