Histopathological and Radiological Validation of Continuous Wave (CW) Near Infrared Spectroscopy (NIRS) Recordings During Cerebral Intravascular Manipulations

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Abstract: An experimental model of stroke in Bonnet Macaques, complicated with subarachnoid hemorrhage, was monitored using CW-NIRS DOT. Comparison of results with histopathology and radiology findings demonstrate the utility of CW-NIRS for functional imaging and monitoring.

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Introduction

Many different NIRS measurement technologies have been used in successful demonstrations of detection and monitoring of physiological and pathological alterations, via the changes in relative hemoglobin concentrations and oxygen saturation that can occur in brain tissue [1-4]. A currently unresolved issue is the problem of determining which measurement strategies provide an optimal tradeoff between the quality and quantity of clinically relevant information that can be derived, and economic factors such as ease of use and system cost. As a practical matter, most systems that are widely in use today are based on the combination of CW illumination and a small number of optodes. An alternative strategy offering theoretical advantages is the use of time-resolved methods. The practical utility of these systems however, invariably is limited by their substantially greater cost, and space and expertise requirements, among other factors (to some extent, the same argument applies to the theoretically equivalent frequency-domain illumination approach). On the other hand, previous reports from our group have shown that substantial performance improvement can be achieved, while staying with the CW illumination approach, simply by adopting high-density, large-area arrays of NIRS optodes [6-8]. Our observations are consistent with published findings that noninvasive NIRS measurements of cerebral perfusion deficits correlates well with perfusion-weighted MRI findings in acute stroke patients [9], and with transcranial doppler assessments of the microcirculation in carotid artery disease patients [10]. However, available independent validation techniques are limited in their ability to examine precisely the same regions of tissue as NIRS cerebral monitoring devices. Equally or even more limited is the researcher's ability to experimentally manipulate human subjects' cerebral circulation.

We have addressed the preceding issues by developing an experimental animal model to use for validation studies on the spatial and temporal capabilities of CW-NIRS diffuse optical tomography (DOT) imager technology. Here we present findings obtained from Bonnet Macaques, from data collected during an experimentally-induced stroke procedure. Results include successful detection and localization of the stroke, and successful discrimination between the induced stroke (deep) and sub-arachnoid hemorrhaging (superficial). All DOT-based findings are independently validated with post-surgical radiological and histological studies.

Methods

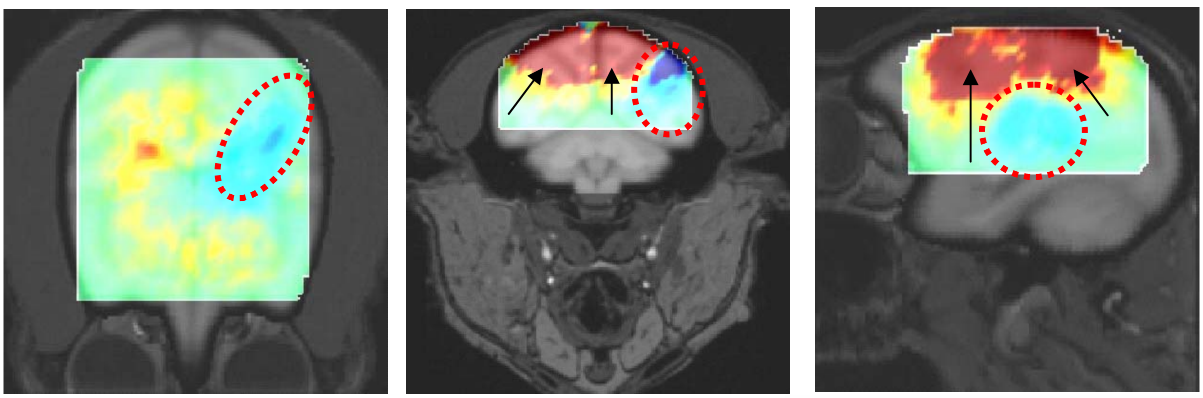
The strokes were achieved via unilateral microcatheter occlusion of the left or right internal carotid artery (ICA) and/or middle cerebral artery (MCA). Two-wavelength (760 and 830 nm) light-intensity data were collected, at an 8 Hz image framing rate, by a 270-channel array (30 detector optodes, 9 of which also are used as sources) placed over a 4×5 cm^2 area in the mid frontal-parietal region of the exposed skull. Optical data were registered to a developed macaque atlas (Xu *et al.*, this conference), preprocessed to remove noise dominated data and subjected to 3D image reconstruction using the Normalized Difference Method [11]. All significant events relevant to the experiment were recorded in real time. Post-surgical CT and MRI scans, as well as post-mortem histopathological examination of the animals' brain, revealed the presence of diverse pathologies (including cortical infarction and subarachnoid bleeding) in each monkey. The post-surgical evaluations acted as a gold standard to compare with the NIRS data.

Results

Figure 1 shows standard anatomical views of the reconstructed changes in total Hb level seen in response to induced stroke accompanied by sub-arachnoid hemorrhage. Comparison of these findings to pathologies noted in histopathological examinations (Fig. 2) and in MR (Fig. 3) and CT images match with the locations indicated in the images, demonstrating the ability of large-area, dense-array CW-NIRS measurement data to spatially localize hemodynamic perturbations. Additional studies (not shown) have also revealed spatial and temporal coincidence between effects of various infusion agents (contrast dye, verapamil) and the associated hemodynamic responses.

Conclusion

The spatial and temporal specificity of responses to the different types of events indicate that continuous-wave NIRS imager technology can be deployed as an effective tool for functional imaging.



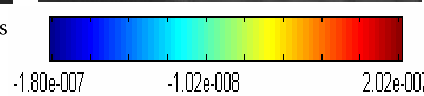


Figure 1. CW-NIRS DOT images of reconstructed change in total Hb level in the monkey's head, with bilateral subarachnoid bleeding (arrows) and left temporal stroke (red dotted circle) indicated.

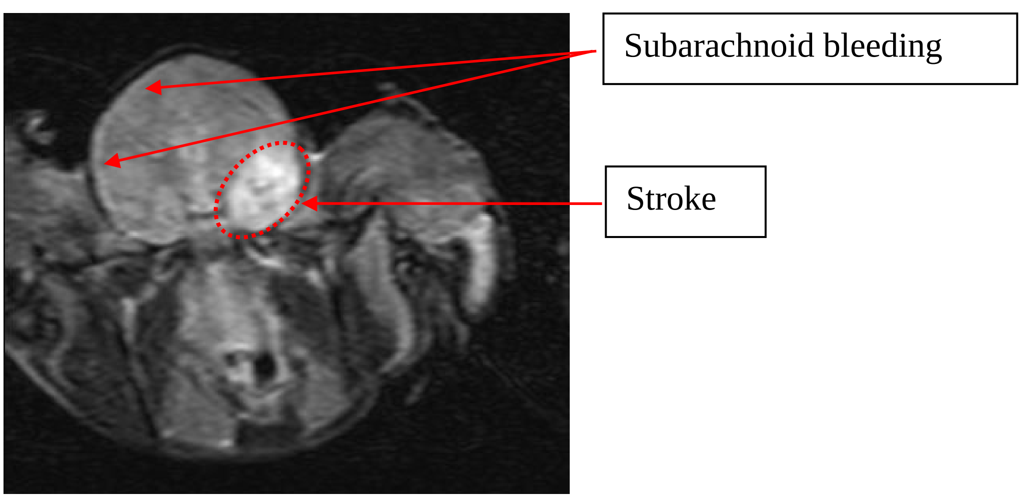


Figure 2. FLAIR MRI coronal image of the head of the animal after the experiment.

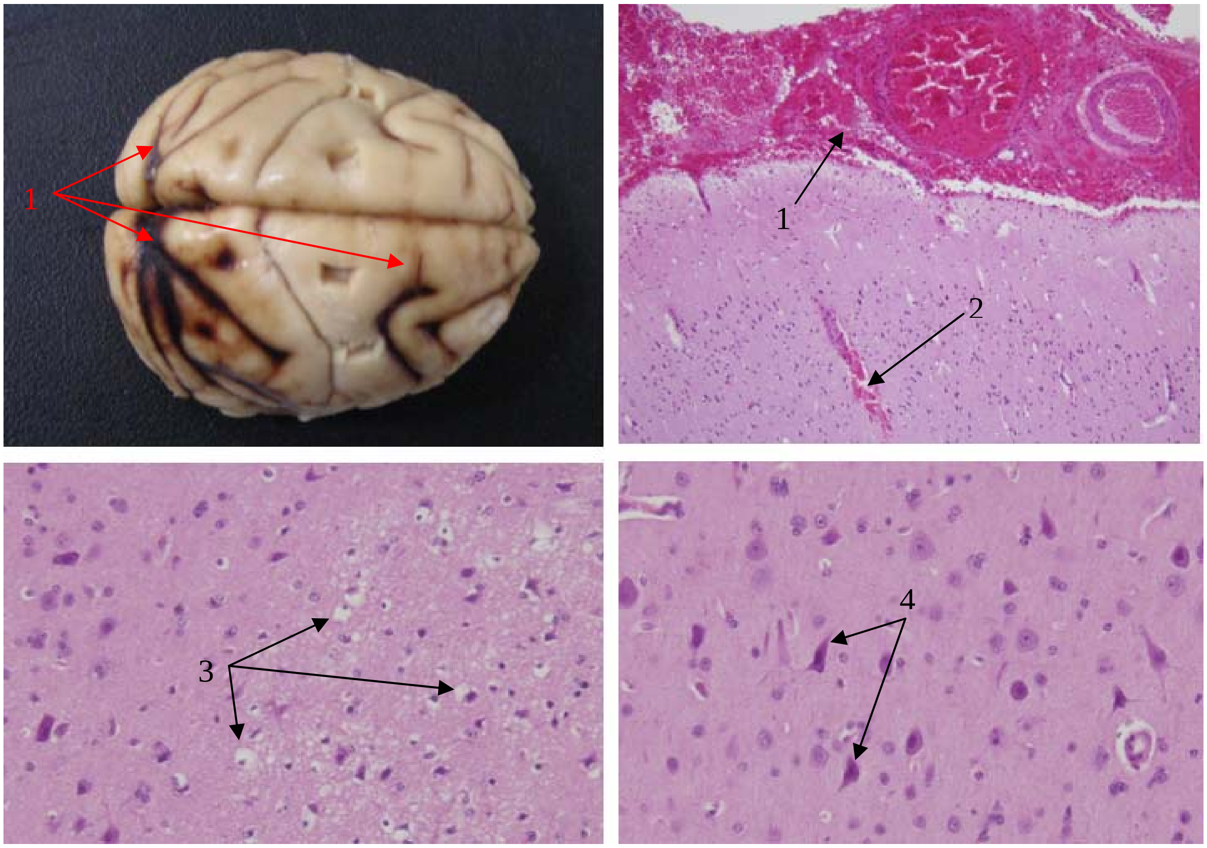


Figure 3. Histopathologic examination confirmed the presence of subarachnoid hemorrhage (1) in two animals (exemplary results for one of the animals are shown here). There also were perivascular petechial hemorrhages (2) in the superficial cortical layers, and many of the small blood vessels appeared congested. Presence of focal vacuolization of the neuropil (3) and acute ischemic neurons (4), with many shrunken neurons with hypereosinophilic cytoplasm and pyknotic nuclei, were identified in the frontal cortex and temporal cortices. These findings are evidence of developing stroke process in these areas of the brain.

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