Cerebral monitoring during acute stroke and subarachnoid hemorrhage in the Bonnet Macaque with functional near infrared spectroscopy (fNIRS)

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INTRODUCTION

As near-infrared spectroscopic (NIRS) monitoring technology becomes more prevalent in the experimental and clinical settings, it becomes increasingly important to validate the sensing and image reconstruction techniques that are used. NIRS monitoring of cerebral oxygenation is utilized clinically and was well described by Wolf in 2007 [3], but in 2009 it was suggested that there is not enough clinical data for safe use of this technique in management of patients susceptible to cerebral ischemia [1]. Some authors even question the ability of continuous-wave (CW) NIRS to detect ischemic stroke, since it does not provide quantitative values of baseline hemoglobin concentrations, as does time-resolved near-infrared spectroscopy (TR-NIRS) [2]. At the same time, recent studies are very promising. Leistner et al. demonstrate that patients with subacute ischemic stroke will benefit from simultaneous and noninvasive monitoring of neuronal ***(DC-magnetoencephalography)*** and vascular (NIRS) signal changes [5]. Noninvasive measurements of cerebral perfusion deficits by NIRS correlates well with ***perfusion-weighted MRI (PWMRI)*** in patients with acute stroke [6] and also with ***transcranial doppler (TCD)*** assessment of microcirculation in proximal cerebral vessels in patients with carotid artery disease [4].

We have conducted validation studies on the spatial and temporal capabilities of CW NIRS technology for studying a variety of cerebrovascular conditions in Bonnet Macaques, by performing CW-NIRS cerebral monitoring during experimentally induced stroke and subarachnoid hemorrhage. A stroke was achieved via unilateral microcatheter wedge occlusion of the Left internal carotid artery (ICA) / Middle Cerebral Artery (MCA). A subarachnoid hemorrhage was detected during the experiment, as a complication following intravascular manipulations of the left cerebral vessels during microcatheter placement.

METHODS

Data Collection

Experimental data, acquisition-channel data and reconstructed images are presented, for the case of an animal that developed diffuse subarachnoid hemorrhage and a large infarct in the left temporal cortex.

For monitoring and data collection we used a CW NIRS-Diffuse Optical Tomography (DOT) imager, sampling two wavelengths (760 and 830nm) to distinguish the hemoglobin (Hb) oxygenation states, at a 7.96 Hz rate, with 9 co-located illumination source-detector sites and 21 detection-only sites (30 detectors total), resulting in 9×30 = 270 data acquisition channels. From these channels, we selected those which for the source and detector optodes both lay over the right hemisphere (70 channels), or both lay over the left hemisphere (61 channels), removing all channels that involved crossing the midline between the hemispheres. Channels with very high noise levels (baseline coefficient of variation > 25%) also were eliminated (6 from the right and 7 from left side).

The fibers were placed over a 4×5 cm area in the mid fronto-parietal region on the exposed skull, after removal of overlying tissues (skin, muscles, etc.) to achieve optimal fiber contact and light penetration over the full cerebral volume, and to minimize the potential for artifacts in the Hb signal arising from blood vessels in those tissues (Fig. 14).

All significant events during the experiment, either medical (introduction of medications/contrast/intravascular manipulations locations, types/changes in vital signs, etc.) or non-medical (physical movements of animal or table, etc.) were recorded in real time.

Mandatory post-experimental observation included x-ray CT, perfusion CT, MRI (diffusion, T2 and FLAIR) and brain histopathology.

Description of the Experiment

The animal was placed under general anesthesia. Skull muscles were dissected, and the NIRS probes were positioned in direct contact with the skull. DOT recordings were commenced prior to any surgical intervention. An initial attempt to occlude the right MCA was unsuccessful, owing to vasospasm and to the small size of the relevant vessels. During the occlusion attempt, verapamil (a vasodilator) was locally injected, intra-arterially into the right MCA. Several contrast injections also were performed, to assist in guidance of the catheter. At ~ 95 min, the catheter was repositioned into the left ICA system. To induce stroke, the microcatheter was placed for ~ 2 hr. in the distal intracranial left ICA bifurcation at the origin of the left MCA, and the guide catheter in the cervical ICA, creating a left ICA/MCA occlusion. During the attempts, perforation and subarachnoid hemorrhage was suspected. NIRS recordings stopped after the first hour of reperfusion after removal of the occluding catheter. The animal was then moved to the imaging suite for recording of CT and MRI. The animal was moved to autopsy and the experiment was terminated by euthanasia.

The brain was removed for later histopathology analysis. The animal was then moved to the imaging suite to record CT, perfusion CT, MRI (diffusion, T2 and FLAIR). The experiment was terminated by euthanasia. The brain was removed for later histopathology.

RESULTS

Method Validation

Figs. 1- 4 shows Hboxy, Hbdeoxy and Hbtotal time series computed from two-wavelength data acquisition-channel data. As a data integrity check, we examined all pairs of reciprocal channels and found that they had strong positive correlations (compare Figs.3 and 4).

Figs. 1 and 2 correspond to the left hemisphere channels and Figs. 3 and 4 to right hemisphere channels.

Figs. 5-11 show 2D sections of Hboxy 3D reconstructed images, at different time/event points. Analogous Hbtotal image sections are shown in Fig. 12.

Axial view: slice 30out of 40 (top to bottom) (slice 25 in fig.12.)

Coronal view: frontal = slice 8, parietal = slice 28, out of 40

Sagittal view: right = slice 10, left = slice 30, out of 40

All images in Figs. 5-11 are scaled to a color-axis range from -5.5×10^{-7} to $+5.5\times10^{-7}$. Images in Fig. 12 are scaled to a color axis range from -1.8×10^{-7} to $+2\times10^{-7}$. DOT transparency = 85%, MRI transparency = 50%.

Fig. 5 illustrates the initial baseline recordings prior to any surgical interventions (first 20 min).

Figs. 6 and 9 show changes consistent with vasodilatation in the right parietal region of the brain, at 10 and 80 min after injection of verapamil in the right MCA.

Figs. 7 and 8 correspond to time points 10 sec before (Fig. 7) and during (Fig. 8) right ICA contrast bolus injection. Shown is significant decrease in Hb_{oxy} levels due to replacement of the blood by contrast medium during the bolus time interval.

Fig. 10 corresponds to the final contrast bolus, followed by subarachnoid bleeding (at 121 min.) resulting from cerebral artery damage caused by intravascular catheter manipulations.

Fig. 11 corresponds a time frame 3 min after the beginning of the subarachnoid bleeding (at 124 min). Significant and rapid increase in Hboxy levels is noted consistent with arterial bleeding over both hemispheres of the brain.

Fig. 12 & 13. - 25 min. after Left ICA/MCA occlusion with balloon catheter. Arrows show area of ischemic stroke identified by NIRS(Fig. 12) and confirmed by MRI after the experiment (Fig. 13). It was shown that Hb_{total} view provides the most acceptable value in settings of two combined conditions: subarachnoid bleeding and ischemic stroke.

Fig. 14. - X-ray image of the NIRS array setup.

Fig. 15. - Shown is CW-NIRS array attached directly to the cranium, after soft tissue dissection.

CONCLUSIONS

Time series imaging of the Hb signal provides a simple and direct means to monitor in real time different physiological and pathological processes in cerebral tissue, vessels and surrounding structures in response to a different types of challenges, such a contrast or vasodilator injection, bleeding or ischemia.

Inspection of data and subsequent 3D-DOT image reconstruction showed changes in hemoglobin oxygenation (Hb_{oxy} and Hb_{deoxy}) and relative concentration (Hb_{total}), which closely matched the events recorded during the procedure. At the same time reconstructed NIRS images were matched with MRI and Histopathological localization of the stroke.

We were able to identify, with temporal and spatial specificity, increased Hb_{oxy} content resulting from regional vasodilator (verapamil) injections, and decreased all 3 Hb states (Hb_{oxy}, Hb_{deoxy} and Hb_{total}) with localized injections of contrast boluses. Global bilateral increase in Hb_{oxy} and Hb_{total} content with later subsequent simultaneous decrease in Hb_{oxy} and increase in Hb_{deoxy}, but stable Hb_{total} were noted with diffuse arterial subarachnoid hemorrhage, what is closely matching with expected physiological changes in those conditions. After cerebral vessels occlusion, significant decrease in Hb_{oxy} and subsequent increase in Hb_{deoxy} recorded at occluded side with no significant changes in opposite site.

These data suggest that CW-NIRS is an effective tool for monitoring functional status of the brain during different interventions and acute pathological processes in real time.

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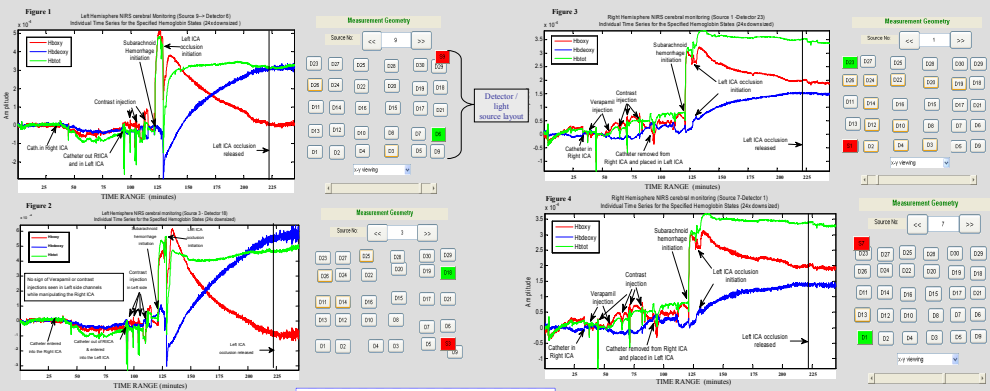
DATA VIEW FOR ALL 3 Hb STATES (Hb_{oxy}, Hb_{deoxy} and Hb_{total})



NIRS 3D-DOT RECONSTRUCTION IMAGES