NIRS: Past, Present, and Future in Functional Urology

Alexander Koven1,2 · Sender Herschorn1,3

Accepted: 27 July 2022 / Published online: 11 August 2022
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Abstract
Purpose of Review Near infrared spectroscopy (NIRS) is a non-invasive optical technique that uses near infrared light to detect the oxygenation status and hemodynamics of various organs. This article reviews the use of NIRS for the non-invasive assessment of lower urinary tract dysfunction (LUTD). Applications include assessment of bladder outlet obstruction, overactive and underactive bladder, neurogenic LUTD, pediatric LUTD, interstitial cystitis/bladder pain syndrome, and pelvic floor dysfunction. In addition, the article describes how NIRS is elucidating more about the brain-bladder connection.

Recent Findings While evidence exists for the application of NIRS throughout a wide range of LUTD, most of these studies are limited by small sample sizes without matched controls. Investigators have experienced problems with reproducibility and motion artifacts contaminating the data. The literature is also becoming dated with use of older technology.

Summary NIRS holds potential for the non-invasive acquisition of urodynamic information over time scales and activities not previously accessible, but it is not yet ready for use in routine clinical practice. Advances in wearable technology will address some of the current limitations of NIRS, but to realize its full potential, larger scale validation studies will be required. Moreover, multidisciplinary collaboration between clinicians, scientists, engineers, and patient advocates will be critical to further optimize these systems.

Keywords Near infrared spectroscopy · Bladder · Voiding dysfunction · Urodynamics · Hemoglobin · Wearable technology

Introduction
Near infrared spectroscopy (NIRS) is a non-invasive optical technique that uses near infrared (NIR) light to detect the oxygenation status and hemodynamics of various organs.
With wavelengths between 650 and 1350 nm, NIR light is invisible to the human eye but has key properties for studying tissue. It penetrates deeper into tissue with less attenuation than visible light. It is also absorbed by multiple biologically relevant molecules, such as hemoglobin (Hb). Similar to a pulse oximeter, the amount of light reflected through the tissue is detected by a photodiode (or light detector) and used to calculate relative concentrations of tissue components, such as oxygenated hemoglobin ($O_2$Hb), deoxygenated hemoglobin (HHb), and total hemoglobin ($t$Hb), using a relationship called the Beer-Lambert law [1]. It has most commonly been applied for monitoring and diagnosing conditions of the brain and skeletal muscle, but there has been increasing speculation and literature on its potential use in functional urology and managing lower urinary tract dysfunction (LUTD).

LUTD is a complex and multifactorial condition leading to disturbances in urine storage and/or voiding. Standard evaluation has relied on invasive urodynamic testing, which takes place under artificial conditions, relying on bladder and rectal catheters to study bladder volume and pressure. It has been hypothesized that bladder storage and emptying leads to hemodynamic variations in the microvasculature of the bladder wall and pelvic floor, which differ in health and disease [2]. Based on this, investigators have explored whether NIRS can non-invasively and continuously monitor these changes using transcutaneous monitors, thus providing previously unavailable physiologic information. These investigators have attempted to prove feasibility and answer the questions: Can NIRS be used to enhance the investigation of patients with LUTD, aid in diagnosis and treatment selection, and offer new insights for further research? This article reviews the answers by summarizing past developments, current knowledge, and potential future advancements of NIRS in functional urology.

The Past: From Lasers to LEDs — The Rise of NIRS in Functional Urology

The first NIRS devices relied on laser powered continuous wave instruments, meaning light was generated by a laser with a constant output [3]. These systems were sensitive with high-resolution sensors but had limited clinical utility due to their large size and large fiber optic cables connecting components. This was especially problematic as arrays of multiple sources and detectors are required to detect regional changes and attain information from different tissue layers. This technical challenge was overcome through the introduction of light emitting diodes (LEDs). These relatively small light sources offered lower power consumption while maintaining high light intensity and ultimately replaced the use of lasers. LEDs have enabled the design of wireless, battery powered NIRS devices with telemetric capabilities.

The Present: Shining Light on the Unexplored Aspects of Bladder Function

LED-based continuous wave NIRS instruments are currently being applied to shed light on the unexplored aspects of functional urology by monitoring real-time changes in oxygenation and hemodynamics as the bladder fills and empties. These devices are typically applied over the skin, across the midline of the lower abdomen superior to the symphysis pubis (Fig. 1a). For research purposes, this can be coupled with simultaneous urodynamics, including filling cystometry and pressure-flow studies. This approach has been applied to study normal bladder function, bladder outlet obstruction (BOO), overactive bladder (OAB), underactive bladder (UAB), neurogenic LUTD, pediatric LUTD, and interstitial cystitis/bladder pain syndrome (IC/BPS) and even adapted for the pelvic floor. Much of this work has been conducted

![Fig. 1](https://example.com/fig1.png)  
**Fig. 1**  
(a) Location of a NIRS device for transcutaneous bladder monitoring, positioned on the abdominal skin superior to the pubic symphysis. Created with BioRender.com.  
(b) An example graph showing NIRS-derived changes in oxygenated, deoxygenated, and total hemoglobin concentration ($O_2$Hb, HHb, $t$Hb) for an asymptomatic subject with simultaneous urolflowmetry, from permission to void (P) and including start (S) to end of uroflow (E) [4]. Adapted from work by Stothers and Macnab
by Macnab and Stothers [2] and extended or reproduced by others. Most are pilot or feasibility studies, which include small sample sizes and questions around generalizability, and conclude with calls for larger, confirmatory trials. Key studies are summarized here.

**The Normal Bladder**

Stothers and Macnab were first to define a NIRS bladder pattern seen in asymptomatic children and adults by monitoring O$_2$Hb, HHb, and tHb throughout the micturition cycle [4]. They demonstrated a reproducible trend with tHb and O$_2$Hb increasing following permission to void, yet before voiding begins, and gradually returning to baseline after voiding ends (Fig. 1b). Based on these findings, they postulated that the bladder detrusor is “primed” with a surplus of O$_2$Hb even before initiation of the voiding phase and continues to rise in O$_2$Hb during the “work” of voiding. O$_2$Hb remains greater than HHb throughout the voiding phase in physiologic voiding, reflecting oxygen supply being greater than demand. Consequently, dysfunction can theoretically be associated with changes in hemodynamics and oxygenation data captured by NIRS [2].

**The Obstructed Bladder**

The association of NIRS parameters with BOO is the most well studied. In contrast to normal bladders, Macnab and Stothers demonstrated a predominately negative trend in tHb over the voiding phase due to a decrease in O$_2$Hb [5]. This implies that the demand for oxygen exceeds supply, a trend reflected in other tissues and muscles under stress. For instance, the heart similarly experiences hypertrophy and ischemia in the context of pressure overload from hypertension or outflow obstruction [6].

These observations led to the development of NIRS-derived algorithms for the diagnosis of BOO, with the goal of developing non-invasive tools that can diagnose BOO with comparative accuracy to invasive urodynamics to detect DO in women with OAB. They found an acceptable sensitivity of 80.6%, but with a specificity of only 28.1%, they concluded it was unreliable in detecting DO ($p=0.028$) [13••]. Farag et al. also demonstrated statistically significant changes in NIRS pattern with DO, giving a range of AUC values of 0.80–0.85 for O$_2$Hb curves and 0.73–0.84 for HHb curves [14].

Like NIRS diagnosis of BOO, there have questions regarding the reliability of the technology for diagnosis of OAB. Mastoroudes et al. conducted a pilot study to evaluate the sensitivity and specificity of NIRS as an alternative to urodynamics to detect DO in women with OAB. They found an acceptable sensitivity of 80.6%, but with a specificity of only 28.1%, they concluded it was unreliable in detecting DO ($p=0.028$) [13••]. Reasons postulated included a high body mass index and darker skin pigmentation in the cohort, motion artifacts, and the possibility that NIRS changes are not synchronized well enough with DO to be used for diagnosis. Experience from Macnab and Stothers suggests that there could potentially be several distinctive NIRS patterns for OAB given its multiple causal mechanisms [2]. The NIRS criteria chosen as indicative of DO in this study might not have been comprehensive enough to cover all the possible causes of DO.

While treatment of OAB has traditionally focused on the bladder, there is increasing recognition of the brain-bladder connection. Functional magnetic resonance imaging (fMRI) has associated bladder control with an extensive network of brain regions, including activation of the anterior cingulate gyrus with urgency and deactivation of the prefrontal cortex with DO [16, 17]. Functional NIRS (or fNIRS) of the brain can map these regional differences and provide similar non-invasive monitoring but is more affordable, portable, and easier to operate [18]. Macnab et al. demonstrated feasibility of brain fNIRS using simultaneous bladder NIRS and a validated patient controlled sensory meter. In a patient with OAB, they demonstrated increased neuroexcitation of the anterior cortex with a strong urge to void, and then a subsequent decrease in neuroexcitation in response to a distractor.
stimulus (e.g., phone call) [19•]. While this requires further verification, it points to brain-mediated mechanisms involved in OAB and the possibility of using brain fNIRS to objectively evaluate lower urinary tract sensation.

The Underactive Bladder (UAB)

Compared to OAB, there is a paucity of data on UAB, a syndrome characterized by “a slow urinary stream, hesitancy and straining to void, with or without a feeling of incomplete bladder emptying, sometimes with storage symptoms” [20]. Like DO for OAB, detrusor underactivity (DU) is the urodynamic counterpart, defined as “a contraction of reduced strength and/or duration, resulting in prolonged bladder emptying and/or a failure to achieve complete bladder emptying within a normal time span” [20]. It is often clinically challenging to distinguish UAB from BOO in men with LUTD. Romai et al. investigated the use of NIRS for this by performing simultaneous urodynamics and bladder NIRS in men with moderate to severe symptoms and maximum urine flowrates <15 cc/s. Results revealed that a flat NIRS tracing correlated with a bladder contractility index (BCI) <100, i.e., a weak bladder, with a good concordance (kappa = 0.63) for discriminating DU from BOO [21•]. This may provide insight into the potential pathogenesis and diagnostic criteria in this poorly understood area.

The Neurogenic Bladder

Neurogenic LUTD or “neurogenic bladder” refers to “abnormal or difficult function of the bladder, urethra (and/or prostate in men) in the context of clinically confirmed relevant neurologic disorder” [22]. This may be due to congenital anomalies, acquired neurologic diseases, or trauma to the brain and spinal cord [23]. Patients can experience a wide range of urinary tract conditions and complications, including OAB, incontinence, infections, obstruction, and renal failure [24]. They require ongoing management and surveillance, with urodynamics being the gold standard test due to the absence of normal sensation [25]. Given the potential difficulties of invasive urodynamics in this population and regularity of assessment, non-invasive NIRS monitoring would be particularly valuable.

Shadgan et al. investigated the use of simultaneous bladder NIRS and urodynamics in 10 adult paraplegic patients with neurogenic LUTD [22]. Urinary incontinence occurred in 5 patients, which was associated with a rise in detrusor pressure on urodynamics and a simultaneous fall in detrusor O$_2$Hb on bladder NIRS. Detrusor tissue saturation index (TSI), which is O$_2$Hb as a percentage of tHb, also decreased significantly during episodes of incontinence (mean change in TSI = −3.9 ± 2.1%, P < 0.005) [26•]. This finding is consistent with previous literature relating to bladder blood flow detected using a laser Doppler flow probe with bladder wall compliance [27].

Like non-neurogenic OAB, Sakakibara et al. used fNIRS to study neurogenic OAB. They showed that during bladder storage the prefrontal cortex, which normally suppresses the bladder, is relatively deactivated in patients with neurogenic OAB and DO, compared to controls [28]. They subsequently investigated the effect of anticholinergics, such as tolterodine and fesoterodine. They found that initiation of these medications could reverse the deactivation seen; however, tolterodine activated the right prefrontal area, while fesoterodine led to activation of the left prefrontal area [29•, 30]. The reason for this discrepancy was not fully explained, but the studies were limited by sample sizes and patients included had a wide spectrum of neurologic conditions that might have influenced the results.

The Pediatric Bladder

Non-neurogenic LUTD in children is LUTD without any neurological basis and is a common condition in childhood, reported in up to 15% of 6-year-olds [31]. While certain abnormal urodynamic features have been identified, underlying causes remain unexplained. Moreover, invasive urodynamic testing in children is challenging because of catheterization. NIRS has the potential to further explain symptoms and monitor patients non-invasively.

Afshar et al. compared changes in NIRS parameters during voiding in children (3–14 years old) with LUTD and asymptomatic controls. O$_2$Hb, HHb, and tHb were monitored from permission to void to the end of urination. Asymptomatic children demonstrated the same trend as described in asymptomatic adults (i.e., increasing tHb following permission to void and during urination, mainly from increasing O$_2$Hb). Conversely, children with LUTD exhibited a blunted or absent increase in tHb and HHb was greater than O$_2$Hb [32••]. This implies a lack of hemodynamic response required to provide energy for detrusor contraction and the potential for physiologic fatigue during voiding, like adult males with BOO.

The Painful Bladder

IC/BPS is defined as “an unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6-week duration, in the absence of infection or other identifiable causes” [33]. Given insufficient publications regarding diagnosis and overall management, the American Urological Association and Canadian Urological Association guidelines on IC/BPS are based mainly on clinical principles, expert opinion, and lower quality evidence [34, 35]. This leads to subjective assessments, wide variations in diagnostic approaches, and delays in diagnosis [36].

While pathogenesis remains uncertain and likely multifactorial, bladder biopsies in certain patient populations with IC/BPS have
identified histologic findings suggesting chronic submucosal inflammatory disease [37]. Shadgan et al. hypothesized these changes may result in changes in oxygenation parameters and that bladder NIRS could be used to diagnose IC/BPS. They tested 24 patients with LUTD, divided into 4 with IC/BPS and 20 without. Patients with IC/BPS had significantly higher detrusor TSI (74.2 ± 4.9% in IC/BPS vs. 63.6 ± 5.5% in non-IC/BPS, p < 0.0005) [38••].

Abnormalities in the brain’s processing of sensory input has also been hypothesized to contribute to IC/BPS. Consequently, Pang et al. investigated the use of brain fNIRS on patients with IC/BPS. They assessed functional connectivity in the prefrontal cortex, which is a measure of temporal correlations between anatomically separate regions. Compared to healthy controls, functional connectivity was decreased in IC/BPS patients with an empty bladder and with a strong desire to void (p < 0.05) [39•]. While this requires further validation, it points to possible frontal lobe disorders and new brain biomarkers for diagnosis of IC/BPS.

The Pelvic Floor

Lower urinary tract function relies on normally functioning pelvic floor muscles. This is apparent with stress urinary incontinence (SUI), when a weakened pelvic floor leads to urine leakage during increases in abdominal pressure (e.g., coughing, sneezing, lifting). First-line treatment involves strengthening these muscles with pelvic floor muscle therapy (PFMT); however, current measures of pelvic floor strength are subjective, including maximal voluntary contraction assessed by palpation. Conversely, in sports medicine, quantitative measures of skeletal muscle are frequently performed with NIRS instruments to measure function in both normal and pathologic skeletal muscle [40].

Macnab et al. hypothesized that NIRS could be used to interrogate the pelvic floor muscles in women and developed a NIRS device housed in a transvaginal probe [41]. They studied pelvic floor contractions and applied validated NIRS-derived oxygenation parameters from sports medicine, including half-time recovery of hemoglobin difference, HbDiff (½RT), which is a measure of muscle recovery time [40]. In a pilot study, they tested pelvic floor muscles in 7 symptomatic and 11 asymptomatic women, before and after 8-week, home-based PFMT. Results demonstrated a post-treatment improvement with a decrease in HbDiff (½RT) (p < 0.01) [42•]. Overall, measurements proved to be feasible, well tolerated by participants, and consistent with muscle oxygenation seen in other skeletal muscle.

The Future: Developing and Leveraging New NIRS Technologies

While there have been promising findings using NIRS in functional urology, there have also been some discrepancies in results, with devices still limited to a small group of investigators for research purposes. Several major limitations have prevented more widespread testing and use. Firstly, while a main advantage of NIRS is its ability to be used noninvasively during regular activity, reproducibility of the data has been an issue due to contamination by motion artifacts. To control this, most studies have involved carefully restricting body movement, with some using surface electromyogram monitoring to rule out motion artifacts. The second major limitation is the NIRS form factor. While the LED-based systems described can be made wireless, their relatively large size, rigid design, and heavy construction limit their ability to be truly wearable during regular, real-world activity. Finally, the NIRS devices described have focused on monitoring oxygenation and do not provide direct information about volume and pressure, key factors typically used to manage LUTD. Multiple technologies are being developed in parallel to correct for motion artifacts, enhance wearability, and detect additional metrics.

Correcting Motion Artifacts

Motion artifact is a well-known limitation of NIRS [43]. For example, Farag et al. had to exclude 28% of participants in their OAB NIRS study due to data being contaminated by motion and concluded NIRS could not be used reliably enough for routine clinical practice [14]. Consequently, there have been efforts to exclude motion artifacts from NIRS data so that it may be used reliably in real-world, ambulatory patients.

Much of this work comes from the use of fNIRS in monitoring brain activity. Like the bladder, brain measurements are limited by motion in real-world applications, which can cause fluctuations unrelated to the event of interest and loss of the contact between the sensor and the skin. Several methods have been proposed to solve this problem, including the use of an accelerometer to measure motion [44], and various post-processing algorithms to identify motion artifacts based on different characteristics (like frequency, amplitude and duration of signal) [45]. These algorithms include principal component analysis [46], Wiener filtering [47], Kalman filtering [48], and wavelet-based denoising algorithms [49]. Molavi and Dumont demonstrated the latter on fNIRS data and significantly attenuated motion artifacts without distorting signal [50].

Despite progress with post-processing algorithms, they are typically limited by reliance on expert opinion and post hoc tuning of parameters. Machine learning is emerging as a powerful tool to identify signal from noise and address these shortcomings by learning optimal parameters from the data. Russel-Buckland et al. developed a novel process using machine learning methods to detect common motion artifacts [51], while Lee et al. used an artificial neural network to reinforce a more traditional wavelet-based method [52]. More recently, Kim et al. reported on the use of a deep convolutional neural network to remove motion artifacts from
NIRS data [53]. This model outperformed conventional methods using simulated and semi-simulated data. Next steps will be to apply these methods to real-world NIRS data and translate from monitoring the brain to the bladder.

Enhancing Wearability

Wearable technologies are projected to change our understanding of basic physiology by obtaining complex, multimodal data over time scales and activities not previously accessible [54]. Light-based sensors, like NIRS, serve as the fundamental mechanism for many of these devices, which currently still rely on very basic electrooptic componentry. The next generation of NIRS sensors will leverage more recent advances in wireless device platforms, miniaturized spectrometers, and advanced light sources to expand the capabilities of light-based measurement strategies in wearable biomedical devices.

Like motion-invariance technology, brain fNIRS offers a case study for what may be possible for bladder monitoring. Rwei et al. reported on a soft, flexible, and wireless cerebral hemodynamic monitoring device capable of measuring cerebral and peripheral oxygenation, designed specifically for infants and children [55]. The system utilizes standard, cost-effective components, including a photodiode array, a pair of LEDs, rechargeable battery, and a compact circuit design, which can wirelessly communicate with an external device via Bluetooth. The device is encapsulated using medical-grade silicone with a compact size of $33 \times 16 \times 3$ mm and mass of 2.8 g, an order of magnitude lighter than current NIRS probes. A clinical study has also demonstrated measurements comparable to existing clinical standards [55].

Detecting Volume and Pressure

While the majority of NIRS research has focused on measuring oxygenation, other useful parameters may be feasible. Non-invasive, ambulatory bladder volume and pressure assessment would be particularly important in patients with neurogenic LUTD who cannot independently sense the fullness of their bladders, providing them with a warning to electively empty or catheterize before accidental incontinence, as well as minimize bladder pressure and risk of renal injury. This could also be a valuable tool for the management of nocturnal enuresis in children and overflow incontinence in the elderly.

Several techniques for ambulatory bladder volume monitoring exist and are at various stages of development, including ultrasound, implantable sensors, and bioelectrical impedance analysis, which estimates body composition through measurement of electrical resistance. While ultrasonic devices are the most established, they require high frequency sensors and coupling gel, making them more expensive and challenging to use. Implantable body sensors would theoretically be most accurate and allow for direct pressure measurements, but in-vivo testing is complex and research on them is not yet mature. Bioelectrical impedance analysis is low cost, but also low accuracy. An optimal approach might be NIRS, which has higher accuracy compared to bioelectrical impedance analysis, yet more affordable and easier to use than ultrasound [56].

NIRS bladder volume monitoring has been tested by incorporating light sources around 975 nm, which is the absorption peak of water. Jeyalakshmi evaluated such a device using a bladder phantom and showed a significant difference in light absorption between a full and empty state [57]. Molavi et al. used a similar device in a pilot study involving one healthy volunteer and similarly observed a significant difference in light absorption between full and empty [58]. Fong et al. extended this work using Monte Carlo simulation to model light transport through the bladder wall and inform the ideal position of light sensors. Furthermore, they developed a machine learning algorithm to determine bladder fullness. Like Molavi et al., they confirmed a significant difference between the full and empty bladder of a healthy volunteer [59, 60].

In addition to volume, NIRS measurements have been correlated with pressure. As mentioned, Shadgan et al. noted consistency between a drop in bladder TSI and a rise in detrusor pressure in patients with neurogenic LUTD [21]. While not a direct measurement, mathematical or machine learning algorithms might be used to model detrusor pressure over time. This will require larger clinical trials to analyze the NIRS signal and find correlation with urodynamic data.

Conclusion

As NIRS has evolved over time, from lasers to LEDs and from studying brains to bladders, it has opened the door to the non-invasive acquisition of urodynamic information over time scales and activities not previously accessible. This article has reviewed the ability of NIRS to measure oxygenation of the bladder and pelvic floor during micturition and identify various LUTD, such as BOO, OAB, UAB, neurogenic LUTD, and IC/BPS. Additionally, this article has described how NIRS is elucidating more about the brain-bladder connection. There have been promising signals in the data, but also key limitations. Most of these studies are limited by small sample sizes without matched controls. Investigators have experienced problems with reproducibility and motion artifacts contaminating the data. There has also been uncertainty in what the signals mean physiologically and what role NIRS will have in the future of urodynamic testing, if any. These issues have dampened enthusiasm and much of the literature is becoming outdated.
NIRS is still not ready for use in routine practice or as a consumer product, but the time is right for some additional attention. The wearable device landscape has exploded in recent years, led by advances in miniaturized hardware, machine learning and data analytics, and further accelerated by the COVID-19 pandemic as remote care has become an increasingly critical part of healthcare [61]. Patients are seeing these devices make diagnostics more accessible and less invasive, trigger more timely intervention, and empower better self-care. NIRS holds potential to do the same for functional urology, enhancing quality of care across a wide range of conditions and uses. However, technological advances will only get us so far without updated, larger-scale studies validating and ensuring correct interpretation of the data. Moreover, multidisciplinary collaboration between clinicians, scientists, engineers, and patient advocates will be critical to further optimize these systems. It is this next phase of work that will determine the role of NIRS in functional urology and if it will fade into obsolescence, act as an adjunct to existing tools, or someday power a new category of wearable, non-invasive urodynamic systems.

Declarations

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Conflict of Interest The authors declare no competing interests.

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Papers of particular interest, published recently, have been highlighted as:

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●● Of major importance

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