# High-resolution Spectroscopic Photoacoustic Tomography for Non-invasive Functional Imaging of Small-animal Brains *in vivo*

Lihong V. Wang*, Xueding Wang, Geng Ku, Xueyi Xie, George Stoica
Optical Imaging Laboratory, Department of Biomedical Engineering
Texas A&M University, 3120 TAMU, College Station, Texas 77843-3120 USA
Phone: (1) 979-847-9040, Fax: (1) 979-845-4450, Email: LWang@tamu.edu

Abstract — Based on the multi-wavelength laser-based photoacoustic tomography, non-invasive imaging of cerebral blood oxygenation and blood volume in small-animal brains *in vivo* was realized. The high sensitivity of this technique is based on the spectroscopic differences between oxy- and deoxy-hemoglobins whereas its spatial resolution is diffraction-limited by the photoacoustic signals. The point-by-point distributions of hemoglobin oxygen saturation and total concentration of hemoglobin in the cerebral cortical venous vessels, altered by systemic physiological modulations including hyperoxia and hypoxia, were visualized successfully through the intact skin and skull. This technique can potentially accelerate the progress in neuroscience and provide important new insights into cerebrovascular physiology and brain function.

## I. INTRODUCTION

Photoacoustic tomography (PAT, also referred to as optoacoustic or thermoacoustic tomography) involves both photons and ultrasound. A short-pulsed laser source is used to irradiate the biological tissue samples under investigation. A temperature rise of the order of mK is produced in a short time frame. Consequently, thermoelastic expansion causes emission of acoustic waves, referred to as photoacoustic waves. The photoacoustic waves are measured by wideband ultrasonic transducers around the sample, and the acquired photoacoustic waves are used to reconstruct the optical absorption distributions. Because the laser pulse is short, proportionately high-frequency ultrasonic waves are produced and used to provide diffraction-limited spatial resolution. The contrast in PAT is determined primarily by the optical properties of the biological tissues, and the spatial resolution in PAT is determined primarily by the photoacoustic waves originating from within the biological tissues. We developed a multi-wavelength laser-based PAT system for functional imaging of small-animal brains *in vivo*. With this system, cerebral hemoglobin oxygen saturation ($SO_2$) and total concentration of hemoglobin (HbT) in rat brains were imaged non-invasively with high spatial resolution.

## II. METHOD

In order to produce photoacoustic waves—based on laser-induced thermoelastic expansion—in biological tissues efficiently, the laser pulse must be short. When the laser pulse duration is much shorter than the thermal diffusion time over the length scale of resolution, thermal diffusion can be neglected; this is known as the assumption of thermal confinement. Our recent development of an accurate reconstruction algorithm [1] and the configuration of laser illumination relative to the acoustic detection plane in combination with the full-view detection of the imaging cross-section played a crucial role in the effort reported here. For cases where the scanning radius in a circular-scan configuration is much greater than the photoacoustic wavelengths (which is true in our experiments), we have

$$A(\mathbf{r}) = -\frac{r_0^2 C_p}{2\pi v_s^4 \beta} \int_{\theta_0} d\theta_0 \frac{1}{t} \frac{\partial p(\mathbf{r}_0, t)}{\partial t}\bigg|_{t=|\mathbf{r}_0-\mathbf{r}|/v_s}, \tag{1}$$

where $A(\mathbf{r})$ denotes the optical absorption within the sample at position $\mathbf{r}$; $p(\mathbf{r}_0, t)$ is the photoacoustic signals detected at each scanning angle $\theta_0$; $C_p$ is the specific heat; $v_s$ is the acoustic velocity; $\beta$ is the thermal coefficient of volume expansion; and $\mathbf{r}_0$ is the detector position with respect to the imaging center.

The experimental system for PAT of a rat brain *in vivo* has been introduced before [2]. In this work, through the modulation of the inhaled oxygen concentration, we changed the systemic physiological status of the rat. First, provided with pure oxygen, the rat was under the hyperoxia status. Two photoacoustic images of the optical absorptions in the rat brain cerebral cortex were acquired with the laser light at the 584-nm and the 600-nm wavelengths, respectively. Then the breathing gas was changed slowly to a mixed gas with a low concentration of oxygen (~8% $O_2$, ~5% $CO_2$ and ~87% $N_2$). Then under the hypoxia status, two more images of the rat brain cerebral cortex corresponding to the same two wavelengths were acquired.

For each physiological status, the two images of the relative optical absorptions corresponding to the two wavelengths enable us to compute the point-by-point $SO_2$ and HbT in the area of cortical venous vessels through the following equations:

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$$SO_2 = \frac{[HbO_2]}{[HbO_2]+[Hb]} = \frac{\mu_a^{\lambda_2}\varepsilon_{Hb}^{\lambda_1} - \mu_a^{\lambda_1}\varepsilon_{Hb}^{\lambda_2}}{\mu_a^{\lambda_1}\varepsilon_{\Delta Hb}^{\lambda_2} - \mu_a^{\lambda_2}\varepsilon_{\Delta Hb}^{\lambda_1}}, \quad (2)$$

$$HbT = [HbO_2]+[Hb] = \frac{\mu_a^{\lambda_1}\varepsilon_{\Delta Hb}^{\lambda_2} - \mu_a^{\lambda_2}\varepsilon_{\Delta Hb}^{\lambda_1}}{\varepsilon_{Hb}^{\lambda_1}\varepsilon_{HbO_2}^{\lambda_2} - \varepsilon_{Hb}^{\lambda_2}\varepsilon_{HbO_2}^{\lambda_1}}, \quad (3)$$

where $\mu_a$ is the absorption coefficient; $\lambda_1$ and $\lambda_2$ are the two wavelengths; $\varepsilon_{Hb}$ and $\varepsilon_{HbO_2}$ are the known molar extinction coefficients of the oxy- and deoxy-hemoglobin, respectively; and $[Hb]$ and $[HbO_2]$ are, respectively, the concentrations of the two forms of hemoglobin.

## III. RESULTS

With the high optical contrast between the blood and background brain tissues, each brain image presents the vascular structure in the rat cerebral cortex clearly and matches well with the open-skull anatomic photograph obtained after the imaging experiment (see Fig. 1). The average $SO_2$ levels in the area of cortical venous vessels were ~86% and ~61% under the hyperoxia and the hypoxia statuses, respectively. The average HbT value under the hypoxia status was about ~11% larger than that under the hyperoxia status.

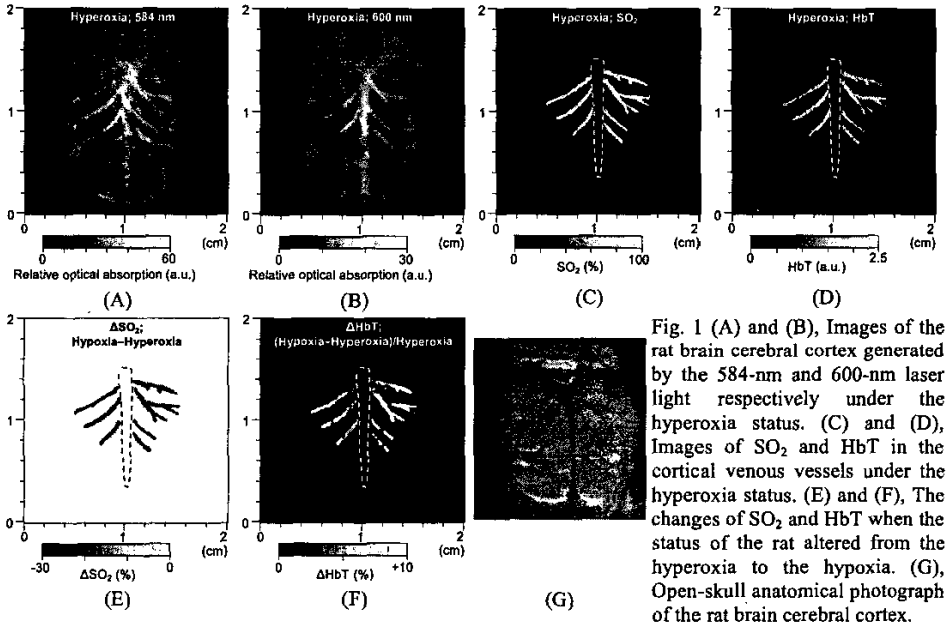


Fig. 1 (A) and (B), Images of the rat brain cerebral cortex generated by the 584-nm and 600-nm laser light respectively under the hyperoxia status. (C) and (D), Images of $SO_2$ and HbT in the cortical venous vessels under the hyperoxia status. (E) and (F), The changes of $SO_2$ and HbT when the status of the rat altered from the hyperoxia to the hypoxia. (G), Open-skull anatomical photograph of the rat brain cerebral cortex.

## IV. CONCLUSION

Non-invasive high-resolution imaging of functional parameters in the rat brain was realized with spectroscopic photoacoustic tomography. This capability of PAT opens up a new window to studying brain function and disorders.

## V. REFERENCES

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