Near-InfraRed Spectrometry (NIRS) and Venous-side Monitoring of the Circulation

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Learning Objectives

• Understand the rationale for venous-side monitoring
• Understand the technology of near-infrared spectrometry
• Gain a framework for understanding application of current and future technology

Physiologic rationale

The heart and cardiovascular system serve a complex but primary function of adequate substrate delivery to meet changing metabolic needs of different organ systems. The global substrate supply and demand, and systemic blood flow distribution, are dynamic state-dependent functions of anatomic, environmental, autonomic, endocrine, autocrine, cytokine, and intracellular controls. The integrated functioning of these mechanisms generally serves efficient distribution of substrate in health; such functioning can be multiply affected in disease, and is broadly affected by surgical and anesthetic interventions. Standard hemodynamic monitors provide a minimal data set which only crudely characterizes the circulation. Repetitive measurement and recording of heart rate, arterial blood pressure, and, recently, arterial oxygen saturation have been the basis for safety monitoring of the circulation in anesthesia and critical care, but in many instances these parameters do not have adequate predictive or heuristic value. These supply-side measures are to the circulation what the fiO2 and breathing rate are to the respiratory system: inadequately powered to reliably characterize system function or detect failure.

Limitations of Standard Domain Measurements

Measurement of arterial blood pressure, or organ perfusion pressure (mean arterial minus central venous pressure), provides an indirect measure of the output from the heart and the input to the systemic circulation. As a function of both cardiac and systemic vascular resistance (PP = CI*SVRI), only when one factor is constant will blood pressure directly reflect changes in the other. High and low pressure baroreceptors supply afferent input to the brain stem, and integrated neuroendocrine responses alter both vasomotor tone and cardiac output in the short and medium term to minimize changes in blood pressure. These cardiovascular reflexes make blood pressure a poor indicator of cardiac output, although partial decoupling of this integration in the sick patient or deliberately by anesthetic pharmacology may be exploited to allow for earlier detection of changes in cardiac output. However, inferences about CO from BP are both unreliable and counterintuitive: when invasively measured at hourly intervals, there was no relationship (r<0.2) between MABP and the Fick-derived systemic cardiac index in neonates with one or two ventricle anatomy; over ten minute periods of observation, the relationship between BP and CI was inverse (r=-0.4). [1] These observations imply that SVR is the more dynamic and important determinant of blood pressure in the critically-ill neonate, and help quantify the inferential limitations of blood pressure.
The model of \( PP = CI \times SVRI \) also implies that SVRI is a scalar variable, although the total resistance is actually composed of the inverse of sums of regional conductances, which are not clinically measurable and which are somewhat independent of each other. Thus, perfusion pressure does not measure organ perfusion; with relatively fixed cardiac output, an increase in blood pressure will occur through a net increase in SVRI which is not likely to be evenly distributed across all vascular beds, and thus will result from a change in the distribution of blood flow across organs. This implies that increasing blood pressure occurs through a reduction in blood flow to some regions.

Measurement of whole-body oxygen economy by exploiting the Fick principle is the physiologic rationale for SvO2 monitoring. By Fick, \( SvO2 = SaO2 - \frac{VO2}{DO2} \), and thus SvO2 will change with changes in whole-body balance of oxygen supply and demand. In experimental shock, SvO2 below a critical level is a quantitative measure of the degree of oxygen debt (a measure of the ‘dose’ of hypoxia) that is highly predictive of mortality. [2,3] However, measurement of whole-body SvO2 is technically challenging even in immobilized infants, and with abnormal circulatory anatomy, whole-body mixed SvO2 is only a theoretical construct. The ScvO2 is a close approximation of SvO2, with good evidence for improved outcomes in critical illness and high-risk surgery if ScvO2 is a primary hemodynamic target. [4-7] A limitation of SvO2 monitoring is that it is relatively insensitive to changes in the distribution of cardiac output, and thus significant organ ischemia may occur with SvO2 in the normal range.

**NIRS measurement rationale**
Part of the rationale for NIRS monitoring is an extension of the rationale for SvO2 monitoring: to detect changes in cardiac output or oxygen economy before blood pressure falls, when blood pressure monitoring is unavailable, or when pre-existing or anticipated hemodynamic changes are significant threats to patient wellness. Because even ScvO2 is invasive and sometimes technically formidable, a non-invasive SvO2 proxy would be a significant advance in the care of neonates, infants, and children. Additional rationale derives from recognition of the heterogeneity of the systemic circulation, with organ blood flow dependent on regional resistances that are subject to complex influences in the perioperative period. The mixed SvO2 is the flow-weighted average of regional venous saturations, and thus measurement of regional venous saturation would allow not only the reconstruction of SvO2 but also the detection of changes in regional or organ blood flow.

**NIRS methodology**
The principle of NIRS monitoring is optical spectroscopy: the differential absorption of different light wavelengths with changes in the concentration of an absorber. Current NIRS monitors target the hemoglobin molecule, like pulse oximetry, SvO2 catheters, and laboratory co-oximeters. Simply, these devices quantify the color of blood, and extend our visual capability by defined spatial and temporal resolution, tireless repetition, algorithmic computation, and numerical output. [8,9]

The ear oximeter was a five-wavelength transmission NIRS device that measured arterial saturation accurately by induction of thermal hyperemia. [10] Non-arterial measures of organ hemoglobin saturation by NIRS has a firm laboratory basis that culminated in the publication by Jobsis in 1977 of the in-vivo optical measurement of oxyhemoglobin concentration and cytochrome aa3 redox state in a transilluminated cat head and dog heart. [11] The theoretic feasibility of transmission NIRS was impeded
by the attenuation of photons by the amount of absorber in the whole brain or heart, and established the fundamental trade-off in NIRS monitoring, that of sample size vs. signal intensity. Clinically useable devices relied on the development of reflectance NIRS technology, with recognition of the importance of both absorption and scatter of photons as they traverse biologic tissue, which is better characterized as a suspension than a solution. The two major obstacles are the absorption of photons by non-heme absorbers, and the unquantifiable scatter which makes absolute measures of absorber impossible. If the target measure is hemoglobin saturation, then the absolute concentration of oxy- or deoxy-hemoglobin is not a required measure, and the saturation can be computed from the red/infrared ratio as in pulse oximetry. [8] This field saturation measure is derived from relative ratios even in devices advertized as ‘absolute’, and has been variously reported as tissue saturation (StO2), tissue oxygenation index (TOI), or regional saturation (rSO2). The uptake of oxygen from hemoglobin by mitochondria follows from diffusion down concentration gradients that are determined by supply and demand, and thus the rSO2 can be described from the regional Fick relationship as \( rSO2 = SaO2 - rVO2/rDO2 \).

Current devices, which inject and count photons on the same side of the body, capitalize on theoretic and empiric refinements of modified Beer-Lambert equations, emitter and detector characteristics, and methods to characterize the optical path for injected photons; significant contributions to this knowledgebase have been made by Dean Kurth. [12-14] Although the scatter and absorption of a single photon is essentially random as it traverses biologic tissue, the average path of photons that are continuously registered by a detector on the same side as an injector will be an arc of a circle, with a depth of about half the source-detector distance in continuous-wave spectrometers. This path length can also be characterized by restricting the registration to temporal windows following picosecond-wide pulses of photons (time-domain spectrometers) or by measuring the phase-shift of a frequency-modulated light source (phase shift spectrometers). Most current devices are continuous-wave devices, with a source-detector distance of 4 cm and a depth of penetration of about 2 cm. Additional spatial resolution can result from an additional near detector with a shorter source-detector distance that registers photons from more shallow tissue, such that subtraction of this near signal from the far will result in greater rejection of signal from shallow tissue, effectively focusing the measurement on deeper tissue. [8,9]

**NIRS Validation**

The fundamental challenge in validation of NIRS oxyhemoglobin saturation measurement is that the field of measurement is regional, diffuse, and internally heterogeneous, such that there is no single place to obtain blood that will be equal to the NIRS field. This obstacle is usually surmounted by characterizing the field as lying between the arterial and venous points, and by modeling the field saturation from arterial and regional venous measures. Both the anatomic and optical properties of tissue make recovery of photons from arteries less likely than from capillaries or veins, and thus the rSO2 will be close to the regional vein saturation.[15] The relationship between cerebral rSO2 and SjvO2 is much stronger in small heads than in large heads. [8,9,15,16]

Hyperemia will result in greater regional oxygen delivery and rSO2 will rise; the converse will occur with ischemia. This relationship can be mathematically stated by the regional Fick principle, such the regional blood flow (RBF) = k/(SaO2-rSO2). Thus the regional arterial-venous difference is inversely related to
blood flow when hemoglobin and organ oxygen demand are constant. Consideration of both the rSO2 and the SaO2-rSO2 difference will help interpretation. The fractional regional oxygen extraction has also been characterized as \( f_{OE} = \frac{(SaO2-rSO2)}{SaO2}. \) [17]

Non-cerebral measurements have been described for adult muscle, [18] neonatal mesentery, [9,19,20] and neonatal and infant kidney. [9,21,22] The anatomic basis for these measures relies on the accessibility of the target tissue within 1-2 cm of the body surface, knowledge of regional anatomy, and the predictability of the optical light path from the sensor placement. An anterior abdominal probe site is specific for the mesenteric circulation, and the T12-L2 flank probe site is specific for the ipsilateral renal circulation in a neonatal piglet model, with 50-70% of the signal deriving from the target organs. [23,24] The renal vein saturation is close to the regional rSO2 in infants undergoing cardiac catheterization, but the organ specificity for renal measurements may be limited in children greater than 10 kg. [25]

**Clinical NIRS observations**

**Normals**
The cerebral and somatic/renal rSO2 has been described in normal, awake neonates over the first five days of life: the average cerebral rSO2 was 78% and average renal rSO2 was 87%. [26] The cerebral and particularly somatic-renal rSO2 demonstrated short-term variability, reflecting changes in blood flow related to activity, blood oxygen and carbon dioxide levels, and sympathetic tone. The difference between somatic-renal and cerebral rSO2 in this normal population was 9%, an index of the relative distribution of blood flow between cerebral and somatic beds. The renal rSO2 exceeded the cerebral rSO2 in 24/25 of these normal neonates, reflecting the relatively high blood flow to metabolism ratio in the kidney that renders it susceptible to injury when sympathetic tone is high. Feeding did not have significant effects in these normal newborns.

**Cerebral NIRS**
Normothermic cerebral desaturation to the 30-45% range is associated with biochemical and histologic evidence of injury in a wide variety of animal models, and time-dependency has been demonstrated. [27,28] Thresholds at hypothermia are less well defined but are probably higher. [29] Cerebral desaturation during rewarming and after cardiopulmonary bypass is common, and associated with cerebral injury. [22,30-34] Thresholds and intervention strategies based on cerebral NIRS that improve outcome only partly validated. [35] Online detection of the lower limit of autoregulation, a concept fundamental to neurologic protection but elusive in individual determination, has been validated by automated detection of the coherency of cerebral rSO2 in arterial blood pressure. [36,37]

**Mesenteric NIRS**
Mesenteric rSO2 in infants shows a close relationship to ScvO2 and lactate in the early postoperative period following cardiopulmonary bypass. [20] Mesenteric desaturation by NIRS was related to the development of necrotizing enterocolitis in medical neonates, [19] but an even stronger relationship was found for the somatic/cerebral rSO2 ratio, presumably as an index relatively resistant to patient-specific
non-heme absorbers and changes in arterial saturation. Further validation of mesenteric rSO2 for outcome is necessary.

**Renal NIRS**

Measures of rSO2 from the T12-L2 flank region show abrupt profound drop with aortic cross-clamping during repair of coarctation, validating this measure as region-specific. [38] The T12-L2 somatic rSO2 in the first 24 hours following cardiopulmonary bypass predicts the extent of creatinine elevation at 48-72 hours, suggesting the relationship of this regional measure to ischemic organ injury. [21,39]

**Multisite Models**

Although both cerebral and somatic rSO2 contribute to mixed venous blood, the SvO2 can be better approximated by a linear combination of cerebral and renal rSO2 than by either alone, [21,40-44] and multiple-site models would be even better. The predictive accuracy [45] is high enough to identify children at significant risk of low SvO2, and thus this approach can serve a proxy for SvO2 in goal-directed therapy, with multisite rSO2 reconstruction of SvO2 related to some outcome. [42,46,47]

Changes in the relationship between cerebral and somatic rSO2 can provide a window on changes in the distribution of cardiac output with surgical, anesthetic, or pathologic influences. As somatic blood flow decreases during sympathetic activation, the somatic-cerebral difference will be reduced. This non-invasive measure of flow redistribution is related to biochemical shock and organ dysfunction, [40,41,48] and is returned to normal by intervention. [49] Changes in the distribution of cardiac output with changes in ventilation and arterial pCO2 are also evident using this approach. [50]

**Sources of error**

Errors in clinical application of NIRS devices are largely related to misunderstanding of the optical limitations, which are much more significant in large patients,[8,9,51] in whom organ-specific measures may be invalid. The optical field of current 4cm source-detector distance devices will interrogate only about 1 cm3 of tissue, and intra-organ heterogeneity must be appreciated; again, this limitation is extremely dependent on patient size. Direct hyperbilirubinemia will cause a reduction in the rSO2 relative to the regional venous measure, and this effect needs further quantification. [52,53]

Other sources of error are interpretive or inferential. The relationship between rSO2 and regional pO2 will depend on temperature, pCO2, and local factors, and both overly high and overly low tissue pO2 are associated with injury. Overinterpretation of a single regional rSO2 measure as a global characteristic may be misguided. Conversely, disregard of worrisome rSO2 information in the face of normal blood pressure may not reflect understanding of the complexity of circulatory physiology.

**Summary**

The cardiovascular system is complex, and multidimensional measures are necessary to more fully describe and monitor its characteristics and function. Measures in both the pressure and oxygen domain can help decode whole body and regional pressure and flow changes, which are often in opposite directions; thus the continuous availability of information from NIRS can be disruptive and challenging to interpret. Non-invasive measurement of regional venous oxygen saturation with NIRS can provide a probe of organ-specific blood flow or oxygen supply-demand relationships that are good enough for use
in a wide variety of clinical scenarios, and the current technology is more suitable for neonates, infants and small children. Future developments will permit more accurate measures in larger patients and those with other optical confounders, and will allow greater spatial resolution. NIRS monitors should do for the circulation monitoring what pulse oximetry has done for respiratory monitoring, with the prospect of elimination of unrecognized venous desaturation, organ ischemia, and shock-like states. However, understanding both the principles and limitations of current and future devices is fundamental to appropriate application of technology.

References


