REVIEW

# Chronic monitoring of bladder volume: a critical review and assessment of measurement methods

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MENDEZ A, SAWAN M. Chronic monitoring of bladder volume: a critical review and assessment of measurement methods. The Canadian Journal of Urology. 2011;18(1):5504-5516.

*Chronic monitoring of bladder volume can improve the clinical diagnosis and the choice of therapeutic approach for patients suffering from urinary dysfunction. It can also be employed to notify patients or healthcare personnel when the bladder should be emptied. An early warning can be triggered either when functional bladder capacity is reached or when an abnormally high postvoiding residual volume remains in the bladder after an unfinished voiding. Currently, neuroprosthetic implants are used in the treatment of refractory patients with overactive bladder, with urgency-frequency or with voiding complications. These implants can further enhance their performance, and also reduce their adverse-effects, by implementing a conditional stimulation based on the ongoing information of bladder volume. In this paper, we review the measurement methods used in past studies, we analyze and assess them, and lastly we pinpoint the one that we consider the optimal one for chronic monitoring of bladder volume.*

**Key Words:** bladder volume, chronic monitoring, conditional stimulation, neuroprosthetic implants, overactive bladder, urgency-frequency, voiding dysfunction

## Background

The bladder functions of storing and voiding urine can fail as a consequence of several causes, ranging from a simple and reversible urinary tract infection to more severe diseases or conditions. Without pretending to write an exhaustive list, we can mention the following:[1-4] prostatic hypertrophy or bladder cancer, spinal cord injury (SCI), strokes and other cerebral vascular incidents (CVIs), neurological diseases (e.g., Parkinson's, multiple sclerosis, Alzheimer's, etc.), arthritis, iatrogenic incontinence (e.g. following radical prostatectomy or hysterectomy), nocturnal enuresis, fistula, neuropathic bladder and nonorganic causes, urethral hypermobility with or without associated pelvic organ prolapse, prostatitis, pharmacologic side effects, weak or damaged pelvic floor muscles or nerves, and neurologic dysfunctions anywhere along the neuraxis from the brain to the spinal cord, or in the peripheral nerves or ganglia. As a result of bladder malfunction owing to any of the above mentioned causes, serious complications in a patient's health and a continuous deterioration in their quality of life will occur.

Chronic monitoring of bladder volume will allow a more suitable clinical diagnosis and a better choice of therapeutic approach. It can also be employed to notify the patients or the healthcare personnel when the bladder should be emptied. This situation can arise either when functional bladder capacity is reached or when an abnormally high postvoiding residual volume remains after an incomplete micturition.

Nowadays, there are alternative therapeutic approaches that are being used in patients that do not respond to, or that do not tolerate conservative

Accepted for publication November 2010

Acknowledgements
The authors would like to thank the Canada Research Chair of Smart Medical Device and the Natural Sciences and Engineering Research Council (NSERC) of Canada and to Le Fonds Québécois de la Recherche sur la nature et les technologies (FQRNT) for their support.

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treatments. These approaches are based on implanted neuroprosthesis that perform electrical stimulation of the lower urinary tract (LUT) nerves. The electrical stimulation of these nerves helps the patients with urge incontinence or abnormal urgency-frequency due to an overactive bladder (OAB), and it can also assist patients with urinary retention owing to non-mechanical obstructions.[5] Some studies published in recent years have proposed different approaches based on the permanent stimulation of LUT nerves.[6-11]

It has been stated that conditional stimulation, i.e. depending on the ongoing bladder state, can improve overall performance and prevent or reduce adverse effects.[12] The conditional stimulation can also decrease the deleterious effects produced by a continuous electrostimulation, for instance, the noxious electrochemical reactions at the electrode-tissue interface and nerve degeneration.[13] Moreover, it has been affirmed that supplying the neurostimulation device with sensorial information could significantly improve the neuroprosthesis effectiveness.[14] In this way, a closed-loop control can be implemented, adding intrinsic auto-regulation advantages, which allows considering the differences of the physiological responses among patients or even in the same patient over time.

Despite the few attempts carried out the last few years, which will be reviewed and analyzed in the next sections, to date, there is no device for a continuous and reliable monitoring of bladder volume.[12]

We found that some physiological and anatomical characteristics of the urinary bladder have been the principal causes that could account for the failure of past attempts. These characteristics will be summarized in the following section. Furthermore, the complexity of the bladder's autonomic and somatic neural system as well as the technical limitations of today's available technology for the chronic monitoring of biological variables, have greatly hindered the development of such a device.

In this paper, we analyze the published studies related to bladder volume measurement, and also we assess several measurement methods, in order to pinpoint the most promising one for chronic monitoring of bladder volume. The analysis was carried out by critically and exhaustively reviewing up-to-date literature from different sources indexed by Medline-PubMed, Compendex, Inspec and Derwent Innovation (patents), as well as the websites of companies that sell neuroprosthetic devices. To ensure, as far as possible, an unbiased analysis of the measuring methods, we used evaluation matrices with weighted criteria that will be briefly described below.

## The anatomical and physiological characteristics of the bladder that challenge chronic monitoring

In the past, many attempts to monitor bladder volume have failed or have not overcome the laboratory boundaries due to difficulties arising from the complexity of bladder anatomy and physiology and the proper decoding of its neural activity. The main difficulties that we found influencing failures in bladder volume monitoring were: 1) the low change in intravesical pressure during filling due to high bladder compliance (viscoelasticity) and wall accommodation (< 10 cm $H_2O$); 2) the substantial changes in the size of the bladder during filling and voiding (~ 75% of surface variation); 3) the irregular shape of the bladder when full due to the influence of the surrounding pelvic organs; 4) the variations in bladder pressure depending on the patient's posture and the influence of many stress conditions, e.g. coughing, sneezing, vomiting, etc.; 5) the chemical properties of urine, e.g. its high corrosiveness, variable conductivity, its high concentration of salts that can adhere to any sensor or device inserted into the vesical lumen, etc.; 6) bladder smooth muscle is less electrically coupled than other smooth muscle and 7) the high complexity of bladder control, partly because the bladder is the only smooth muscle organ driven by both the somatic and the autonomic neural system.

## An exploration of methods used for bladder volume monitoring

The methods that could be used for chronic monitoring of bladder volume will be explored and analyzed in the following paragraphs in order to assess their efficacy in a subsequent analysis.

Most of the *in vivo* studies that will be analyzed below used the typical setup depicted in Figure 1, with roughly similar kind of equipment and accessories. This set up allows mimicking bladder filling and voiding (with known limitations), performing a similar procedure to that used in urodynamic studies.

The procedure usually performed with the setup depicted in Figure 1 consists of injecting saline (NaCl 0.9% at 37$^{o}$ C) into the bladder through one barrel of a double-lumen transurethral catheter. However, in small animal models like rats, a double lumen cannula is inserted through the bladder dome. An infusion pump allows setting up different filling rates (physiological or fast filling) depending on the experiment goals and on the functional bladder capacity of the experimental model (relatively high filling rates generally elicit overactivity). The second

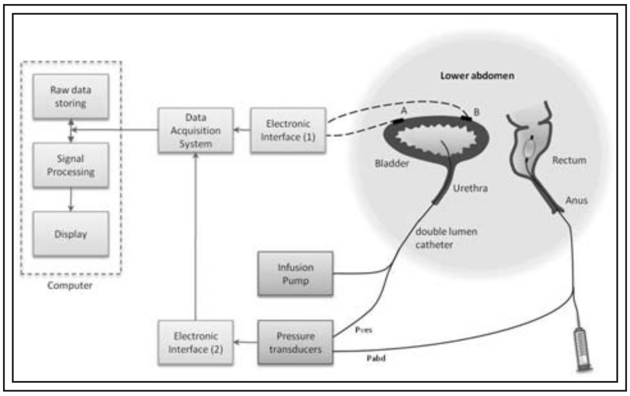


**Figure 1.** Typical set up used for studies of bladder activity. A and B are generic transducer or electrodes located on different parts of the lower abdomen depending on experiment goals.

barrel is connected to a pressure transducer to record simultaneously the intravesical pressure ($P_{ves}$). In some studies the abdominal pressure ($P_{abd}$) can also be measured. To perform this measurement a balloon is inserted into the rectum and connected to a second pressure transducer. This allows determining the pressure exerted by the detrusor ($P_{det}$), because as known, $P_{ves}$ results from the addition of pressures produced by the contraction of the detrusor muscle and the abdominal musculature, i.e. $P_{ves} = P_{abd} + P_{det}$. Thus, $P_{abd}$ measurement allows detecting artifacts produced under several physiological circumstances. In more recent studies, $P_{ves}$ and $P_{abd}$ data have been fed into a computer through a data acquisition system that amplify, filter and convert this data to digital values. Once inside the computer the signal is processed and the results are displayed conveniently.

Depending on the goals of the experiment different types of transducers or electrodes can be used to measure variables such as pressure, displacement, elongation and also images can be obtained using ultrasound transducers. Electrodes, which essentially are ionic to electronic current transducers, are used to inject or to record electrical current, to or from the tissue (bladder wall or nerves). A generic representation of these transducers and electrodes placed on the bladder dome is shown in Figure 1a and 1b. However, their specific location in the lower abdomen varies from study to study. As will be described below, the transducers or the electrodes can be sutured onto the bladder wall, inserted into the vesical lumen or embedded in the submucosal layer. A special type of electrode (cuff-electrode) can be wrapped around the bladder nerves or around the sacral roots to record neural signals produced by bladder distension and contraction. Typically, the ultrasound transducers are externally fixed to the lower abdomen using belts or elastic pants.

Specialized electronic interfaces, see Figure 1 are used to properly drive the transducers or the electrodes and connect them to the computer by means of the data acquisition system. All gathered signals from the transducers and the electrodes are stored in computer memory to be processed on-line and displayed in real-time, or to be further processed off-line using more complex algorithms. Generally, the researcher tries to find out a relationship (correlation) between bladder activity and the signals recorded from the transducers.

### *Intravesical pressure (IVP) measurement*

This method is based on the principle that if we know the value of $P_{ves}$ it could be used to indirectly assess bladder volume. For instance, if we determine in a previous cystometric study the value of $P_{ves}$ along with the volume that elicits a voiding sensation, then we could detect, by mean of an implanted pressure transducer, when the bladder has reached its functional capacity.

Past studies have assessed the feasibility of this approach for monitoring the bladder pressure or volume. However, Westerhof et al showed that bladder pressure variation does not correlate well with the urge sensation.[15] On the other hand, it is known that a detectable pressure increase arises only when a threshold value is reached.[16]

A model proposed by Korkmaz et al[17] allowed describing the stress-strain behavior of the bladder wall during the filling and voiding cycle. By means of this model, and using the data collected from real cystometry and uroflowmetry of different patients, the authors verified that the stress in the bladder wall during the filling and voiding cycle is characterized by a curve with hysteresis, which results from the viscoelastic properties of the bladder. Additionally, they showed that during the filling phase, stress relaxation is the most important issue that accounted for the small increase in the intravesical pressure.

Some experiments performed on dogs in order to track bladder pressure, considering different physiological situations, were carried out by Takayama and coworkers.[18] Pressure transducers were embedded in the submucosal layer of the anterior bladder wall. The authors reported a small increase in intravesical pressure during the bladder filling phase, but they also mentioned that undesirable artifacts produced by animal's movements hindered the extraction of reliable information, which is required to follow the bladder pressure with enough precision.

It has been shown by Koldewijn et al[19] that it is possible to use pressure transducers affixed with non-absorbable sutures in the peritoneal surface of the bladder's dome. However, they reported that the transducers can erode into the vesical lumen or can detach from the wall.

An autonomous monitoring system that measured the intravesical pressure using a capacitive pressure transducer inside the bladder was proposed by Coosemans et al.[20] However, they did not make the packaging for the electronic system required to carry out *in vivo* experiments to evaluate the efficacy of this device in real conditions.

Results from these and other studies confirm that it is difficult to extract volume information from the intravesical pressure, but Jezernik et al.[13] showed that it is possible to spot onset bladder contractions detecting a sudden increase in $P_{ves}$. However, the $P_{ves}$ variation is also produced by stress conditions such as on voiding, coughing, defecating, vomiting and postural changes between the standing and sitting position, etc.[18] These conditions can produce false positives if they are not detected.

### *Electrical impedance plethysmography (EIP)*

Plethysmography is a method for measuring volume changes in specific parts of the body or of the whole body. There are three types of plethysmographic techniques: 1) volume displacement using air or water outside the body; 2) measurement of the electrical impedance or admittance of a body part (bioimpedance); and 3) image plethysmography using x-rays, ultrasound or MRI. The volume displacement technique seems to be impractical for bladder monitoring purposes. A type of image plethysmography, i.e. wearable ultrasonography, will be described later.

Electrical impedance plethysmography (EIP) is typically carried out by injecting a controlled AC current into the tissue. This current passing through the tissue produces a voltage drop between the electrodes (generally one or two pair) placed on the lower abdomen skin or directly on the organ. This voltage can be measured using a specialized amplifier. Then, it is possible to calculate the tissue bioimpedance, since the values of the injected AC current and the voltage drop are known.[21]

Over the last few decades, several studies used EIP for assessing bladder volume. Some of them were focused in whole body impedance measurement while others in bladder impedance measurement. The hypothesis underlying these studies states that there is a correlation between bladder bioimpedance and the volume of urine stored. Nevertheless, the published results are quite controversial, as will be shown below.

The feasibility of the direct impedance measurement method to assess bladder volume was tested by Waltz et al.[22] The authors found a linear relationship between bladder volume and the impedance recorded with an implanted device, using two electrodes attached to a dog's bladder. The measured sensitivity was 7 Ohms per 100 mL. The reproducibility and the long term stability of the method were not reported in this study.

Other researchers have used EIP for measuring bladder volume in a non-invasive way. Denniston and Baker[23] also found a linear relationship between bladder volume and bioimpedance measurements, but using spot (snap) electrodes on the abdomen skin of anesthetized dogs. They described the advantages of a new arrangement of the spot electrodes placed nearer to the bladder boundaries. These authors also reported a linear response but with a lower sensitivity (0.7 Ohms per 100 mL). Similar results were reported by Doyle and Hill,[24] but conducting experiments in humans, which showed a linear response but with even a lower sensitivity (0.1 Ohms per 100 mL).

A comprehensive research using this approach was carried out by Abbey and Close.[25] They conducted studies in men and women (two groups of 20 patients) for measuring several variables simultaneously, using four spot electrodes with the patients resting in the supine position. Their results showed a weak relationship between the impedance and bladder volume during the bladder filling and voiding phases. However, the results were greatly influenced by some patients' specific factors and their sex; in both men and women, the baseline impedance was influenced by the skin surface and by the skin fold thickness, but in women, this baseline also correlated with the time since the last menstrual period (oestrous cycle). Nevertheless, they did not report any results concerning the accuracy of the method used for bladder volume measurement.

Other studies focused their efforts in the detection of bladder fullness. Yamada et al[26] worked on a device for detecting bladder fullness using a pair of spot electrodes placed on the surface of both femoral joints, and another pair near the bladder area. They concluded that a remarkable stability and reproducibility can be achieved using specially designed electrodes placed in those places to detect the urge threshold. However, in their experiments and subsequent analysis they did not consider known issues mentioned in other studies,[25,27] which could interfere with or modify the results.

The electrical impedance tomography (EIT) technique, which produces images from bioimpedance measurements, has also been used for measuring bladder volume. In a study conducted by Hua et al[28] an array of 48 surface electrodes and a two-dimensional computer model was used to display a finite element image of the bladder. This study aimed to show the feasibility of this technique; however, no result was found concerning the effectiveness of the proposed method.

A device based on bioimpedance measurement to estimate bladder volume was proposed by Provost et al.[29] This device was designed to provide feedback to an implantable electrical stimulator[30] intended to drive a neurogenic bladder. The device tried to detect when the urge volume threshold was attained. The authors showed interesting results from the analysis of their measurements using four pairs of electrodes placed on dog's bladder. However, since then they foresaw difficulties in correctly assessing this threshold during the *in vivo* experiments, due to the changes in urine conductivity and the zeroing problems that arose from residual volume. In fact, those issues are still some of the hardest to be addressed by this technique. On the other hand, it is known that bladder smooth muscle is less electrically coupled than other smooth muscles,[31] which could hinder the accuracy of the bioimpedance measurements of the bladder.

In another study carried out by Kim et al[32] in 13 patients with SCI, using surface electrodes placed on the lower abdomen, additional limitations of this method for detecting small changes in bladder volume in long-term measurements were shown. The major limitations found were the influence of body fat and the interference arising from fluid and fecal movements as well as fecal accumulation in the bowels.

A more recent study executed by Keshtkar et al[33] assessed the relationship between the measured bioimpedance and the bladder volume, in *ex vivo* and *in vivo* experiments, using urine-like solutions with different conductivity that could affect the measurements. They concluded that the bladder tissue bioimpedance decreased when it was stretched and all mucosal folds became flattened. The authors also showed that at lower frequencies, the measured impedance increased with bladder volume, i.e. an opposite sign slope. Moreover, an insignificant, weak relationship was found.

A comprehensive study conducted by Gill et al[27] also assessed the feasibility of fluid conductance for measuring bladder volume. Several *in vitro* experiments were developed using four electrodes, latex vessels and bladders excised from pigs, filled with a urine-like saline solution at different temperatures and concentrations. The authors showed that the conductance increased with temperature and concentration but was different for each pair of these variables, except at low concentrations where this relationship was no longer valid. They also showed that the measured conductance was determined by the fluid conductivity, and lastly, that the conductance increased linearly at low volume but approached asymptotically to the high values. Therefore, in order to use this method in practical applications, the authors suggested that it required a real-time compensation of the fluid conductivity for the dynamically varying properties of urine and also an improvement in sensitivity.

As seen above, the EIP has been one of the most used measurement method for monitoring bladder volume by means of electrodes placed on the lower abdomen skin or on the bladder wall, with a preference for the former. Some authors showed the feasibility of using the EIP method to estimate bladder volume, while others have shown that, despite the fact that it is barely possible to correlate bladder bioimpedance with volume, several issues must be addressed in order to use this method for reliably estimating bladder volume. Moreover, electrodes placed on the bladder, continuously exciting the tissue with a current (required for the bioimpedance measurement), can lead to permanent damage and induce changes in the physiological behavior of the bladder wall. Additionally, electrode migration toward the bladder lumen or electrode detachment is possible. Thus, we can state that none of the studies reviewed implementing EIP demonstrated any effective solution for the chronic monitoring of bladder volume.

### *Strain-gauge plethysmography (SGP)*

This method uses transducers that change their impedance or their electrical charge pursuant to the modification of the shape produced by external forces. The measuring principle of these transducers can either be resistive, capacitive, inductive or piezoelectric. Specifically, for this application, the elongation or the contraction of the transducer placed on the bladder will generate a variation in the impedance or in the charge (piezoelectric case). This variation can be measured by a proper electronic circuit (e.g. a bridge or a charge amplifier), then translated into distance, and lastly into volume units.

Few studies using this approach have been published, even if this could be one of the most interesting principles for a reliable monitoring of bladder activity and volume. In fact, this principle is based on the direct measurement of a primary variable, i.e. the bladder distension/contraction. Therefore, these measurements should correlate well enough with bladder activity and volume and not be dependent on the patient's health condition.

We can speculate and say that the small number of studies with this approach might be related to unsuccessful attempts in the past, mainly as consequence of the low reproducibility and the low stability of measurement achieved using this approach, as will be shown below.

An interesting concept using this approach was proposed by Rajagopalan et al.[34] They measured the changes in electrical resistivity of a polypyrrole (a polymer) deposed on a highly elastic fabric used like a pouch covering the bladder. Their results showed that when the fabric with the impregnated polymer was stretched, it produced a linear resistivity change in a range of 20%-40%. The *in vitro* experiments, carried out in a phantom bladder, showed the feasibility of using such a sensor to measure bladder volume, displaying some advantages inherent to the concept. However, some fabrication issues should be solved in order to use this sensor in long-term measurements, because after few days its sensitivity became null. On the other hand, no *in vivo* experiment was performed with the goal of assessing the conductivity, the accuracy, the reproducibility, the stability and the biocompatibility under real conditions.

A patented sensor for measuring changes in any anatomical part, but especially designed for the mammalian bladder, was proposed by Upfal et al.[35] The transducers were made of a silicone elastomeric sheath containing a pair of helically coiled conductive wires. The limited results published in the patent application are not enough to assess the effectiveness of this device. Moreover, an analysis of the known issues affecting this method was omitted. We did not find any additional related studies, either from these authors or from the company that owns the patent.

In order to meet the requirements of chronic monitoring, the materials used for covering and supporting the sensor on the bladder wall should be soft and elastic. These properties allow the transducer to follow the large changes of the bladder's surface during its distension and contraction, but without overloading it. In fact, an increase in the effort required to stretch the bladder wall could substantially affect the measurements, and also overall bladder behavior, particularly in overactive bladders. Additionally, the material should fit the irregular shape of the bladder properly, have high endurance and also be biocompatible. These material requirements, and the intrinsic invasiveness of this method, are identified as the major issues to be addressed in order to use this method in practical applications.

### *Wearable ultrasonography (WUS)*

Ultrasound or ultrasonography is a well-known medical imaging technique that uses sound waves of high frequency and its echoes for determining tissue boundaries by means of image processing algorithms. This technique produces animated two dimensional or three dimensional, black and white or color images. Ultrasonography has become a useful non-invasive method for measuring bladder volume. Currently, it is a common method for measuring postvoid residual urine (PVR). It is an alternative to indwelling catheterization, the most accurate and the gold standard technique but with known adverse effects.

Whereas a standard ultrasound machine with the appropriate software can be used to assess bladder volume, a new type of specialized portable machine today is widely used (e.g. Bladder Scanner series from Verathon Medical Inc., Washington, USA). This machine helps in the clinical surveillance of patients suffering from urinary dysfunctions.

The above mentioned devices cannot be considered wearable, which is a must for chronic monitoring of the bladder. By definition, a wearable device should be very easy to wear, thus a wearable device for measuring bladder volume should be lightweight, smaller, and more ergonomic than a portable one.

A few studies have used the ultrasound technique for continuously monitoring bladder volume by means of a wearable device. Petrican et al[36] proposed a miniaturized ultrasonic bladder volume monitor for children with enuresis. The aim of this device was to alert the patient when the urge threshold was reached during the night. The device was affixed to a belt fastened around the patient's lower abdomen. It was tested in 41 patients showing more than 70% accuracy in determining volume under well controlled conditions. However, a number of shortcomings were found during the testing phase in obese patients, in patients that had undergone abdominal surgery, or were sitting, constipated or had liquid stools. Improved solutions were suggested by the authors based on the use of an array of ultrasound cells affixed to elastic pants that fit the patient better.

These suggestions were taken by Beauchamp et al,[37] who reported that a clinical evaluation carried out in ambulatory patients showed only 40% success. They also mentioned measuring problems arising from even slight changes in probe orientation, which caused artifacts that incorrectly triggered the alert. In a new study,[37] the same authors were seeking a device for preventing bed-wetting, i.e. for alerting enuretic patients before and not after the micturition. The device showed good results in phantom bladder testing, but no clinical trial was carried out to test the measurement robustness.

Kristiansen et al[38] also proposed a similar solution with the same goal. They designed a wearable ultrasonic bladder volume monitor that used 7 phased-array ultrasonic transducers in a circular pattern device. The data collected was sent wirelessly (through a Bluetooth channel) to a portable computer for further processing. They reported good results with their *in vitro* test using a prototype apparatus and a phantom bladder. The measurements showed a mean absolute error of 2.9%, good reproducibility; low drift over time and with temperature and a good correlation versus a volume estimation obtained by MRI. Despite the good results shown under well controlled conditions, none of the intrinsic limitations of this method mentioned above (Petrican et al),[36] were analyzed.

As has been seen so far, the results yielded by this method are greatly affected by the patient's conditions and have only been shown to be effective under well controlled conditions. On the other hand, bladder activity monitoring is more complicated using this method, owing to the small, rapid variations that must be detected by the data processing algorithms. Moreover, the image processing requires a powerful computer for executing the complex algorithms in real-time and for displaying the measured volume. Therefore, for this method to have a practical application in chronic bladder monitoring, an improvement in measurement robustness as well as in the ergonomics issues is required.

### *Electroneurographic (ENG) signal recording and processing*

This method uses information gathered from the bladder's natural sensors (mechanoreceptors) for monitoring its activity. Several studies have shown the presence of mechanoreceptors that respond to the bladder distension and contraction and others that respond, more specifically, to bladder volume.[39,40] The sensorial information produced by these mechanoreceptors during the filling and voiding cycle, coded as action potential firing frequency, is carried by the bladder's afferent nerves (i.e. the pelvic, hypogastric and pudendal nerves). These nerves are part of the complex organization of sympathetic, parasympathetic, and somatic pathways of the pelvis nerves shown in Figure 2. The recording of this neural activity is known as an electroneurogram (ENG).

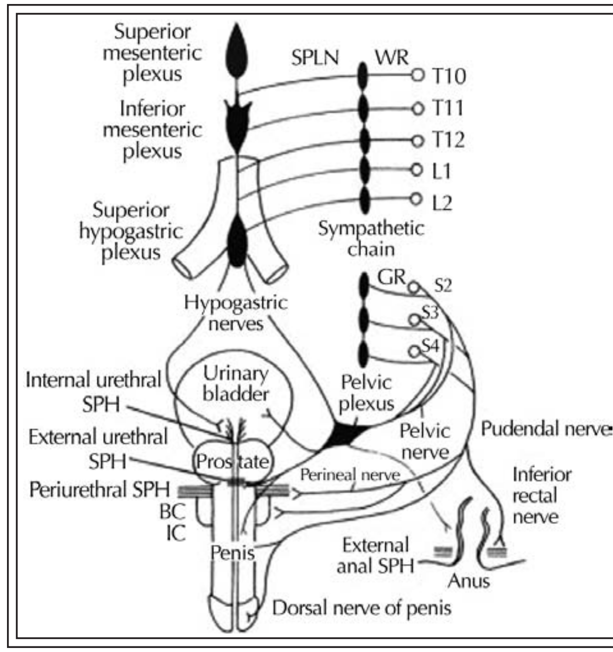


**Figure 2.** Neural pathways of the pelvis showing the afferent nerves commonly used the ENG recordings (see text). SPLN = splanchnic nerves; GR = gray rami; WR = white rami; BC = bulbocavernosus muscle; IC = ischiocavernosus muscle; SPH = sphincter. From[3] with permission from John Wiley and Sons.

The ENG signal arises from the superimposed or compounded action potentials (CAPs) of several firing units present in the nerve.

The recorded ENG signal is processed using algorithms with different degrees of complexity depending on the application. The most common ENG processing method is the signal averaging and low-pass filtering, which is technically known as rectifying and bin integration (RBI). This method allows one to extract rough sensorial information from the ENG amplitude envelope.[41] The sensing interface most commonly used in this type of recording has been the tripolar cuff-electrodes. These electrodes are formed by three rings of metal (platinum or stainless steel) supported by a cylindrical cuff generally made of silicone or its derivatives.[42]

The RBI has shown to be a feasible and quite robust technique for detecting onset bladder contractions using tripolar cuff-electrodes wrapped around pelvic nerve and sacral roots,[13,43-46] albeit it has been less effective at the pudendal nerve.[46] The application of different detection algorithms such as the constant threshold, the adaptable (variable) threshold and the cumulative sums (CUSUM),[46,47] have allowed detecting the sudden increase of $P_{ves}$ due to a detrusor contraction.

A few studies have been conducted with the main goal of establishing whether it is possible to extract volume information from the ENG recorded from the afferent bladder nerves. A preliminary study performed by Harb et al[48] recorded the ENG using tripolar cuff-electrodes on the sacral roots (S2) in dogs with the spinal cord transected at the supralumbar level. The authors, using the RBI technique, showed an increase in S2 neural activity in dogs during the bladder filling, with some lag explained either by a volume threshold required to trigger nerve activity or by a delayed bladder response to filling.

The feasibility of bladder activity monitoring from ENG activity was assessed by Jezernik and coworkers in acute experiments performed in pigs.[43] They showed the possibility of recording bladder afferent activity by mean of tripolar cuff-electrodes placed on the pelvic nerve and on the sacral root S3. Their results revealed that bladder response was more phasic than tonic, since the recorded activity was higher during fast filling or during detrusor contraction than during isovolumetric volume measurements or slow filling. This behavior was considered good for detecting bladder contraction (e.g. overactivity) but it was considered bad for detecting bladder fullness.

A study carried out by Sinkjaer et al[45] in one human patient with a suprasacral SCI also showed that passive filling and bladder contraction activity can be detected from the ENG of the sacral dorsal root S3 using tripolar cuff-electrodes.

A comprehensive study performed in cats by Jezernik et al[13] stated that monitoring the bladder fullness (volume) directly from cuff recordings of the sacral root S1, using the RBI technique, was not feasible. However, the authors suggested that maybe it was possible by measuring the time elapsed between reflex contractions in overactive bladders. Nevertheless, the single result shown is not enough to confirm this. Moreover, they commented on the limitations of the cuff-electrode recordings in achieving higher signal levels, a better signal to noise ratio (SNR) and also the shortcomings due to the low selectiveness of sacral root recordings. As was mentioned above, these signals arise from the superposition of the efferent and afferent activity from the bladder, rectum and dermatomes. Therefore, they suggested that recording of the pelvic nerve activity could improve the selectiveness, eliminating some interference from visceral and dermatome activity. However, the long term effects of placing cuff-electrodes on the pelvic nerve have not yet been assessed.

Another important study carried out in human patients with SCI, was performed by Kurstjens et al.[44] The authors investigated the afferent activity of the bladder, the rectum and the skin (dermatomes), performing intraoperative recording of the ENG elicited by these sources in the extradural sacral root S3. They showed the feasibility of performing these recordings in humans using cuff-electrodes and confirmed or questioned some previous published results. For instance, the authors confirmed that the ENG signal recorded using tripolar cuff-electrodes was influenced by the number of fibers, by the diameter, and by the proximity of the firing axons to the electrode surface. They found that skin responses were larger than those from the bladder and the rectum, depending on the type of conducting fibers. The authors also showed that during bladder filling, both the phasic and the tonic responses were elicited. Conversely, Jezernik et al[43] observed mainly phasic responses in animal models, as was mentioned above. In fact, Kurstjens and coworkers questioned the extension of this conclusion to humans, based on the tonic response that they recorded for $P_{ves}$ over 40 cm $H_2O$. However, this is not sufficiently supported in their publication, and a final conclusion similar to that given by the Jezernik et al[43] was stated, favoring the detection of bladder contraction based on the phasic nature of neural response. Lastly, they considered difficult to monitor bladder volume from the ENG recordings of the sacral roots S3 using tripolar cuff-electrodes.

More recently Saleh et al[49] published an interesting acute study performed in anesthetized dogs. They proposed a method that recorded the voltage drop ($V_{out}$) across a section of the extradural sacral root S2 when a sinusoidal constant low current (4 µA p-p, 30 Hz) was applied to it by means of a tripolar cuff-electrode. The authors reported a correlation between bladder volume and the $V_{out}$ amplitude recorded, which can be roughly observed in some graphic results. However, no analysis of the specificity of the processed signal was presented. Lastly, the authors stated the feasibility of bladder volume measurement based on recorded nerve activity when a sinusoidal current was applied to the S2 sacral root. Even so, more exhaustive analysis and experiments should be done to test the robustness of the proposed method.

None of the above reviewed studies have shown robust results demonstrating the feasibility of bladder volume monitoring from ENG recordings. In fact, there are few published studies whose principal goal was the detection of bladder volume from the ENG recording, while in other related studies this feasibility was marginally analyzed. Some possible shortcomings could be identified, e.g. inaccuracies in the methodology used and in the analysis of the results. For instance, in some acute experiments performed with anaesthetized animals the spinal cord was transected at a supralumbar level to produce a SCI, and immediately the researchers started the recordings of the ENG activity in the targeted nerve.

It is known that after a spinal cord trauma (i.e. SCI) a spinal shock period will arise. This period is characterized by motor paralysis, by a loss of sensation and the by the abrupt disruption of the reflex pathways, which lead to a condition of hyporeflexia or areflexia.[50] It might take 3 to 4 weeks on average to recover some reflexes, depending on the SCI site and its extension. Thus, the information recorded during the spinal shock period could yield misleading results. Moreover, some studies reviewed did not establish either the specificity of the measured signal or the identification of animal's physiological conditions (e.g. bladder compliance), which could greatly influence the results.

Furthermore, very low levels of ENG signals (under 10 μV) should be detected to measure the amplitude variation in the processed signal. However, it was shown that recordings performed using tripolar cuff-electrodes feature a low signal to noise ratio. The measurements are also affected by the low selectiveness of sacral root recordings using tripolar cuff-electrodes, because they result from superimposed action potentials of efferent and afferent nerves from different viscera and dermatomes. This hinders the extraction of bladder information because the signal produced by the bladder afferents is the weakest. Consequently, the low selectiveness of the recording could lead to erroneous signal interpretation.

Recent studies have shown that it is possible to improve the quality and the selectiveness of the ENG recording of the peripheral neural system using different types of multicontact electrodes[51] and more complex processing algorithms.[52-54] Therefore, the ENG recording method requires more in depth research to determine whether it is suitable for bladder volume monitoring using other electrodes and processing techniques.

### *Electromagnetic plethysmography (EMP)*

The measurement of the distance between points by means of Hall Effect crystals sutured onto the bladder wall was used to estimate topographical bladder movement during isovolumetric reflex activity. The approach correlated the distance with changes in magnetic flux emanated from a permanent magnet also affixed in the bladder wall and then sensed by nearby Hall Effect transducers. This set up was used by Woltjen et al[55] for monitoring bladder activity during isovolumetric reflexive contraction in cats and dogs. They measured a displacement between the Hall Effect transducer and the permanent magnet with a precision error in a range of 0.5 mm to 3 mm and the speed of contractions was estimated in a range of 2 cm to 4 cm. These results could be useful for bladder volume monitoring, if it is possible to establish a correlation between the measured distances and bladder volume. However, the authors did not report any results concerning bladder volume measurement.

A more recent implementation of this measurement principle was carried out in dogs by Wang et al.[56] A permanent magnet sutured onto the anterior bladder wall was magnetically coupled to an external warning unit sutured onto the inferior abdominal wall. The external unit contained a compass-like switch that triggered a buzzer when the magnet movement showed that the volume had reached the programmed threshold. This method has been reported by the authors to be effective under very well controlled lab conditions, but no test in humans has been published to prove its efficacy, or patient's tolerance or comfort. Moreover, robustness is a pending issue because the positioning of the magnet on the bladder wall and the sensor in the reading unit is critical. Thus, any relative displacement between them will yield wrong results.

In general, this measurement method, as well as others mentioned above, still has major issues to be addressed; i.e. the long term stability of fixing the sensor to the bladder wall. As was shown,[19] any sensor or electrode affixed to bladder wall can detach or migrate toward the bladder lumen. Therefore, for long term or chronic monitoring, an improvement in the method for fixation to the bladder wall is required.

Once this issue is resolved (a hard task), another interesting and potentially effective method could be applied to monitoring bladder volume; i.e. sonomicrometry. This technique uses several tiny piezoelectric crystal sensors attached or embedded in an organ (e.g. the cardiac muscle) forming a network. One crystal sends an ultrasound wave that is detected later by another crystal. The time elapsed between the emission and the reception of the ultrasound wave can be related to the distances between the crystals. Properly calibrating the system and using the information from all of the crystals in the network, it is possible to measure several mechanical variables such as the volume, the pressure, and the speed of the distension or contraction, etc. Currently, this method is considered the gold standard for the measurement of mechanical cardiac variables in acute studies,[57] because of its accuracy and reproducibility. It has been proposed for use in Medtronic pacemakers to improve their performance, according to a patent owned by the company.[58]

## Assessment of the measurement methods

In order to assess the methods described above and to pinpoint the one with the greatest promise to succeed in chronic monitoring of bladder volume it is necessary to define some evaluation criteria, then assign a weight to them and lastly to evaluate each measurement method accordingly. This evaluation methodology allows quantitative analysis to select the optimum method more objectively than, for instance, pros versus cons, thereby overcoming the most evident bias always present in the researcher, his analysis and his preferences.

The International Continence Society (ICS) has published some standards[59,60] for the measurement of volume and pressure of the bladder, which could be used as references during this evaluation process. However, it must be taken into account that these standards have been suggested for urodynamic equipment used in the diagnostic of LUT diseases, for non-chronic applications under very well controlled conditions. Consequently, the ICS standards could hardly be met by such a type of chronic monitoring device, considering the limitations of both medical knowledge and technological feasibility. On the other hand, it is known that monitoring devices do not always have to meet the same specifications that diagnostic devices do (commonly less demanding), because the clinical purpose and the operating conditions are often quite different.

The following evaluation criteria have been established from the analysis of the measurement methods for chronic monitoring of bladder volume:
- Effectiveness in chronic use;
- Ease of implantation (minimally invasive);
- Reproducibility of volume measurements;
- Immunity to postural changes, urge stress, urine conductivity, temperature, and other artifacts;
- Detection of bladder overactivity;
- Safety in use with minimal deleterious effects;
- Accuracy of volume measurements (more important for diagnostic than for monitoring);
- Ease of set-up, calibration, and adjustment to the patient's particularities;
- Low power consumption (from a battery);
- Availability and cost of materials and components required for its implementation.

An analysis based on an evaluation matrix was carried out to pinpoint the monitoring method that best meets the criteria mentioned above. The results of this analysis are shown in Table 1 and the computation of the scores was performed as described below.

TABLE 1. **Assessment result**

| | Measurement method | | | | | |
|---|---|---|---|---|---|---|
| **Selection criteria** | **IVP** | **EIP** | **SGP** | **WUS** | **EMP** | **ENG** |
| Effectiveness in chronic use | 0.2 | 0.2 | 0.3 | 0.3 | 0.4 | 0.5 |
| Immunity to postural changes, urge stress, urine conductivity and temperature and other artifacts | 0.1 | 0.1 | 0.4 | 0.2 | 0.2 | 0.4 |
| Ease of calibration and adjustment to the patient's particularities | 0.2 | 0.2 | 0.1 | 0.2 | 0.1 | 0.2 |
| Ease of implantation (minimally invasive) | 0.4 | 0.4 | 0.2 | 0.6 | 0.4 | 0.5 |
| Safety in use with minimal deleterious effects | 0.4 | 0.1 | 0.4 | 0.6 | 0.5 | 0.5 |
| Efficacy of volume measurement (accuracy) | 0.1 | 0.2 | 0.4 | 0.3 | 0.3 | 0.2 |
| Precision of volume measurement (reproducibility) | 0.1 | 0.2 | 0.6 | 0.5 | 0.5 | 0.4 |
| Detection of bladder overactivity | 0.5 | 0.3 | 0.5 | 0.4 | 0.3 | 0.4 |
| Low power consumption | 0.3 | 0.2 | 0.1 | 0.2 | 0.5 | 0.5 |
| Availability and cost of materials and components | 0.4 | 0.5 | 0.1 | 0.4 | 0.4 | 0.4 |
| **Total score** (over 5) | 2.7 | 2.4 | 3.1 | 3.7 | 3.5 | 3.9 |
| **Score percentage** | 53% | 49% | 62% | 75% | 70% | 77% |
| **Rank** | 5 | 6 | 4 | 2 | 3 | 1 |

IVP = indirect volume measurement from intravesical pressure; EIP = electrical impedance plethysmography; SGP = strain-gauge plethysmography; WUS = wearable ultrasonography; EMP = electromagnetic plethysmography; ENG = electroneurographics recordings

To rate each method, we employed a qualitative scale ranging from 1 to 5 (very poor, poor, passable, good and very good). Consequently, the final score is given on this scale as well as a total percentage. The methods were rated from 1 to 5 for each individual criterion. Then, each method's rate was multiplied by the weight assigned to the criterion. To ensure that the selection of the optimum method was robust enough, i.e. less dependent on small weighting variations, five sets of appropriate weights were used. The final score, which appears in the cells of Table 1, was calculated averaging the score for each set while keeping the rate given to each method. Lastly, the total score for the measurement method is the sum of each rate (column sum). Note that for the sake of simplicity only the final score obtained using this procedure is shown in Table 1.

Considering its consistency throughout the analysis, the recording of the ENG afferent activity of the bladder mechanoreceptors has been identified as the chronic bladder volume monitoring method that best satisfies the evaluation criteria defined in this paper.

## Discussion

Knowing and understanding the anatomy, the physiology and the neural control of LUT is essential to accomplishing any successful work in bladder monitoring. We found that some studies overlooked very important elements of bladder physiology, which either were ignored at the time of publication or perhaps were considered irrelevant. It might happen that the eagerness to quickly get results sometimes leads the researchers to skip over essential steps.

For monitoring bladder volume, two types of sensing options have been used; those based on artificial sensors (pressure, displacement, ultrasound, etc.) or those that use the natural sensors present in the bladder wall (mechanoreceptors). The information gathered from the artificial bladder sensors is more independent of the patient's condition, so it can be more reproducible over time in the same patient and among different patients. Furthermore, accuracy could potentially be higher than that provided by natural receptors. Major drawbacks are the decreasing reliability over a long period of time, a higher degree of invasiveness, the problems arising from their location within the lower abdomen on or near a moving organ, and the biocompatibility of the materials employed. On the other hand, the information gathered from natural mechanoreceptors is more reliable, the implantation procedure of the neuroprosthesis is less invasive and the cuff-electrodes used as interfaces for ENG recordings are well tolerated in chronic applications.[14] However, in the pathologic bladders of patients with SCI and other neural conditions, bladder cancer, cystitis, etc., the information collected from mechanoreceptors could be misleading. Additionally, the selectiveness and the signal to noise ratio of recorded ENG signal using tripolar cuff-electrodes are still pending issues.

Analyzing the results of the studies reviewed concerning bladder volume monitoring, it can be stated that the sensorial information produced by the bladder mechanoreceptors is rather more related to the detection of bladder fullness and pain than of a specific volume, particularly when $P_{ves}$ is below the threshold value.

The firing frequency of the tension mechanoreceptors increases during bladder distension, but a relatively rapid adaptation of these receptors along with the viscoelastic accommodation of the bladder, have prevented the extraction of volume information from the measurement of $P_{ves}$. This is in accordance with the finding of the prevalence of phasic over tonic response of the bladder mechanoreceptors. Thus, the mechanoreceptors that specifically respond to bladder volume should be a better target to relate their outflow activity with bladder volume.

It was not evident to pinpoint the optimum method for monitoring bladder volume, considering the anatomical and physiological particularities of the bladder, as well as the discussed limitations of the methods based on natural or artificial sensors, and bearing in mind the technological constraints. As could be seen in Table 1, none of the measurement methods proposed in past years completely met the evaluation criteria. The ENG recording of bladder afferent activity, which could reflect the bladder distension and contraction as well as the volume information, appears to be the most suitable method for this biomedical engineering challenge. Nevertheless, more studies are required to demonstrate its feasibility. An improvement in selectiveness and in the signal to noise ratio seems to be mandatory for success in a new endeavor.

The choice in no way means that this is the only valid method but that it is the most suitable candidate to be studied in future research. Thus, this result should not discourage future works that may use the other methods that have not been favored in the present analysis, provided that the mentioned limitations could be addressed.

Considering the enormous economic and social impact of urinary bladder dysfunctions, which affect millions of people around the world and cost several billion dollars each year,[1,2,61] future research should be carried out to find out new therapeutic methods and to improve the currently available ones.

## Conclusions

We can confirm that there is currently no available method having the effectiveness required for use in current clinical practice for chronic monitoring of bladder volume. This is a critical requirement for more successful application of the neuroprosthetic implants in patients with bladder dysfunctions.

ENG recording was found to be the method that best met the user's needs. However, more studies are required to determine whether this method can be used for bladder volume monitoring.

It is expected that the present study can facilitate the development of a safe and effective method and apparatus for the chronic measurement of bladder volume, clinically useful for patient monitoring or as part of a neuroprosthetic device. □

References


1. Stothers L, Thom DH, Calhoun E. Urinary Incontinence in Men In: Urologic Diseases in America. US Department of Health and Human Services PHS, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, editor. Washington D.C.: US Government Printing Office; 2007:195-219.
2. Nygaard I, Thom DH, Calhoun E. Urinary Incontinence in Women In: Urologic Diseases in America. US Department of Health and Human Services PHS, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, editor. Washington D.C.: US Government Printing Office; 2007:159-86.
3. Margaret MR. Neurophysiology in neurourology. *Muscle Nerve* 2008;38(1):815-836.
4. Wein AJ. Pathophysiology and Classification of Voiding Dysfunction. In: Wein AJ, editor. Campbell-Walsh Urology. 9th. ed. Philadelphia, PA: Saunders Elsevier; 2007.
5. Clinical Sumary: Medtronic InterStim® Therapy. Medtronic Inc.; 2006; Available from: http://professional.medtronic.com/downloads/sacral-nerve-stimulation/interstim-clinical-summary-ma12871a_b_002.pdf.
6. Ba A, Sawan M, Editors. Integrated programmable neurostimulator to recuperate the bladder functions. Electrical and Computer Engineering. IEEE CCECE Canadian Conference ON; 2003.
7. Boyer S, Sawan M, Abdel-Gawad M, Robin S, Elhilali MM. Implantable selective stimulator to improve bladder voiding: design and chronic experiments in dogs. *IEEE Trans Rehabil Eng* 2000;8(4):464-470.
8. Bruns TM, Bhadra N, Gustafson KJ. Variable patterned pudendal nerve stimuli improves reflex bladder activation. *IEEE Trans Neur Syst Rehabil Eng* 2008;16(2):140-148.
9. Rijkhoff NJM, Wijkstra H, van Kerrebroeck PEV, Debruyne FMJ. Urinary bladder control by electrical stimulation: review of electrical stimulation techniques in spinal cord injury. *J Urol* 1998; 160(3, Pt 1):961.
10. Sawan M, Ba A, Mounaim F, Corcos J, Elhilali M. Biomedical circuits and systems dedicated for sensing and neurostimulation: case study on urinary bladder dysfunctions. *Turk J Elec Eng Comp Sci* 2008;16(3):171-187.
11. Peckham PH, Knutson JS. Functional electrical stimulation for neuromuscular applications. *Annu Rev Biomed Eng* 2005;7(1): 327-360.
12. Martens FM, van Kuppevelt HJ, Beekman JA, Rijkhoff NJ, Heesakkers JP. Limited value of bladder sensation as a trigger for conditional neurostimulation in spinal cord injury patients. *Neurourol Urodyn* 2010;29(3):395-400.
13. Jezernik S, Grill WM, Sinkjaer T. Detection and inhibition of hyperreflexia-like bladder contractions in the cat by sacral nerve root recording and electrical stimulation. *Neurourol Urodyn* 2001; 20(2):215-230.
14. Sinkjaer T, Haugland M, Inmann A, Hansen M, Nielsen KD. Biopotentials as command and feedback signals in functional electrical stimulation systems. *Med Eng Phys* 2003;25(1):29-40.
15. Westerhof BE, de Bakker JV, van Duyl WA, Editors. High resolution detector for micromotion in smooth muscle strips. Engineering in Medicine and Biology Society, 1996. Bridging Disciplines for Biomedicine. Proceedings of the 18th Annual International Conference of the IEEE; 1996.
16. Peterson AC, Webster GD. Urodynamic and Videourodynamic Evaluation of Voiding Dysfunction. In: Wein AJ, Editor. Campbell-Walsh Urology. 9th. ed. Philadelphia, PA: Saunders Elsevier; 2007.
17. Korkmaz I, Rogg B. A simple fluid-mechanical model for the prediction of the stress–strain relation of the male urinary bladder. *J Biomech* 2007;40(3):663-668.
18. Takayama K, Takei M, Soejima T, Kumazawa J. Continuous monitoring of bladder pressure in dogs in a completely physiological state. *Urology* 1987;60(5):428-432.
19. Koldewijn EL, Van Kerrebroeck PEV, Schaafsma E, Wijkstra H, Debruyne FMJ, Brindley GS. Bladder pressure sensors in an animal model. *J Urol* 1994;15(5):1379-1384.
20. Coosemans J, Puers R. An autonomous bladder pressure monitoring system. *Sensors and Actuators A: Physical* 2005;123-124:155-161.
21. Northrop RB. Plethysmography. In: Neuman MR, Editor. Noninvasive instrumentation and measurement in medical diagnosis. Boca Raton: CRC Press LLC; 2002:241-252.
22. Waltz FM, Timm GW, Bradley WE. Bladder Volume Sensing by Resistance Measurement. *IEEE Trans Biomed Eng* 1971;BME-18(1):42-46.
23. Denniston JC, Baker LE. Measurement of urinary bladder emptying using electrical impedance. *Med Biol Eng* 1975;13(2): 305-306.
24. Doyle P, Hill D. The measurement of residual urine volume by electrical impedance in man. *Med Biol Eng Comput* 1975;13(2): 307-308.
25. Abbey J, Close L. Electrical impedance measurement of urinary bladder fullness. *J Microw Power* 1983;18(3).
26. Yamada A, Fuse M, Aoyagi T, Hosaka H, Toma H, Yanagisawa H. Preventive equipment for urinary incontinence: a device employing lower abdominal impendance changes. *Int J Artif Organs* 1994;17(3):146-150.
27. Gill BC, Fletter PC, Zaszczurynski PJ, Perlin A, Yachia D, Damaser MS. Feasibility of fluid volume conductance to assess bladder volume. *Neurourol Urodyn* 2008;27(6):525-531.
28. Hua P, Woo EJ, Webster JG, Tompkins WJ, Editors. Bladder fullness detection using multiple electrodes. Engineering in Medicine and Biology Society, 1988. Proceedings of the Annual International Conference of the IEEE; 1988.


 

29. Provost B, Sawan M. Proposed new bladder volume monitoring device based on impedance measurement. *Med Biol Eng Comput* 1997;35(6):691-694.
30. Sawan M, Arabi K, Provost B. Implantable volume monitor and miniaturized stimulator dedicated to bladder control. *Artif Organs* 1997;21(3):4.
31. Yoshimura N, Chancellor MB. Physiology and Pharmacology of the Bladder and Urethra. In: Wein AJ, editor. Campbell-Walsh UROLOGY. 9th. ed. Philadelphia, PA: Saunders Elsevier; 2007.
32. Kim CT, Linsenmeyer TA, Kim H, Yoon H. Bladder volume measurement with electrical impedance analysis in spinal cord-injured patients. *Am J Phys Med Rehabil* 1998;77(6):498-502.
33. Keshtkar A, Mesbahi A, Mehnati P. The effect of bladder volume changes on the measured electrical impedance of the urothelium. *Int J Bio Eng Tec*h 2008;1(3):287-292.
34. Rajagopalan S, Sawan M, Ghafar-Zadeh E, Savadogo O, Chodavarapu V. A Polypyrrole-based strain sensor dedicated to measure bladder volume in patients with urinary dysfunction. *Sensors* 2008;8(8):5081-5095.
35. Upfal J, Roberts A, inventors; Urovid Pty Ltd, assignee. Anatomical sensor. World Intellectual Property Organization patent WO2004037082-A1; AU2003273617-A1. 2004.
36. Petrican P, Sawan MA. Design of a miniaturized ultrasonic bladder volume monitor and subsequent preliminary evaluation on 41 enuretic patients. *IEEE Trans Rehab Eng* 1998;6(1):66-74.
37. Beauchamp-Parent P, Sawan M, Editors. New reconfigurable ultrasonic enuresis monitoring system. Proceedings of the 20th Annual International Conference of the IEEE EMBS; 1998; Hong Kong. China: IEEE;1998.
38. Kristiansen N, Djurhuus J, Nygaard H. Design and evaluation of an ultrasound-based bladder volume monitor. *Med Biol Eng Comput* 2004;42(6):762-769.
39. Morrison J. The activation of bladder wall afferent nerves. *Exp Physiol* 1999;84(1):131-136.
40. Shea VK, Cai R, Crepps B, Mason JL, Perl ER. Sensory fibers of the pelvic nerve innervating the rat's urinary bladder. *J Neurophysiol* 2000;84(4):1924-1933.
41. Sinkjaer T. Integrating sensory nerve signals into neural prosthesis devices. *Neuromodulation* 2001;3(1):34-41.
42. Navarro X, Krueger TB, Lago N, Micera S, Stieglitz T, Dario P. A critical review of interfaces with the peripheral nervous system for the control of neuroprostheses and hybrid bionic systems. *J Peripher Nerv Syst* 2005;10(3):229-258.
43. Jezernik S, Jian Guo WEN, Rijkhoff NJM, Djurhuus JC, Sinkjaer T. Analysis of bladder related nerve cuff electrode recordings from preganglionic pelvic nerve and sacral roots in pigs. *J Urol* 2000; 163(4):1309-1314.
44. Kurstjens GAM, Borau A, Rodríguez A, Rijkhoff NJM, Sinkjaer T. Intraoperative recording of electroneurographic signals from cuff electrodes on extradural sacral roots in spinal cord injured patients. *J Urol* 2005;174(4):1482-1487.
45. Sinkjaer T, Rijkhoff N, Haugland M, Kurstjens M, Kerrebroeck Pv, Casey A, Kirkham A, Knight S, Shah J, Donaldson N, Craggs M, Editors. Electroneurographic (ENG) signals from intradural S3 dorsal sacral nerve roots in a patient with a suprasacral spinal cord injury. The 5th Annual IFESS2000 Conference and The Neural Prostheses; 2000; Aalborg, Denmark Department of Biomedical Engineering and Physics, University of Vienna, Vienna Medical School.
46. Wenzel BJ, Boggs JW, Gustafson KJ, Grill WM. Detecting the onset of hyper-reflexive bladder contractions from the electrical activity of the pudendal nerve. *IEEE Trans Neural Syst Rehabil Eng* 2005;13(3):428-435.
47. Jezernik S, Sinkjaer T, Editors. Detecting sudden bladder pressure increases from the pelvic nerve afferent activity. Proceedings of the 20th Annual International Conference of the IEEE EMBS; 1998; Hong Kong, China: IEEE.
48. Harb A, Sawan M, Crampon M-A, Editors. Monitoring Bladder Activities in Paralysed Dogs: System Design and Acute Experiments. . 4th Annual Conference of the International Functional Electrical Stimulation Society (IFESS); 1999 August 23-27 Sendai, Japan.
49. Saleh A, Sawan M, Elzayat EA, Corcos J, Elhilali MM. Detection of the bladder volume from the neural afferent activities in dogs: experimental results. *Neurol Res* 2008;30(1):28-35.
50. Morrison JFB. Sensations arising from lower urinary tract. In: Torrens M, Morrison JFB, editors. The physiology of the lower urinary tract. London: Springer Verlag; 1987:89-131.
51. Grill WM, Norman SE, Bellamkonda RV. Implanted neural interfaces: biochallenges and engineered solutions. *Annu Rev Biomed Eng* 2009;11:1-24.
52. Micera S, Citi L, Rigosa J, Carpaneto J, Raspopovic S, Di Pino G, Rossini L, Yoshida K, Denaro L, Dario P, Rossini PM. Decoding information from neural signals recorded using intraneural electrodes: toward the development of a neurocontrolled hand prosthesis. Proceedings of the IEEE. 2010;98(3):407-417.
53. Bonfanti A, Borghi T, Gusmeroli R, Zambra G, Oliyink A, Fadiga L, Spinelli AS, Baranauskas G, Editors. A low-power integrated circuit for analog spike detection and sorting in neural prosthesis systems. Biomedical Circuits and Systems Conference, 2008. BioCAS 2008. IEEE; 2008.
54. Durand DN, Tesfayesus W, Yoo PB. Peripheral nerve signals for neural control. 2007 IEEE 10th International Conference on Rehabilitation Robotics, Vols 1 and 2. 2007:999-1002.
55. Woltjen JA, Timm GW, Waltz FM, Bradley WE. Bladder motility detection using the Hall Effect. *IEEE Trans Bio Eng* 1973;BME-20(4): 295-299.
56. Wang J, Hou C, Zhang W et al. Micturition alert device dedicated to neurogenic bladders. *US Nat Lib Med Eng Abst* 2008;22(5): 597-601.
57. Korinek J, Vitek J, Sengupta PP et al. Does implantation of sonomicrometry crystals alter regional cardiac muscle function. *J Am Soc Echocardiogr* 2007;20(12):1407-1412.
58. Stadler RW, Combs WJ, Lipson D, inventors; Medtronic Inc (Medt), assignee. Implantable medical device employing sonomicrometer output signals for detection and measurement of cardiac mechanical function patent US2004176810-A1; US7082330-B2. 2004.
59. Rowan D, James E, Kramer A, Sterling A, Suhel P. Technical aspects. Produced by the International Continence Society Working Party on Urodynamic Equipment. *J Med Eng Technol* 1987;11(2):57-64.
60. Schäfer W, Abrams P, Liao L et al. Good urodynamic practices: uroflowmetry, filling cystometry, and pressure-flow studies. *Neurourol Urodyn* 2002;21(3):261-274.
61. Martel L, Bélanger A, Berthelot J-M. Loss and recovery of independence among seniors. In: Canada S, editor.: Statistics Canada; 2002.