Spectroscopy 22 (2008) 429–436
DOI 10.3233/SPE-2008-0367
IOS Press

A transvaginal probe for near infrared spectroscopic monitoring of the bladder detrusor muscle and urethral sphincter

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Abstract. The majority of *in vivo* applications of near infrared spectroscopic (NIRS) monitoring use transcutaneous optode placement over the tissue of interest. Invasive application of optodes is occasionally described for monitoring tissue too deep for transcutaneous study, principally in animal models, but sometimes in humans. Invasive fibre-optic probes have been developed for a range of other spectroscopic applications including some *in vivo*. We describe the design and feasibility testing in a human subject of a vaginal probe to extend the scope of recently developed techniques for NIRS monitoring in urology.

Design criteria included: use of optodes and cables with dimensions compatible with appropriate overall probe size; dual channel capability (for simultaneous monitoring of bladder wall and urethral sphincter); secure interoptode separation at correct distance for required penetration; ease of insertion, orientation and avoidance of movement artifact.

Components were obtained that met design criteria and allowed use of the probe connected to a commercial NIRS instrument. Iterative development established optimal interoptode distance and secure positioning of a probe that could be housed for *in vivo* study within a disposable vaginal speculum.

The feasibility of monitoring changes in chromophore concentration in the bladder detrusor and urethral sphincter using this intravaginal probe was evident from four separate studies during voiding and a series of physiologic events (cough, Valsalva and Kiegel contractions) in a healthy female volunteer. This small series suggests that reproducible data free of movement artifact, with consistent patterns and magnitudes of chromophore change can be obtained with the probe designed.

Keywords: Chromophore concentration, fibre-optic probes, hemodynamics, near infrared spectroscopy, spectroscopic analysis, urology

1. Introduction

The majority of biomedical applications of near infrared spectroscopy (NIRS) use a transcutaneous optode interface for the transmission of photons into tissue and detection of those returning unabsorbed or unscattered in order to monitor change in concentration of the chromophores oxyhemoglobin (O_2Hb), deoxyhemoglobin (HHb), total hemoglobin (tHb) and cytochrome (CCO) [1,2]. The non-invasive nature of a transcutaneous NIRS interface provides many advantages [3], however, the depth of penetration of NIR light is limited to approximately half the interoptode distance [4,5], which restricts such applications to relatively superficial tissue and organs. Consequently, when tissue in deeper locations is to be interrogated with conventional optodes these have to be applied directly to the surface of the tissue of interest, and this is usually done invasively in animal models, or in isolated organs and tissue samples [2]. For this reason, the majority of *in vivo* applications of NIRS continue to use transcutaneous optodes,

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in reflectance mode, and the principal tissues studied are skeletal muscle and the cortical surface of the brain [1–3,6,7].

Recent research has demonstrated the feasibility of using transcutaneous NIRS as an adjunct to diagnostic evaluation of patients with voiding dysfunction [8,9,11]. A suprapubic optode allows changes in chromophore concentration in the bladder detrusor muscle to be monitored during both the bladder filling and voiding cycles. Studies can be done independently or simultaneously with the current invasive urodynamics testing procedures [10]. Changes in NIRS chromophore concentration are evident during voiding that are different in health and disease. Our hypothesis is that bladder pathologies affect the physiology of the detrusor, and that the alterations in muscle thickness, contractility, oxygenation and hemodynamics that result are reflected in the NIRS changes observed. We have also observed synchrony between the changes in chromophore concentration monitored via NIRS and the pressures measured via urodynamic testing during the bladder voiding cycle [11,12]. This finding also suggests a pressure derived effect on bladder function that can be detected via changes in oxygenation and hemodynamics.

There are however limitations to transcutaneous NIRS of the bladder and elements in addition to detrusor health and activity are involved in normal voiding. In patients with a high body mass index (BMI) body fat can increase the distance between the skin and the surface of the detrusor muscle beyond the effective depth of NIR light penetration. In addition adipose tissue increases the tendency for NIR light to scatter [1,13]. Also, for comprehensive evaluation of the urinary tract the ability to monitor the activity of the urethral sphincter can be required, particularly in female subjects prone to stress incontinence. Current methodology using electromyography (EMG) lacks precision as activity in several muscle groups contribute to the signal [14].

For these reasons we developed a fibre-optic probe that could be used within the vagina to interrogate the bladder detrusor and mid-urethra through the anterior vaginal wall.

Invasive applications of many forms of spectroscopy, including NIRS, have been undertaken. Investigators have overcome multiple challenges related to the physics of optical transmission by various materials and through media such as blood, monitoring during surgical operations, and access to remote tissue of interest [2,15,16]. Many successful applications incorporate the required optical elements into fibre-optic probes and Utzinger has reviewed the design characteristics of such probes for use in reflectance, polarized reflectance, fluorescence and Raman spectroscopy [17]. Investigators using NIRS have developed a variety of probes and direct apposition techniques that successfully allow a NIRS emitter and sensor to be introduced invasively to locations where sufficient penetration of photons occurs for the organ of interest to be monitored, or specific tissue to be studied. Applications have included true *in vivo* human studies, *ex vivo* examination of excised human organs or tissue, studies in animal models and prototype development using various phantoms [2].

An intravaginal NIRS probe was first developed in order to monitor the fetal brain during passage of the fetus through the birth canal. Schmidt trialed application of a pair of optical probes to the fetal scalp [18] and then a single probe on the fetal head with the second on the maternal abdomen [19]. Difficulties with probe attachment and movement, and concerns regarding the adequacy of photon penetration limited this research. Probe refinement next used optodes applied on either side of the fetal head in transmission mode [20], but movement remained a limiting factor. Peebles successfully achieved intrapartum measurement of changes in human fetal cerebral hemoglobin during uterine contractions in 8 fetuses using a silicone rubber molding which held the ends of two fibre-optic cables that ended in 2 glass prisms at a constant optode separation against the side of the fetal head within the vagina [21,22]. The interoptode distance used initially was 3 and 3.5 cm latterly. Investigators using a similar intravaginal probe with a 3.5 cm interoptode distance confirmed the observation of changes in fetal cerebral oxygenation

and perfusion during labour [23], and described important variations in relation to late [24], and variable and prolonged fetal heart rate decelerations [25]. Further probe refinement included the use of light suction [22], although intrapartum monitoring remained prone to movement artifact [3,26].

We describe the design, development and clinical feasibility trials of a vaginal probe incorporating a NIRS emitter and dual channel NIRS sensors for monitoring both the bladder detrusor and the urethral sphincter simultaneously in human volunteers using a commercial NIRS instrument.

2. Methods

2.1. Prototype design

A series of prototype probes were developed iteratively based on the following criteria:

- NIRS optode size compatible with inclusion in a compact probe;
- Fibre-optic cable size compatible with dimensions of required probe, adequate light conduction, and ease of use;
- An optical cable interface to connect the probe's optical cables to a commercial NIRS instrument;
- Paired NIRS sensors for monitoring both the bladder detrusor and the urinary sphincter independently;
- Sensor placement in the probe to allow positioning of the bladder sensor deep in the vagina and the sphincter sensor at the mid-urethral point with both sensors monitoring through the anterior vaginal wall;
- Sensor positioning adjustable initially to optimize placement for data collection, but with interoptode distance maintained to avoid data compromise;
- An interoptode distance between emitter and sensor providing appropriate depth penetration to the tissue of interest;
- Probe housing and design compatible with ease of insertion, maintenance of constant position to control movement, hygiene and patient acceptance.

2.2. Construction and development

The sensors and optical cables chosen were developed for research applications by Artinis Medical Technologies, BV, Holland. The size of the emitter and receiver optodes met our specification (3 mm wide, 8 mm long and 4 mm deep), and the fine glass fiber cables were small enough to incorporate into our probe having an external diameter of 2.0 mm. The 1.5 mm solid tip of each cable was then connected to the standard, larger diameter fibre-optic cables of a commercial NIRS instrument via a custom made interface consisting of a plastic block with screw threaded holders. The NIRS instrument, an Oxymon III (Artinis Medical Systems, BV, Holland) [27] generates NIR light in four wavelengths (764, 855, 904 and 975 nm), incorporates a daylight filter to counter interference from ambient light, and has commercial software for conversion of raw optical densities into chromophore concentration and graphic display.

The paired NIRS sensors were configured so that with the probe in position they would appose the bladder detrusor and mid-urethra respectively through the anterior vaginal wall. The emitter was placed mid-way between sensors. Serial adjustments were made; the finalized distances chosen were 1 and 5 cm

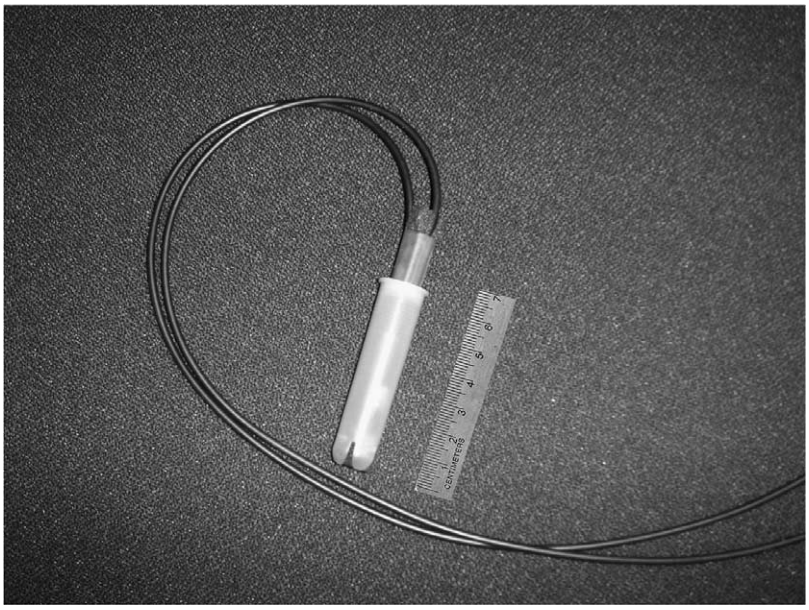

Fig. 1. The initial prototype of the vaginal NIRS probe housed in a plastic tampon cover, showing an early single channel configuration for interrogation of the urethral sphincter (with a single emitter and sensor) and two fibre-optic cables.

from the tip of the probe for the sensors and 3 cm for the emitter. This provided good sampling sensitivity with an interoptode distance of 2 cm. The sensors were laid on high density plastic foam shaped to provide a snug push fit when inserted into the probe housing. This enabled the sensor placement to be held constant during monitoring, but allowed ease of adjustment between studies while the optimal optode positions and interoptode distance were derived.

The housing used in the first iteration of the probe was a plastic tampon cover chosen because of its size and likely acceptance by patients (Fig. 1). This version enabled the subject to insert the probe, and made removal of the foam core and optodes for position adjustments simple. A urologist then optimized the probe position, ensuring that it was in the midline, fully inserted, and oriented so as to direct the sensors at the anterior roof of the vagina. Sensor orientation and correct insertion was aided by a vertical mark on the proximal end of the probe visible to the urologist. Subsequent improvements simplified this process.

The current probe is incorporated into a disposable vaginal speculum made of transparent plastic (Welch Allen, USA) (Fig. 2). Theoretically light piping [7] could allow some light to be transmitted directly from the emitter to the sensors via the clear plastic housing. However, the quality of the data obtained suggests that no extraneous light transmission occurs in our design. The foam insert is cut to position the sensors correctly, and hold them directly against the anterior wall of the housing. In this way they are also correctly aligned when the speculum is inserted and the handle held towards the patient in the midline. This probe is easier to insert and maintain in position than earlier versions. Probably the speculum configuration with an incorporated handle accounts for the lack of movement artifact seen thus far in our feasibility trials. Importantly patients find the design acceptable, and report feeling better able to control the position of this probe following insertion than its predecessor, although all tend to prefer placement by the urologist.

Fig. 2. The current probe housed in a disposable clear plastic vaginal speculum configured for bladder detrusor and mid-urethral monitoring. The emitter and sensors are visible as a small silver square, held in place by a foam insert. The proximal (sphincter) and distal (bladder) sensors and the emitter are attached to the three fine fibre-optic cables. These connect via an optical fibre interface (black block with retaining screws) to standard diameter cables from a NIRS instrument (not shown). The handle of the housing speculum facilitates correct positioning and stabilization during monitoring.

2.3. Feasibility trials

The feasibility of using this vaginal probe for NIRS monitoring, and limited confirmation of the reproducibility of data obtained, was confirmed in a series of measurements made following 8 separate probe insertions in a healthy 67-year-old female volunteer with no history or symptoms of urinary tract disease. With the definitive probe reproducible tracings of change in chromophore concentration (O_2Hb, HHb and tHb) were achieved during spontaneous voiding in all trials attempted. Physiologic events repeated during each trial such as voluntary coughing, Valsalva maneuver, and a series of voluntary pelvic floor contractions each had a characteristic pattern of change. Importantly, there was good reproducibility of the patterns and magnitude of change generated during sequential voluntary pelvic floor contractions in the channel monitoring over the mid-urethra, and an absence of significant movement artifact. An example of one such series of four pelvic floor contractions is shown in Fig. 3. In addition, single probe trials and observations were made in three other asymptomatic female volunteers to confirm the feasibility of using transvaginal NIRS monitoring and make an initial assessment of its acceptability in the context of clinical research.

3. Discussion

We have demonstrated the feasibility of monitoring changes in chromophore concentration in tissue in the bladder detrusor muscle and the mid-urethra (urethral sphincter) via an invasive vaginal probe incorporating the required NIRS sensors and fibre-optic cables.

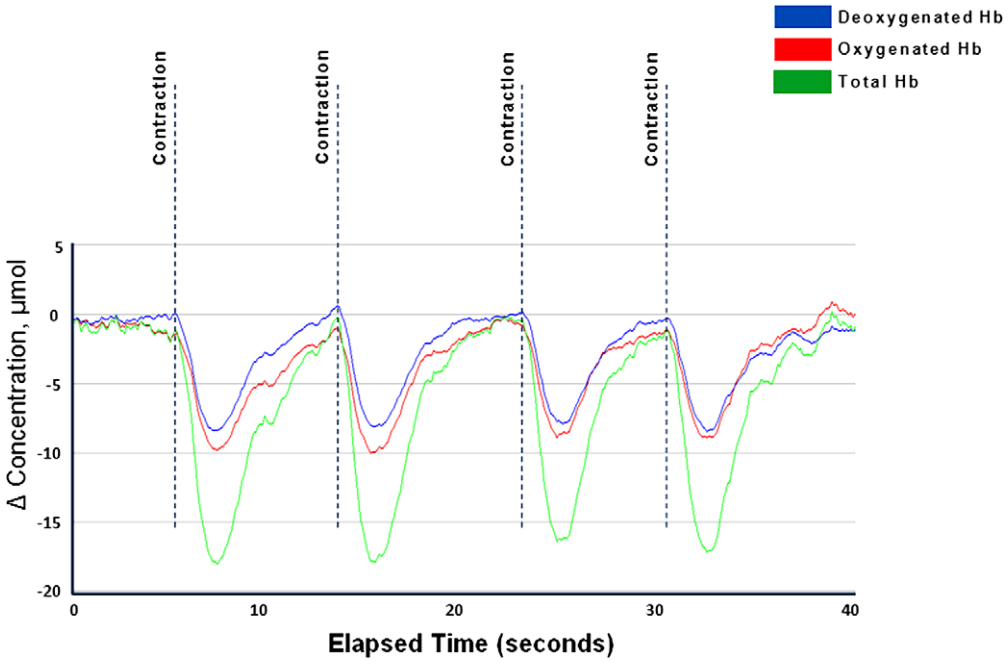

Fig. 3. Representative changes in oxygenated (O_2Hb), deoxygenated (HHb) and total (tHb) hemoglobin during four sequential voluntary pelvic floor contractions using the NIRS vaginal probe prototype.

The probe developed met all the design criteria by providing NIRS monitoring of both sites of interest – the bladder detrusor and mid-urethra – through the anterior vaginal wall; generating reproducible NIRS data during voiding and voluntary physiologic events; being simple to position in the midline and maintain in place so as to avoid movement artifact, and proving acceptable to patients and the urologist collecting the NIRS data. The iterative development process enabled the optimal positioning of the sensors to be established, and confirmed that the method of securing the sensors within the probe by means of a stiff foam insert was reliable. The consistency of the patterns and magnitude of change suggest that the interoptode distance was held constant, as any variation would be expected to corrupt the data collected. Initial design deficiencies were identified, and modifications made that enabled them to be corrected. In particular the shape and size of the tampon cover housing while easy to insert proved difficult to align correctly and maintain in a constant position without movement. In contrast, housing the probe within a disposable vaginal speculum which incorporated a handle made insertion and orientation straightforward for the urologist, and maintenance of the probe in a constant position simple for the patient, while at the same time providing a probe that looked familiar and was acceptable to patients.

The data collected showed promising reproducibility in the patterns and magnitude of change seen in the NIRS data. Although we recognize this reproducibility is limited as our data only comes from a series of eight separate measurements on one volunteer, except for single confirmatory observations in 3 other subjects, and that further trials and validation of our findings are required. However, the trans-vaginal NIRS data collected from the posterior wall of the detrusor muscle during bladder emptying was directly comparable to the patterns of chromophore change seen during transcutaneous monitoring of the anterior wall of the bladder detrusor via a suprapubic sensor in a large series of subjects [8,9,11,12]. Also, the changes in NIRS parameters seen during pelvic floor contractions were particularly consistent by the standards of measurement of other studies of voluntary muscle contractions [28]. There was also a clear

difference between these patterns and those seen on voiding or individual events generated by cough or Valsalva maneuver. In addition, data collected over the detrusor and sphincter respectively were distinct, and were only detected in temporal relationship to voiding or individual events generated by voluntary physiologic activity. The initial impression is that the changes seen during pelvic floor contraction principally reflect a hemodynamic effect, but more studies are required to establish the physiologic nature of the chromophore changes seen. Importantly, in the light of historic difficulties related to movement artifact in NIRS studies of the fetal head made using early intravaginal probe designs [3,26], our data with this probe suggest that it can be maintained in a constant position during monitoring.

By describing the design and rationale for our probe design we hope that other investigators will be able to conduct independent trials, particularly those who are interested in the role of the urinary sphincter in voiding pathology.

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