Using NIR Spatial Illumination for Detection and Mapping Chromophore Changes during Cerebral Edema

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ABSTRACT

We used spatially-modulated near-infrared (NIR) light to detect and map chromophore changes during cerebral edema in the rat neocortex. Cerebral edema was induced by intraperitoneal injections of free water (35% of body weight). Intracranial pressure (ICP) was measured with an optical fiber based Fabry-Perot interferometer sensor inserted into the parenchyma of the right frontal lobe during water administration. Increase in ICP from a baseline value of 10 cm-water to 145 cm-water was observed. Following induction of cerebral edema, there was a 26±1.7% increase in tissue concentration of deoxyhemoglobin and a 47±4.7%, 17±3% and 37±3.7% decrease in oxyhemoglobin, total hemoglobin concentration and cerebral tissue oxygen saturation levels, respectively. To the best of our knowledge, this is the first report describing the use of NIR spatial modulation of light for detecting and mapping changes in tissue concentrations of physiologic chromophores over time in response to cerebral edema.

Keywords: Brain Injury, Edema, Spatially Modulate Light, Optical Properties, Cerebral Hemodynamics, intracranial pressure.

1. INTRODUCTION

Cerebral edema is an increase in brain tissue water content that occurs when free water escapes from within blood vessels into brain tissue.[1,2] Due to water accumulation, the brain swells increasing intracranial pressure (ICP). Increased ICP decreases cerebral perfusion pressure, and this change is progressive with increasing ICP. If the swelling is severe brain herniation occurs and death results from brain stem compression. Cerebral edema can occur as a complication of several disease states such as stroke, traumatic brain injury, brain tumors, and even from surgery.

During cerebral edema there are changes in the concentrations of oxyhemoglobin, deoxyhemoglobin and water in brain tissue. These molecules absorb specific wavelengths of light which alter the optical properties of brain tissue. Several optical imaging techniques have been used so far to detect these optical alterations during cerebral edema with various advantages and disadvantades.[3-6] However, none of them has been able to separate light absorption from scattering and to provide absolute quantitative spectroscopic maps in a non-contact manner. These deficiencies motivated us to propose an alternative non-contact and simple free-scan setup based on spatial light modulation[7] to detect and map tissue chromophore changes in the brain during cerebral edema.

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2. METHODOLOGY

2.1 Animal Procedure

All animals used in this study were treated in accordance with National Institutes of Health (NIH) regulations and under approval of the Institutional Animal Care and Use Committee (IACUC) at the University of California, Irvine.

Adult male Sprague-Dawley rats (n=3) weighted ~320g were anesthetized using barbiturate anesthesia (Sodium Pentobarbital 50 mg/kg initial dose IP, 2mg/kg IP supplements as needed to maintain anesthesia) and were fixed in a stereotactic frame. To decrease respiratory secretions and possibility of syncopal attacks, atropine (0.1mg/kg) was injected intramuscularly, immediately prior to making a surgical incision. A midline skin incision was made and ~8x8mm² square area overlying the left somatosensory cortex was outlined. The skull over this area was thinned to about 150μm with a dental drill until the cerebral veins were visible. All surgical procedures were performed using a surgical microscope (Carl Zeiss). A thin film of saline was placed over the thinned skull and covered with a coverglass and the entire set up served as an imaging window. The saline filled in the cranial window to prevent the skull from drying and to increase its transparency. Cerebral edema was induced by slowly injecting free water (35% of body weight) intraperitoneally over time. Free water administration creates cerebral edema. Known as the water intoxication model, this is a well established model for creating brain edema.[8] To prevent hypothermia body temperature was kept constant by a using a rectal thermometer that is connected to an electric heating pad by feedback mechanism that maintained the body temperature at 37±0.5º during the entire experiment.

2.2 System Description

A schematic diagram of our setup is shown in Fig. 1. NIR periodic illumination patterns of two spatial frequencies (0, 0.19 mm^{-1}) with a 120º phase shifting between three adjacent patterns were projected onto the brain from a modified commercial digital light projector. The pattern passes through five bandpass filters (680, 760, 800, 880 and 980nm) placed on a five-position automatic filter wheel placed immediately at the output of the projector. Polarized filters in both the illumination and the detector were placed with orthogonal polarization planes to eliminate specular elimination. The diffusely reflected light (deformed pattern) recorded by a CCD camera and analyzed off-line on a PC computer using Matlab software. To determine quantitatively the absorption (μ_a) and reduced scattering (μ_s') coefficients, and hence also the chromophore parameters, we used the diffusion approximation to the radiative transport theory to relate the measured reflected light intensity to the optical coefficients.[9] The entire system was controlled by a personal computer through the LabView platform.

2.3 Image Collection and Processing

Imaging was performed through the surgically created imaging window over a period of three hours following edema induction. The reflected image of the region-of interest (ROI) of the cortex was acquired with a CCD camera while projecting spatially modulated NIR light onto the ROI. The modulated images were obtained from ROI selected by the investigators, and processed to obtain quantitative chromophore maps. These maps were generated every two minutes to study the changes in cortical perfusion with time following experimental manipulation. Imaging started before induction of edema to establish baseline concentrations of oxyhemoglobin, deoxyhemoglobin, and hemoglobin oxygen saturation and repeated during and after experimental intervention. Baseline images were obtained between 15-25 minutes before induction of edema. Thus, each rat served as its own control decreasing the number of animals required for the study. Custom software wrtitten in Matlab was developed to acquire and process the images off-line. To reduce noise, images before analysis were digitally filtered by a two-dimensional Gaussian lowpass filter using *fspecial* function in Matlab. During the entire imaging procedure, the animal remained anesthetized.

2.4 Statistical analysis

Results are expressed as mean ± standard error of the mean. A paired *t*-test was used to verify change in the chromophores at baseline and at peak edema. Difference in the chromophores was considered to be significant at a probability level of less than 0.05 ($p<0.05$).

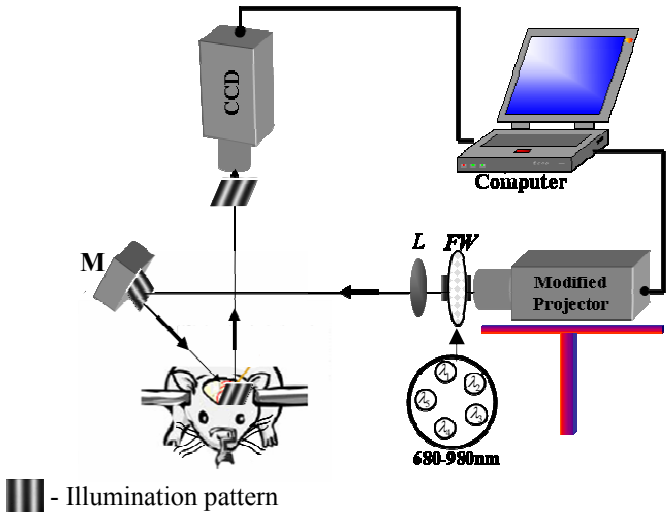

Figure 1. Schematic illustration of setup for brain edema imaging.
FW, filter wheel; L, lens; M, mirror.

3. RESULTS AND DISCUSSION

The region-of interest (ROI) photograph of the rat cortex is shown in Fig. 2(*a*). The size of this ROI is about 4.4×4.4 mm. During the experiments an ICP monitor (Samba 3200) was inserted through the skull in the right hemisphere to provide a constant pressure reading. ICP was measured in centimeter water (cm H_20) and, at rest, is normally less than 13-20 cm H_2O. ICP between 30 and 40 cm H_20 are usually fatal if prolonged and above 50 cm H_20 is very likely to cause severe harm to the brain (death). The time-course of both the chromophores (oxyhemoglobin, deoxyhemoglobin, total hemoglobin concentration, tissue oxygen saturation, and water) and ICP in response to edema are shown in Fig. 2(*b*). During the first 25 minutes of baseline imaging, the ICP and chrmophore concentrations were found to be stable at baseline values previously established using this technique.[10] Following intraperitoneal (IP) administration of free water, ICP was found to increase in a non-linear fashion with time. Each animal (n=3) underwent sudden cessation of respiration accompanied by a brief extensor jerk at a peak ICP of 140 to 160 cm of water. Following this each animal died from lack of respiratory effort. The occurrence of this sudden death is consistent with cerebral herniation, which is the final event causing death in patients with cerebral edema and raised ICP. The accumulation of water in the brain through osmotic pressure gradients causes cerebral edema. Since the volume of the cranial cavity is fixed, the ICP rises. The rising ICP initially squeezes out CSF and later venous blood from the cerebral sinuses based on the Monro-Kellie doctrine.[11] At higher pressures (above the mean arterial pressures) blood flow to the brain is compromised resulting in tissue hypoxia resulting in progressive decrease in hemoglobin oxygen saturation. These events result in changes in cerebral chromophore concentration which are depicted in Figure 2(*b*). HbO_2, THC, and StO_2 were found to temporally decrease in a linear fashion with time, while Hbr increased.

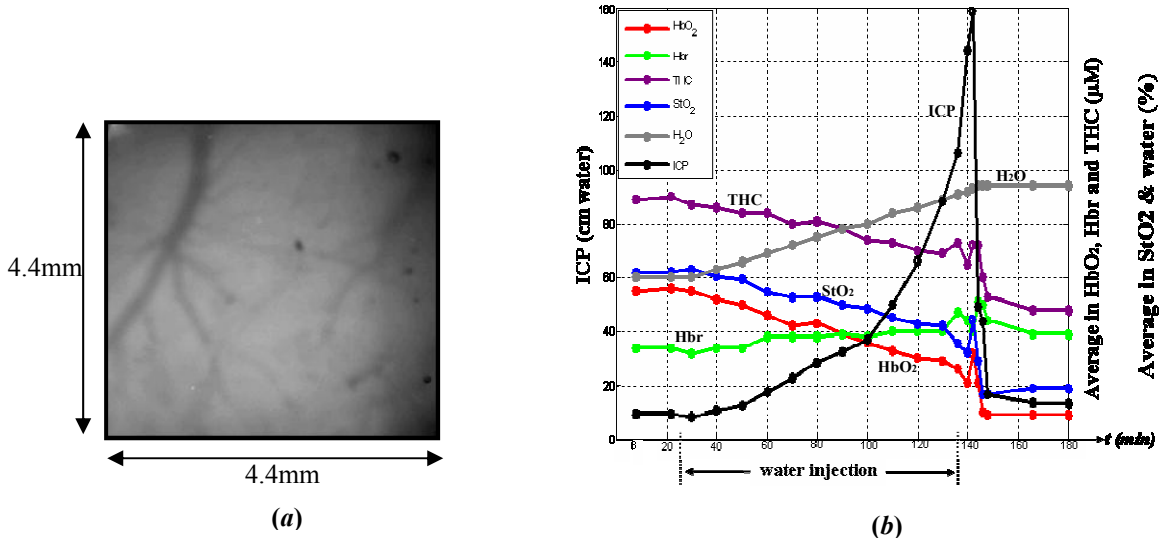

Figure 2. (*a*) 4.4×4.4mm^2 ROI of the rat cortex selected by the investigator for data processing. (*b*) Time-course of the chromophore changes of the cortex in response to edema.
Legend: HbO2-oxyhemoglobin, Hbr-deoxyhemoglobin, THC(=HbO2+Hbr)-total hemoglobin concentration, StO2(=HbO2/THC)×100)-tissue oxygen saturation, H2O-water, and ICP-intracranial pressure.

We repeated the above experiments in three rats with same setup and approximately similar body weights and confirmed the reproducibility of our results. Figure 3 illustrates the average changes in chromophore concentrations following cerebral edema.

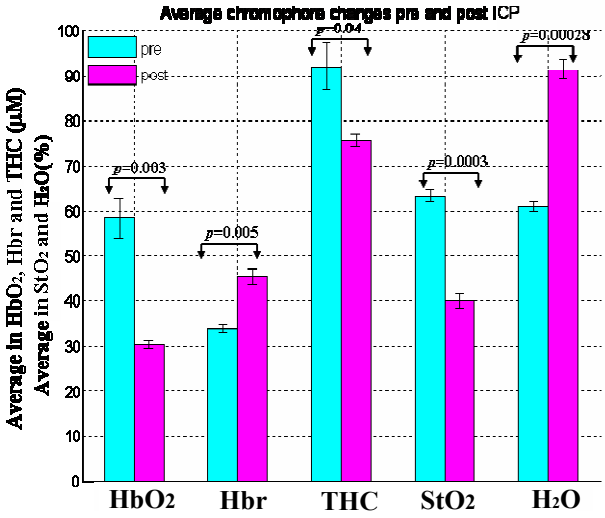

Figure 3. Bar graph summarizing the mean chromophore concentrations pre- (turquoise) and post (purple) cerebral edema in three rats.

Time-series images illustrating the dynamic spatial and temporal changes in chromophore maps over the ROI, during the cerebral edema state are shown in Fig. 4. Each image features 352×352 pixels equivalent to size of

4.4×4.4 mm^2, results in spatial resolution of 0.0125 mm/pixel. Higher concentration values correspond to brighter pixel scale values and vice verse represented by the scale bar to the right of each panel map. The effects of cerebral edema on tissue chromophore concentrations are clearly visible in this figure. As we progress from normal state (baseline) to brain herniation the progressive increase in Hbr and progressive decrease in HbO2, THC, and S_tO_2 is mapped spatiotemporally by our system. These changes reflect the pathophysiologic state of the brain during edema and the ability of the spatially modulated light technique to quantify changes in chromophore concentration with time.

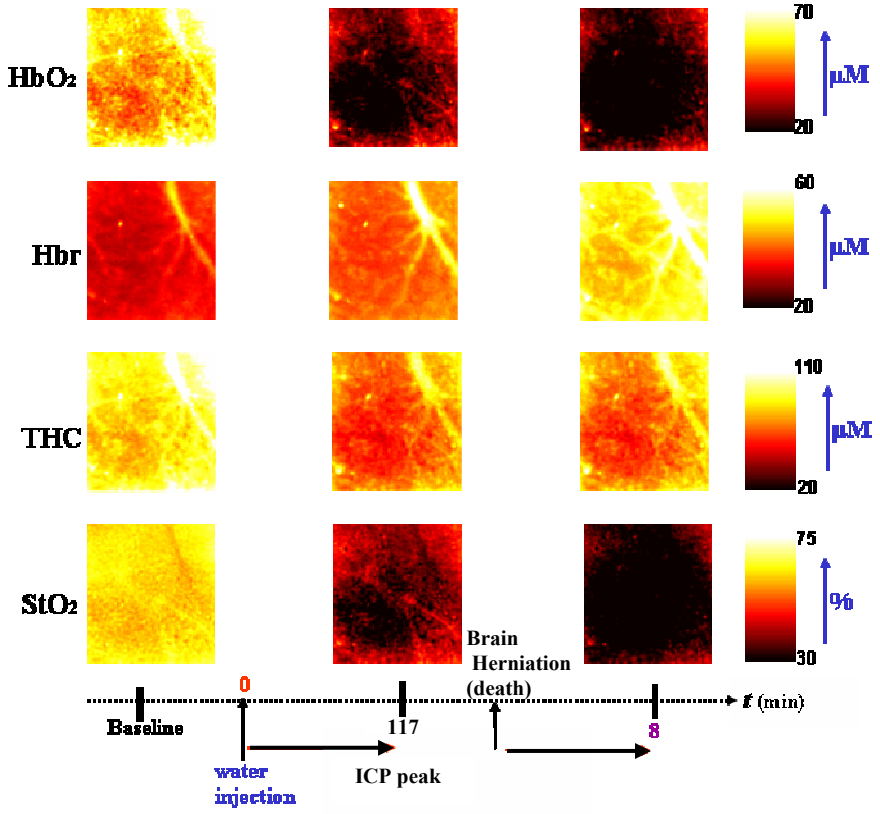

Figure 4. Selected time points of the hemodynamic distribution map changes in cortical perfusion during cerebral edema. The magnitude of changes is clearly visualized in these maps. note, different color scales for each parameter quantified.

4. CONCLUSION

In summary, quantitative information on the spatiotemporal distribution of physiologic chromophores during cerebral edema was obtained by spatially modulated NIR light. Experimental results show a 26±1.7% increase in tissue molecular concentration of deoxyhemoglobin and a 47±4.7% and 37±3.7% decrease in oxyhemoglobin, and cerebral tissue oxygen saturation levels, respectively, following induction of cerebral edema. Also detected is a decrease of 17±3% in the THC from the baseline. During cerebral edema, blood flow decreases in regions of brain tissue swelling as a result of high ICP.[12] This effect can be detected from the THC difference pre- and post-cerebral edema as we observed during our experiments. The present study is the first to show the ability of spatially-modulated NIR light to

detect and map changes in chromphores in real time during cerebral edema. Changes in scattering parameters (scattering amplitude and power) during cerebral edema have been investigated during this study and will be separately evaluated. Our preliminary results suggest that spatial modulation of light can be valuable tool in monitoring the course and severity of cerebral edema. The reported technique is simple, inexpensive, easy to implement, and can therefore be adapted for edema monitoring in clinical and laboratory settings.

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