Measuring Tissue Blood Flow using Ultrasound Modulated Diffused Light

A. Ron[a], N. Racheli[a], I. Breskin[a], Y. Metzger[a], Z. Silman[a], M. Kamar[a], A. Nini[a], R. Shechter[a], M. Balberg[a]

[a] Ornim Medical Ltd, Israel

Highlights:

- **Non-invasive and continuous monitoring of cerebral blood flow in swine, based on the acousto-optic effect.**
- **High sensitivity and specificity for detecting changes in cerebral blood flow.**
- **Very good agreement with concurrent invasive blood flow monitoring by Laser Doppler probes.**

Introduction:

Monitoring microcirculatory blood flow is essential during treatment of patients in whom brain perfusion may be compromised. However, there are currently no noninvasive devices that continuously monitor cerebral blood flow (CBF). A novel monitor (CerOx), that uses the acousto-optic effect, enables real time continuous, noninvasive monitoring of CBF and oxygenation. The aim of this study is to examine the ability of the CerOx to monitor CBF during controlled manipulations of blood flow and compare it to invasive Laser Doppler (LD) measurements.

Methods:

- 20 Kg Piglets were anesthetized and ventilated.
- Increased CBF by:
  - Epinephrine.
  - Hypercarbia (FiCO_2=7%)
  - Hypoxia (FiO_2=10%)
- Decreased CBF by:
  - Nitropruside.
  - Hyperventilation
- CBF was monitored using the Cerox and an invasive Laser Doppler Electrode (Moore Instruments, UK).
- Cerox probes were placed on the head and a Laser Doppler probe was inserted to the cerebral cortex (through a skull bore hole) for cerebral monitoring.
- Receiver Operator Curves (ROC) analysis was performed as a test for the discriminative power of the measurements to accurately identify these manipulations. For each of the five manipulations, a ROC analysis was calculated.

Technology:

- Coherent (BW<300MHz) near infrared light illuminates the tissue, and ultrasound waves are introduced simultaneously
- Photons that travel through the path of the ultrasound wave are “tagged” and can be identified upon detection, by detecting an artificial Doppler shift induced by the moving ultrasound waves.
- The cross correlation between the intensity of the light reaching the detector and the ultrasound signal is calculated.
- A flow index (CFI) is calculated from the amplitude of this cross correlation divided by the light intensity.

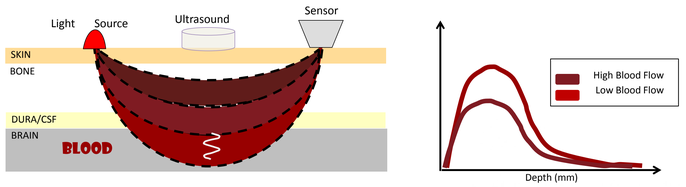

Figure 1 : (Left) An illustration of the light path and the ultrasound field. (Right) Cross correlation signal

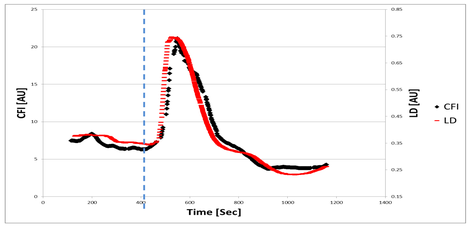

Figure 2 : Epinephrine manipulation

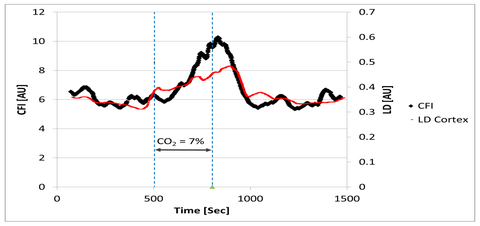

Figure 5 : Hypercarbia

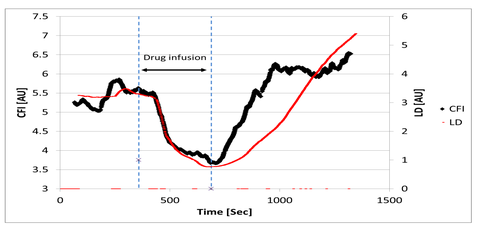

Figure 3 : Nitropruside infusion

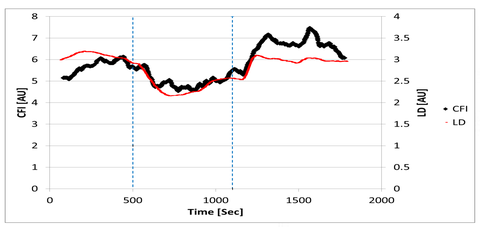

Figure 6 : hyperventilation

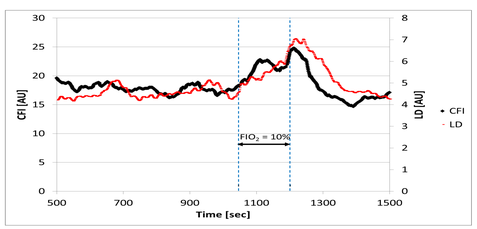

Figure 4 :Hypoxia

Manipulation	Method	Area Under Curve	95% Confidence Interval	
			Lower Bound	Upper Bound
Epinephrine	CFI	0.816	0.758	0.875
	LD	0.794	0.733	0.854
Nitropruside	CFI	0.914	0.887	0.940
	LD	0.919	0.893	0.945
Hypoxia	CFI	0.838	0.797	0.878
	LD	0.976	0.965	0.987
Hypercarbia	CFI	0.875	0.833	0.918
	LD	1.000	1.000	1.000
Hyperventilation	CFI	1.000	1.000	1.000
	LD	1.000	1.000	1.000

Table 1 : CFI and LD ROC analysis per manipulation

Results:

Epinephrine: (Figure 2) significant correlations between two methods were observed, showing a substantial increase in CBF following Epinephrine injection (dashed line). This is a result of an increase in cardiac output and blood pressure.

Nitropruside: (Figure 3) a large drop in CBF was observed during Nitropruside infusion (dashed line). This is a result of vasodilatation and decrease in systemic blood pressure.

Hypoxia: (Figure 4) demonstrating a modest increase in CBF during inhalation of a reduced fraction of oxygen (FiO_2) using up to 10% O_2 mixture. This is a result of the increase in PCO_2 during this manipulation.

*Hypercarbia: (*Figure 5), induced by inhalation of 7% CO_2 and 93% O_2, demonstrating a significant increase in CBF (period of ventilation with 7% CO_2 is marked on the figure).

Hyperventilation: (figure 6), PCO_2 was reduced leading to a reduction in CBF (dashed line).

Sensitivity and Specificity:

For each of the five manipulations, a ROC analysis is presented in Table 1.

In addition, ROC analysis for 23 Epinephrine manipulations produced an area under the curve (AUC) of 0.953 [95% CI (0.942, 0.960)]for the CerOx readings and AUC of 0.943 [95% CI (0.933, 0.953)] for the LD.

Discussion:

The agreement between CerOx and Laser Doppler readings in detecting changes in flow demonstrates that CFI responds to changes in blood flow in a similar way to LD. The two techniques measure different tissue volumes, but the measured signals are correlated and have similar direction of change and dynamics.