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Blood flow measurements and clot detection with near-infrared spectroscopy

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Abstract: Detecting impeded blood flow and locating the clot causing it is a major challenge in neurosurgery. We propose an instrument that uses near -infrared spectroscopy to simultaneously detect clots and measure blood flow.

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1. Introduction

The formation of blood clots and the restriction of blood flow to brain tissue is a major cause of brain damage and death during neurosurgery. Surgeons can remove clots and repair the blood vessels if they can locate the clot and determine when blood flow has been restored. Current techniques for measuring blood flow are limited by the size of vessel to which they can be applied and the frequency with which they can be used. None of these techniques can locate the blood clot itself or determine its extent. In this paper we present preliminary data for the design of an instrument that uses near infrared spectroscopy to measure blood flow and detect blood clots simultaneously.

Two techniques are currently used to measure blood flow in the brain during surgery; fluorescent angiography and Doppler measurements. In fluorescent angiography a fluorescent dye (indocyanin green) is injected into the patient and the surgeon uses an appropriate light source to observe the dye as it flows into the brain. Any vessels that do not fill with dye are not experiencing significant blood flow and possibly contain clots. This technique is limited because once the vessels are filled with dye no further information can be obtained; fluorescence will be present if new dye is flowing into a vessel or if dye is trapped in a blocked blood vessel. Additionally, the amount of dye a patient can be exposed to is limited due to safety concerns. Doppler instruments are also used to measure blood flow. This technique relies on measuring the Doppler shift of laser or ultrasound radiation that is reflected off moving blood. Current ultrasound Doppler instruments are limited in that they can only be used with larger blood vessels. Neither technique can detect the location and size of the clot causing the restriction in blood flow.

2. Using Temporal Correlation to Measure Flow

The technique we propose to measure flow makes use of fluctuations in transmitted light. A light source is placed on one side of the blood vessel and two or mores detectors on the other. As particles, in this case blood cells, pass between the source and the detectors the intensity of the transmitted light fluctuates. For larger, slow particles the temporal separation of these fluctuations will be obvious to the eye and the velocity of the particle can be determined directly from the spacing of the detectors. In situations such as blood vessels where there are smaller particles, higher backgrounds, and higher concentrations of particles the fluctuations are less intense and less clearly separated. The cross correlation function can be used to extract the time scale of regular fluctuations from noisy data. The normalized cross correlation of two signals $G(\tau)$ of two signals, F_1 and F_2 is

$$G(\tau) = \frac{< \delta F_1(t) \delta F_2(t+\tau) >}{< F_1 >< F_2 >} \quad (1)$$

Where <…> is the mean over time, τ is the correlation delay time and $\delta F_i(t) = F_i(t) - < F_i >$ [1]. In order to extract useful information, the cross correlated data is fit with an expression for $G(\tau)$ in terms of the parameter of interest, the velocity:

$$G(\tau) = \frac{1}{N}\exp\left[-\frac{R^2}{\omega_0^2}\left(\tau^2 + \tau_F^2 + 2\tau\tau_F\right)\right] \quad (2)$$

In this expression N is the average number of particles, R is the spacing between observation volumes, τ_f is the average time of transit between observation volumes and ω_0 is the $1/e^2$ radius of the observation volume [2,3]. Equation 2 will have a peak at $\tau = \tau_f = R/|V|$ where V is the velocity of flow.

To test this technique a model of blood flow was used. Milk served to model blood since the fat globules in homogenized milk are similar in size to blood cells, around 2-3 μm in diameter [4]. A micro channel 250μm wide was created in PDMS elastomer to represent a blood vessel [5]. Milk was forced through the channel with a syringe. The light source used was white light from a tungsten lamp. The spectrum is unimportant to the flow measurement aspect of this system as long as it corresponds to the range of the detector. It is important that the detection volume be similar in size to the particles passing through it so that the optical fluctuations are significant. Towards this end these initial experiments were performed using a microscope mounted camera for the detection system. Each pixel in conjunction with the optical system of the microscope defines a square detection area approximately .5μm on a side. Using a camera had the additionally advantage of directly providing an image of the moving particles.

3. Near-infrared spectroscopy and blood clot measurements

Near infrared spectroscopy has proven its usefulness in studying brain processes such as hemodynamics and neuronal activity [6]. Recent experiments to be published shortly indicate that the near-infrared can also be used to detect blood clots. The absorption and scattering properties of blood in the liquid state is different from that of clotted blood. The optical cross correlation technique for measuring flow described above can be easily combined with this technique to measure blood clots to create an instrument that can do both simultaneously.

4. Results and Discussion

In theory, only two detectors are needed for cross correlation measurements. Our experiments indicate that the best results can be obtained by using a camera and treating each pixel as a separate detector. This is a simple way to have thousands of data points for comparison. There are many approaches that can be taken for processing the data from multiple pixels. The cross correlation between each pixel and every other pixel can be calculated. Pixels in one spatial region can be averaged and correlation with the average from another spatial region. Or the autocorrelation of each pixel can be calculated. We discovered that the most robust analysis technique for temporal autocorrelation was to take the cross correlation of all pixels at a fixed distance to each other and average the results. This method makes it more likely that fluctuations will be due to the same particle passing by each detector at different times. Figure 1 presents measurements taken on the model flow channel described above and analyzed in this manner. As the pixel spacing increases the time of peak correlation increases as well. The particle velocity of calculated from this data is approximately 21 pixels per second, or 10.5μm/s.

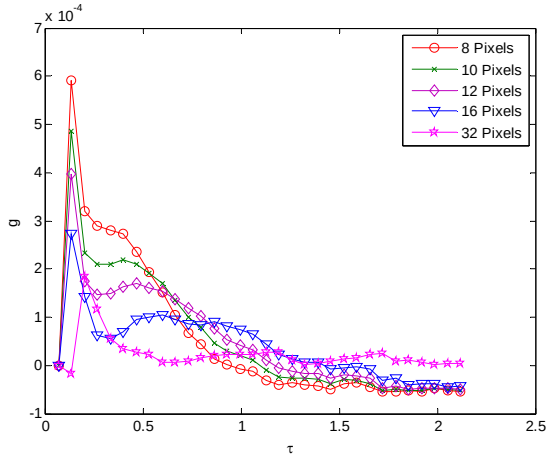

Fig 1. Cross correlation of optical fluctuations caused by milk particles flowing through a micro channel. Each curve represents the average cross correlation of all pixels at a fixed distance.

5. Conclusion

Optical correlation spectroscopy can be used to measure flow. This technique can be combed with near-infrared spectroscopy clot detection to create an instrument that will overcome some of the limitations of traditional techniques for measuring blood flow during neurosurgery. This instrument could be used repeatedly on blood vessels of all sizes and would detect the exact location of the clot, not only the rate of blood flow.

1. Acknowledgements

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6. References

1. Elson, E. L. and D. Madge (1974). "Fluorescence Correlation Spectroscopy: I. Conceptual Basis and Theory." Biopolymers **13**: 1-27.
2. Madge, D., W. W. Webb, et al. (1978). "Fluorescence Correlation Spectroscopy. III. Uniform Translation and Laminar Flow." Biopolymers **17**: 361-376.
3. Brinkmeier, M., K. Dorre, et al. (1999). "Two-Beam Cross-Correlation: A Method to Characterize Transport Phenomena in Micrometer-Sized Structures." Analytical Chemistry **71**: 609-616.
4. Woodcock, J. P. (1975). "Physical Properties of Blood and their Influence on Blood Flow Measurement." Reports on Progress in Physics 39: 65-127.
5. Jo, B.-H., L. M. Van Lerberghe, et al. (2000). "Three-Dimensional Micro-Channel Fabrication in Polydimethylsiloxane (PDMS) Elastomer." Journal of Microectromechanical Systems 9(1).
6. Gratton, E., V. Toronov, et al. (2005). "Measurement of brain activity by near-infrared light." Journal of Biomedical Optics **10**(1): 011008.