RESEARCH PROPOSAL – CONCEPTUAL PAPER

Title:

Transcutaneous Doppler (laser Doppler) monitoring device for microvascular circulation

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Objective:

To develop an effective, sensitive and reliable assessment device to monitor microvascular circulation for diagnostic, monitoring and research use

Methodology and Design:

Using Doppler or laser Doppler principles

Outcome / usefulness:

To allow effective assessment of microvascular blood flow

Principles of Laser Doppler Flowmetry

Laser Doppler flowmetry (LDF) is a method for determining blood flow through tissue capillaries, arterioles to assess the tissue perfusion. LDF works by directing laser beam from a probe containing optical fiber light guides (transmitter) to an area of tissue to be investigated. Laser light from one fiber is scattered within the tissue and some is scattered back to the probe. Another optical fiber (receiver) collects the backscattered light from the tissue and returns it to the monitor.

Laser Doppler detects shifts in the frequency of laser light (Doppler shift) after it interacts with moving components of tissue such as red blood cells (Bonner et al. 1981). The greater the net movement within tissue, the greater the broadening of the frequency of light detected and the greater the Doppler shift. The laser Doppler measures the frequency shift of light rather than the sound waves used in standard ultrasound Doppler. The photodetector converts the broadened light frequencies into an electrical signal that is processed to provide an estimation of blood flow, termed *flux*. Flux is proportional to the average speed and number of red blood cells in the area of light penetration. For most tissues the mean sampling depth is in the region of 0.5-1.0 mm with a typical sampling volume in the region of 0.3-0.5 mm^3.

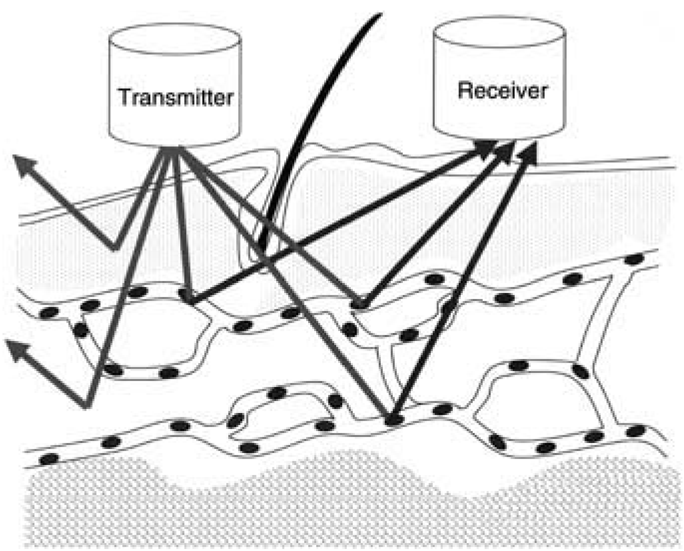


Figure: Basic operating principles of laser Doppler flowmetry. A laser beam is directed to an area of tissue. Upon contact with red blood cells in the target tissue, light waves are reflected and scattered, resulting in broadening of the light wave frequency, which is detected and received by a photodector.

The light returned to the monitor undergoes signal processing whereby the emitted and returned signals are compared to extract the Doppler shift related to moving red blood cells. Microvascular blood perfusion is electronically calculated as the product of mean red blood cell velocity and mean red blood cell concentration. It is not possible to determine absolute measurements of blood flow because the changes in wavelength that occur are unrelated to their direction of movement of red blood cells.

The LDF technique offers substantial advantages over other methods in the measurement of microvascular blood perfusion. Studies have shown that it is both highly sensitive and responsive to local blood perfusion and is also versatile and easy to use for continuous real-time monitoring. The method is potentially non-invasive and does not disturb the normal physiological state of the microcirculation. Furthermore, the small dimensions of the probes have enabled it to be employed in experimental and clinical environments not readily accessible using other techniques.

The two types of laser Doppler instruments used to measure blood flow are single point fiber optic monitors and laser Doppler images. The single point fiber optic monitor is the instrumentation most frequently used to measure flux. Laser light is transmitted via a fiber optic probe placed in direct contact with the tissue under investigation. Several fiber optic probes are commercially available. Noninvasive continuous measurements of flux are made with skin surface probes. Needle probes are designed to penetrate tissues and therefore are more invasive than surface probes. They can be used intraoperatively to measure flow within tissues such as the brain or liver. Endoscopic probes are less invasive than needle probes and measure flow to mucosal surfaces.

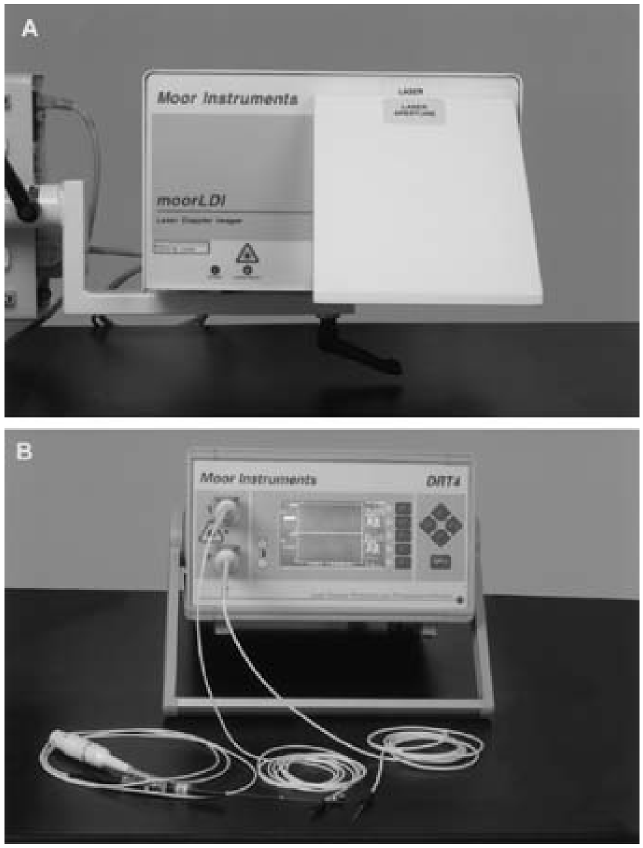


Figure: Laser Doppler instrumentation. (A) Scanning laser Doppler imager (LDI) (B) single point fiber optic monitor with fiber optic probes (LDF)

Figure: Laser Doppler flowmetry machine

The laser Doppler imager is a noninvasive system that measures flux within tissues by scanning tissues measuring 25 to 2500 cm^2 via a low-power collimated laser beam directed in a rectilinear pattern, displaying results in a two-dimensional color-coded image of flux. Low flux level is expressed in blue, with green, yellow, and red indicating increasingly higher level regions of flux. Gray areas represent regions where no flux can be detected.

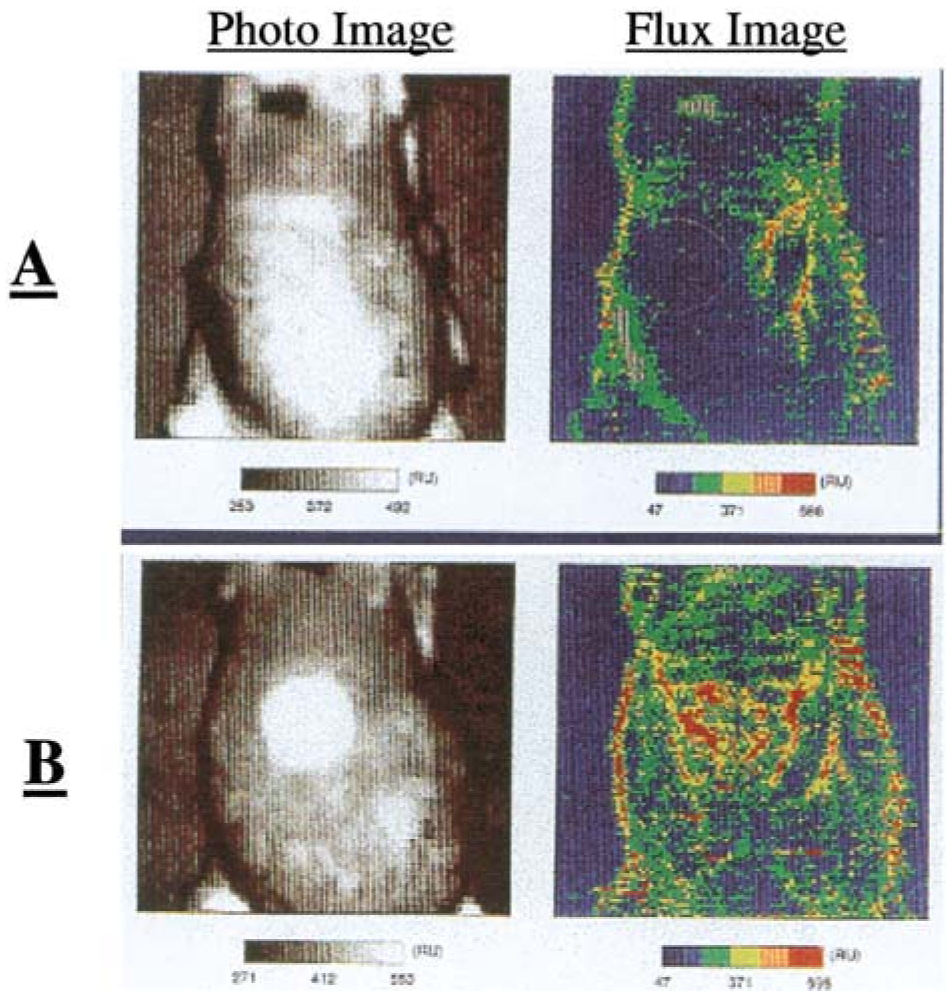


Figure: Laser Doppler images of a dorsal air sac mouse model of angiogenesis

Applications of LDF

This technique is commonly used to monitor the effect of environmental conditions, physical manipulations, and drug treatments on tissue perfusion. It has been used extensively in biomedical research and clinical settings. LDF has been used for ocular, cerebral, cutaneous, auricular, splanchnic, and renal blood flow in a wide range of laboratory animal species. The clinical research and applications include tumour research, cerebral monitoring, flap transfer surgery, transplantation surgery and vital organ monitoring, pharmacology, as well as peripheral vascular disease research.

1. Post-operative monitoring of free tissue transfer

Monitoring circulation of flaps post-operatively is critical to success in microvascular transplantation. Disruption of perfusion to a flap can result in partial or complete flap loss. To be effective, changes in perfusion need to be recognized quickly to correct any treatable problems. Monitoring and quick recognition of ischemia reduces the chance of a no-reflow phenomenon and flap failure.

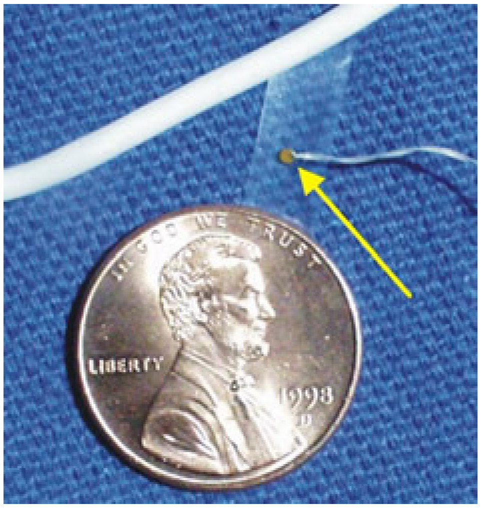
The gold standard for assessing viability of transferred tissue is clinical examination. Identification of a failing or insufficiently perfused flap can occasionally be challenging even for the experienced microsurgeon.

More sophisticated devices to monitor flap are required. The ideal monitor is reliable, accurate, simple to operative, continuous and inexpensive. Several different monitoring devices are in use.

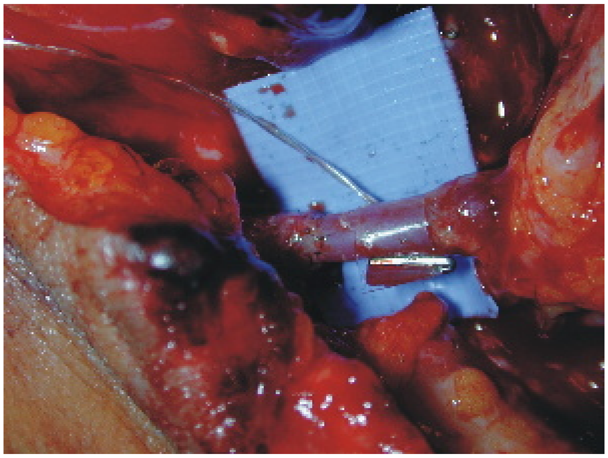
a) Doppler Ultrasonography

Doppler ultrasound converts sound waves reflected by a moving column of blood into an audible signal or wave form. The probe can be placed directly on the vessel or used on the skin surface. When used on the skin surface, the probe may detect a vessel in the vicinity of the vessel in question, resulting in false-positive readings. Venous flow problems may go undetected for several hours because of the persistence of arterial pulsations in the flap pedicle.

For flaps with no perforator signal that is easily accessible (such as a buried flap), an implantable Doppler ultrasonic probe can be used. This consists of a small probe attached to a polymer sleeve that is placed around a pedicle vein and/or artery adjacent to the anastomosis, with a thin probe lead wire exiting through the incision. The lead wire easily detaches from the probe and is removed through the incision with gentle traction on the wire. Doppler signals have a characteristic pattern that can, with experience, be identified as arterial (pulsatile) or venous (undulating). A change in the character of the signals from strong to diminished or undetectable may indicate vascular occlusion. Doppler monitoring is, however, subject to error, both false-positive and false-negative readings, and thus should always be used in conjunction with clinical assessments.



THE IMPLANTABLE DOPPLER PROBE CRYSTAL (ARROW)



The Doppler is Secured Around a Draining Vein with the Cuff and Ligaclips

b) Laser Doppler Flowmetry

The laser Doppler apparatus consists of a probe that is surface-mounted to the cutaneous portion of a free flap. The probe is connected to a portable monitor displaying continuous variations in flow. The reflected light has very limited penetration and surface measurements only capture the movement of red blood cells in the cutaneous microcirculation. It is unable to differentiate between venous and arterial flow. Significant perfusion abnormalities leading to flap compromise can go undetected using this system. However, it is probably the most accurate of the commonly used systems for monitoring. The accuracy of this method may be improved if the Doppler flowmeter is linked to a computerized data acquisition system that can process and detect more subtle signal abnormalities.

c) Temperature Probe

The temperature probe is placed on the skin to provide continuous measurement of skin temperature. Due to the poor correlation of blood flow to surface temperature, this method is unreliable.

d) Pulse Oximetry

Pulse oximetry is commonly used for continuously monitoring digital pulse and oxygen saturation by measuring the difference between wavelengths of light absorbed by reduced and oxygenated hemoglobin. It has been used successfully for digit replants by monitoring differences between the replanted digit and a normal digit.

e) Fluorescein Dye

Fluorescein dye is administered systemically and is detectable in non-pigmented skin in 20 minutes by Wood's lamp. The fluorescein is deposited in the extracellular space and is cleared slowly, requiring several hours between observations. It may be useful for determining the initial viability of flaps, including pedicled flaps. More frequent observations are possible using a quantitative fluorometer probe that allows detection of smaller amounts of dye.

f) Thermocouple Probe

The thermocouple probe is based on the physical finding that when two different metals are in contact, a change in temperature causes proportional changes in the rate of electron transport. Placement of probes distal and proximal to an anastomosis allows differential temperature measurements. Clot or static blood cool is cooler and causes a difference in the readings of the probes, indicating a perfusion problem. This technique is invasive and is prone to errors in probe placement as well as to iatrogenic vascular trauma.

2. Allergy study

The nasal muscosa and skin are two sites particularly exposed to allergic reaction. The situation for assessing the nasal mucosa is more complex: choice of site and type of probe are important considerations. The preferred site is the anterior tip of the inferior turbinate mucosa. Endoscopic probes are particularly appropriate because of the rounded tip although needle probes may be considered.

3. Cerebral Blood Flow

Laser Doppler assessment of cerebral blood flow is used in conjunction with other techniques for multi modal monitoring of head injured patients. Failure of autoregulation at intercranial pressures (ICP) of less than 58mmHg were noted by Kirkpatrick et al (1994) and CO_2 evoked responses have been described by Bolognese et al (1995). These assessments have been made using invasive procedures but non-invasive blood flow assessments have also been performed using skin probes on the forehead and the gross changes at brain death recorded (Litscher et al, 1995).

4. Gastroenterology

Endoscopic probes can be used in conjunction with gastroscopes or NG tubes to assess flow of the gastric mucosa and disorders. This can be used as a predictor of non-healing of benign gastric ulcers (Clarke et al, 2002) or to measure the effect of treatment intervention on mucosal flow.

5. Pharmacology

The effects of topical or systemic vasoactive drugs on human tissue blood flow can be assessed by laser Doppler allowing dose response measurements to be made.

6. Tooth Vitality Testing

Cardiac cycle blood flow pulsation in the supplying artery is transmitted to the pulp capillaries as pulsations in blood velocity. These pulsations are apparent on laser Doppler monitor traces of vital teeth and are absent from non-vital teeth. The mean blood flux level in healthy teeth is much higher than for non-vital teeth. However in vital teeth with impaired blood supply the flux level can be low and the presence of pulsation is the only indication of vitality.