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Near-infrared spectroscopy for monitoring peripheral tissue perfusion in critically ill patients

Espectroscopia no infravermelho próximo para a monitorização da perfusão tecidual

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ABSTRACT

Near infrared spectroscopy (NIRS) is a non-invasive technique that allows determination of tissue oxygenation based on spectrophotometric quantitation of oxy- and deoxyhemoglobin within a tissue. This technique has gained acceptance as a tool to monitor peripheral tissue perfusion in critically ill patient. NIRS principle is based on the use of near-infrared electromagnetic waves for qualitative and quantitative assessments of molecular factors related to tissue oxygenation. Although this technique can be apllied in any tissue, it is primarily used for monitoring peripheral oxygenation in the muscle. Parameters that are determined using NIRS can be either directly calculated or can be derived from physiological interventions, such as arterial and venous occlusions methods. Information regarding muscle oxygen saturation, muscle oxygen consumption and regional blood flow can therefore be obtained. Clinical applications of NIRS include peripheral oxygenation monitoring during resuscitation of trauma and septic shock as well as the assessment of regional microcirculatory disorders. This review provides a brief discussion of NIRS basic principles and main clinical uses of this technique, with a specific focus on studies that assess the usefulness of NIRS in intensive care and emergency patients.

Keywords: Spectroscopy, near-infrared; Monitoring, physiologic/methods

INTRODUCTION

Near-infrared radiation consists of light with wavelengths near of the visible portion of electromagnetic spectrum. This concept is simple to understand when one bears in mind that light is an electromagnetic wave that propagates as energy. The use of electromagnetic waves is very common in daily life, e.g., in radios, TVs and microwave ovens. These waves are also frequently used in medical procedures, e.g., in X ray- and magnetic resonance imaging-based diagnoses. Electromagnetic waves are identified by their frequency and wavelength, which is often given in nanometers (nm) (Table 1). The electromagnetic spectrum between 390 and 900 nm encompasses the visible portion of the spectrum. In addition to visible light, this spectrum also includes both infrared and ultraviolet light. The infrared (IR) region extends from $3x10^{11}$ Hz to approximately $4x10^{14}$ Hz and is divided into three spectral regions: Near-IR (i.e., near to the visible light: 780 – 2,500 nm); Mid-IR (2,500 – 50,000 nm) and

Conflicts of interest: None.

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Table 1 – Electromagnetic spectrum

		Frequency (Hz)			Wavelength		
Radio waves		Less than		$3x10^{11}$	Above		0.3 m
Microwave		10^9 Hz	to	$3x10^{11}$	0.3 m	to	1 mm
Infrared		$3x10^{11}$ Hz	to	$3.8x10^{14}$	1 mm	to	789 nm
Visible	Red	$3.8x10^{14}$ Hz	to	$4.8x10^{14}$	789 nm	to	625 nm
	Orange	$4.8x10^{14}$ Hz	to	$5x10^{14}$	625 nm	to	600 nm
	Yellow	$5x10^{14}$ Hz	to	$5.2x10^{14}$	600 nm	to	577 nm
	Green	$5.2x10^{14}$ Hz	to	$6.1x10^{14}$	577 nm	to	491 nm
	Blue	$6.1x10^{14}$ Hz	to	$6.59x10^{14}$	491 nm	to	455 nm
	Violet	$6.59x10^{14}$ Hz	to	$8x10^{14}$	455 nm	to	390 nm
Ultraviolet		$8x10^{14}$ Hz	to	$2.4x10^{16}$	390 nm	to	8.82 nm
X ray		$2.4x10^{16}$ Hz	to	$5x10^{19}$	8.82 nm	to	6 pm
Gamma ray		Above		$5x10^{19}$	Less than		6 pm

Far-IR (50,000 nm – 1 mm).

Near-IR was first described in 1800 by William Herschel.[1] However, it was not until 1968 that the agricultural engineer Karl Norris described the near-infrared spectrum using spectroscopy.[2] In 1977, the American Frans F. Jobsis demonstrated the usefulness of near-infrared spectroscopy (NIRS) for the non-invasive monitoring of tissue oxygenation and he is also considered the frontrunner of research into the use of near-IR spectroscopy to assess cell oxygenation and metabolism.[3] Following the study of Jobsis in the late 1970s several other clinical trials were published on the subject of monitoring tissue oxygenation using NIRS, both in patients and in healthy subjects.[4-6]

NIRS uses specific and calibrated wavelengths of near-IR light to noninvasively illuminate the tissue below a sensor placed on the skin. A detailed description of the physical bases of NIRS can be found in articles that focus specifically on this subject.[7,8] This review will focus on the physics of NIRS and on its clinical uses, especially in intensive care medicine.

Technical considerations

NIRS analysis is based on the use of different near-IR wavelengths. The different absorption and dispersion characteristics of light of various wavelengths can be used to both quantitatively and qualitatively evaluate biological tissue contents. When light reaches a biological tissue, its subsequent path depends on reflection, dispersion and absorption. Whereas reflection is dependent only on the angle of incidence of the light, dispersion and absorption depend on the light's wavelength. Light with longer wavelengths are less dispersed into the tissues, thus favoring IR transmission, as it has longer wavelength within light spectrum. Absorption, however, is determined by the molecular properties of the tissue. For example, light with a wavelength above 1,300 nm is fully absorbed by water in the superficial skin layers. Light in the visible portion of the spectrum (below ~700 nm) is completely absorbed by hemoglobin (Hb) and myoglobin. Moreover, visible light is highly dispersed, limiting its penetration into tissues. Near-IR (between 700 and 1,300 nm) has superior tissue penetration ability; it can pass through the skin into subcutaneous tissue, the underlying muscles or any other tissue. As light enters the body, it is absorbed by tissue components (chromophores), reducing the intensity of light. The relationship between the chromophore concentration and light absorption is described by the Beer-Lambert equation:

$$A = \log \frac{(I_0)}{(I)} = \varepsilon.c.d$$

In this equation, A is the measured absorbance, I_0 is the light intensity at a given wavelength, I is the sample-transmitted intensity, d is the optical path through the sample, ε is the extinction coefficient (also known as molar absorptivity) and c is the substance concentration. The Beer-Lambert law states that when light of a known wavelength passes through a solution of an unknown concentration,

this concentration may be determined based on the extinction coefficient and the distance that the light travels through the sample. Therefore, the extinction coefficient (which varies according to the substance) can be used to establish the optical absorbance characteristics of a given substance at a given wavelength. This formula is applicable only for solutions; in tissues, however, light does not follow a straight path but is absorbed or reflected by tissue components. Therefore, the emitted light is not directly transmitted to the receptor, which is generally parallel to the emitter. The light path through the tissue (known as the 'optical pathlength', or PF) acquires a curved shape (the 'banana shape'), and the distance covered is longer than the emitter-receptor distance. A modification of the Beer-Lambert law was made to account for this difference:[9]

$$A = \Sigma\varepsilon.c.d.DPF$$

Here, *d* is the distance between the light emitter and the receptor, and DPF is the PF differential. Knowledge of the DPF is essential for quantitative NIRS measurements and is one of the primary components of the algorithm used in a given NIRS device. Near-IR penetration is primarily dependent on *d*. The majority of sensors have *d* value between 2.5 and 3 cm, providing a tissue penetration ability of between 2.0 and 2.5 cm (Figure 1). Therefore, near-IR light crosses the skin, subcutaneous tissue, muscle and bone; brain and muscle tissues are therefore the easiest tissues to assess using NIRS.

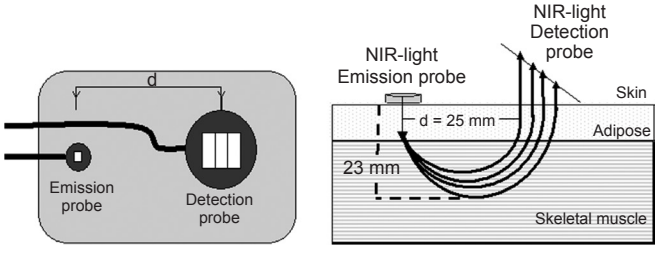

Figure 1- Diagram of a distal tip of the NIRS optical cable (A). With 25 mm spacing (d) between emission and detection probes, approximately 95% of the detected optical signal is from 23 mm of tissue penetration (B). Note the curved shape of the light path (banana shape).

Methodological considerations

The difficulty to quantify the NIRS signal led to the development of different measurement methods. Currently, near-IR spectrophotometers have variable degrees of sophistication, applicability, algorithms and wavelengths. It is generally accepted that at least four near-IR wavelengths are required to differentiate the absorption spectra of different tissue chromophores. Continuous wave (cw) spectrophotometers are commonly used commercial devices; these apparatuses, however, do not provide quantitative measures of absolute chromophores concentrations but rather determine changes in concentrations from a baseline value, reflecting, therefore, changes in tissue oxygenation. This methodological limitation is based on the need to obtain accurate PF values for each wavelength and estimations of tissue light dispersion. As new technologies were developed, more sophisticated devices were designed to provide quantitative data. Phase modulation and spatially resolved spectroscopy employ different algorithms to obtain tissue absorption coefficients and consequently are able to calculate absolute concentrations of tissue chromophores. These devices also use multichannel NIRS technology, i.e., several detectors at different distances within a same sensor, providing measurement of a larger portion of tissue. Although these spectrophotometers can quantify tissue chromophore concentrations, few studies have compared the different measurement methods currently in use. As these spectrophotometers use different algorithms, their quantifications will also differ, rendering their clinical application difficult.[10]

With the aim of designing devices for bedside use, some manufacturers have developed more easily operated spectrophotometers using simpler algorithms, which in turn are not able to provide absolute tissue chromophore concentrations. However, their ability to be used continuously at the bedside and relatively consistent tissue oxygenation readings make these devices advantageous.

At a fundamental level, NIRS spectrophotometers comprise a light detection microprocessor and a monitor (Figure 2). The device is connected to an optical fiber cable that has a light source connected to an optical sensor. The distance between the light emitter and the light receptor of the optical sensor varies from 12 to 25 mm. An optical converter is used to export the collected signals to the monitor, where the data are graphically displayed.

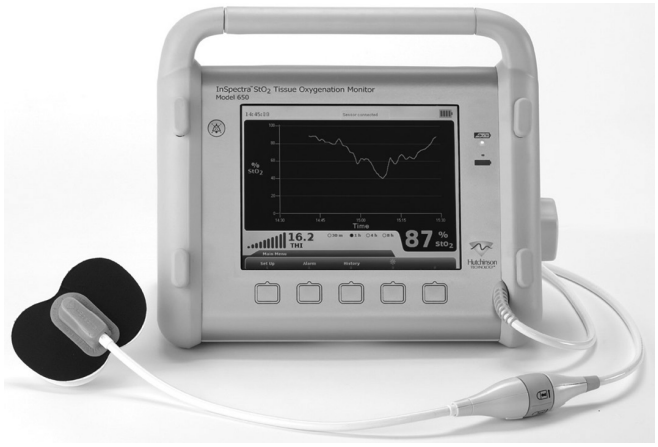

Figure 2 – An example of a near-infrared spectrophotometer (Inspectra, Hutchinson Technology Incorporated).

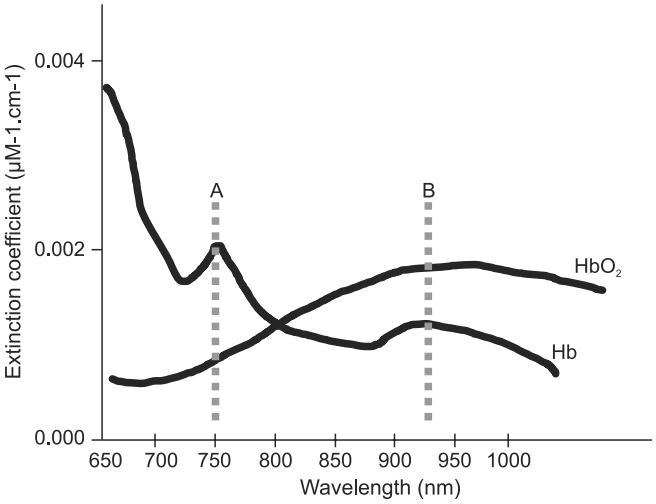

Figure 3 – Near-infrared spectrophotometer absorption spectra for oxyhemoglobin (HbO_2) and deoxyhemoglobin (Hb). Dotted lines correspond to peak Hb (line A) and HbO_2 (line B) absorptions.

Parameters measured with NIRS

Tissue oxygenation-related molecules that absorb near-IR are primarily hemoglobin, myoglobin and mitochondrial cytochrome oxidase ($citaa_3$). The absorption peaks of these three components in the near-IR region differ; deoxyhemoglobin (Hb) and oxyhemoglobin (HbO_2) have absorption peaks at 760 nm and 920 nm, respectively (Figure 3).

Although both Hb and HbO_2 are more strongly absorbed in the visible light spectral (~500 to 600 nm), this wavelength of light cannot penetrate the tissue as deeply. $Citaa_3$ is the final electron transportation chain receptor in the internal mitochondrial membrane and is the endpoint for cellular aerobic metabolism. The absorption peak for $citaa_3$ in the near-IR spectrum is between 800 and 865 nm. During hypoxemia, $citaa_3$ is in the reduced state, altering its absorbance properties in the IR spectrum.

NIRS-measured parameters may be calculated either direct or indirectly (Table 2). Directly calculated measurements depend on the device used. For example, phase modulation and spatially resolved spectroscopy provide absolute HbO_2 and Hb concentrations. Most NIRS devices provide information regarding changes in concentration from a baseline value at an arbitrary unit and tissue oxygen saturation, which is the clinically most relevant direct parameter. Measures calculated indirectly are obtained using physiological interventions to alter circulation at the assessed area; this is most frequently performed using arterial and venous occlusion.[4,11] This technique provides quantitative information regarding blood flow and local oxygen consumption.

Table 2 – Directly near-infrared spectrophotometer measured parameters

Parameter	Unit	Modality	Physiological intervention to obtain the parameter
Peripheral tissue O_2 saturation (StO_2)	%	D	None
Δ HbO_2 and Δ Hb	A.U., μM	D (with PMS, SRS) or I	AO, VO
$Citaa_3$	μM	D	None
Peripheral O_2 consumption	$mlO_2.min^{-1}.100\ g^{-1}$	I	AO, VO
Peripheral blood flow	$mlO_2.min^{-1}.100\ g^{-1}$	I	VO
Deoxygenation velocity	%/min	D	AO
Reoxygenation velocity	%/min	D	AO

O_2 - oxygen; HbO_2 - oxyhemoglobin; Hb - deoxyhemoglobin; Δ – difference in value prior to and following physiological intervention; A.U. – arbitrary unit; D - direct; I - indirect; AO – arterial occlusion; VO – venous occlusion; PMS - phase modulate spectroscopy; SRS - spatially resolved spectroscopy; s - seconds.

Tissue muscle oxygen saturation (StO_2)

Based on the Hb and HbO_2 concentration ratio, NIRS provides data to calculate StO_2, which is also expressed as tissue oxygenation index. This information can be derived from the equation [HbO_2/(HbO_2 + Hb)] x 100, which is defined as the functional saturation percentage. StO_2 is a measure of blood oxygen saturation in the tissue area assessed by the spectrophotometer. Based on the tissue's blood distribution, the contribution of arteriolar, capillary and venous compartment to the NIRS signal are estimated to be 10%:20%:70%, respectively. Thus, resting StO_2 values measured by NIRS reflect mainly the venous compartment. However, studies have failed to show a correlation between NIRS-determined StO_2 and actual venous blood saturation.[12-14] These studies support the theory that in conditions where oxygen demand is increased, e.g., during exercise or in arteriovascular disease, the proportion of blood in the different vascular compartments is changed due to capillary recruitment. Although venous, arterial and capillary blood contributions cannot be practically determined, StO_2 has been shown to be an excellent parameter for determining the balance between oxygen supply and oxygen demand.[15]

Muscle oxygen consumption and regional blood flow

Using the venous and arterial occlusion methods, NIRS can be applied to measure oxygen consumption (mVO_2) and regional blood flow (BF) by following the rate of HbO2 and Hb changes. In the venous occlusion method, a conventional pneumatic cuff is inflated to a pressure of approximately 50 mmHg. Such a pressure blocks venous occlusion, but does not impede arterial inflow. As a result, venous blood volume and pressure increase. NIRS can reflect this change by an increase in HbO_2, Hb and total hemoglobin.[16] In arterial occlusion method, the pneumatic cuff is inflated to a pressure of approximately 30 mmHg greater than systolic pressure. Such a pressure blocks both venous outflow and arterial inflow. Depletion of local available O_2 is monitored by NIRS as a decrease in HbO_2 and a simultaneous increase in Hb, whereas total Hb remains constant. For venous occlusion, mVO_2 is calculated using the rate of Hb increase. As venous blood flow is blocked, the increase of Hb levels is primarily due to conversion of HbO_2 to Hb, therefore reflecting mVO_2. The calculation of mVO_2 using arterial occlusion is based on the same principle as venous occlusion. The difference is that blocking both arterial and venous blood flow results in a static blood compartment where HbO_2 levels drop as a direct result of mVO_2, which displaces oxygen from hemoglobin (Figure 4). Absolute HbO_2 and Hb concentration changes (ΔHbO_2 and ΔHb) are expressed in units of $\mu M.s^{-1}$. Considering the molecular relationships between hemoglobin with oxygen (i.e., 1:4) and the molecular weight of hemoglobin, mVO_2 can be indirectly obtained and converted into units of $mlO_2.min^{-1}.100\ g^{-1}$.

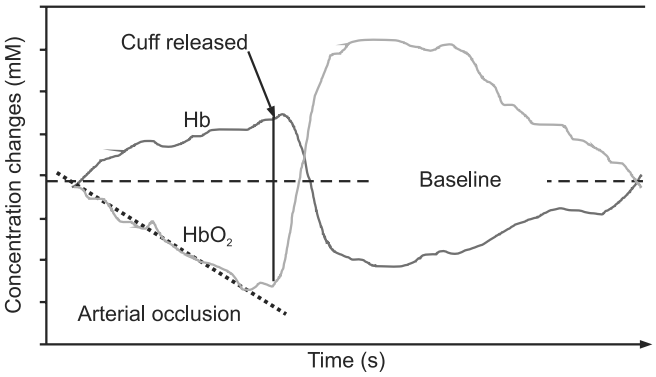

Figure 4 – Quantitative NIRS measurements during arterial occlusion. After release of the occluding cuff, blood volume increases rapidly, resulting in an increase in HbO_2 and a quick washout of Hb, followed by a hyperaemic response. Oxygen consumption is calculated as the rate of decrease of HbO_2 indicated by the dotted line.

Blood flow (BF) measurements using NIRS are calculated using venous occlusion method, which results in a volume increase of the distal part of examined limb due to continuous arterial blood flow combined with blocked venous outflow. BF is calculated as a linear function of total hemoglobin (HbO_2 + Hb) during occlusion. Absolute concentrations variations of HbO_2 and Hb (Δ HbO_2 and Δ Hb) are expressed as $\mu M.s^{-1}$. Using laboratory-assessed blood hemoglobin levels, BF is calculated and converted into units of $ml.min^{-1}.100\ ml^{-1}$. These calculations can only be obtained from NIRS devices that provide quantitative HbO_2 and Hb data.

Rate of StO2 deoxygenation

An alternative method exists for estimating mVO_2 using devices that do not return absolute concentrations, which is determining the rate of StO_2 decrease during an ischemic period, normally calculated during a 3-minute arterial occlusion and expressed as StO_2 variation in %/minute (Figure 5). This parameter was

only recently introduced in the intensive care setting and has not been properly evaluated. The drop in StO_2 during arterial occlusion is believed to reflect the local oxygen extraction rate at the NIRS-assessed area; this analysis may provide an important estimate of the balance between oxygen supply and oxygen demand.[5]

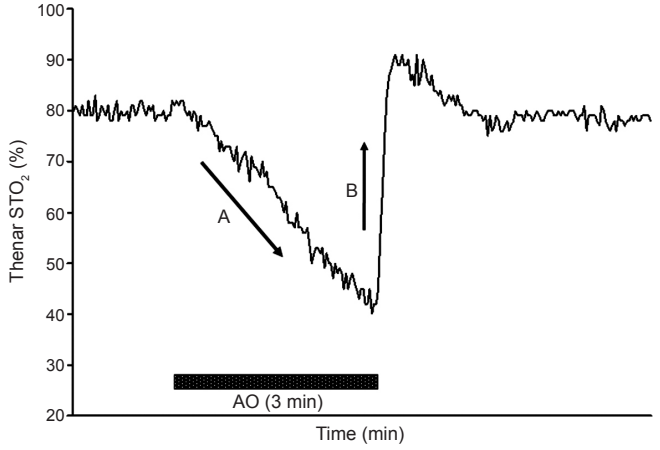

Figure 5 – Tissue muscle oxygen saturation (StO_2) during 3 minutes of arterial occlusion (AO). (A) Rate of StO2 deoxygenation: the velocity at which StO_2 decreases during AO, expressed as %/min. Rapid deoxygenation rate corresponds to higher oxygen extraction rates. (B) Rate of StO2 reoxygenation: the velocity at which StO_2 increases from cuff release to the maximal reoxygenation during reactive hyperemia. Reflect mainly microcirculatory vascular reactivity.

Rate of StO2 reoxygenation

The rate of StO2 reoxygenation is calculated as the velocity of StO_2 increase between the end of arterial occlusion (starting after the pneumatic cuff is emptied) and the degree of maximal reoxygenation during reactive hyperemia. After release of the occluding cuff, a hyperaemic response is observed (Figure 5). Blood volume increases rapidly, resulting in an increase in HbO_2 and a quick washout of Hb. This overshoot of StO2 represents the balance between arterial blood inflow and mVO_2 and depends mainly on microcirculation function. Delayed reoxygenation velocity implies microcirculatory changes, e.g., those that occur with severe sepsis. Similar to deoxygenation velocity, reoxygenation velocity has not been evaluated properly in the setting of intensive care.

Mitochondrial cytochrome oxidase ($citaa_3$)

$Citaa_3$ remains reduced during oxygen deprivation, resulting in a loss of its near-IR absorbance. NIRS is able to detect this change during intracellular dysoxia conditions; however, monitoring this parameter is still technically complicated because tissue $citaa_3$ concentrations are low compared to hemoglobin and because these changes are not synchronized with the ischemic insult. Simultaneous $citaa_3$ and StO_2 measurements allow for the detection of cellular dysoxia secondary to mitochondrial dysfunction. In normal conditions, changes in StO_2 and $citaa_3$ are coupled, i.e., when StO_2 decreases, $citaa_3$ is in the reduced, and when StO_2 levels increase, $citaa_3$ is less reduced. When StO_2 and $citaa_3$ changes are disparate (e.g., more reduced $citaa_3$ with normal or high StO_2 levels), one may anticipate that a change in the mitochondrial electron transport chain is occurring during cell oxygenation, suggesting mitochondrial dysfunction.

Clinical uses of NIRS

NIRS is currently useful in a number of clinical conditions and, although it can be applied in any organ, it has been primarily used for assessment of brain and muscle tissue oxygenation. Cerebral NIRS monitoring is used in surgical procedures with high brain ischemia risks, such as carotid endarterectomy, brain aneurism surgeries, brain perfusion monitoring during extracorporeal circulation and head trauma. For intensive care setting and in emergency departments, the use of NIRS to assess tissue oxygenation has been focused on peripheral muscle oxygenation.[17] Monitoring muscle oxygenation is used for the following reasons: (a) peripheral muscle tissue is easily accessible compared to brain tissues; (b) during shock, brain oxygenation is maintained at expense of blood flow redistribution from peripheral tissues to vital organs; and (c) vascular control mechanism in the muscle tissue is more sensitive to systemic perfusion alterations due to its predominant sympathetic control. Therefore, the physiological bases for the use of NIRS in critically ill patients is based on the fact that monitoring peripheral perfusion can be used as early marker of tissue hypoperfusion.[18]

Trauma

Experimental models of animal hemorrhagic shock have shown that NIRS-determined StO_2 can be used as a resuscitation parameter.[19-22] In these studies, a pre-defined 50% StO_2 value in peripheral muscle was showed to reflect appropriate systemic oxygen supply. Moreover, muscle StO_2 values were shown to be low even with normal systemic resuscitation parameters, corroborating the idea that normalizing conventional hemodynamic parameters

does not restore oxygenation to all tissue vessels.

Studies investigating the usefulness of NIRS for peripheral monitoring in trauma patients have been focused mainly on shock resuscitation. The primary differences among these trials were related to the party of the body at which StO_2 was assessed, which were the deltoid area and the thenar eminence.

Three studies that measured the deltoid muscle with NIRS should be emphasized. Cairns et al.[23] investigated the ability of NIRS to detect mitochondrial dysfunction in shock patients and to determine the risk of multiple organ failure. Both StO_2 and $citaa_3$ were monitored from the deltoid and the relative differences in these measurements were determined. Out 9 patients developing multiple organ failure, 8 exhibited disparate StO_2 and $citaa_3$ values. In contrast, this disagreement between StO_2 and $citaa_3$ measurements was observed in only 2 of the 16 patients who did not develop organ failure. Mckinley et al.[24] compared peripheral muscle StO_2 with other resuscitation parameters, including system oxygen delivery, arterial lactate and central venous oxygen saturation during the resuscitation of 8 trauma patients admitted to the intensive care unit (ICU). StO_2 measurements were obtained from the deltoid using NIRS during resuscitation and 12 hours following patient stabilization. In this trial, a significant StO_2 increase was observed during the 36 hours of resuscitation, and a good correlation between StO_2 and tissue perfusion parameters was also observed; the results were statistically significant for systemic oxygen delivery, base deficit and blood lactate concentration. More recently, Ikossi et al.[25] assessed deltoid StO_2 in 28 trauma patients admitted to the ICU and reported a mean 63% ± 27% StO_2 as a reference for successful resuscitation. Patients whose values were below this level exhibited an increased risk for infection or multiple organ failure.

Three other studies stand out, which evaluated StO_2 from the thenar eminence. Crookes et al.[26] investigated the ability of NIRS to determine shock severity in trauma patients. In this study, StO_2 assessed on thenar eminence was compared between healthy subjects and patients. No StO_2 differences were shown between healthy subjects (87% ± 6%) and non-shock patients (83% ± 10%). StO_2 assessed in patients was able to discriminate the degrees of shock severity (80% ± 12% for moderate shock and 45% ± 26% for severe shock). Another trial by Cohn et al.[27] showed that StO_2 as measured using NIRS on thenar eminence had a similar prognostic power as base deficit in predicting multiple organ dysfunction in a large group of patients with shock secondary to trauma. In this trial, StO_2 values below 75% were related to a worse outcome, defined as organ dysfunction and death. Moreover, recently Gomez et al.[15] measured StO_2 on thenar eminence in trauma patients with hemodynamic instability admitted to the ICU. In this study, similar to that of Crookes,[26] StO_2 was measured in healthy subjects and no difference was shown for StO_2 between healthy adults (88% ± 5%) and trauma patients (85.5% ± 8.9%). However, in contrast to the study mentioned above, an arterial occlusion test was conducted. The rate of StO2 deoxygenation (which reflects mVO_2) was not significantly different from healthy subjects, whereas the rate of StO2 reoxygenation demonstrated an altered microvascular response in trauma patients.

From these studies is clear that StO_2 is lower in the deltoid muscle than at the thenar eminence. This difference may be explained by the larger subcutaneous tissue layer in the deltoid region, which may faint the NIRS signal from the muscle, as will be discussed below. In addition, some studies performed in healthy subjects have showed low sensitivity of thenar StO2 to detect changes in central blood volume in a model of hypovolemia induced by lower limb negative pressure, indicating.[28,29] However, the advantage of assessing StO_2 at the thenar eminence is the feasibility of the arterial occlusion test, allowing the mVO_2 and microcirculation function to be estimated, i.e., a more complete evaluation of peripheral perfusion. In spite of this difference, independent of the assessed region, the prognostic value of StO_2 comes from repeated measurements performed within the first hours of resuscitation and not from one time measurement.

Severe sepsis and septic shock

Although a large number of clinical trials have investigated StO_2 in septic patients, few were able to report any predictive value. Some authors have shown similar StO_2 values for healthy subjects and septic patients, while others have shown lower StO_2 values for septic shock patients when compared with healthy subjects. This inconsistency is speculated to be related to different types of resuscitation as well as to the moment of measurement. However, a prospective observational study demonstrated that repeated StO_2 assessments in septic patients within the first hours of ICU admission was predictive of unfavorable outcomes.[30] In this study, the lack of StO_2 normalization, as shown by a sustained StO_2 below 70% within the first 8 hours following resuscitation, was reported to be associated with organ and metabolic dysfunctions.

NIRS can be used in sepsis to evaluate the integrity of the microvasculature and mVO_2 with the analysis of

changes in StO_2 during the vascular occlusion test. Three studies have focused in measuring regional mVO_2. Girardis et al.[31] applied venous occlusion to estimate mVO_2 and BF in patients with shock. The NIRS sensor was placed on the ventral face of the brachioradialis muscle, 5 cm above the proximal radius head. Both the mVO_2 and BF values following venous occlusion were higher in septic shock when compared with non-septic shock patients. However, oxygen extraction was similar for both groups, highlighting the microcirculatory dysfunction in sepsis. In a similar study, De Blasi et al.[32] performed a series of venous and arterial occlusions to assess microcirculation in septic shock patients, post-operative patients and healthy subjects. The measurements were made using quantitative NIRS with the sensor placed on the ventral face of the brachioradialis muscle and included StO_2, mVO_2, rate of StO2 reoxygenation and vascular reactivity (defined as ΔStO_2) No differences in StO_2 were observed between the three groups, and mVO_2 was shown to be significantly lower in septic shock patients. Vascular reactivity, as reflected by ΔStO_2 and rate of StO2 reoxygenation, was also reduced in septic shock patients. The discrepant mVO_2 results among these studies challenges the effectiveness of NIRS as a non-invasive regional oxygenation assessment method. However, these differences are most likely related to the different device models and the study designs used, e.g., both did not use repeated mVO_2 assessments prior to or following any therapeutic intervention.

In an attempt to make these variables simpler for bedside use, Pareznik et al.[33] evaluated StO_2 and rate of StO2 deoxygenation during arterial occlusion. Patients with localized infection without sepsis, with severe sepsis and with septic shock were compared. The measurements were performed using non-quantitative NIRS with the sensor on the thenar eminence following admission to the ICU, at stabilization, on the seventh day of the hospital stay and at discharge. The variable that was more strongly related with sepsis prognosis was the rate of StO2 deoxygenation. Septic shock patients exhibited a lower StO2 deoxygenation rate at admission when compared with severe sepsis or infection without sepsis. On the last hospitalization day, the StO2 deoxygenation rate was higher than that at admission in septic patients; however, the value on the last day of hospitalization was still lower when compared to both other groups. The rate of StO2 deoxygenation was also observed to be significantly correlated to the SOFA (Sequential Organ Failure Assessment) score (r = 0.79). The pathophysiological mechanism of StO2 deoxygenation during the ischemic period is related to alterations in the diffusive transport of oxygen in microcirculation.

Creuter et al.[34] evaluated the predictive value of StO2 reoxygenation rate in 72 septic patients and demonstrated that the reoxygenation rate were lower in shock than in non-shock patients. Moreover, non-surviving septic patients were shown to have slower reoxygenation rate than survivors. Other studies, however, failed to reproduce these predictive findings related to StO2 reoxygenation rate, but confirmed that this parameter is strongly altered in sepsis, highlighting the ability of NIRS to continuously monitor microcirculation in septic patients.[35,36]

Other clinical uses in intensive care medicine

Some clinical trials have used NIRS for diagnosing lower limb compartmental syndrome.[37-39] In an observational study, 9 patients with lower limb compartmental syndrome confirmed by physical examination and increased compartment pressure (64 ± 17 mmHg) were evaluated prior to and following fasciotomy.[39] The mean StO_2 in the affected limb (56 ± 27%) was significantly lower than the mean in controls (87 ± 7%) and was normalized following the fasciotomy (82 ± 16%).

NIRS can also be applied for the assessment of brain vascular reactivity in sepsis.[40] Changes in brain vascular reactivity following mechanical ventilation-induced hypercapnia were measured based on quantitative changes in HbO_2 and Hb levels. During septic shock, changes in both HbO_2 and Hb were significantly attenuated when compared with those observed in severe sepsis. Although the therapeutic value of this parameter may be controversial, this finding has helped the understanding of the pathophysiology of septic encephalopathy.[41]

Because resting StO_2 values reflect mainly the venous compartment, some investigators have used StO2 to indirectly estimate central venous oxygen saturation. Some studies have compared central venous oxygen saturation with thenar StO_2 measurements in septic patients and failed to show a strong correlation between these two parameters. A plausible explanation may be that StO_2 is much more related to the peripheral perfusion status than with the systemic hemodynamic, emphasizing that microcirculation and macro-hemodynamic measurements cannot be directly related.[42]

NIRS limitations

The main limitations of NIRS include the following: a) the influence of the bone or fatty tissue thickness on assessments performed in the brain and muscle, respectively; b) the role of myoglobin on tissue oxygenation assessments; and c) the influence of interstitial edema on

the NIRS signal. Regarding brain oxygenation monitoring, modern devices can account for bone thickness by the appropriate modification of the distance between the light emitter and the receptor, thereby improving NIRS sensitivity.[43]

The role of fatty tissue interference is still controversial in the literature, most likely due to the different methodologies and devices used in the trials. However, tissue oxygenation variations are considered primarily from regions of muscle, even when fatty tissues are as thick as 1.5 cm.[44,45]

Hemoglobin and myoglobin absorption spectra are superimposed, and because their absorption spectra are identical, NIRS is not able to discriminate between them. Experimental studies have shown that the signal from myoglobin corresponds to only 10% of the absorbed light and that myoglobin saturation is stable even during conditions that impair cell oxygen transportation.[5,46] Therefore, the majority of the NIRS signal is considered to come from hemoglobin.

The effect of tissue edema gained interest following the introduction of NIRS for the assessment of peripheral oxygenation in septic shock patients with interstitial edema from vascular leakage syndrome. One study showed that the degree of interstitial edema may affect NIRS oxygenation measurements. However, this influence is less important when NIRS is used in muscle areas that are less impacted by edema, such as the thenar region.[47]

CLOSING REMARKS

Near infrared spectroscopy (NIRS) is a non-invasive technique that allows determination of tissue oxygenation based on spectro-photometric quantitation of oxy- and deoxyhemoglobin within a tissue. As NIRS technology develops, the design of the spectrophotometer may be simplified, rendering it more feasible for bedside use in intensive care settings. Although NIRS can potentially be very useful for tissue oxygenation and perfusion assessments, additional studies are warranted to clarify its role in the clinical management of ICU patients.

RESUMO

A espectroscopia no infravermelho próximo (NIRS) tem sido principalmente usada na investigação da oxigenação periférica tecidual de forma não invasiva e contínua. O princípio da espectroscopia consiste na aplicação da luz no comprimento de onda do infravermelho-próximo para avaliar, de forma quantitativa e qualitativa, os componentes moleculares relacionadas à oxigenação tecidual. Baseado na relação das concentrações da deoxiemoglobina e da oxiemoglobina no tecido, a NIRS obtém informações para o cálculo da oxigenação tecidual. Embora possa ser aplicada em qualquer órgão, como método não invasivo é principalmente usada para a monitorização da oxigenação muscular periférica. Os parâmetros medidos pela NIRS podem ser calculados diretamente ou através de intervenções fisiológicas para alterar a circulação no local da aferição, sendo as mais usadas a oclusão arterial e a oclusão venosa. Deste modo, pode-se obter informações sobre a saturação do oxigênio muscular periférico e tecidual, bem como do fluxo sanguíneo e consumo de oxigênio local. Seu uso é direcionado principalmente para a monitorização da oxigenação tecidual periférica durante ressuscitação do choque no trauma e em pacientes sépticos, bem como a monitorização dos distúrbios da microcirculação regional. Esta revisão abordará os princípios físicos da espectroscopia no IV-próximo, e das principais aplicações clínicas deste instrumento de monitorização, com ênfase nos estudos que investigaram a utilidade da NIRS na área de terapia intensiva e também no setor de emergência clínica.

Descritores: Espectroscopia de luz próxima ao infravermelho; Monitorização fisiológica/métodos

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