Monitoring Hemodynamic Changes in Brain Infarct Area of Rats Using Diffuse Optical Imaging

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Abstract—**Stroke is a heterogeneous syndrome caused by various diseases resulting from disruption of cerebral blood flow (CBF) and brain tissue necrosis. Ischemic stroke is the major type of this syndrome induced by brain infarction. The infarct area will accompany with cerebral edema which could change the optical properties of the brain tissue. Near infrared spectroscopy (NIRS) was commonly used in measuring the concentration of the main chromophores in the blood – oxy- and deoxy- hemoglobin for acquiring the hemodynamic or metabolic change in the tissue. In our previous studies, we have shown the hemodynamic activity of stroke rat using frequency domain NIRS (FDNIRS). To precisely locate the ischemic infarct region within whole brain, we develop a non-invasive, diffuse optical imaging (DOI) system based on NIRS. To localize the infarct area and morphological information, the 2D scanning system with DOI technique was developed. The optical properties of the tissue i.e. absorption and scattering coefficient, representing the photon transmission model in the tissue, were applied to observe the structural changes of the brain tissue. In the pilot study, we have applied FDNIRS to monitor the changes of blood oxygen level controlled by neurovascular coupling in ischemic brain. By comparing the FDNIRS measurement result of the sham group with the middle carotid arterial occlusion (MCAO) group stroke rat on post operation day 3. We found that there is a high correlation between the reduced scattering coefficient and the infarct area tissue. The system has been applied to observe the *in-vivo* experiment of ischemic animal stroke model. Further study can develop optical techniques for monitoring and diagnosing the progress of stroke and the novel therapy methods.**

Keywords—**stroke, infarction, near infrared spectroscopy, diffuse optical imaging, hemodynamic.**

I. Introduction

Human brain plays an important role as a control center of human body. The damage of brain tissue not only caused disability, moreover, it may take our lives. The brain tissue damage could result from many causes. In this paper, we concerned about the reason which is brain vascular related syndrome — stroke. Generally, we categorized stroke into two types, one is hemorrhagic stroke, and the other is ischemic stroke. Ischemic stroke is the major type of this syndrome, which induced by brain infarction. The insufficient blood flow caused by infarction will damage the brain tissue due to lack of nutrient and oxygen. It has been reported that there were approximately 90% of strokes was identified with this type (Sacco et al., 1998).The damaged brain tissue caused by ischemia could separate into two region, one is infarct core and the other is penumbra region. The infarct core is the earliest illness position during the acute ischemic stroke syndrome, which is irrecoverable area regardless of reperfusion. On the other hand, the area surrounds infarct core, which is called penumbra region, defined as a hypoperfused tissue whose blood flow is too low to keep the electric activity except the ion channel mechanism. The infarct core continuously propagating the harmful metabolic process to the nearby region such as excitotoxicty, spreading depolarization, inflammatory response(Ramos-Cabrer et al., 2011). Whether or not the brain tissue is intact depends on one of these responses which is called spreading depolarization (Kawauchi et al., 2014; Strong et al., 2007). This key phenomenon will extend the infarction area of ischemic stroke from the infarct core as time goes on. Massive ionic migration in the cellular membrane often accompanies with spreading depolarization. This mechanism influences the morphological properties of the tissue which may also directly affects the light transmission in the tissue, especially the scattering event.

Near infrared spectroscopy (NIRS) has been used as a clinical diagnostic technique since 1977 by Dr. Jobsis who had tried to use NIR light to get the oxidation and circulation in the superficial tissue (Jobsis, 1977). The NIRS is a technique which applied the infrared light wavelength in the range from 600 nm to 1000 nm, and then detect the light that transmitted through the sample or tissue. The light propagating in the media was described by radioactive transport equation (RTE). It is hard to derive an analytical solution form RTE so the simplified form base on some assumption was developed and applied to NIRS study. This form was called diffuse approximation (DA), with appropriate boundary condition, we could get the analytical model of light intensity and optical properties. By analyzing the change of light signal, NIRS could provide a quantitative parameter to monitor real time hemodynamic response. The main optical properties of tissue – absorption coefficient (μ_a) and reduced scattering coefficient (μ_s'), which are

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wavelength dependent, are the key indices that reflect the physiological information of the tissue or sample(Zhao et al., 2005). The absorption rapidly decrease the intensity of the light, meanwhile the multiple scattering also happened and randomize the propagating direction of the photon. This two factor let us hard to detect the residue light which escape the tissue. In biomedical materials or tissues, the major substances which absorb the light are water, the others are some lipid(Hillman, 2007). However, these substances s have relative lower absorption coefficient in the near infrared region which we called biomedical window(Nissilä et al., 2005). By applying proper optical model, for example, modified Beer-Lambert's law, we could easily compute the change of hemoglobin concentration. In order to monitor and acquire the spatial and temporal information while the ischemic stroke processing, we develop a non-invasive, real-time, fast scanning system which based on NIRS technique.

II. Materials and Methods

A. 2D Galvos Mirror Scanning System

To achieve fast and two dimensional scanning, we used the Galvos Mirror TSH-8203 (Sunny Technology, Inc.) which controlled by LabVIEW program through NI-DAQ 6363 (National Instrument, Inc.). The scanning type could choose two different mode, one is pixel by pixel, the other is line by line. The pixel size was 1mm depend on the diameter of the focused laser light beam (690 nm). The scanning angle and range could be set by the maximum input voltage. Figure.1 shows the scanning track of this two different mode. The fast moving speed of pixel by pixel is 1 ms, and the scanning speed of line by line mode could reach 1 ms each line.

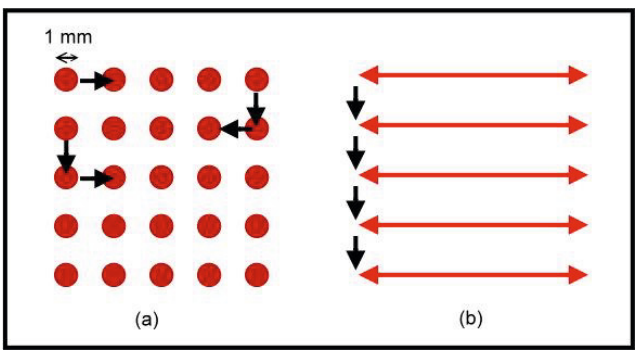


Figure 1. (a) pixel by pixel scanning, (b) line by line scanning.

B. NIR signal measurement

The back scattering light was collected by a home-made multi-mode (MM) optical fiber probe with diameter 200 μm. The one end of the probe was coupled with FC connector and then fixed on the avalanche photon diode (APD) C54060-01 (Hamamatsu, Inc.), and the other end was directly contact the surface of phantom to avoid the surface reflection noise. The APD output a DC voltage signal which was acquired by NI-DAQ 6363 with LabVIEW user interface. The scanning and acquisition system was showed in Figure 2.

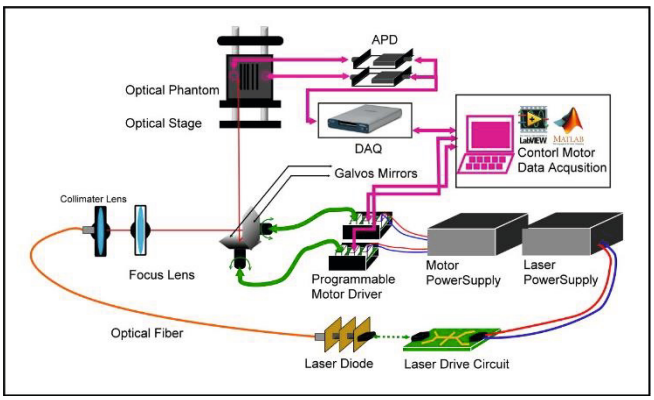


Figure 2. Scanning and optical signal acuqisition system diagram.

C. Optical Phantoms & Simulation Pattern

The phantoms was consist of PDMS subtrate (Sigma, Inc.) with mixture of TiO_2 solution and diluted black ink. This two matters form a basic scattering and absorption coeffiecient, respectively. The scattering and absorption coeffcient was measured ISS imagent frequency domain NIRS (ISS, Inc.). The absoulte oxygen saturation of the simulation phantoms were also measured. The test pattern was used to simulate the change of optical properties of the tissue. In this study, we use bar code print on a transparent plastic paper as a test pattern to observe the NIR reflected signal change by measuring the light intensity. The bar code pattern will paste on and burry in the phantoms to test the depth limitation.

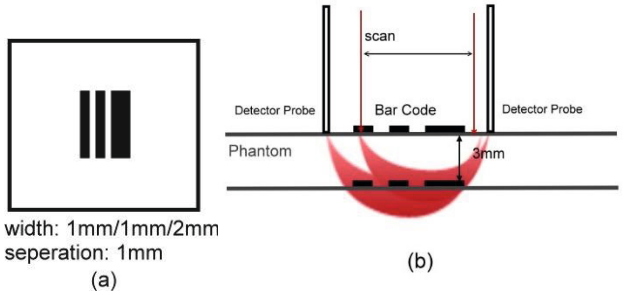


Figure 3. (a) Bar code pattern, (b) Bar code scanning and two different positions.

Table 1 Optical Phantom Content

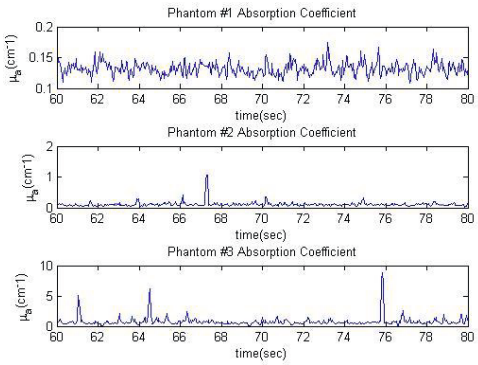
No.	Ink	TiO2
Phantom #1	0.2%	0.2%
Phantom #2	0.2%	0.4%
Phantom #3	0.1%	0.4%

The phantom #1 was simulate the optical properties of normal rat brain.

III. RESULTS

A. μ_a , μ_s' of optical phantoms

We use commercial instrument to measure the phantom optical properties, we collect the 690 nm to correspond with the scanning light source. In here we compute the mean value of this two coefficient with different time length. Figure 4. shows the short time period variation of absorption and scattering coefficient. From Table 1 and Table 2, we know that while the absorbent(Ink) concentration is fixed, the scattering difference slightly influence on the mean value of μ_a, on the other hand, we could see obvious change and instability from both μ_a and μ_s' in the fixed high scattering concentration phantom.



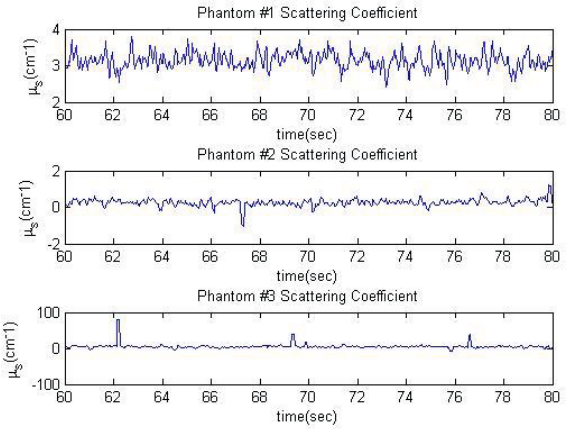


Figure 4. Measurement of absorption and scattering coefficients of different phantoms.

Table 2 Phantom Absorption and Scattering Mean Values

No.	μ_a (cm^{-1}) 90sec/20sec	$\mu_s'(cm^{-1})$ 90sec/20sec
Phantom #1	0.1324/0.1320	3.1891/3.1467
Phantom #2	0.1196/0.1125	0.2638/0.2701
Phantom #3	1.6510/0.7601	3.8878/5.3222

B. Scanning Pattern

We could observe the main trend of the light intensity signal attenuation through Fig. 5. The bar code pattern shows good SNR in superficial scanning, the deep pattern (3mm) has poor SNR but the intensity change correspond to the bar code pattern could still be identified.

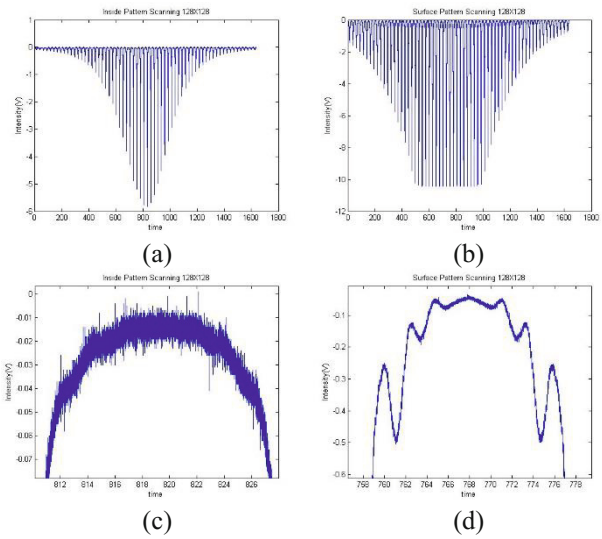


Figure 5. (a)(b) Scanning inside and superficial pattern, (c)(d) one period of scanning inside and superficial pattern.

IV. CONCLUSIONS

The pattern scanning presents good sensitivity between light intensity and optical property. The scanning depth could reach to 3 mm. The μ_a, μ_s' of optical phantoms were not stable due to the non-uniform mixture and solubility this may result in uncertainty while calculating oxygen saturation and hemoglobin concentration change.

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Format the Acknowledgment and References headlines without numbering.

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