Blood phantom verification of a new compact DOT system

Bertan Hallacoglu[1], Jason W. Trobaugh[1,2], Kate L. Bechtel[3], Chandran V. Seshagiri[1]

(1) Cephalogics, LLC, 33 Arch St. Suite 320, Boston, MA 02110,
(2) Department of Electrical and Systems Engineering, Washington University in St. Louis, MO 63110, (3) Triple Ring Technologies, Newark, CA 94560

Outline

Patients with a variety of neural disease states including cerebral hemorrhage, ischemia, and head trauma are at risk of impaired cerebral perfusion. Reliable, accurate, continuous, bedside imaging of cerebral tissue oxygen saturation (StO_2) could help clinicians manage perfusion in these patients.

However, demonstrating the accuracy of cerebral StO_2 images *in vivo* is unfeasible since no reference standard exists. Measurements in tissue-mimicking phantoms provide a reasonable first-step towards verification of system performance and characterization [1,2]. Intralipid (IL) and ink phantoms have been commonly used to verify measurements of optical properties; blood phantoms have been used to better mimic physiology and incorporate physiologically relevant absorption and scattering spectra; other phantom experiments have included multi-layer designs to approximate the layered composition of the human head.

Combining these ideas, we have designed a two-layered blood phantom for verification of blood oxygen saturation (SO_2) measurements in the "brain" layer. In this poster, we report preliminary measurements on this phantom using a new compact diffuse optical tomography (DOT) system for quantitative, non-invasive, continuous bedside imaging of cerebral oxygenation and perfusion in patients with cerebrovascular disease.

Methods

DOT System

- High-density arrangement: 10x18 (sources x detectors) on rigid-flex circuit boards (Fig. 1a).
- 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).
- Dynamic range of over 10^7, or 140 dB.

Blood Phantoms

- Noryl enclosure: dimensions 120x60x45mm (RI ~1.58).
- Front wall with cutouts to house the DOT sensor-array.
- Optical windows: ~0.1mm thick Lexan polycarbonate film (RI ~1.6).
- Slits for placement of diffuse separator to create distinct regions inside the enclosure (Fig.1b and c).
- Diffuse separator material: C-HH20 (Brightview Tech, Durham, NC), Polyethylene Terephthalate (PET), 0.178mm thickness (RI ~1.46).
- Mixture: IL 20% (Sigma Aldrich, St. Louis, MO), water, and fresh bovine blood mixed to create suspensions with μ_s' and fraction of blood representative of blood to brain tissue volume.
- Typical mixtures used by volume were 6% IL to water (μ_s' ~10cm^{-1} at 800nm), and 3.5% blood to IL+water (~60 μM total hemoglobin concentration).

Testing

- Desaturation achieved by adding yeast/sugar into suspensions [2].
- DOT measurements acquired continuously through the front wall before and during desaturation.
- Oxygen tension (PO_2) and temperature of the desaturated layer were recorded (Neofox O_2 sensor, Ocean Optics, Dunedin, FL) and converted to SO_2 using the hemoglobin disassociation curve to serve as a reference (Fig 2).
- Experiment 1: Extracerebral layer desaturated, and brain layer kept constant (Fig.1b).
- Experiment 2: Extracerebral layer kept constant, and brain layer desaturated (also, Fig.1b).
- Experiment 3: Diffuse separator repositioned, and half of brain layer desaturated (Fig. 1c).

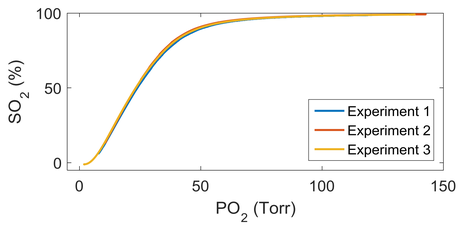

Fig.2. Hemoglobin disassociation curves were used to convert local oxygen tension (PO_2) and temperature measurements to hemoglobin oxygen saturation (SO_2) values. SO_2 values were used as reference for the DOT measurements ("Reference" in Figs 3-5).

Data Processing

- Bulk μ_s' spectrum, and oxy- (HbO) and deoxy-hemoglobin (HbR) concentrations were determined by iteratively fitting the data (*e.g.* Fig. 1d) with a homogenous diffusion model [4]. Following scattering power relationship was used in the fitting procedure: $\mu_s'(\lambda) = \mu_s'(\lambda_{ref})(\lambda/\lambda_{ref})^{-b}$.
- Two-layer HbO and HbR concentrations were determined by fitting the data with a two-layer diffusion model [5].
- Rytov approximation, expressed as $y = -\log(\phi/\phi_0) = Ax$, was used for estimation of voxelized HbO and HbR perturbations, where:
  - ϕ is the measured light intensities (*e.g.* Fig. 1d),
  - ϕ_0 is a two-layer diffusion model [5],
  - x is HbO and HbR perturbation images in a vector form,
  - A is the chromophore sensitivity matrix for the specific sensor-array geometry constructed according to [6]. Finite-element modeling in a two-layered slab model was performed using NIRFAST to generate Green's functions for the sensitivities of each source and detector for all wavelengths [7].
- Moore-Penrose generalized inverse [5] was used for the estimation of HbO and HbR perturbation images, $x = A^{\#}y$, by minimizing the objective function: $\min\{\|(y - Ax)\|_2^2 + \alpha\|Lx\|_2^2\}$, where $A^{\#} = L^{-1}A^T(A^TA + \alpha I)^{-1}$, $L = \sqrt{diag(A^TA) + \beta}$, and α and β represent regularization values [6].
- HbO and HbR perturbations were added back to background values to evaluate oxygen saturation of hemoglobin (SO_2).
- Measurements were processed into 2-D images of layer 2 and image means were compared to reference SO_2 values (Figs. 3-5).

Discussion and Conclusion

- The blood phantom platform presented here models the human head as a two-layer medium, wherein layers 1 and 2 represent extracerebral tissue (scalp, skull, CSF) and brain tissue (gray and white matter), respectively.
- In this platform, we have demonstrated the sensitivity of our quantitative SO_2 imaging approach to flat-field and spatially-varying SO_2 values beneath a 15mm thickness (representative of typical scalp-to-cortex distance) while remaining insensitive to SO_2 values within that thickness using a new compact DOT system.
- It should be noted that covered SO_2 range (0-100%) was beyond physiological limits (~30-80%), which may affect accuracy of measurements. The atmosphere around the phantom may be controlled to improve this limitation in future studies.
- To our knowledge, these are some of the few quantitative SO_2 images in the literature and are important steps towards developing validation strategies in the absence of a reference standard for quantitative cerebral StO_2 imaging *in vivo*.

Results

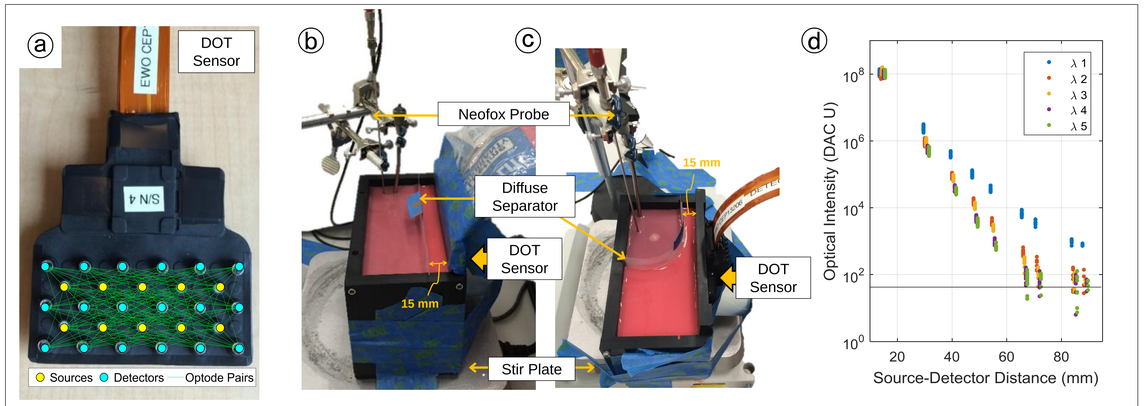

Fig.1. Experimental setup: ⓐ The DOT sensor-array with a high-density imaging arrangement of 10 sources (yellow circles) and 18 detectors (blue circles). Green lines indicate all measurement pairs, ranging from 1–9 nearest neighbors; ⓑ blood phantom setup for experiments 1 and 2 showing the placement of the DOT sensor-array and the Neofox PO_2/temperature probes during measurements; ⓒ setup for experiment 3, where the "brain layer" is split in two regions; and ⓓ representative detected optical intensity levels for five wavelengths vs. source-detector distances in a blood phantom.

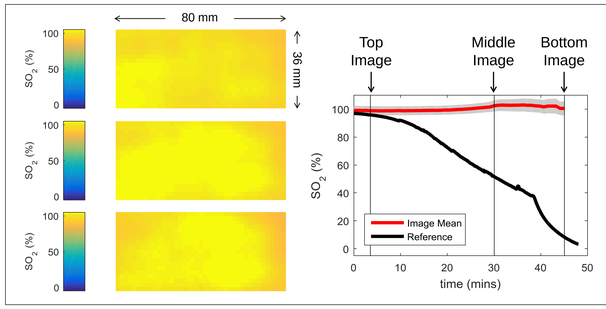

Fig.3. Results of experiment 1, wherein extracerebral layer is desaturated and brain layer is kept constant. SO_2 images of layer 2 at discrete time points are shown on the left; temporally plotted mean±stdev of images of layer 2 (red line) and the reference measurement (black line) are shown on the right. Time points of the images are indicated by the vertical lines. Reference measurement is of the desaturated extracerebral layer.

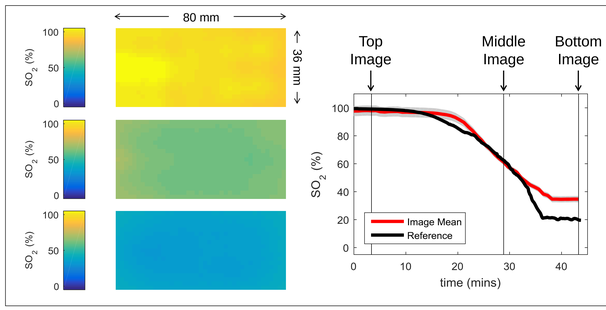

Fig.4. Results of experiment 2, wherein extracerebral layer is kept constant and brain layer is desaturated. SO_2 images of layer 2 at discrete time points are shown on the left; temporally plotted mean±stdev of images of layer 2 (red line) and the reference measurement (black line) are shown on the right. Time points of the images are indicated by the vertical lines. Reference measurement is of the desaturated brain layer.

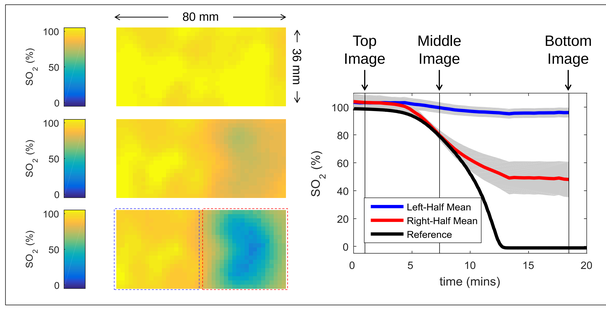

Fig.5. Results of experiment 3, wherein extracerebral layer and half of the brain layer is kept constant, and the other half of the brain layer is desaturated. SO_2 images of layer 2 at discrete time points are shown on the left; temporally plotted mean±stdev of the images of layer 2 (right half in red, and left half in blue), and the reference measurement (black line) are shown on the right. Time points of the images are indicated by the vertical lines. Reference measurement is of the desaturated half of the brain layer.

References

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