VOIDING DYSFUNCTION EVALUATION (B BRUCKER AND B PEYRONNET, SECTION EDITORS)



NIRS: Past, Present, and Future in Functional Urology

Alexander Koven^{1,2} • Sender Herschorn^{1,3}

Accepted: 27 July 2022 / Published online: 11 August 2022 © The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

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. Technological advancements enabling these applications are also discussed.

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

Abbreviations		BOO	Bladder outlet obstruction
NIRS	Near infrared spectroscopy	OAB	Overactive bladder
NIR	Near infrared	UAB	Underactive bladder
Hb	Hemoglobin	IC/BPS	Interstitial cystitis/bladder pain syndrome
O_2Hb	Oxygenated hemoglobin	AUC	Area under the curve
HHb	Deoxygenated hemoglobin	DO	Detrusor overactivity
tHb	Total hemoglobin	fMRI	Functional magnetic resonance imaging
LUTD	Lower urinary tract dysfunction	fNIRS	Functional near infrared spectroscopy
LEDs	Light emitting diodes	DU	Detrusor underactivity
		TSI	Tissue saturation index
		SUI	Stress urinary incontinence
This article is part of the Topical Collection on Voiding Dysfunction		PFMT	Pelvic floor muscle therapy
Evaluation		HbDiff (½RT)	Half-time recovery of hemoglobin

Alexander Koven alexander.koven@mail.utoronto.ca

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.

difference



Department of Surgery, University of Toronto, Toronto, ON, Canada

Institute of Medical Science, University of Toronto, Toronto, ON, Canada

Division of Urology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada

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 (O₂Hb), deoxygenated hemoglobin (HHb), and total hemoglobin (tHb), 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

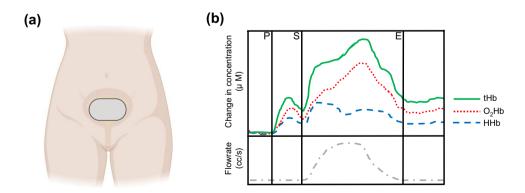


Fig. 1 a Location of a NIRS device for transcutaneous bladder monitoring, positioned on the abdominal skin superior to the pubic symphysis. Created with BioRender.com. **b** An example graph showing NIRS-derived changes in oxygenated, deoxygenated, and total hemo-

globin concentration (O_2 Hb, HHb, tHb) for an asymptomatic subject with simultaneous uroflowmetry, 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 O₂Hb, HHb, and tHb throughout the micturition cycle [4]. They demonstrated a reproducible trend with tHb and O₂Hb 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 O₂Hb even before initiation of the voiding phase and continues to rise in O₂Hb during the "work" of voiding. O₂Hb 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 predominantly 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 urodynamic pressure-flow studies [2]. An initial algorithm by Macnab and Stothers combined NIRS data with maximum flowrate on uroflowmetry and post-void residual to obtain a sensitivity and specificity of 87.7% and 88.9%, respectively [7]. A later version used classification and regression tree analysis with NIRS data alone for a specificity and precision of 88% and 94%, respectively [8••].

Other investigators have tested and produced NIRS-derived algorithms with varying results. Farag et al. developed a model for diagnosing BOO with sensitivity and specificity of 89.3% and 87.5%, respectively [9]. Chung et al. applied an algorithm based on NIRS patterns, maximum flowrate, and post-void residual but did not demonstrate any significant correlation between NIRS and BOO with an area under the curve

(AUC) for diagnosing BOO of 0.484 [10]. This was attributed to issues with reproducibility and reliability of the technology, motion artifacts, sensitivity of their NIRS equipment and using an older algorithm. As of 2012, the group concluded NIRS was "not yet ready for clinical use" [11].

The Overactive Bladder (OAB)

NIRS has been explored as a diagnostic tool for non-neurogenic OAB, "a complex syndrome characterized by urinary urgency, usually with frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other pathology" [12]. In particular, investigators have studied NIRS parameters in patients with evidence of detrusor overactivity (DO), the primary urodynamic abnormality underlying OAB, with the aim of identifying a distinctive NIRS pattern. Vijaya et al. noted a statistically significant rise in HHb in the detrusor with DO, not seen during voluntary voiding (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 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 [15••]. 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_2Hb on bladder NIRS. Detrusor tissue saturation index (TSI), which is O_2Hb as a percentage of tHb, also decreased significantly during episodes of incontinence (mean change in $TSI = -3.9 \pm 2.1\%$, 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_2Hb , 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_2Hb). Conversely, children with LUTD exhibited a blunted or absent increase in tHb and HHb was greater than O_2Hb [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 $(74.2\pm4.9\%$ in IC/BPS vs. $63.6\pm5.5\%$ 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 ($\frac{1}{2}$ RT), 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 ($\frac{1}{2}$ RT) (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, realworld 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

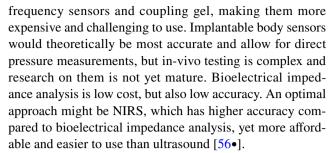
Wearable technologies are projected to change our understanding of basic physiology by obtaining complex, multimodal data over time scales and activities not previously accessible [54]. Light-based sensors, like NIRS, serve as the fundamental mechanism for many of these devices, which currently still 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



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.

References

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

- Of importance
- Of major importance
- Delpy DT, Cope M, van der Zee P, Arridge S, Wray S, Wyatt J. Estimation of optical pathlength through tissue from direct time of flight measurement. Phys Med Biol. 1988;33(12):1433–42. https://doi.org/10.1088/0031-9155/33/12/008.
- Macnab AJ, Shadgan B, Stothers L. The evolution of wireless near infrared spectroscopy applications in urology and rationale for clinical use. J Near Infrared Spec. 2012;20(1):57–73. https:// doi.org/10.1255/jnirs.963.
- Macnab AJ, Gagnon RE, Stothers L. Clinical NIRS of the urinary bladder - a demonstration case report. Spectroscopy. 2005;19(4):207–12.
- Stothers L, Macnab AJ. Near-infrared spectroscopy (NIRS) changes in oxy and deoxyhemoglobin during natural bladder filling and voiding in normal volunteers. J Urol. 2007;177:506.
- Macnab AJ, Stothers L. Receiver operator curves describing near infrared spectroscopy (NIRS) changes during pressure flow studies in men with obstruction. J Urol. 2007;177(4):502–3. https:// doi.org/10.1016/S0022-5347(18)31723-3.

- Koeck I, Burkhard FC, Monastyrskaya K. Activation of common signaling pathways during remodeling of the heart and the bladder. Biochem Pharmacol. 2016;102:7–19. https://doi.org/10.1016/j.bcp.2015.09.012.
- Macnab AJ, Stothers L. Near infrared spectroscopy (NIRS): Validation of bladder-outlet obstruction assessment using noninvasive parameters. Can J Urol. 2008;15(2):4241–8.
- Guevara R, Stothers L, Macnab AJ. Mathematical modeling methodology for generation of a diagnostic algorithm using near-infrared data. Spectroscopy. 2011;25(1):1-11. Applied classification and regression analysis in NIRS monitoring applications to classify patients into those with and without lower urinary tract pathology.
- Farag F, Martens F, D'Hauwers K, Feitz W, Heesakkers JP. Near infrared spectroscopy: a novel non- invasive diagnostic method for detrusor overactivity in patients with overactive bladder symptoms a preliminary and experimental study. Eur Urol Suppl. 2011;10(2):289–90. https://doi.org/10.1016/S1569-9056(11) 60905-6.
- Chung DE, Lee RK, Kaplan SA, Te AE. Concordance of near infrared spectroscopy with pressure flow studies in men with lower urinary tract symptoms. J Urol. 2010;184(6):2434–9. https://doi.org/10.1016/j.juro.2010.08.027.
- Shadgan B, Macnab A, Stothers L. Re: Concordance of near infrared spectroscopy with pressure flow studies in men with lower urinary tract symptoms. J Urol. 2012;187(1):359–61. https://doi.org/10.1016/j.juro.2011.09.022.
- Haylen BT, de Ridder D, Freeman RM, et al. An international urogynecological association (IUGA)/international continence society (ICS) joint report on the terminology for female pelvic floor dysfunction. Neurourol Urodyn. 2010;29(1):4–20. https:// doi.org/10.1002/nau.20798.
- 13. Vijaya G, Digesu GA, Derpapas A, Panayi DC, Fernando R, Khullar V. Changes in detrusor muscle oxygenation during detrusor overactivity contractions. Eur J Obstet Gynecol Reprod Biol. 2012;163(1):104–7. https://doi.org/10.1016/j.ejogrb. 2012.03.030. Investigated changes in O₂Hb and HHb of the bladder wall during voluntary and involuntary detrusor contractions.
- Farag FF, Martens FM, D'Hauwers KW, Feitz WF, Heesakkers JP. Near-infrared spectroscopy: a novel, noninvasive, diagnostic method for detrusor overactivity in patients with overactive bladder Symptoms—A preliminary and experimental study. Eur Urol. 2011;59(5):757–62.
- Mastoroudes H, Giarenis I, Vella M, et al. Use of near infrared spectroscopy as an alternative to videourodynamics to detect detrusor overactivity in women with the overactive bladder syndrome. Urology. 2012;80(3):547–50. https://doi.org/10.1016/j. urology.2012.05.036. Evaluated NIRS for detecting DO in women with OAB.
- Komesu YM, Ketai LH, Mayer AR, Teshiba TM, Rogers RG. Functional MRI of the brain in women with overactive bladder: brain activation during urinary urgency. Female Pelvic Med Reconstr Surg. 2011;17(1):50–4. https://doi.org/10.1097/SPV.0b013e3182065507.
- Griffiths D, Tadic SD. Bladder control, urgency, and urge incontinence: evidence from functional brain imaging. Neurourol Urodyn. 2008;27(6):466–74. https://doi.org/10.1002/nau.20549.
- Mehagnoul-Schipper D, van der Kallen BFW, Colier WNJM, et al. Simultaneous measurements of cerebral oxygenation changes during brain activation by near-infrared spectroscopy and functional magnetic resonance imaging in healthy young and elderly subjects. Hum Brain Mapp. 2002;16(1):14–23. https:// doi.org/10.1002/hbm.10026.
- Macnab AJ, Stothers L, Speich J, Klausner A. Evaluation of cortical neuroexcitation in urinary urgency using simultaneous



- near infrared spectroscopy of the brain and bladder with quantification of sensation. Proceedings Volume 11028, Optical Sensors 2019. Evaluated the use of simultaneous brain fNIRS, bladder NIRS and sensation quantification in the evaluation of OAB
- Chapple CR, Osman NI, Birder L, et al. Terminology report from the international continence society (ICS) working group on underactive bladder (UAB). Neurourol Urodyn. 2018;37(8):2928–31. https://doi.org/10.1002/nau.23701.
- Romai L, Tuzzolo P, Civitella A, et al. Bladder NIRS: a non-invasive method functional to distinguish between detrusor underactivity (DU) and bladder outlet obstruction (BOO), in men with LUTS. Eur Urol. 2020;20:S177–8. Evaluated NIRS for differentiating BOO from DU in men.
- Gajewski JB, Schurch B, Hamid R, et al. An international continence society (ICS) report on the terminology for adult neurogenic lower urinary tract dysfunction (ANLUTD). Neurourol Urodyn. 2018;37(3):1152–61. https://doi.org/10.1002/nau. 23397.
- Gajewski JB, Drake MJ. Neurological lower urinary tract dysfunction essential terminology. Neurourol Urodyn. 2018;37:S25–31. https://doi.org/10.1002/nau.23758.
- Nseyo U, Santiago-Lastra Y. Long-term complications of the neurogenic bladder. Urol Clin North Am. 2017;44:355–66.
- Kavanagh A, Baverstock R, Campeau L, et al. Canadian urological association guideline: Diagnosis, management, and surveillance of neurogenic lower urinary tract dysfunction. Can Urol Assoc J. 2019;13(6):E157–76. https://doi.org/10.5489/cuaj.5912.
- 26. Shadgan B, Macnab A, Nigro M, Stothers L. Monitoring of lower urinary tract function in patients with spinal cord injury using near infrared spectroscopy. Proceedings Volume 8207, Photonic Therapeutics and Diagnostics VIII. 2012. Investigated NIRS for monitoring bladder function in patients with spinal cord injury.
- Kershen RT, Azadzoi KM, Siroky MB. Blood flow, pressure, and compliance in the male human bladder. J Urol. 2002;168(1):121– 5. https://doi.org/10.1016/S0022-5347(05)64843-4.
- Sakakibara R, Tsunoyama K, Takahashi O, et al. Real-time measurement of oxyhemoglobin concentration changes in the frontal micturition area: an fNIRS study. Neurourol Urodyam. 2010;29(5):757–64. https://doi.org/10.1002/nau.20815.
- 29. Sakakibara R, Tateno F, Yano M, Takahashi O, Aiba Y, Yamamoto T. Fesoterodine normalizes the brain function in overactive bladder patients due to central nervous system lesion: a real-time measure of oxyhemoglobin concentration changes during urodynamics. Int J Urol. 2019;26(10):1014–5. https://doi.org/10.1111/iju.14072. Investigated the effect of anticholinergic medication on brain function in OAB patients.
- Sakakibara TF, Yano M, et al. Tolterodine activates the prefrontal cortex during bladder filling in OAB patients: A real-time NIRSurodynamics study. Neurourol Urodynam. 2014;33(7):1110–5.
- Hoebeke P. Voiding dysfunction, recurrent UTI, constipation and vesicoureteric reflux: a common disease complex. Dialog Pediatr Urol. 2002:252–253.
- Afshar K, Shadgan B, Stothers L, Macnab A. Near infrared spectroscopy (NIRS) and altered detrusor oxygen consumption in non-neurogenic lower urinary tract dysfunction in children. J Urol. 2010;183(4):e629. https://doi.org/10.1016/j.juro.2010.02. 1408. Compared changes in NIRS parameters during voiding in asymptomatic controls to children with LUTD.
- Hanno P, Dmochowski R. Status of international consensus on interstitial cystitis/bladder pain syndrome/painful bladder syndrome: 2008 snapshot. Neurourol Urodynam. 2009;28(4):274– 86. https://doi.org/10.1002/nau.20687.

- Cox A, Golda N, Nadeau G, et al. CUA guideline: diagnosis and treatment of interstitial cystitis/bladder pain syndrome. Can Urol Assoc J. 2016;10(5–6):E136–55. https://doi.org/10.5489/cuaj.3786.
- Clemens JQ, Calhoun EA, Litwin MS, et al. A survey of primary care physician practices in the diagnosis and management of women with interstitial cystitis/painful bladder syndrome. Urology. 2010;76(2):323–8. https://doi.org/10.1016/j.urology.2009.12.047.
- Lynes WL, Flynn SD, Shortliffe LD, Stamey TA. The histology of interstitial cystitis. Am J Surg Pathol. 1990;14(10):969–76. https://doi.org/10.1097/00000478-199010000-00011.
- Shadgan B, Stothers L, Macnab AJ. Noninvasive diagnosis of bladder dysfunction in patients with interstitial cystitis/painful bladder syndrome using near infrared spectroscopy. J Urol. 2012;187(4):e935. https://doi.org/10.1016/j.juro.2012.02.2497. Investigated the ability of NIRS to differentiate subjects identified as IC/BPS from other bladder conditions.
- 39. Pang D, Liao L. Abnormal functional connectivity within the prefrontal cortex in interstitial cystitis/bladder pain syndrome (IC/BPS): a pilot study using resting state functional near-infrared spectroscopy (rs-fNIRS). Neurourol Urodyn. 2021;40(6):1634–42. https://doi.org/10.1002/nau.24729. Investigated abnormalities within the prefrontal cortex of patients with IC/BPS based on fNIRS.
- Buchheit M, Ufland P, Haydar B, Laursen PB, Ahmaidi S. Reproducibility and sensitivity of muscle reoxygenation and oxygen uptake recovery kinetics following running exercise in the field. Clin Physiol Funct Imaging. 2011;31(5):337–46. https://doi.org/10.1111/j.1475-097X.2011.01020.x.
- 41. Shadgan B, Stothers L, Macnab AJ. A transvaginal probe for near-infrared spectroscopic monitoring of the bladder detrusor muscle and urethral sphincter. Spectroscopy. 2008;22(6):429–36.
- 42. Macnab AJ, Stothers L. Measurement of exercise treatment effect from pelvic floor muscle therapy for lower urinary tract dysfunction using near infrared spectroscopy. Proc. SPIE 11638, Biophotonics in Exercise Science, Sports Medicine, Health Monitoring Technologies, and Wearables II. March 5, 2021. Evaluated if the effect of PFMT could be detected using NIRS in women with SUI.
- Huppert TJ, Diamond SG, Franceschini MA, Boas DA. HomER: a review of time-series analysis methods for near-infrared spectroscopy of the brain. Appl Opt. 2009;48(10):D280–98. https://doi.org/10.1364/AO.48.00D280.
- 44. Kim C, Lee S, Koh D, Kim B. Development of wireless NIRS system with dynamic removal of motion artifacts. Biomed Eng Lett. 2011;1(4):254–9. https://doi.org/10.1007/s13534-011-0042-7.
- Brigadoi S, Ceccherini L, Cutini S, et al. Motion artifacts in functional near-infrared spectroscopy: a comparison of motion correction techniques applied to real cognitive data. Neuroimage. 2014;85(1):181– 91. https://doi.org/10.1016/j.neuroimage.2013.04.082.
- Yucel MA, Selb J, Boas DA. Targeted principle component analysis: a new motion artifact correction approach for near-infrared spectroscopy. J Innov Opt Heal Sci. 2014;7(2). https://doi.org/10.1142/S1793545813500661.
- Izzetoglu M, Devaraj A, Onaral B. Motion artifact cancellation in NIR spectroscopy using wiener filtering. IEEE T Bio-Med Eng. 2005;52(5):934–8. https://doi.org/10.1109/TBME.2005. 845243.
- Izzetoglu M, Chitrapu P, Onaral B. Motion artifact cancellation in NIR spectroscopy using discrete kalman filtering. Biomed Eng Online. 2010;9. https://doi.org/10.1186/1475-925X-9-16



- Lang M, Guo H, Odegard JE, Burrus CS, Wells RO. Noise reduction using an undecimated discrete wavelet transform. LSP. 1996;3(1):10–2. https://doi.org/10.1109/97.475823.
- Molavi B, Dumont GD, Shadgan B, Macnab AJ. Attenuation of motion artifact in near infrared spectroscopy signals using a wavelet based method. Proc. SPIE. 2011;7890
- Russell-Buckland J, Bale G, de Roever I, Tachtsidis I. ABroAD: a machine learning based approach to detect broadband NIRS artefacts. Oxygen Transport to Tissue XL. 2018:319–324. https://doi.org/10.1007/978-3-319-91287-5_51
- Lee G, Jin SH, An J. Motion artifact correction of multi-measured functional near-infrared spectroscopy signals based on signal reconstruction using an artificial neural network. Sensors (Basel, Switzerland). 2018;18(9):2957. https://doi.org/10.3390/s18092957.
- Kim M, Lee S, Dan I, Tak S. A deep convolutional neural network for estimating hemodynamic response function with reduction of motion artifacts in fNIRS. JNE. 2022;19(1). https://doi.org/10.1088/1741-2552/ac4bfc
- Kim J, Campbell AS, de Ávila BE, Wang J. Wearable biosensors for healthcare monitoring. Nat Biotechnol. 2019;37(4):389–406. https://doi.org/10.1038/s41587-019-0045-y.
- Rwei AY, Lu W, Wu C, et al. A wireless, skin-interfaced biosensor for cerebral hemodynamic monitoring in pediatric care. P Natl Acad Sci USA. 2020;117(50):31674–84. https://doi.org/10.1073/pnas.2019786117.
- Nasrabadi MZ, Tabibi H, Salmani M, Torkashvand M, Zarepour E. A comprehensive survey on non-invasive wearable bladder volume monitoring systems. Med Biol Eng Comput. 2021;59(7–8):1373–402. https://doi.org/10.1007/s11517-021-02395-x. A review of wearable bladder volume monitoring technologies.

- Jeyalakshmi MS. Wearable system design for detecting urinary bladder fullness. Int J Pure Appl Math. 2018;119(15):2183-9.
- Molavi B, Shadgan B, Macnab AJ, Dumont GA. Noninvasive optical monitoring of bladder filling to capacity using a wireless near infrared spectroscopy device. TBCAS. 2014;8(3):325–33. https://doi.org/10.1109/TBCAS.2013. 2272013.
- Fong D, Alcantar AV, Gupta P, Kurzrock E, Ghiasi S. Noninvasive bladder volume sensing for neurogenic bladder dysfunction management. 2018 IEEE 15th International Conference on Wearable and Implantable Body Sensor Networks (BSN). 2018:82–85. https://doi.org/10.1109/BSN.2018.83296 64.
- Fong DD, Yu X, Mao J, et al. Restoring the sense of bladder fullness for spinal cord injury patients. Smart Health. 2018;9–10:12–22.
- Best J. Wearable technology: COVID-19 and the rise of remote clinical monitoring. BMJ. 2021;372:n413. https://doi.org/10. 1136/bmj.n413.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

