

Non-invasive near infrared spectroscopy (NIRS) of the bladder: questions frequently asked by clinicians

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When most clinicians first see the term *near infrared spectroscopy* (NIRS), they do not recognize that this is an application of physics to medicine that they do in fact have some experience using. Transillumination of a scrotal mass employs the basic physics of light transmission through tissue, and oximetry is able to provide measurement of oxygen saturation (SaO₂) because of application of spectroscopic principles. Oximeters use wavelengths that optimize light penetration into tissue and allow measurement of changes in the concentration of hemoglobin because light absorption by this molecule varies depending on the wavelengths used and whether or not it is carrying oxygen. The net result, derived with the aid of signal averaging and software algorithms, is a value of such importance that it is now widely regarded as “the fifth vital sign.”

NIRS has been used for 30 years to measure changes in hemoglobin concentration occurring in the microcirculation of various tissues that reflect alterations in oxygenation and hemodynamics. Brain and muscle have been the principle tissues studied, and validated methodologies exist for a range of NIRS-derived measurement parameters.¹⁴ Since 1990, urologic research has employed NIRS methodology, with the most recent application being noninvasive transcutaneous monitoring of the bladder detrusor as a means of evaluating voiding dysfunction.⁵ Understandably, clinicians and researchers have questions regarding application of this optical technology to urology and to the evaluation of bladder dysfunction in particular. This article provides answers to some of the most frequently asked questions relating to NIRS of the bladder.

What is near infrared spectroscopy?

NIRS is a basic science technique that uses photons of light in the near-infrared spectrum to interrogate tissue noninvasively. The physics principles underlying NIRS include the relative transparency of tissue to light in the NIR spectrum (NIR photons penetrate through skin and scatter widely into underlying tissue) and the different absorption spectra of hemoglobin at specific wavelengths, which depend on whether or not the hemoglobin molecule is carrying oxygen.^{3,6} NIRS instruments generate light using multiple lasers or photodiodes that emit photons at several different wavelengths between 700 nm and 1000 nm.⁷ A transcutaneous interface with an emitter and a sensor allows the photons generated to penetrate into tissue and measures the number returning. Photons are variably absorbed by chromophores, which are naturally occurring chemicals in tissue that absorb light. The principal chromophores of interest in human tissue are oxygenated hemoglobin (O₂Hb) and reduced hemoglobin (HHb). Given that the absorption spectra of O₂Hb and HHb are different, a set of linear equations can be solved simultaneously to derive the changes occurring in the concentration of these chromophores, using the difference between the number of photons transmitted and the number detected returning from the tissue by the instrument.

Most NIRS instruments are continuous-wave systems that contain the following components⁵:

- at least 1 pulsed laser diode for each chromophore being sampled; typically the lasers emit light using 1, 2, or 4 wavelengths in the 729–920 nm range,
- fiberoptic bundles that transmit light from the source to a tissue interface (probe or patch) and

back to the instrument's photon-counting hardware,

- optodes in the tissue interface that emit light into the tissue and receive the photons returning,
- photon-counting hardware: photodiode, photomultiplier, or charge-coupled device (CCD) computer with software containing algorithms for converting raw optical data into chromophore concentrations, and storing and displaying data,
- a visual display where NIRS data are displayed numerically and/ or graphically against time.

The benefits of NIRS technology include its noninvasive nature, nontoxic energy source, and ability to monitor a range of physiologic change continuously, in real time, with high temporal resolution (6–10 Hz) at the bedside. NIRS can be used simultaneously with other technology such as ultrasound and during urodynamic pressure-flow studies. Patients find the simplicity of the technology attractive and like the transcutaneous interface; it is also not an expensive technology.

Limitations of NIRS include the ability to provide only measurement of change in chromophore concentration from baseline rather than an absolute quantitative measurement. This is because the exact concentration of hemoglobin within the tissue being studied is not known. Consequently, NIRS data are most informative where there is a temporary change in the physiologic state of the tissue (e.g., induced hypoxia, ischemia, or a change in blood volume) or where physiologic changes occur as a result of organ

function (e.g., striated muscle contraction, including the urethral sphincter and pelvic floor) or detrusor muscle activity.^{18,9} When photons are transmitted into tissue, some light is lost because of scattering beyond the field of the transcutaneous sensor; as a result, only a proportion of the photons transmitted are detected returning from the tissue of interest. For reasons such as these, NIRS relies on software algorithms to enable the basic principles of NIRS physics to be applied in a clinical context and to facilitate data interpretation. In this regard NIRS is no different from other technologies already in the medical mainstream such as oximetry (the most widely used application of photonics technology), computed tomography (CT), and magnetic resonance imaging (MRI). Similarly, it is important to recognize when comparing a novel technology such as NIRS to a current gold standard that virtually all extant technologies also make similar concessions through their software algorithms to a range of basic science principles in order for them to have clinical applicability.

What does NIRS measure?

NIRS measures changes in concentration of the chromophores oxy- and deoxyhemoglobin in tissue, as described above. A multiple-wavelength continuous-wave instrument and appropriate inter-optode distance allow changes in O₂Hb and HHb concentrations to be monitored in real time. These changes allow tissue oxygenation and hemodynamic trends from baseline to be monitored; changes in O₂Hb, HHb, and total hemoglobin (tHb) reflect oxygen supply, oxygen consumption, and alteration in total blood volume, respectively. The principles underlying such measurement have been shown to be reproducible in a variety of tissues, including brain and muscle, and validated methodologies have also been reported for measurement of several specific parameters in these tissues, including noninvasive quantification of blood volume and blood flow.¹ Muscle function is strongly dependent on oxidative metabolism as, during contraction, O₂ consumption (VO₂) rises many-fold in association with an increase in O₂ delivery (DO₂). Consequently, pathology that

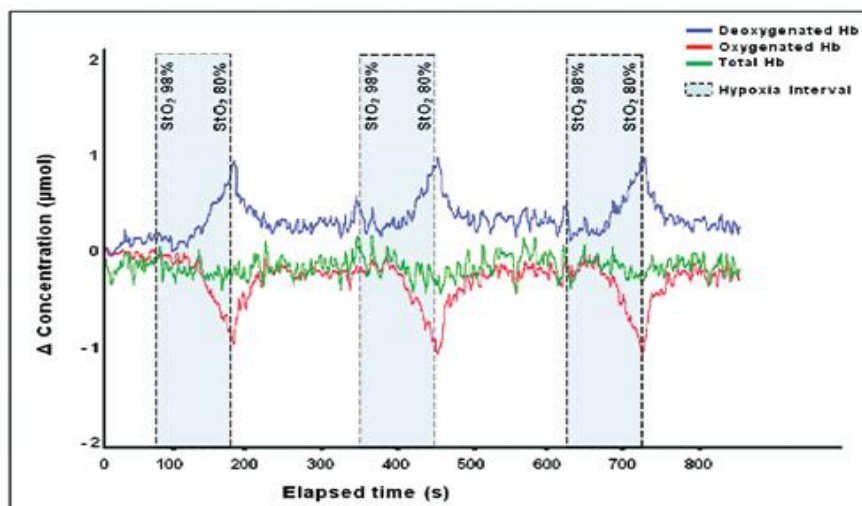


Figure. Patterns of change in hemoglobin (Hb) concentration in response to 3 episodes of systemic hypoxia in surgically exposed rabbit bladder.

impairs VO_2 or DO_2 through either a hemodynamic or a metabolic mechanism can adversely affect the functional capacity of muscle or a muscular organ. Characteristic patterns of change in chromophore concentration occur in response to physiologic events that alter tissue oxygen demand, including hypoxia, ischemia, and muscle contraction.^{2,4,5,10} The figure shows the pattern of change and reproducibility of variations in chromophore concentration in response to 3 episodes of systemic hypoxia detected via NIRS optodes placed directly on the surgically exposed rabbit bladder.

Following demonstration of the feasibility of using NIRS to monitor changes in O_2Hb , HHb , and tHb in the human bladder detrusor,¹¹ a NIRS instrument specifically designed for applications in urology was developed,⁸ and prospective studies were conducted that combined noninvasive transcutaneous NIRS monitoring of the anterior bladder wall with simultaneous invasive urodynamic evaluation (UDS).^{5,12} This research has established that a NIRS emitter and a sensor placed on the abdominal skin in a suprapubic location provide a means of monitoring changes in O_2Hb , HHb , and tHb occurring in the detrusor during the filling and voiding cycle, and that these parameters differ in health and disease.

Why does bladder emptying generate changes in NIRS?

Voiding involves contraction of the detrusor smooth muscle, which requires provision of oxygen and energy substrates to meet increased metabolic demand within the detrusor. Oxygen and glucose delivery to striated muscle is known to alter in response to varying demand by the interplay of neural and chemical changes within the microcirculation. Complex mechanisms interact to alter vessel caliber and permeability, blood volume (flow), and O_2Hb and HHb concentration in response to these alterations in metabolic demand. Research has established that the bladder has a rich blood supply that alters as the organ fills and empties.

Why do NIRS measurements differ in health and disease?

Systemic pathologies affecting the vasculature probably alter the ability of the detrusor microcirculation to respond adequately to an increase in oxygen demand during contraction. Some bladder pathology such as bladder outlet obstruction likely also generates organ-specific changes in muscle that result in alterations in blood flow and muscle

metabolism. The pattern of NIRS changes reported in brain and muscle reflects effects of systemic pathology on the microcirculation and organ-specific pathology. Our hypothesis is that where local or systemic pathology adversely affects the detrusor microcirculation sufficiently to generate voiding dysfunction, patterns of change in NIRS parameters different from those seen in subjects will occur. As experience with bladder NIRS grows, it is probable that distinction will be evident among specific bladder pathologies, based on the nature of the physiologic effects generated on oxygenation and hemodynamics. This is already possible in patients with lower urinary tract symptoms in the context of the presence or absence of bladder outlet obstruction.²

How do we know the detrusor is being monitored?

Confidence comes from the basic physics principles of NIR light transmission, and from research indicating that the depth of photon penetration is principally determined by the interoptode distance (IOD)—the distance separating emitter and sensor on the skin surface.^{3,13} Although tissue structure and the quantity of adipose tissue present have some influence, the principal way of altering the path of NIR light through tissue is to select an appropriate IOD to enable the photon path's area of maximum sensitivity to be directed to interrogate the detrusor. While the photon path extends above and below the point of maximum sensitivity, this point is usually at a depth that approximates half the IOD. Our animal experiments also provide an additional measure of confidence, as comparable patterns of change are observed in response to increased oxygen demand when NIRS monitoring is done with transcutaneous optodes and when optodes are placed directly on the wall of the surgically exposed bladder. Appropriate IOD is used in each circumstance to reflect the depth of light penetration required. In addition, significant variations in NIRS parameters occur only in direct temporal relationship to events in the voiding cycle; patterns compatible with physiologic change are detected only over the bladder and not from a control channel with the same IOD sited elsewhere on the abdomen.

What is the contribution of subcutaneous tissue?

As stated above, adequate IOD allows light to travel through the skin and subcutaneous tissue so that most attenuation takes place within the anterior

wall of the bladder. The literature on brain studies provides research data on the same issue, with confidence that appropriate instrumentation and sound methodology ensure that the cortical brain surface is interrogated reliably in spite of NIR photons having to travel through skin, muscle, bone, and cerebrospinal fluid. Our animal studies showing comparable patterns of change in NIRS parameters with and without tissue between the optodes and the bladder also add confidence to the premise that the principal tissue being interrogated is the bladder. Hence it is most probable that in bladder studies subcutaneous tissue does not significantly influence light attenuation.

What effect does movement have on NIRS data collection?

Spontaneous patient movement, such as occurs commonly with change of position during urodynamic measurements, is readily evident in the NIRS data stream as abrupt unidirectional change of a magnitude and duration that are incompatible with a physiologic effect. Small-magnitude fluctuations due to respiratory movement and vascular pulsation can also be detected, but these fluctuations are rhythmic, regular, and of low amplitude. Software algorithms and filters for smoothing data can be incorporated to remove movement artifact. It is evident from muscle studies involving isometric contraction, and from NIRS monitoring during exercise physiology research and a variety of sporting activities, that meaningful data can be obtained in the presence of movement. NIRS data have been successfully measured during sports activities, including wrestling, running, and skiing, and during other voluntary activities where significant movement occurs. During such studies, in addition to trend monitoring of chromophore concentration, a range of specific parameters relating to muscle oxygenation and hemodynamics is routinely measured.^{12,4}

How does change in bladder size impact NIRS measurements?

This is a central and legitimate question regarding NIRS bladder studies. However, it is important to recognize that, as referred to above, published data provide confidence that meaningful monitoring can be achieved in multiple situations without movement contaminating the data. With reference to the bladder, our pelvic ultrasound measurements made in 24 females during simultaneous NIRS and urodynamics indicate⁴ that the

relationship of the anterior wall of the bladder to the abdominal sensor probably remains relatively constant during voiding. Also, the site chosen for the NIRS sensor patch following our preliminary research (2 cm above the pubis and across the midline) is probably optimal in the context of change in bladder size having the least influence on the signal obtained. These pelvic ultrasound measurements suggest that the dome of the bladder is where movement predominantly occurs as the organ changes in size during voiding. At volumes less than 250 cm³, all planes of the bladder move comparably, but at greater volumes it is predominantly the dome that moves to accommodate the additional urine volume. Consequently, what likely occurs is some change in the thickness of the bladder wall as the bladder fills and empties, rather than frank movement in front of the optodes. As with the question relating to the potential contribution of subcutaneous tissue to the signal, some effect is probable; however, the effect of change appears to be sufficiently small that the value of the NIRS signal is not compromised, based on the consistency of the NIRS data obtained, the fact that the patterns of change appear to reflect physiologic variations in the detrusor, and the ability of NIRS data to distinguish the presence or absence of pathology in males with lower urinary tract symptoms.

In terms of classifying symptomatic males as obstructed or unobstructed, research indicates that NIRS data obtained during the voiding cycle has discriminant ability comparable to invasive pressure flow studies. This applies when using NIRS data combined with maximum flow rate (Q_{max}) and postvoid residual urine volume (PVR),² or when using NIRS data alone analyzed with a classification and regression tree (CART) algorithm.⁵ Such discriminant ability would be unlikely if change in bladder size contributed significantly to the NIRS data obtained. It is far more probable that physiologic changes in the detrusor underlie the NIRS monitoring parameters measured and their ability to correctly classify subjects as either obstructed or unobstructed. The probability that NIRS bladder monitoring provides important information regarding physiologic change is supported by two other observations. NIRS data recorded between permission to void and uroflow start often show significant hemodynamic change (usually an increase in tHb made up predominantly of O₂Hb) before voiding begins—that is, while the bladder volume remains constant and no change in bladder size occurs. Additional evidence that alterations in detrusor oxygenation and hemodynamics occur in the absence of any change in bladder size is also seen where there is voiding delay.

Significant alterations in oxy- and deoxyhemoglobin indicative of variations in blood volume, increased availability of O₂Hb, and increased oxygen consumption have been recorded. Such changes most likely result from isotonic contraction as urge is sustained and from related effects in the microcirculation that NIRS monitoring is able to detect.

Consequently, because effects indicative of physiologic change in the detrusor are observed when bladder volume remains constant and during voiding, it is probable that change in bladder size does not negatively impact the ability of NIRS to provide monitoring data of value during assessment of patients with voiding dysfunction.

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