Concurrence of significant cerebrovascular events with fNIRS and CT, MRI and histopathology

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INTRODUCTION

Monitoring of cerebral tissue oxygenation via fNIRS is widely utilized in experimental and clinical settings.[1]

CW-fNIRS measurements of cerebral perfusion deficits correlates well with:

- Perfusion-weighted MRI in acute stroke.[2]
- Transcranial doppler assessment of microcirculation in carotid artery disease.[3]
- DC-magnetoencephalography monitoring of neuronal activity in subacute ischemic stroke.[4]

The sensitivity of CW-NIRS to detect ischemic stroke needs further validation.[5]

To evaluate the spatial and temporal capabilities of CW-fNIRS 3D diffuse optical tomography (3D-DOT) we conducted validation studies of experimental stroke in 2 Bonnet Macaques (BM-1 and BM-2).

METHODS

Data Collection

Acquisition-channel data and reconstructed images are recorded in real time in BM-1 and BM-2.

Equipment:

- CW-fNIRS 3D-DOT imager used (760nm and 830nm) at a 7.96 Hz rate
- 30 detectors, 9 co-located illumination source-detector sites and 21 detection-only sites resulting in 270 channels (Figs. 1,2).
- The detectors were placed over a 4×5 cm area in the mid frontal-parietal region on the exposed skull (Fig. 2).
- The NAVI® software (NIRx Medical Technologies) was used for fNIRS data pre-processing and 3D image reconstruction.
- All significant events and procedures during the experiment were recorded in real time.

Description of the Experiment

- Dissection of skull muscles and positioning of the fNIRS probes in direct contact with the skull under general anesthesia.
- fNIRS recording commenced prior to any intervention and stopped 1 hour after reperfusion (Figs. 3-6).
- Multiple injections of verapamil (0.35-0.53 mg) and iodinated contrast medium (Omnipaque 300) into ICA/MCA. .
- Acute cerebral ischemia was achieved via 5-Fr diagnostic microcatheter occlusion of the ICA and/or MCA.
- Intraoperative angiography ascertained arterial perforation with subarachnoid hemorrhage (SAH) (Fig. 11).
- Completion postoperative CT-scan and diffusion, T2 and FLAIR MRI (Fig. 12) were performed prior to euthanasia.
- Brain histopathology was obtained. The brains were removed and fixed in 10% buffered formalin for > 2 weeks, after which 5 mm coronal sections were obtained for histopathology. (Fig.13).

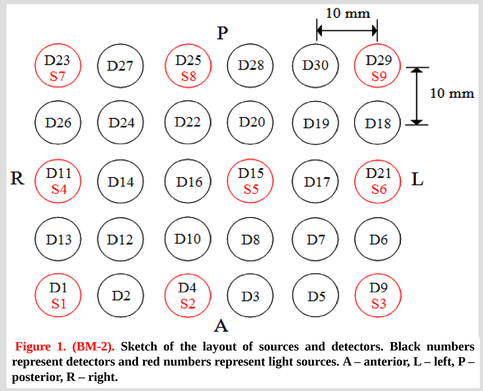


Figure 1. (BM-2). Sketch of the layout of sources and detectors. Black numbers represent detectors and red numbers represent light sources. A – anterior, L – left, P – posterior, R – right.

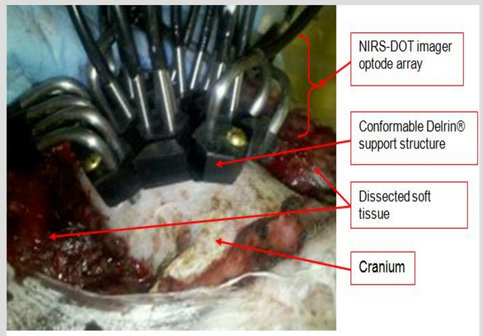


Figure 2. (BM-1). Photograph of fNIRS optode array secured to the animal's skull after dissection of the overlying soft tissues.

TIME SERIES DATA VIEW FOR Hb STATES (Hb_{oxy}, Hb_{deoxy} and Hb_{total})

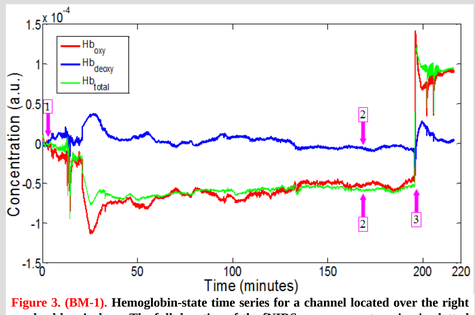


Figure 3. (BM-1). Hemoglobin-state time series for a channel located over the right cerebral hemisphere. The full duration of the fNIRS measurement session is plotted on the time axis. Purple arrows indicate time frames highlighted in subsequent reconstructed image results: 1 (5 min into the measurement) = pre-intervention baseline; 2 (168 min) = during cerebral ischemia; 3 (198 min) = time of removal of the occluding microcatheter.

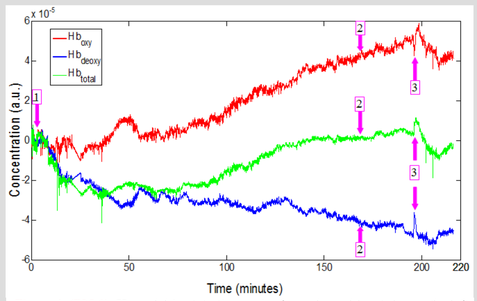


Figure 4. (BM-1). Hemoglobin-state time series for a channel located over the left cerebral hemisphere. Significance of purple arrows is the same as in Fig. 3.

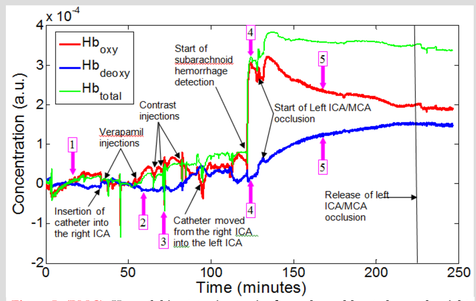


Figure 5. (BM-2). Hemoglobin-state time series for a channel located over the right cerebral hemisphere. The full duration of the NIRS measurement session is plotted on the time axis. Times of occurrence of intraoperative events are indicated. Purple arrows indicate time frames highlighted in subsequent reconstructed image results: 1 (20 min into the measurement) = pre-intervention baseline; 2 (60 min) = response to verapamil injection; 3 (72 min) = response to contrast injection; 4 (126 min) = 4 minutes after NIRS detection of SAH and 3.5 min. before occlusion; 5 (166 min) = after 36.5 min of induction of cerebral ischemia.

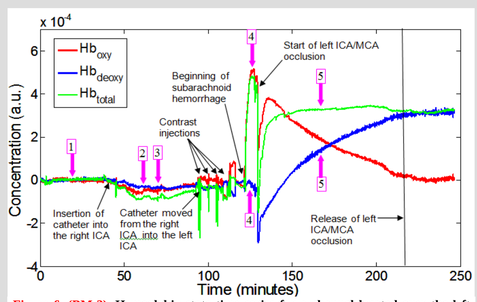


Figure 6. (BM-2). Hemoglobin-state time series for a channel located over the left cerebral hemisphere. Significance of purple colored arrows is the same as in Fig. 5.

2D SECTIONS OF THE fNIRS 3D-DOT RECONSTRUCTED IMAGES

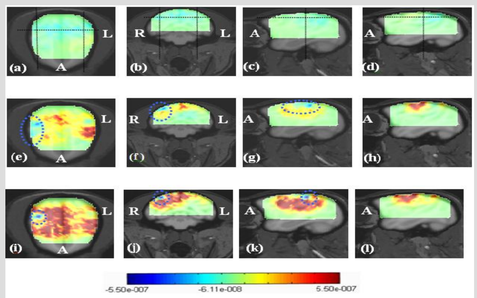


Figure 7. (BM-1). 2D sections of 3D ΔHb_{oxy} images reconstructed from the fNIRS data collected during the 5th [(a)-(d)], 168th [(e)-(h)] and 198th minutes [(i)-(l)]. (a)-(d): prior to all intravascular interventions; (e)-(h): approximately 2-1/4 hr. post-occlusion; (i)-(l): 1 minute after release of the occlusion. (a),(e),(i): axial section; (b),(f),(j): coronal section; (c),(g),(k): left-hemisphere sagittal section; (d),(h),(l): right-hemisphere sagittal section. Dotted lines in (a)-(d) indicate the intersections among the plotted 2D sections. Dotted circles in (e)-(g);(i)-(k) show location of cerebral ischemia.

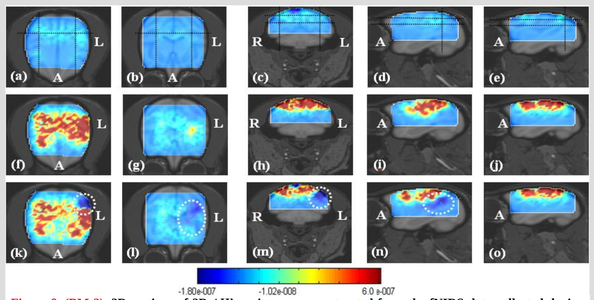


Figure 8. (BM-2). 2D sections of 3D ΔHb_{total} images reconstructed from the fNIRS data collected during 20th [(a)-(e)], 126th [(f)-(j)] and 166th minutes [(k)-(o)]. (a)-(e): baseline, prior to any intravascular intervention; (f)-(j): 4 minutes after NIRS detection of SAH and 3.5 min. before occlusion; (k)-(o): 37 minutes post-occlusion. (a),(f),(k): superficial axial section; (b),(g),(l): deep axial section; (c),(h),(m): coronal section; (d),(i),(n): left hemisphere sagittal section; (e),(j),(o): right hemisphere sagittal section. Dotted lines in (a)-(e) indicate the intersections among the plotted 2D sections. Dotted circles in (k)-(n) show location of cerebral ischemia.

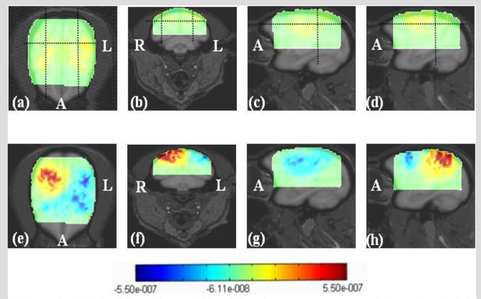


Figure 9. (BM-2). 2D sections of 3D ΔHb_{oxy} images reconstructed from the fNIRS data collected during the 20th [(a)-(d)] and 60th [(e)-(h)] minutes. (a)-(d): prior to right MCA verapamil injection; (e)-(h): following the injection. (a),(e): axial section; (b),(f): coronal section; (c),(g): left-hemisphere sagittal section; (d),(h): right-hemisphere sagittal section. Dotted lines in (a)-(d) indicate the intersections among the plotted 2D sections. A = anterior, L = left, R = right.

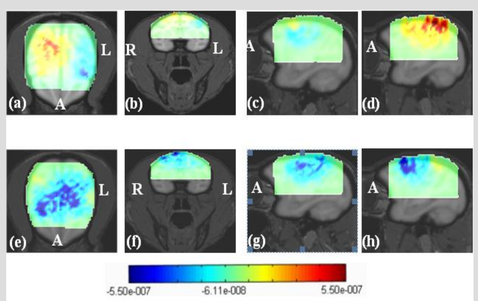


Figure 10. (BM-2). 2D sections of 3D ΔHb_{oxy} images reconstructed from the fNIRS data collected during the 71th minute [(a)-(d)] and 10 seconds later [(e)-(h)]. (a)-(d): prior to right MCA x-ray contrast medium injection; (e)-(h): following the injection. (a),(e): axial section; (b),(f): coronal section; (c),(g): left-hemisphere sagittal section; (d),(h): right-hemisphere sagittal section. Section locations are the same as in Fig. 6.

Figure 11. Intraoperative angiography

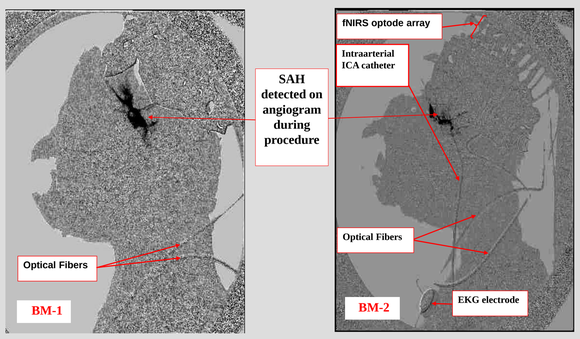


Figure 12. Postoperative coronal FLAIR MRI

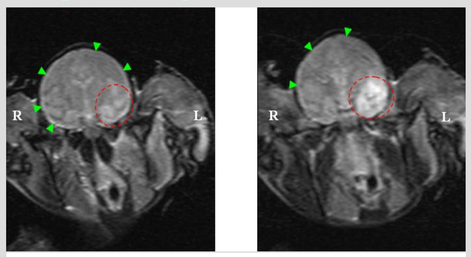
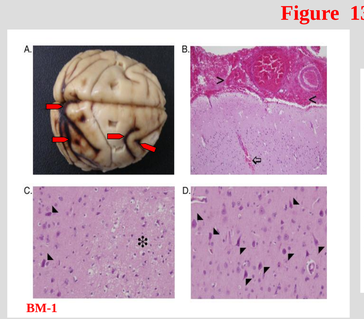


Figure 11. (BM-2). Post-surgical coronal FLAIR MRI sequences confirm presence of ischemia (dotted circle) in the left temporal and inferior frontal lobe following the production of a period of left MCA occlusion. Images also confirm the presence of subarachnoid hemorrhage (arrow points). (L – left, R – right)

Figure 13. Gross and Microscopic Pathology



Red arrows marking subarachnoid hemorrhage present in the sulci.

(>) - Hemorrhage present in the subarachnoid space and surrounding blood vessels.

Vacuolization of neuropil (✱) and shrunken neurons with hypereosinophilic cytoplasm (◀) indicate acute ischemic damage of the cerebral tissue.

Hematoxylin and eosin-stained sections, each 8-10 µm in thickness, were examined by light microscopy.

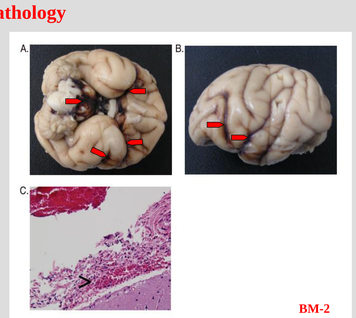


Figure 14(a) **Figure 14(b)**

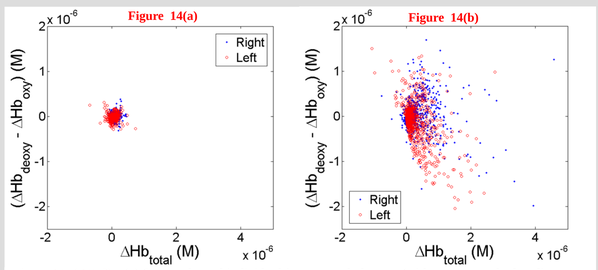


Figure 14. (BM-2). (a) Scatterplots of individual image-voxel changes (with respect to the baseline mean value) in cerebral oxygen exchange and in total Hb concentration. Plotted quantities are derived from images reconstructed from data collected during the 20th minute of the fNIRS measurement session (see Fig. 7, top row). Data points are color coded by cerebral hemisphere: red – left, blue – right. (b) Corresponding scatterplots derived from images reconstructed from data collected during the 166th minute of the fNIRS measurement session (see Fig. 7, bottom row).

RESULTS

We were able to identify, with high temporal and spatial specificity:

- Global bilateral increases in Hb_{oxy} and Hb_{total} levels during diffuse SAH (Figs. 7,8).
- Regional decrease in Hb_{oxy} and Hb_{total} following cerebral ischemia (Figs. 7,8).
- Increased Hb_{oxy} and Hb_{total} levels, on the ipsilateral side, resulting from verapamil injections into the MCA (Fig .9).
- Decreases in Hb_{oxy}, Hb_{deoxy} and Hb_{total} produced by contrast injections into the ICA/MCA (Fig. 10).
- Concurrence between f-NIRS findings and localization of the acute cerebral ischemia and SAH based on CT, MRI and histopathology.
- Increased dispersion in the post-SAH distributions of Hb_{total} and O_2 exchange (Hb_{deoxy} – Hb_{oxy}) values [Fig. 14(b)], in comparison to the baseline time interval [Fig. 14(a)].
  - But the Hb_{total} and O_2 exchange variables are negatively correlated in the left (ischemia and SAH) hemisphere and uncorrelated in the right (SAH only).
  - The left hemisphere has many more points (image pixels) in the ↑Hb_{total}, ↓O_2-exchange quadrant of the graph.

CONCLUSION

CW-fNIRS tomography performs real-time monitoring of the Hb oxygenation status of the brain during and after occlusion, hemorrhage and pharmacological interventions enabling detection of acute cortical pathologies such as cerebral ischemia and intracranial bleeding.

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[5] **K. Sakatani *et al.*, "Progress in NIRS Monitoring of Cerebral Blood Flow." *Brain and Nerve*, 63(9):955-961, (2011).**

ACKNOWLEDGMENTS

This research was supported in part by the National Institutes of Health (NIH) under Grants nos. R21NS067278, R42NS050007 and 5R44NS049734; by the Defense Advanced Research Projects Agency project N66001-10-C-2008; and by the New York State Department of Health.