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Optical microprobe for blood clot detection

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Abstract: One of the mayor complications during vascular surgery is the formation of blood clot. We tested an animal model and assembled a prototype device that shows the blood clot signature spectrum and its temporary growth.
OCIS codes: (230.0230) Optical devices:(230.0040) Detectors.

Introduction:

Optical flow meters can detect blood flow, or its absence, during surgery using a laser Doppler detection scheme. Other approach is, for example, the use of ultrasound methodologies (flow changes the pitch of the sound wave traversing the vessels). The difficulty with the flow technology is that it identifies a vessel obstruction, most likely a blood clot, but it doesn't localize the position or the extent of the obstruction [5,7]. Consequently, the surgeon is required to painstakingly backtrack along the vessel to find a region where flow can be detected and then to surgically search in the intervening length of the vessel for the clot. This can be a time consuming procedure, which places the patient at additional risk. Furthermore, multiple cuts to the vessel are not conducive to vascular health.

Materials and Methods:

During these experiments we use a microvascular rat model. We obtained the proper Animal Committee Care protocol approval from our institution and no pain or discomfort was induced during the procedures.

We used 10 male rats (Rattus Norvergicus Wistard). They weighted 500gms and they were 6 months old. During the procedure the animals were anesthetized with Ketamine100mg/Kg, Xylazine 5mg/Kg and Acepromazine 1.0mg/Kg. Depth of anesthesia was tested by foot pinch every 15 minutes. Supplemental doses of Ketamine 30mg/Kg and Xylasaline1.75mg/kg were given if necessary. In order to have an adequate ventilatory and oxygenation pattern of the tissues, we performed a traqueostomy connecting the airway to a ventilator machine. The ventilator machine was settled by using visual degree of lung expansion. The average breath per minute was about 85, which was producing an average tide volume of 1.5ml. The minute volume was 100/ml/min (range 75-130ml/min). Because this technique is highly sensible to changes in hematocrit and the animal can bleed profusely due to the surgery, we include measurements of capillary hematocrit and hemoglobin concentration (Hematocrit point H2, Stanbio, Tx.) in order to evaluate the blood loss.

Flexible fibers optics (Ocean optics, FL) were used and held in place by a microsurgical force tip. One of the fiber optics was used to illuminate the vessel, and the other was used to collect the signal in transmission geometry. The signal was acquired by spectrometer and processed in computer software developed by the Laboratory of fluorescence and dynamics at Urbana Champaign.

Procedure:

We placed the animal in the surgical field. It was shaved and prepared with Betadine, a midline incision was madden from the sternum to the pelvis. We retracted the peritoneal organs to one side and isolate the abdominal vessels. Under a surgery microscope, the abdominal aortic artery and inferior vena cava vein were dissected using microsurgical technique. Once the artery was prepared, we placed our device in contact with the vessel. The purpose of this instrument is the isolation of the vessel in order to focus the light beam directly through the vessel without any light sources interferences.

After the placement of the probe, the inductions of the blood clot through a microsurgical clamping were performed following the subsequent protocol. Short and long clamping protocols were consecutively made in order to avoid the wash out effect due to the simultaneous proximal-distal unclamping. Our initial work was based in the *in-vitro* spectroscopical analysis of the blood clot. The blood of the animal was taken and deposited in a cuvette letting it clot. Once the blood was completely clotted inside the cuvette using a spectrometer we were capable of characterize and store the spectral components. We believe because the main component of the blood clot are trapped red blood cell unable of being re- oxygenated the blood clot spectrum was very similar the HHb spectrum.

During in-vivo baseline measurements over the vessels described, the relative amount of oxyhemoglobin (HBO2) and deoxyhemoglobin (HHb) were correlated with the specific vessel involved.

Results:

We have performed tests that show that the blood clot has a signature spectrum **(Fig. 1),** which allows for its identification *in vivo.* We have demonstrated that we can track the growth of the clot over time and that we can localize the spatial dimensions of the clot in the vessel (to a resolution of a few millimeters (Fig 2). We have excellent temporal resolution for data acquisition, ranging from 500 spectra/second to a total acquisition time of minutes to hours. We have tested the concept with an animal model (rat) and we have assembled a prototype device **(Fig. 3).**

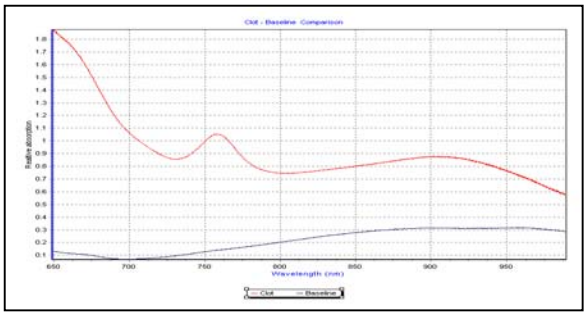

Fig.1 *Comparison between baseline blood (blue) and blood clot spectrum (red).*

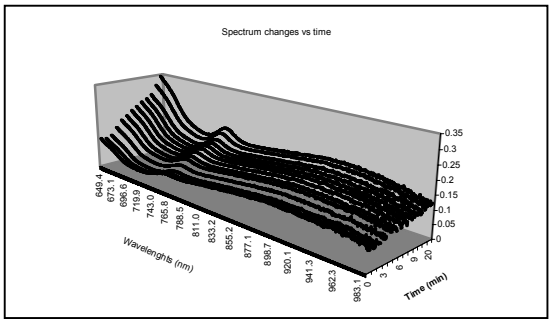

Fig.2 *Temporal spectroscopical changes from blood to clot*

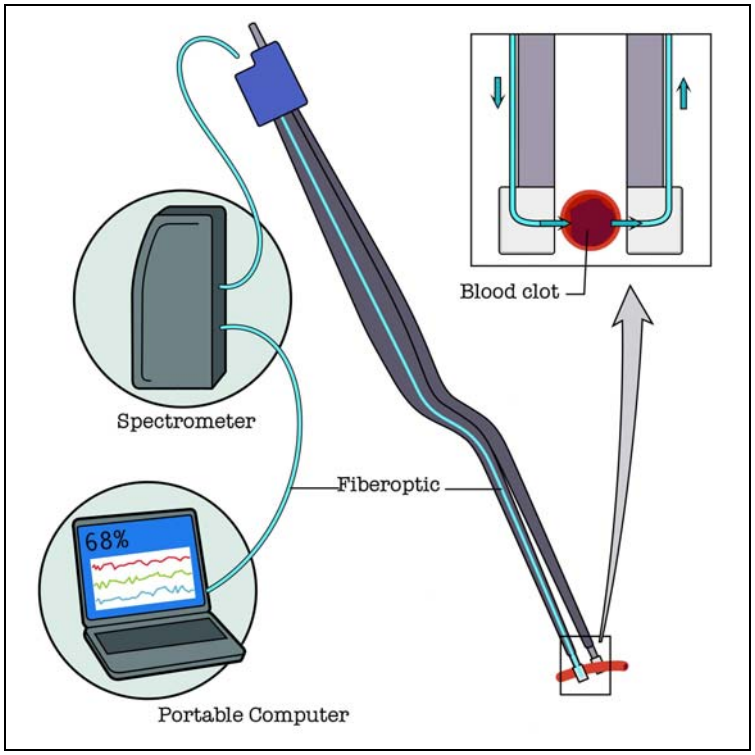

Fig. 3 *–Surgical optical probe tracking a blood clot inside an occluded vessel.*

The spectral acquisition hardware is quite robust, but the forceps like support with fiber optic attachments could benefit from some engineering design refinements. For use in surgery, feedback from surgical personnel vis-à-vis ergonomic issues will be important. We believe that our proof of principle experiments with the rat model are quite general, nonetheless, the procedure will require testing in human subjects at some point.

Discussion:

When blood clots form during neurosurgery, the brain tissue volume irrigated by that vessel becomes deprived of oxygenated blood (arterial blood is rich in oxy-hemoglobin). If this deficit persists over time, temporary or even permanent brain damage may result. In general, depriving tissue of oxygenated blood is detrimental in other forms of surgery. While flow measuring devices are useful to the neurosurgeon in establishing poor or non-existent blood flow in the surgical field [3], these

devices do not tell the surgeon the actual upstream location of the clot. Consequently, common practice involves sequential upstream surgical incisions into the vessel to locate and excise the clot. Our optical microprobe would rapidly and accurately identify the location and the extent of the blood clot in the vessel and would facilitate a timely intervention by the surgeon. A rapid response to a blood clot would minimize tissue damage and lessen the likelihood of serious complications such as stroke.
The optical microprobe is used to locate, identify and localize (the extent of) blood clots in the vasculature. Information about blood clots is particularly important for neurosurgery [6], but it is also useful in other surgeries. This optical method relies on the transmission of near infrared light in tissue. White light (all wavelengths-colors) is generated by a lamp or other suitable source and is delivered to the exposed vessel by a flexible fiber optic strand attached to a forceps like support. (The purpose of the support is to facilitate easy movement of the microprobe from position to position.) After this light passes through the vessel, a second fiber optic strand (also connected to the support) collects the transmitted light and delivers it to a spectrometer for spectral analysis (intensity vs. wavelength). Since tissue primarily transmits near infrared light the spectrum is generally examined in the region 600 to 1200nm [2]. The dominant and characteristic tissue components absorbing light in this spectral window include hemoglobin (oxy- and deoxy- forms), water, fat (lipids) [11,12] and a variety of minor miscellaneous compounds. We have developed software that facilitates determination of the fractional contributions of each component by spectral decomposition based on a weighting procedure. In addition to absorption, transmission of the light in tissue involves scattering in a wavelength dependent manner. The combination of the absorbed and scattered light yields the spectrum measured by the spectrometer. We have determined that the measured spectrum of tissue or blood flowing in a vessel differs from that of a blood clot . In short, the clot has a signature or characteristic spectrum. By tracing the microprobe along a vessel, and simultaneously measuring the spectrum, one can quickly identify if that region of the vessel contains a blood clot or not.
Our optical microprobe is based on a variety of methods, such as absorption spectroscopy, that have been used by scientists for decades [4,10]. Wavelength resolution of the spectrum by a spectrometer is also a well-established technology. However, realization that the blood clot spectrum differs from that of the surrounding medium and that this difference has utility in localizing the clot quickly and with good spatial resolution is our contribution. We have also developed algorithms and experimental methods for resolving the measured spectrum into its (additive) component parts. The other part of our work is the realization (and subsequent implementation) that the various known technologies, such as absorption spectroscopy or fiber optic light delivery and transmission, can be combined into a functional device suitable for resolving this surgical problem

Summary:

One of he mayor complication during vascular surgery is the formation of blood clot. We tested an animal model and assembled a prototype device that shows the blood clot signature spectrum and its temporary growth.

References:

[1]-Adams H, Adams R, and Del Zoppo G (2005). “Guidelines for the early management of patients with ischemic stroke: 2005 guidelines update”. A scientific statement from the Stroke Council of the American Heart Association/American Stroke Association. Stroke 36: 916-923.
[2]-Andre Roggan, Moritz Friebel, Klaus Dorschel (1999): “Optical properties of circulating human blood in the wavelength range 400-2500 nm”. Journal of biomedical Optics 4 (1): 36-46.
[3]-Andreas Raabe, MD, PhD: Jurgen Beck, MD (2003). “Near infrared Indocyanine green video angiography: A new method for Intraoperative Assessment of vascular flow”. Neurosurgery 52:132-139.
[4]-Annika M.K. Enejder, Johannes Swartling (2003): “Influence of cell shape and aggregate formation on the optical properties of flowing whole blood”. Applied optics 42(7): 1384-1393.
[5]-Charbel FT, Hoffman WE, Misra M, Ostergren L (1998): “Ultrasonic perivascular flow probe: technique and application in Neurosurgery”. Neurological Research 20: 439-442:
[6]-Charbel FT, MD: Guido Meglio, MD (2005).”Superficial temporal artery-to-middle cerebral artery Bypass”. Neurosurgery 56 (ONS Suppl. 1) 186-190.
[7]-Charbel FT, Hoffman WE, Misra M, Hannigan K, Ausman JI (1998).”Role of a perivascular ultrasonic micro flow probe in aneurysm surgery”. Neurologia Medico-Chirurgica 38: 35-38.
[8]-F. Neudel, S. Takatani (2004): “Effect of Hemolysis on oxygen and hematocrit measurements by near infrared reflectance spectroscopy”. Medical Engineering Physics 24: 301-307.
[9]-Frank A. Greco, MD, PhD (2004). “Reflectance Spectroscopy of Clotting Blood. A description of the Time-Dependent Behavior”. Arch Pathol. Lab Med.128: 173-180.
[10]-Jarold C. Finlay, Thomas Foster (2004): “Effect of pigment packaging on diffuse reflectance spectroscopy of samples containing red blood cells”. Optical Society of America 29(9): 965-967.
[11]-Werner Jaross, Volker Neumeister (1999): “Determination of Cholesterol in arteriosclerotic plaques using near infrared diffuse reflection spectroscopy”. Arteriosclerosis 147: 327-337.
[12]-Wiendelt Steenberg, Roy Kolkman (1999). “Light-scattering properties of undiluted human blood subjected to simple shear”. J. Opt Soc Am. 16(12): 2959-2967.