In Vivo Applications of Diffuse Optical Techniques For Measuring Hemodynamics in Mouse Models of Cerebral Stroke

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What is Diffuse Optics?

- Uses non-invasive light at visible-near-infrared spectrum (400-900 nm) to study tissue dynamics
- A spectrum of light interacts with tissue, and this interaction is dependent on the contents of absorbers and scatterers in the media (e.g. red blood cells)
- The properties of the absorbers and scatterers gives us dynamic information about tissue (e.g. blood flow or oxygenation)

What is Hemodynamics? Why is it Relevant?

- Study of blood flow and its dynamics in tissue
- Blood carries oxygen and nutrients to body parts, while also removing CO_2 and waste.
- Measuring the variations in oxygenated hemoglobin and flow rate in superficial tissue can give hints towards disease detection and prevention.

What is a Stroke?

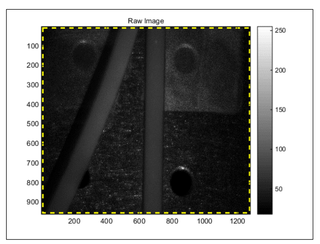
- There are two types of stroke: hemorrhagic and ischemic
- Hemorrhagic strokes result from an aneurysm.
  - Can be under the skull (intracerebral) or out (subarachnoid)
- Ischemic strokes result from blood clots.
  - Can be a thrombosis or embolism
  - Accounts for 87% of strokes

Objectives

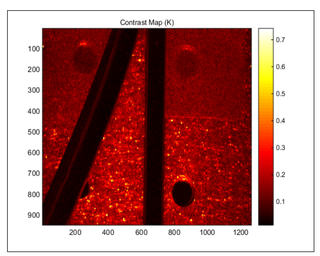
- Observe changes in superficial cerebral blood flow (LASCI) and blood volume/oxygenation (DRS) after chemically inducing strokes in adolescent mice.
- Laser Speckle Contrast Imaging (LASCI) is a technique that uses variations in a light interference pattern to detect superficial blood flow.
- Diffuse Reflectance Spectroscopy (DRS) is a non-invasive way of utilizing the reflectance, absorption, and scattering of light off a turbid medium to measure tissue oxygenation and hemoglobin content.

Speckle

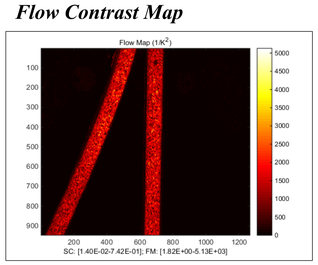
- A Speckle pattern is the result of interference of scattered wave fronts from a coherent (laser) source at a detector (camera) location
- During the exposure time for a single image acquisition the variation in speckle pattern can indicate sub-surface flow and is quantified as
  - K=standard deviation (σ) / mean intensity (<I>)
- Flow contrast is inversely proportional to **flow**
  - Flow~1/K²



Raw Image



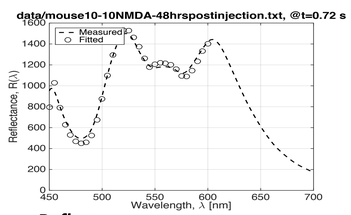
Flow Contrast Map



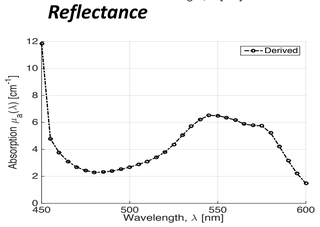
LASCI Flow

Diffuse Reflectance Spectroscopy

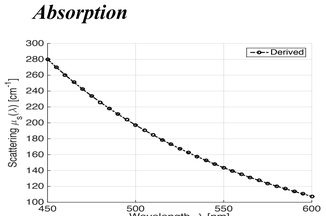
- The diffuse reflectance of a scattering medium can be easily measured using a broad-spectrum light source, spectrometer, and fiber optical probes.
- Light propagation in a turbid medium can be modeled Monte Carlo Model which can be used to fit experimental data
  - Thus the model can be used to derive scattering (μ_s) and absorption (μ_a) spectra for each measurement
- Scattering (μ_s) coefficient
  - Depends on water content, cell structural parts (ECM), etc.
- Absorption (μ_a) coefficient
  - Derives total hemoglobin (THb), concentration of oxygenated hemoglobin (HbO_2), and blood-oxygen saturation (SO_2)



Reflectance



Absorption



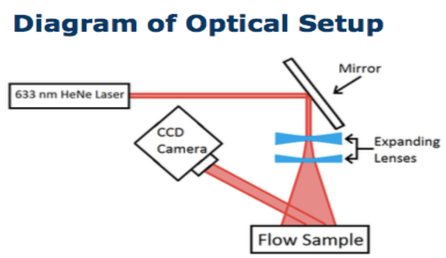
Scattering

Methods

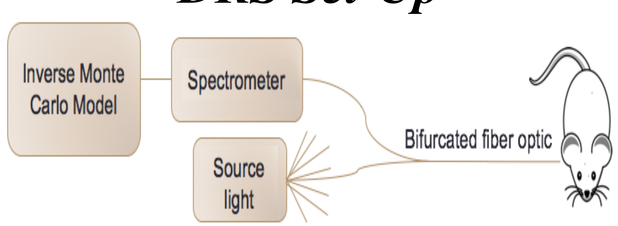
Animal Model:

- Adolescent mice (1-2 years of age)
- Record raw/baseline measurements before injection
  - DRS – 100 scans (30 ms exposure time)
    - Raw reflectance spectrum
  - Speckle – 40 images (20 ms exposure time)
    - Raw image → Flow contrast
- Induce stroke chemically via transcranial injections of
  - NMDA of different concentrations (10 nM, 20nM, etc.)
  - Buffer (Controls)
- Record measurements immediately after injection
  - DRS – 100 scans (30 ms exposure time)
  - Speckle – 40 images (20 ms exposure time)
- Process data
  - DRS – absorption and scattering
    - How did the amount of hemoglobin, and its relative level of oxygenation change after inducing a stroke, using NMDA?
  - Speckle – Flow contrast → LASCI flow
    - How did flow rate change as a result of inducing a stroke, chemically, with NMDA?

Speckle Set-Up

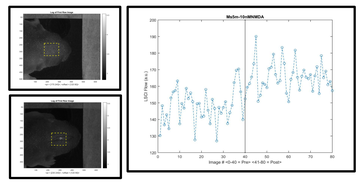


DRS Set-Up

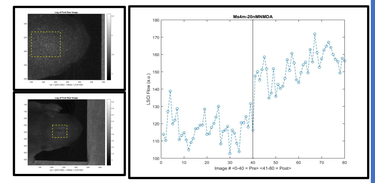


Results

Speckle

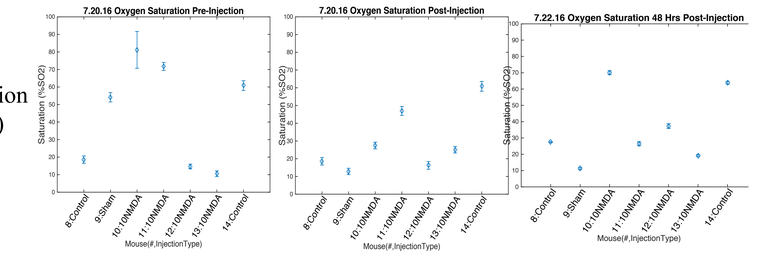


Mouse 5 (male) Flow Analysis -- Injection of 10 nM NMDA



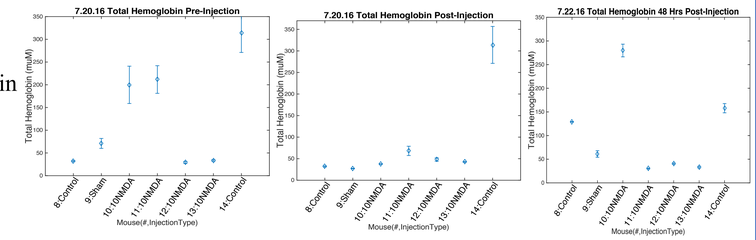
Mouse 4 (male) Flow Analysis -- Injection of 20 nM NMDA

Saturation ($\%SO_2$)



DRS

Total Hemoglobin (mμM)



Pre-injection | Post injection | 48 hours post injection

- Injection caused local hemodynamic changes
- Both systems were able to distinguish between **buffer** (control) and **NMDA**-injected subjects
- Speckle detected different changes in flow rates between injections of NMDA and buffer
  - Efficacy of Speckle in detecting superficial, microvascular flow
- DRS was able to detect lowered saturation ($\%SO_2$) and hemoglobin levels (THb) post injection
  - Levels returned closely to pre-injection values
  - Efficacy for DRS to detect changes in $\%SO_2$ and THb
- Detection of reactive hyperemia

Clinical Significance and Future Research

- ***Being able to non-invasively assess a suspected stroke patient.***
- ***Materials are not expensive, and are easy to transport.***
- ***Knowledge of tissue hemodynamics can be applied to many places of the body (Hands, arms, feet, legs).***

Acknowledgements and Citations

Young, A, Vishwanath, K. Using Laser Speckle Contrast Imaging Detect Changes in Flow. Miami University. 16 March 2017.

Darkens, L, Vishwanath, K. Using Diffuse Reflectance Spectroscopy to detect stroke in a mouse model. Miami University Physics Department, Cincinnati Children's Hospital Medical Center.

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