Noninvasive Continuous Imaging of Reduced Cerebral Perfusion with a Novel Diffuse Optical Tomography (DOT) System: A Preliminary Hyperventilation Study in Pig and Human

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Outline

Cephalogics has developed a wearable Diffuse Optical Tomography (DOT) imaging device to help clinicians monitor perfusion and oxygenation from multiple brain regions on the bedside in disease states such as ischemic stroke, vasospasm, and traumatic brain injury [1]. This study investigated the sensitivity of the system to changes in cerebral tissue oxygenation (StO_2) during hyperventilation induced hypocapnia in a pig and three healthy human volunteers.

Methods

Portable Diffuse Optical Tomography (DOT) System

- A picture of the portable DOT sensor is provided in (Fig.1 a).
- High-density arrangement: 10x18 (sources x detectors) on rigid-flex circuit boards.
- Five time-encoded, amplitude-modulated VCSELs operating at five wavelengths ranging 690-850nm within each source optode.
- Photodiodes, synchronous detection, overlapping CW measurements.
- Source-detector distances: 13-87mm over 9 nearest-neighbors.
- 180 channels per wavelength at 5Hz frame-rate. Acquired data is digitized, processed, and transmitted to a laptop via Ethernet connection for post-processing (fiber-free interface).

Experimental Protocol

- **Pig:** A 45kg Yorkshire pig was placed in prone position, anesthetized (isoflurane), and mechanically ventilated. A Cephalogics DOT sensor was positioned over the pig's cranium; the sensor was secured using an elastic bandage wrap. A second sensor was placed on the hind leg of the pig for monitoring systemic perfusion during the protocol (Fig.1 b). DOT measurements were acquired continuously during baseline (8 mins, $PaCO_2$ = 40mmHg), transient hypercapnia (4 mins, $PaCO_2$ = 15mmHg), and recovery (25 min, $PaCO_2$ = 40mmHg) periods controlled by the respiratory rate of a ventilator. DOT data were recorded to a laptop for offline analysis. Oxygen Saturation images were reconstructed every minute, and image means (±SD) were computed for comparison of results across measurements. All animal procedures were approved by the Institutional Animal Care and Use Committee of Tufts Medical Center and the Human Nutrition Research Center on Aging.

- **Humans:** Hyperventilation testing was also investigated in three healthy human volunteers (mean age, 38.3 years; 3 males). Two DOT sensors were positioned on both sides of the head above the ears over the MCA territory. DOT measurements were acquired during normal-breathing baseline period (~5 mins), rapid-breathing hyperventilation period (~3 mins), and normal-breathing recovery period (~15 mins). Oxygen Saturation images were reconstructed every minute, and image means (±SD) were computed for comparison of results across measurements. The research protocol was approved by Western Institutional Review Board (WIRB: 1132591), and informed consent was obtained from all subjects prior to measurements.

Discussion and Conclusion

Cephalogics noninvasive DOT system measured reduced cerebral tissue O_2 saturation ($StcO_2$) during hyperventilation in human subjects and a pig despite the large scalp-cortex distance in pig. $StcO_2$ estimates in pig markedly decreased during hyperventilation from baseline (–15%±4%), consistent with the known vasoconstrictive response of cerebral tissues to hypocapnia [2]. In contrast, $SstO_2$ estimates modestly increased during hyperventilation (3%±3%), indicating elevated systemic perfusion. Both parameters fully returned to baseline values during the recovery period (Fig. 2).

$StcO_2$ reductions due to hyperventilation in human volunteers (–8%±4%) were consistent between the two hemispheres and the results in pig. Interspecies differences in $StcO_2$ response to hyperventilation were likely due to differences between protocols (free-breathing vs. mechanical ventilation).

The results of this study demonstrate the sensitivity of the Cephalogics' DOT system to $StcO_2$ values and its ability to separate $StcO_2$ from systemic perfusion in a clinically relevant scenario.

Protocol

Fig.1. Illustration of the hyperventilation test setups in pig and human. ⓐ The DOT sensor with a high-density imaging arrangement of 10 sources (yellow circles) and 18 detectors (blue circles). Green lines represent all measurement pairs, ranging from 1–9 nearest neighbors; ⓑ setup for hyperventilation testing in pig showing the placement of DOT sensors on the leg (left panel) for monitoring systemic perfusion, and on the head (right panel) for monitoring brain perfusion; ⓒ setup for hyperventilation testing in human showing the placement of the DOT sensor above the ear over the MCA territory on both sides of the subject's head.

Results

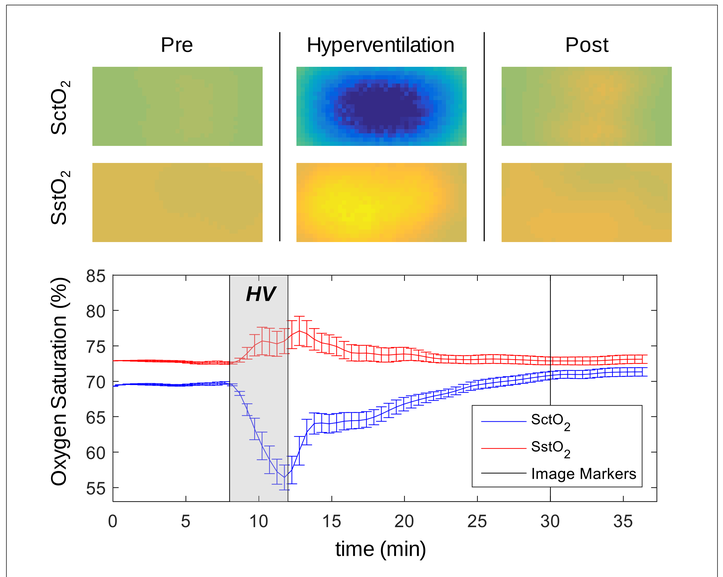

Fig.2. Results of DOT measurements during hyperventilation testing in pig. Cerebral tissue oxygen saturation ($StcO_2$) and leg tissue oxygen saturation ($SstO_2$) are presented. Oxygen saturation images at discrete time points (marked by vertical lines) are provided on the top; and temporally plotted image means (±SD) are provided on the bottom. Hyperventilation period is highlighted in grey.

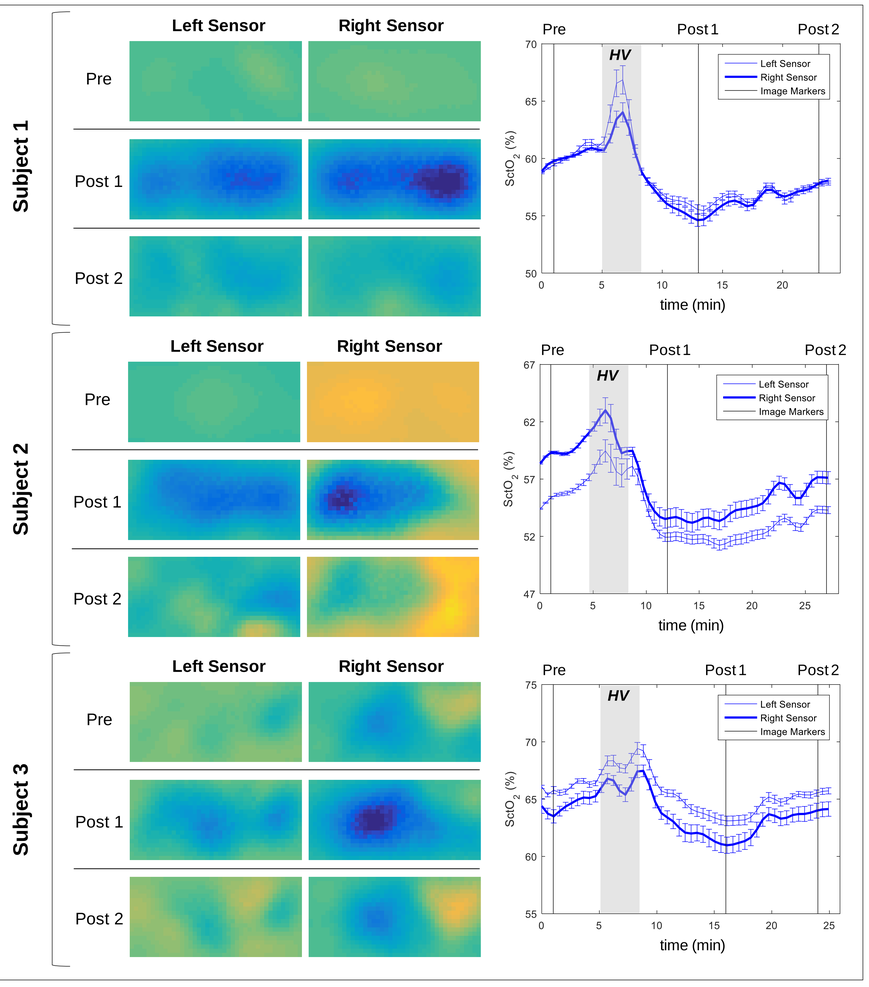

Fig. 3. Results of DOT measurements during hyperventilation testing in three healthy volunteers. Temporal trends and images of cerebral tissue oxygen saturation ($StcO_2$) are presented. Oxygen saturation images at discrete time points (marked by vertical lines) are provided on the left; and temporally plotted image means (±SD) are provided on the right. Hyperventilation periods are highlighted in grey.

References

[1] Hallacoglu, Bertan, Jason W. Trobaugh, Kate L. Bechtel, and Chandran V. Seshagiri. "Blood phantom verification of a new compact DOT system." In Cancer Imaging and Therapy, pp. JM3A-3. Optical Society of America, 2016.

[2] Laffey, John G., and Brian P. Kavanagh. "Hypocapnia." New England Journal of Medicine 347, no. 1 (2002): 43-53.